



Article

Evolution of European Resuscitation and End-of-Life Practices from 2015 to 2019: A Survey-Based Comparative Evaluation

Spyros D. Mentzelopoulos ^{1,*} , Keith Couper ^{2,3}, Violetta Raffay ^{4,5} , Jana Djakow ^{6,7} and Leo Bossaert ⁸

- ¹ First Department of Intensive Care Medicine, National and Kapodistrian University of Athens Medical School, Evaggelismos General Hospital, 45-47 Ipsilandou Street, 10675 Athens, Greece
- ² UK Critical Care Unit, University Hospitals Birmingham, NHS Foundation Trust, Birmingham B15 2TH, UK; k.couper@warwick.ac.uk
- ³ Warwick Medical School, University of Warwick, Coventry CV4 7AL, UK
- ⁴ School of Medicine, European University Cyprus, Nicosia 2404, Cyprus; violetta.raffay@gmail.com
- ⁵ Serbian Resuscitation Council, 21102 Novi Sad, Serbia
- ⁶ Paediatric Intensive Care Unit, NH Hospital, 26801 Hořovice, Czech Republic; jana.djakow@gmail.com
- ⁷ Department of Paediatric Anaesthesiology and Intensive Care Medicine, University Hospital Brno and Faculty of Medicine, Masaryk University, 62500 Brno, Czech Republic
- ⁸ University of Antwerp, 2000 Antwerp, Belgium; leo.bossaert@erc.edu
- * Correspondence: sdmentzelopoulos@yahoo.com or sdmentzelopoulos@gmail.com; Tel.: +30-697-530-4909; Fax: +30-213-204-3307



Citation: Mentzelopoulos, S.D.; Couper, K.; Raffay, V.; Djakow, J.; Bossaert, L. Evolution of European Resuscitation and End-of-Life Practices from 2015 to 2019: A Survey-Based Comparative Evaluation. *J. Clin. Med.* **2022**, *11*, 4005. <https://doi.org/10.3390/jcm11144005>

Academic Editors: Karim Bendjelid and Peter Markus Spieth

Received: 23 May 2022

Accepted: 6 July 2022

Published: 11 July 2022

Publisher's Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



Copyright: © 2022 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

Abstract: Background: In concordance with the results of large, observational studies, a 2015 European survey suggested variation in resuscitation/end-of-life practices and emergency care organization across 31 countries. The current survey-based study aimed to comparatively assess the evolution of practices from 2015 to 2019, especially in countries with “low” (i.e., average or lower) 2015 questionnaire domain scores. Methods: The 2015 questionnaire with additional consensus-based questions was used. The 2019 questionnaire covered practices/decisions related to end-of-life care (domain A); determinants of access to resuscitation/post-resuscitation care (domain B); diagnosis of death/organ donation (domain C); and emergency care organization (domain D). Responses from 25 countries were analyzed. Positive or negative responses were graded by 1 or 0, respectively. Domain scores were calculated by summation of practice-specific response grades. Results: Domain A and B scores for 2015 and 2019 were similar. Domain C score decreased by 1 point [95% confidence interval (CI): 1–3; $p = 0.02$]. Domain D score increased by 2.6 points (95% CI: 0.2–5.0; $p = 0.035$); this improvement was driven by countries with “low” 2015 domain D scores. In countries with “low” 2015 domain A scores, domain A score increased by 5.5 points (95% CI: 0.4–10.6; $p = 0.047$). Conclusions: In 2019, improvements in emergency care organization and an increasing frequency of end-of-life practices were observed primarily in countries with previously “low” scores in the corresponding domains of the 2015 questionnaire.

Keywords: ethics; resuscitation; terminal care; surveys and questionnaires; emergency care

1. Introduction

Data from multinational, observational studies suggest a substantial variation in end-of-life practices across European countries, and an increasing frequency of decisions to limit life-sustaining treatments, especially in southern Europe [1,2]. End-of-life practices are evolving continuously as a result of new evidence-based guidelines, publication of randomized controlled trials supporting complex advance care planning (ACP), new laws/policies, and educational activities [3–23].

In 2015, we conducted a survey of experts from 31 European countries. We administered a comprehensive questionnaire spanning the following four domains: A: practices/decisions related to end-of-life care; B: access to best available care; C: death diagnosis and organ donation; and D: emergency care organization. Practices and organization of care

were scored by numerical summation of positive responses. Results showed substantial variability in country-specific approaches to resuscitation/end-of-life care, indicating the presence of space for evidence-supported progress in all the aforementioned domains [3].

In 2019, we undertook a methodologically improved version of the 2015 survey to address the following questions: (1) How did resuscitation/end-of-life care and emergency care organization evolve over the 2015–2019 period? and (2) Could such evolution, be more marked in countries with “low” (i.e., at or below average) practice/organization scores for 2015?

2. Materials and Methods

The current survey conforms with the Checklist for Reporting Results of Internet E-Surveys (<https://www.jmir.org/2004/3/e34/>; accessed on 20 July 2019 see Supplementary Materials).

Potential study participants from 33 European countries were contacted via e-mail. Participant inclusion criteria comprised nationally and/or internationally recognized, specific, clinical, and/or research expertise in resuscitation and end-of-life care; pertinent evidence should be classifiable in 1 or more of the following categories: (1) European Resuscitation Council (ERC) National Resuscitation Council representative; and/or member of the European Registry of Cardiac Arrest investigators network or other ERC related clinical research networks (e.g., ERC Dispatch Center Survey, Reappropriate Trial, Euro-call); (2) Established researcher in the field: first, second or last author of published, scholarly articles in this field; and (3) At least 3 years of prior service as lead clinician in emergency and/or intensive care.

To reduce the risk of recall/social desirability bias, we aimed for at least three participants from each country. However, this did not constitute an inclusion criterion for country-specific responses. Consequently, responses from countries with just one or two participants were to be anyway included in the data analyses. Following the obtainment of informed consent (see Supplementary Materials), participants were able to electronically access the study questionnaire (Table 1).

Table 1. The 2019 Ethical Practices Questionnaire.

DOMAIN A. PRACTICES/DECISIONS RELATED TO END-OF-LIFE CARE *

A1. End-of-life practices

1. Do-not-attempt cardiopulmonary resuscitation (DNACPR) orders (legally allowed, supported, and applied in your country (3 questions)? applied in single tier, or first and second tier ambulance [†] (3 questions)? applied in-hospital? written in medical record? reviewed?) No. of discrete questions (N) = 9; Maximum score if all responses positive (Max. Score) = 9.
 2. Advance directives (respect for advance directives legally allowed, and supported in your country (2 questions)? applied in the out-of-hospital, and in-hospital setting (2 questions)? applied to start/stop cardiopulmonary resuscitation (CPR) in single tier, or first and second tier ambulance (3-questions)? applied to start/stop CPR in-hospital? N = 8, 4-choice; Max. Score = 8.
 3. Advance Care Planning (same questions as for advance directives). N = 8, 4-choice; Max. Score = 8.
 4. Terminal analgesia/sedation (legally allowed in your country? applied?). N = 2; Max. Score = 2.
 5. Termination of Resuscitation protocols (TOR) (legally allowed? applied in single tier, or first and second tier ambulance (3-questions)? applied in-hospital? N = 5, 4-choice; Max. Score = 5.
 6. Limitation of in-hospital treatment level (If applied, does it pertain to withholding, and withdrawing CPR (2 questions)? does it include TOR, withholding of invasive treatments, and withdrawing of feeding and hydration?). N = 5; Max. Score = 5.
 7. Euthanasia in adults (legally allowed in your country? applied?); euthanasia in children (legally allowed in your country? applied? Physician-assisted suicide (legally allowed in your country?). N = 5; Max. Score = 5.
 8. During patient transportation: Is CPR continued in the prospect of organ donation? Is CPR continued in the prospect of access to higher-level treatment (e.g., extracorporeal CPR)? N = 2; Max. Score = 2.
-

Table 1. *Cont.*

Max. Subscore for end-of-life practices (A1) = sum of Max. Scores of 1 to 8 = 44.

A2. End-of-life Decisions

1. Adults/children: Family participating in Decisions? N = 2; Max. Score = 2.
2. Adults/children: Are end-of-life decisions reached through a shared decision-making process? N = 2; Max. Score = 2.

Max. Subscore end-of-life decisions (A2) = sum of Max. Scores of 1 and 2 = 4.

A3. Family presence during CPR

1. Adults: Family present during CPR? Children: Parents present during CPR? Children:

Other family members present during CPR? N = 3; Max. Score = 3.

Max. Subscore for family presence during CPR (A3) = 3.

Max. Score for Domain A = sum of max. Subscores of A1, A2 and A3 = 51.

Questions pertaining to law and those included in A1.6 and A1.7 had 2-choice responses (i.e., *yes* or *no*); Questions pertaining to what is applied had 4-choice responses (i.e., *never*, *sometimes*, *usually*, and *always*).

B. ACCESS TO BEST RESUSCITATION AND POSTRESUSCITATION CARE †**B1–B3. Out-of-hospital (B1) and in-hospital (B2) resuscitation care, and postresuscitation care (B3)**

1. Is access to best available care (including extracorporeal CPR wherever available) affected by age? race? religion? comorbidity? socioeconomic status? urban-rural (area of occurrence)? type of receiving hospital (out-of-hospital setting) or type of treating hospital (in-hospital setting)? minority? language? high-risk presentation (e.g., acute physiology and chronic health evaluation II score > 25 corresponding to >50% mortality probability)? suicide attempt? knowledge of patient's wish against undergoing CPR? other? The same group of questions was asked about B1, B2, and B3. For each of B1, B2, and B3: N = 13; Max. Score = 13.

Max. Score for Domain B = sum of max. Subscores of B1, B2, and B3 = 39. All questions had 2-choice responses (i.e., *yes* or *no*).

C. DIAGNOSIS OF DEATH AND ORGAN DONATION**C1. Death diagnosis**

1. Legally allowed to diagnose death: physician, out-of-hospital or in-hospital (2 questions)? nurse, out-of-hospital or in-hospital (2 questions)? ambulance person [advanced life support (ALS) provider]? ambulance person [basic life support (BLS) provider]? N = 6; Max. Score = 6.
2. Legally allowed to diagnose death in the absence of obvious signs of death such as rigor mortis or decapitation, and after 20 minutes of asystole without reversible cause: same questions as above; N = 6; Max. Score = 6.
3. Diagnostic criteria for death: Brain death criteria used in out-of-hospital cardiac arrest (after hospital admission) or in-hospital cardiac arrest, and written on death certificate (3 questions)? Cardiorespiratory death criteria used in out-of-hospital or in-hospital cardiac arrest, and written on death certificate (3 questions)? N=6; Max. Score=6.

Max. Subscore for death diagnosis (C1) = sum of max. Scores of 1 to 3 = 18.

C2. Organ donation

1. Heart beating organ donation allowed? Non-heart beating organ donation allowed? Organ donation applied by opting in? Organ donation applied by opting out. N = 4; Max. Score = 4.

Max. Subscore for organ donation (C2) = 4.

Max. Score for Domain C = sum of Max. Subscores of C1 and C2 = 22. All questions had 2-choice responses (i.e., *yes* or *no*).

D. EMERGENCY CARE ORGANIZATION †**D1. Access to emergency care**

1. Out-of-hospital: rural areas: emergency number 112 or another (2 questions)? ambulance arrival within 10 min? N = 3; Max. Score = 3.
2. Out-of-hospital: urban areas emergency number 112 or another (2 questions)? ambulance arrival within 10 min? N = 3; Max. Score = 3.
3. In-hospital: emergency number 112 or another (2 questions)? cardiac arrest team arrival within 10 min? N = 2; Max. Score = 2.

Max. Subscore for access to emergency care (D1) = sum of Max. Scores of 1 to 3 = 8.

D2. Defibrillation

1. Legally allowed to defibrillate using an automated external defibrillator (AED): physician? nurse? ambulance personnel? police? On-site responder? Citizen? Other (specify)? N = 7; Max. Score = 7.
2. AEDs available in: single tier ambulance? first tier ambulance? fire cars? police cars? public places? mass gatherings? first responder dispatch projects? other? N = 8; Max. Score=8.
3. Are AED data (electrocardiographic sequence, waveform, time) available in the patient record? N = 1; Max. Score = 1.
4. Ongoing public access defibrillation programs in place? home AED? school AED? in-hospital AED?-Is there a registry of all AEDs, at national or regional level (2 questions)? N = 6; Max. Score = 6.

Table 1. *Cont.*

Max. Subscore for defibrillation (D2) = sum of Max. Scores of 1 to 4 = 22.

D3. Organization of out-of-hospital emergency care

1. Is there a system in place to alert trained lay rescuers (and/or first responders) by text message or app? N = 1; Max. Score = 1.
2. [A] Is dispatcher assisted bystander CPR practiced in rural areas? Does guidance include compressions or ventilations (2 questions)? N = 3; Max. Score = 3.
3. [B] Is dispatcher assisted bystander CPR practiced in urban areas? Does guidance include compressions or ventilations (2 questions)? N = 3; Max. Score = 3. Single tier ambulance: ALS? First tier ambulance: BLS plus defibrillation or ALS (2 questions)? Second tier ambulance: ALS? N = 4; Max. Score = 4.
4. In traumatic cardiac arrest: in single tier ambulance, or first and second tier ambulance:
 - A. Is the intervention unit qualified for prompt confirmation and management of life-threatening injuries (3 questions, one for each type of ambulance)?
 - B. Are specific criteria applied for withholding or terminating resuscitation (3 questions, one for each type of ambulance)? yes-no, specify.

N = 6; Max. Score = 6.

Max. Subscore for level of out-of-hospital care (D3) = sum of Max. Scores of 1 to 4 = 17.

D4. Organization of in-hospital emergency services

1. Are in-hospital Rapid Response Teams Programs in place? N = 1; Max. Score = 1
2. Is CPR feedback, debriefing, and audit applied (3 questions)? N = 3; Max. Score = 3.
3. Is CPR training on the recently dead legally allowed?-is CPR training practiced? N = 2; Max. Score = 2.

Max. Subscore for organization of in-hospital emergency services (D4) = sum of Max. Scores of 1 to 3 = 6.

D. EMERGENCY CARE ORGANIZATION**D5. Registry reporting of cardiac arrest**

1. Out-of-hospital or in-hospital cardiac arrest data reported to a Registry? N = 2; Max. Score = 2.

Max. Subscore for registry reporting of cardiac arrest (D5) = 2

D6. Education

1. Are there ongoing programs of (a) theoretical education and (b) practice training (e.g., clinical scenario-based) in the field of ethics at pregraduate level (2 questions)? postgraduate level (2 questions)? medical specialty/subspecialty registrar level (2 questions)? specialist level (2 questions)? N = 8; Max. Score = 8.
2. Certified CPR training mandatory for in-hospital healthcare providers: physicians? nurses? other staff? N = 3; Max. Score = 3.

Max. Subscore education (D6) = sum of Max. Scores of 1 and 2 = 11.

D7. Research

1. Enrollment of adults legally allowed without consent in: observational research? interventional research involving drugs? interventional research involving non-drug interventions? N = 3; Max. Score=3.

Max. Subscore for research (D7) = 3

Max. Score for Domain D = sum of Max. Subscores of D1, D2, D3, D4, D5, D6, and D7 = 67. Questions D1.1-3, D2.3, D3.4A, D4.1-3, and D5.1 had 4-choice responses (i.e., *never, sometimes, usually, and always*); all other questions had 2-choice responses (i.e. *yes or no*)

*, Related to the application of the following Ethical Principles: Autonomy, Beneficence, Non-maleficence, Dignity, and Honesty. †, the first tier ambulance corresponds to the capability of BLS plus defibrillation, whereas the second tier ambulance corresponds to the capability of ALS and monitored mechanical ventilatory and hemodynamic support offered by specifically trained and certified personnel. ‡, Related to the application of the Principles of Justice and Beneficence. Scores of Domain A subsections A1.3 and A2.2; and scores of Domain subsections D1.3 (question about 112 as emergency number); D2.3; D3.1; D3.2; D3.4, D6, and D7 were not included in the 2019 vs. 2015 comparative analysis, because the corresponding questions were not included in the 2015 Survey [3]. Therefore, for the purpose of this comparative analysis, the Max. Scores for the 2019 domain A and D were 41 and 40, respectively.

Respondents chose either among four options, that is, *never, sometimes, usually and always* or between *no* and *yes* [3]. Subsequently, responses of *never/sometimes* and *usually/always* were categorized as *no* and *yes*, respectively. All data were entered in an original, “anonymized” Excel Masterfile. Original responses were received from 1 September 2019, to 25 October 2019. Participants from each country were asked to reconfirm their answers and provide any missing answers, approximately 3 months after the initial email invitation. Participants were also asked whether they agreed or disagreed with answers provided by other participants from the same country. In cases of disagreement, we encouraged resolution through consensus. The process of data finalization lasted from 1 December 2019

to 31 January 2020. Only consensus-based, country-specific responses were ultimately analyzed, besides the case(s) of having to include responses from just one country-specific respondent. This resulted in a final Excel Masterfile that included a single, country-specific response to each one of the survey questions [3]. For data analysis, we used a dichotomous quantizing approach by grading a positive response with 1 and a negative response with 0 [24].

2.1. Questionnaire Structure and Grading

The 2019 questionnaire was organized into four domains (Table 1), precisely like the 2015 questionnaire [3]. Domain A (practices/decisions related to end-of-life care) included subdivisions that included sets of questions pertaining to (1) eight end-of-life practices (e.g., do-not-attempt cardiopulmonary resuscitation (DNACPR), advance directives, advance care planning); (2) end-of life decisions and (3) family presence during resuscitation. Each domain A subdivision could reach a maximum subscore if the responses to all of its subcomponent questions were positive. Domain A score was calculated as the sum of the aforementioned subscores (Table 1).

Domain B, C, and D scores were also calculated by summation of the respective subscores (Table 1). Domain B included subdivisions with sets of questions pertaining to access to (1) best out-of-hospital resuscitation care; (2) best in-hospital resuscitation care; and (3) best postresuscitation care. Domain C subdivisions concerned (1) death diagnosis; and (2) organ donation. Domain D subdivisions included sets of questions related to (1) access to emergency care; (2) defibrillation; (3) organization of out-of-hospital emergency care; (4) organization of in-hospital emergency services; (5) registry reporting of cardiac arrest and (6) education (Table 1).

As further detailed in the footnote of Table 1, Domains A and D of the 2019 questionnaire had a total of 10 sets of questions (concerning specific variables, for example, advance care planning (ACP)) that were not included in the 2015 questionnaire. These “new—2019-only” questions were not taken into account in the calculation of the 2019 Domain A and D scores for the purpose of the below-presented 2019 vs. 2015 comparisons.

2.2. Study Outcomes

The primary outcome was the presence/absence of statistically significant differences between 2015 and 2019 in domain A to D scores of all participating countries.

The secondary outcome was the presence/absence of significant differences between 2015 and 2019 domain A to D scores of countries with “low” domain scores in 2015. “Low” 2015 scores were defined as domain scores equal to or lower than the corresponding, overall mean score values of 2015 [3]; more specifically, “low” 2015 scores for domains A, B, C and D were those not exceeding 18, 7, 12 and 23, respectively [3]. Accordingly, “high” (or above average) 2015 scores for domains A, B, C, and D were those exceeding 18, 7, 12 and 23, respectively [3].

The tertiary outcome was the presence/absence of significant differences between changes in “low” 2015 domain scores from 2015 to 2019, and changes in “high” 2015 domain scores from 2015 to 2019.

2.3. Additional Data Collection in the Context of Un-Prespecified, Exploratory Analyses

In an effort to determine any potential effect of the coronavirus disease-19 (COVID-19), we asked respondents to determine whether the pandemic could have resulted in changes in any of their original responses to the questionnaire (Table 1). Pertinent data collection started on 15 May 2020 and ended on 29 June 2020.

2.4. Protocol Approval and Registration

The study protocol was approved by the Ethics and Scientific Committee of Evaggelismos General Hospital Athens, Greece. The approval was used for study conduct in 32/44 European countries (73%) and Turkey. Countries are listed in the online supplement, along

with details for informed consent and personal data protection. The protocol was registered with Clinicaltrials.gov (Identifier: NCT04078815).

2.5. Statistical Analyses

The internal consistency of the 2019 and the 2015 questionnaires was assessed by the determination of domain-specific Cronbach’s alpha. The distribution normality of domain scores and subscores was assessed by the Kolmogorov–Smirnov test with Lilliefors significance correction. Data are reported as number, number (percentage) and median (IQR) or mean ± SD unless otherwise specified. Comparisons pertaining to (1) study outcomes; and (2) domain subscores were conducted using an independent samples *t*-test or the Mann–Whitney *U* test.

Bivariate linear regression was used to explore possible associations between (1) the 2019 domain A and D scores with and without the “new—2019-only” questions [3]; and (2) the 2019 variable-specific scores for DNACPR or advance directives and ACP. All analyses were performed using SPSS version 28 (IBM Corporation, Armonk, NY, USA). All reported P values are two-sided. Statistical significance was set at $p < 0.05$.

3. Results

3.1. Respondents and Countries Participating in the Analysis

A study flow diagram is presented in Figure 1. Initial responses were received from 1 September 2019, to 28 October 2019 from 85 respondents originating from 31/33 European countries (93.9%). The median number (IQR) of respondents per country was 2 (1–4) and ranged from 1 (9 countries) to 9 (1 country). Details on conflicting and/or initially missing responses are presented in Supplemental Table S1. Consensus on conflicting responses and provision of initially missing responses was accomplished for 25/33 countries (75.8%), which were ultimately included in the analyses.

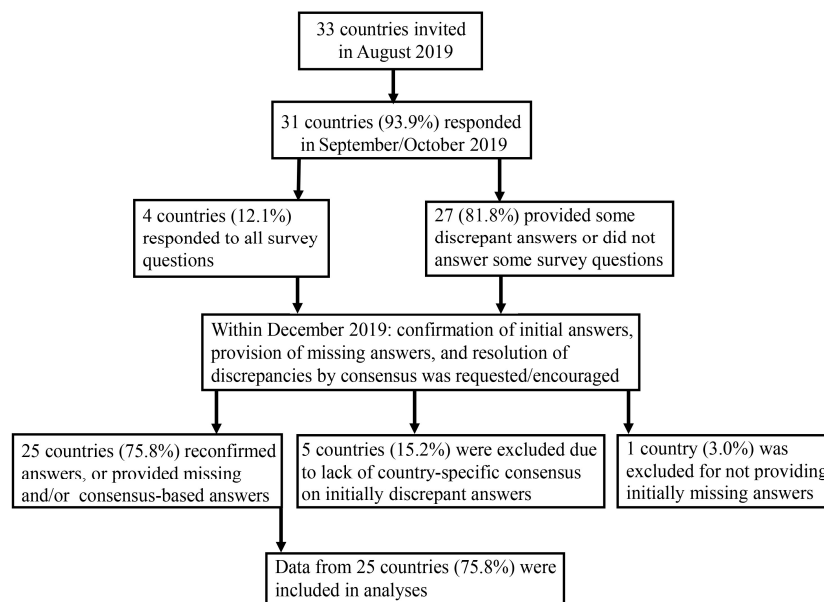


Figure 1. Flow diagram of responses to the 2019 questionnaire.

3.2. Internal Consistency of the 2019 and 2015 Questionnaires

Domains A (end-of-life care practices/decisions), B (access to best resuscitation/postresuscitation care), C (death diagnosis/organ donation) and D (emergency care organization) of the 2019 questionnaire had Cronbach’s alpha values of 0.94, 0.94, 0.63 and 0.74, respectively. Domains A, B, C and D of the 2015 questionnaire, had Cronbach’s alpha values of 0.94, 0.88, 0.61 and 0.78, respectively. Regarding domain C, deletion of a question regarding “organ donation by opting in” in the 2019 questionnaire (Table 1), and deletion

of a question about “use of brain death criteria in “out-of-hospital cardiac arrest” in the 2015 questionnaire [3] (Table 1) would result in respective alpha values of 0.70 and 0.68.

3.3. Results on Study Outcomes

Results on the primary and secondary outcomes are summarized in Figures 2 and 3, respectively; further details, including scores of variable-specific sets of questions, and additional, subgroup-specific data are presented in Supplemental Tables S2–S5.

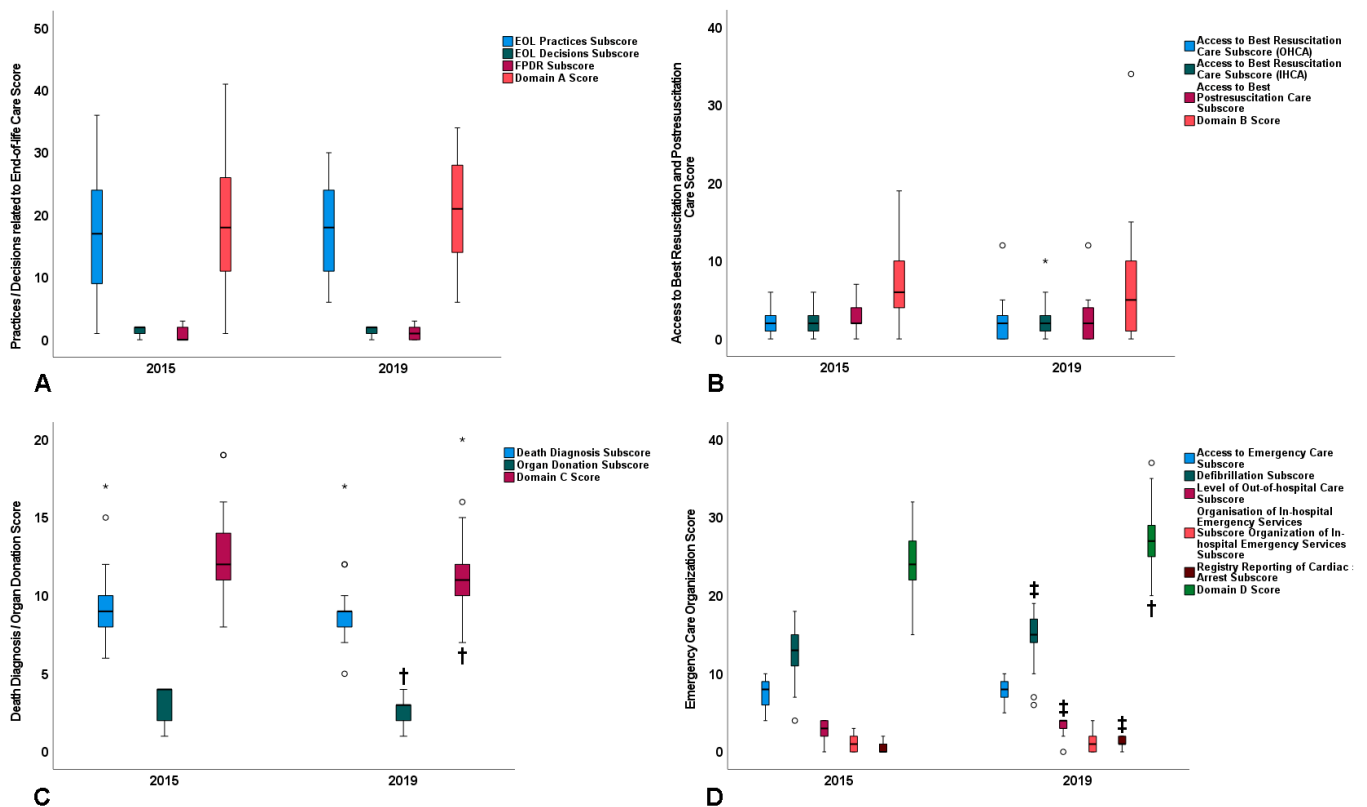


Figure 2. Summary results on the primary study outcome. Boxplot presentation of subscores and scores of domains (A–D) of the study questionnaire. Data originate from the 25 participating countries. Bars reflect median value; box height reflects interquartile range; bars on top or bottom of the boxes reflect actual range of values; symbols (circles and asterisk) reflect countries with outlier score values, that is, score values outside the range that corresponds to box height plus the bars. †, $p < 0.05$ vs. 2015; ‡, $p \leq 0.01$ vs. 2015.

Regarding the primary outcome, domain A and B scores did not differ significantly between 2015 and 2019 (Figure 2). However, domain C score was lower by 1 point in 2019 vs. 2015 (95% confidence interval (CI): 1 to 3; $p = 0.02$); this change was driven by a reduction in the organ donation subscore (Figure 2, Table S3). In contrast, from 2015 to 2019, domain D score exhibited a significant increase of 2.6 points (95% CI: 0.2 to 5.0; $p = 0.035$) (Figure 2, Table S3). Regarding domains A and D, the comparable ranges of score values (Figure 2) and coefficients of variation in 2019 (Table S3) suggest the persistence of the considerable variation in end-of-life practices and emergency care organization observed in 2015 [3].

Regarding the secondary outcome, in countries with “low” 2015 domain scores, domain B and C scores did not differ significantly between 2015 and 2019 (Figure 3). However, from 2015 to 2019, the domain A score increased by 5.5 points (95% CI: 0.4 to 10.6; $p = 0.047$) (Figure 3, Table S4). The domain D score also increased by 4.7 points (95% CI: 2.1 to 7.3;

$p = 0.009$) (Figure 3, Table S4), thereby driving the “overall increase” reported above and in Figure 2 and Table S3.

In the context of a “pragmatic”, practice-level presentation, Table 2 presents the main, observed, proportional changes in positive responses to variable-specific questions from 2015 to 2019.

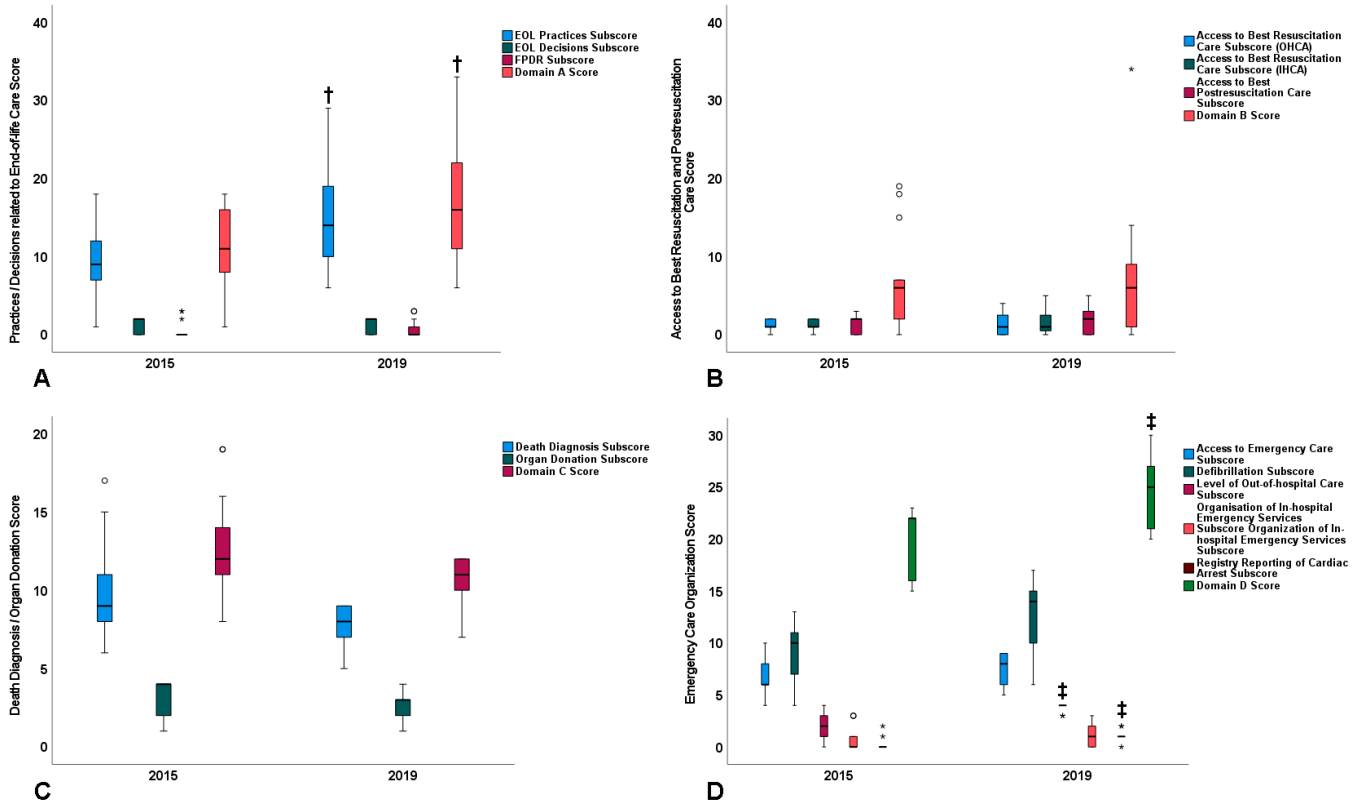


Figure 3. Summary results on the secondary study outcome. Boxplot presentation of subscores and scores of domains (A–D) of the study questionnaire. Data originate from countries with “low” 2015 domain scores ($n = 13$ for domains (A,C); $n = 15$ for domain (B); and $n = 9$ for domain (D)). Bars reflect median value; box height reflects interquartile range; bars on top or bottom of the boxes reflect actual range of values; symbols (circles and asterisk) reflect countries with outlier score values, that is, score values outside the range that corresponds to box height plus the bars. †, $p < 0.05$ vs. 2015; ‡, $p \leq 0.01$ vs. 2015.

Table 2. Main proportional (%) changes in positive responses to variable-specific questions from 2015 to 2019.

Domain A—End-of-Life Care Practices/Decisions	Legally Allowed	Legally Supported	Application out-of-/in-Hospital	Application Related to Start/Stop CPR			Written in Medical Records	Reviewed	
				STIER AMB	1st TIER AMB	2nd TIER AMB			
				Hospital					
DNACPR—all countries (n = 25)	16%	0%	+28%/+28%	8%	4%	24%	12%	24%	0%
DNACPR—low 2015 score (n = 13)	31%	23%	+46%/+46%	15%	15%	31%	23%	31%	15%
Ads—all countries (n = 25)	20%	12%	+20%/+24%	0%	−8%	8%	8%		
Ads—low 2015 score (n = 13)	46%	46%	0.794872	8%	15%	23%	31%		
Term. Analg/Sed - all countries (n = 25)	−12%		−12%						
Domain A	Legally allowed	STIER AMB	1st TIER AMB	2nd TIER AMB	Hospital				
TOR Protocols—all countries (n = 25)	−4%	−12%	−4%	0%	−28%				
Domain C -Death diagnosis/organ donation	Heart beating	Non-heart beating	Opt in	Opt out	Opt in and/or Opt out				

Table 2. Cont.

Organ donation—all countries (n = 25)	0%	0%	−48%	−8%	−8%				
Domain D -Emergency care organization	STIER AMB	1st TIER AMB	Fire Cars	Police Cars	Public Places	Mass gatherings	FRDP	Other	
Defibrillation Av/ty—all countries (n = 25)	32%	12%	12%	20%	0%	12%	−4%	−8%	
Defibrillation Av/ty—low 2015 score (n = 9)	78%	33%	33%	56%	0%	22%	11%	0%	
Domain D	PAD programs	Home AED	School AED	In-hospital AED	AED Registry—Nat.	AED Registry—Reg.			
PAD—all countries (n = 25)	8%	4%	28%	12%	12%	36%			
Domain D	Physician	Nurse	AMB Personnel	Police	On-site Responder	Citizen			
Legally allowed to defibrillate—low 2015 score (n = 9)	0%	0%	−11%	0%	−11%	22%			
Domain D	STIER—ALS	1st TIER—ALS	1st TIER—Defibrillation	2nd TIER—ALS					
AMB level of care—all countries (n = 25)	36%	36%	12%	0%					
AMB level of care—low 2015 score (n = 9)	67%	78%	33%	11%					
	OHCA	IHCA							
Registry reporting—all countries (n = 25)	36%	40%							
Registry reporting—low 2015 score (n = 9)	33%	44%							

STIER, single tier; AMB, ambulance; DNACPR, do-not-attempt cardiopulmonary resuscitation; ADs, advance directives; Term. Analg/Sed, terminal analgesia/sedation; TOR, termination of resuscitation; Av/ty, availability; FRDP, first responder dispatch project; PAD, public access defibrillation; AED, automated external defibrillator; Nat., national; Reg., regional; ALS, advanced life support; OHCA, out-of-hospital cardiac arrest; IHCA, in-hospital cardiac arrest. Regarding “all participating countries (n = 25)”, proportional changes of $\geq 12\%$ in ≥ 3 countries are highlighted in bold script. Domain A: regarding “countries with low 2015 scores (n = 13)” proportional changes of $\geq 15\%$ in ≥ 2 countries are highlighted in bold script. Domain D: regarding “countries with low 2015 scores (n = 9)” proportional changes of $\geq 22\%$ in ≥ 2 countries are highlighted in bold script.

Regarding the tertiary outcome, in countries with “low” 2015 domain A to D scores, all changes in the scores of domains A, C and D from 2015 to 2019 were arithmetically positive and differed significantly from the respective changes determined for countries with “high” 2015 domain A to D scores ($p \leq 0.02$) (Table 3).

Table 3. Summary results on the tertiary outcome.

	Domain A ΔScore 2015 to 2019	Domain B ΔScore 2015 to 2019	Domain C ΔScore 2015 to 2019	Domain D ΔScore 2015 to 2019
Low 2015 score countries, n, median (IQR) or mean ± SD	n = 13 4.0 (−0.5–10.0) *	n = 15 0.8 ± 5.4	n = 13 0.5 ± 1.9 †	n = 9 4.8 ± 4.4 ‡
High 2015 score countries, n, median (IQR) or mean ± SD	n = 12 −2.0 (−6.0–−0.3)	n = 10 −2.8 ± 9.0	n = 12 −3.2 ± 4.3	n = 16 1.4 ± 4.6

Domain A, Practices/decisions related to end-of-life care; Domain B, Access to Best Resuscitation and Postresuscitation Care; Domain C, Death Diagnosis and Organ Donation; Domain D, Emergency Care Organization; ΔScore, Change in Score (from 2015 to 2019). The tertiary outcome comprises the comparison of ΔScores from 2015 to 2019 between countries with low 2015 scores and countries with high 2015 scores; low and high 2015 scores are defined in Methods. *, $p = 0.01$ vs. high-score countries †, $p = 0.01$ vs. high-score countries ‡, $p = 0.02$ vs. high score countries.

3.4. Responses Pertaining Only to the 2019 Survey

Responses to questions included only in the 2019 survey are detailed in the supplement. Country-specific, positive response rates of >50% pertained primarily to ACP, shared decision making, dispatcher-assisted CPR and guidance about compressions/ventilation, quality features of prehospital (ambulance) care and educational programs for ethics.

3.5. Exploratory Analyses

Linear regression revealed significant associations between 2019 domain A (end-of-life care practices/decisions) and domain D (emergency care organization) scores (adjusted $r^2 = 0.35$ to 0.43 ; $p \leq 0.001$; Supplemental Figure S1A,B). There were also strong linear relationships between the 2019 variable-specific score for DNACPR and ACP ($r^2 = 0.68$, $p < 0.001$; supplemental Figure S1C) and the 2019 variable-specific score for advance directives and ACP ($r^2 = 0.79$, $p < 0.001$; Supplemental Figure S1D). Additional details are reported in the supplement.

Results on the effect of COVID-19 were remarkable mainly for changes in access to resuscitation care; for further details see the supplement’s text and Table S6.

4. Discussion

The current comparison of responses to the 2015 and 2019 questionnaires from 25 countries revealed no overall significant changes in end-of-life practices and access to best resuscitation/postresuscitation care. There was an apparent decline in organ donation practices in just two countries. There was a significant improvement in the 2019 emergency care organization, driven by countries with “low” 2015 domain D scores. Furthermore, from 2015 to 2019, the frequency of application of end-of-life practices increased significantly in countries with “low” 2015 domain A scores, as opposed to countries with “high” 2015 domain A scores. The considerable variation in practices and emergency care organization noted in 2015 persisted in 2019. As in 2015, a higher 2019 end-of-life practice score was predictive of an improved 2019 emergency care organization [3].

Regarding end-of-life practices, our results are consistent with recent papers on new legislation [25,26] by suggesting a country-level expansion of legal support [3] and application/implementation of DNACPR and advance directives. Integration of DNACPR/advance directives with ACP has been recently advocated in the context of a holistic approach to honoring patient preferences [4,18]. Accordingly, exploratory analyses revealed that the 2019 variable-specific scores for DNACPR and advance directives were predictive of the variable-specific score for ACP.

Current European guidelines support using terminal analgesia and sedation, without hastening death [7,27]. Accordingly, the new Italian law entitled “Rules about informed consent and advance directives” supports prescribing clinically indicated, deep sedation for terminally ill patients, in the presence of valid informed consent [26]. The right to deep continuous sedation is also established by the recent, French Claeys–Leonetti law [28]. The use of sedation and analgesia does not seem to shorten the dying process of terminally ill

patients [4,27,29]. Furthermore, terminal sedation and analgesia are recommended by recent Canadian guidelines for the alleviation of any pain/distress after LST withdrawal [30]. This clearly differs from the practice of euthanasia, that is, the intentional and painless termination of the patient's life upon their request [31]. Despite the fundamental difference as regards the main objective of the intervention (i.e., alleviation of distress vs. termination of life), several authors have expressed concerns about a potential "practice overlap" between deep sedation until death and euthanasia [26,28,32–42]. This could partly explain our results of declining legal support/application of terminal analgesia and sedation, despite the recently reported increase of treatment limitation decisions over time in Europe [1]. Indeed, if certain respondents (subjectively/erratically) viewed "terminal analgesia and sedation" as a form of "euthanasia" [40], they might have provided negative responses for legal support/application [2,31].

In Western countries, out-of-hospital termination-of-resuscitation rules perform well, with proportions of cardiac arrest survivors recommended for termination (i.e., miss rates) of <1% [43,44]. However, miss rates may exceed 6% in countries with lower proportions of in-field defibrillation attempts and shorter in-field resuscitation before patient transportation [44]. Furthermore, the application of termination-of-resuscitation protocols may vary widely at the country level (according to legal support) [6,44], regional health-care system level (depending on the local frequency of witnessed arrest and bystander CPR) [45], emergency medical service (EMS) or hospital level (according to service-specific or institution-specific resuscitation policies) [44,46] and healthcare professional level (according to pertinent knowledge/expertise, confidence and right/responsibility to decide, possible fear of litigation and personal views) [6,47–49]. Such multiple sources of variation and the concurrent inability to issue a "universal/clear-cut" recommendation for a rule [4] may explain our results of the declining application of termination-of-resuscitation protocols.

Organ transplantation prolongs the life of recipients and improves its quality [50]. An ongoing shortage of organs for transplantation has led to the consideration of uncontrolled donation after circulatory death (DCD) [51]. Over the past 16 years, there has been a steady increase in DCD in the United Kingdom, the Netherlands, Belgium and Spain [50,52]. Such country-specific increases in organ donation could not be detected by our survey questions (Table 1).

Automated external defibrillator (AED) availability and use improve survival and neurological outcome after shockable out-of-hospital cardiac arrest [53–58]. Barriers and facilitators of bystander defibrillation are related to knowledge/awareness, training, willingness, AED availability/accessibility, medicolegal issues, AED registration and dispatcher assistance [59]. Major problems contributing to AED underutilization comprise AED retrieval distance and time-dependent availability (e.g., functional AED not available at night) [60,61]. Recently proposed improvements included mathematical optimization of AED placement and AED drone delivery to lay rescuers [62,63]. Our results are consistent with an ongoing and expanding effort to increase AED availability in various locations and emergency vehicles and improve AED data collection by creating new AED registries.

Our results of increased defibrillation availability are consistent with the reported improvements in ambulance/pre-hospital level of care. However, the pertinent key determinant was the reported increase in ambulance advanced life support (ALS) (Table 1). Prehospital ALS is cost-effective [64] and efficient paramedic training in ALS interventions may lead to better patient outcomes [65–68]. Physician-staffed ambulances have been associated with improved neurological outcomes in bystander-witnessed cardiac arrest [69]. EMS physician attendance has been associated with improved survival after cardiac arrest in Norwegian rural areas [70].

As elsewhere detailed [6], registry-based analyses offer valuable insights into regional variation, temporal trends and determinants of cardiac arrest outcomes, the potential efficacy of therapeutic interventions, and the extent of evidence-based clinical practice [70–73]. The EuReCa projects combined data from the national cardiac arrest registries of 28 European

countries and have already reported on key modifiable variables (e.g., bystander CPR and defibrillation rates) affecting patient outcomes [73]. Accordingly, our results suggest an improvement in registry reporting of cardiac arrest from 2015 to 2019.

Responses to domain A and D “2019-only” questions suggested variation in end-of-life practices and emergency care organization, respectively. Variable-specific scores for DNACPR and advance directives were predictive of the variable-specific score for ACP, possibly implying increasing integration of advance directives with ACP [6,18]. Overall and “2019-only” results on emergency care organization indicate a need for multilevel improvement in many countries and are consistent with the observed large variation in cardiac arrest outcomes [71,73].

The current questionnaire was not specifically designed to detect pandemic-induced changes in resuscitation practices and patient outcomes [74–76]. Our results are consistent with the recently reported less CPR initiation by bystanders/first aid providers and mobile medical teams, and less AED use [74,75].

Strengths and Limitations

The current survey’s strengths include coverage of multiple aspects of resuscitation and end-of-life practices/care and comparative determination of their time-dependent changes [3,31].

Limitations (including subjectivity-related bias) exhibit similarities to those acknowledged in our 2015 survey [3]. In 2019, we attempted to increase the number of 1–2 respondents per country in 2015; this was not feasible for 9/25 countries (36%; Supplemental Table S1). Consequently, the current work is still primarily based on the opinion of just a few experts from each participating country. We also requested confirmation of original answers and provision of missing answers within 3 months (as opposed to 6 months in 2015). Furthermore, in contrast to 2015, we analyzed only consensus-based data from most (i.e., 16/25; 64%) of the participating countries. Arguably, these methodological differences between the current and the 2015 survey may have limited their comparability. Nevertheless, in 2015, we employed similar criteria for respondent selection and also analyzed consensus-based data from 4/25 (16%) participating countries.

As in 2015, we assumed that respondents had a thorough knowledge of multiple aspects of practice/care or access to information concerning survey items [3]. Furthermore, we employed a dichotomous quantizing approach, which may risk the loss of critical information but also limit respondent subjectivity [3,24]. Arguably, our approach could be regarded as more suitable for questions answerable with a “clear yes or no” (e.g., are DNACPR orders legally allowed?) and less suitable for differentiated questions (e.g., are DNACPR orders applied in the out-of-hospital or in-hospital setting?). However, the determined Cronbach’s alpha values indicated similarly good-to-strong internal consistency of the 2015 and 2019 survey domains [77–79]; this further suggests homogenous and replicable patterns of participant responses in both surveys [79], thereby also supporting domain scores’ comparability.

Our results were derived by simple summation of positive responses and should therefore be interpreted with caution as a higher domain A score may not always indicate better practice. Controversial end-of-life practices such as euthanasia and physician-assisted suicide (PHAD) [80,81] should not be considered equivalent to practices aimed at safeguarding patient autonomy, such as advance directives and ACP [4–6]. However, euthanasia/PHAD are rarely requested/practiced [2], and pertinent positive responses (increasing domain A scores by $\leq 15\%$) were provided by just 4/25 (16%) and 5/25 (20%) countries in 2015 and 2019, respectively.

Finally, in 5/25 countries (20%; respondents, $n = 1$ and ≥ 3 , in three and two countries, respectively), we noted domain A score changes of >10 points from 2015 to 2019 (supplemental Tables S1 and S2); pertinent contributing factors could include improved adherence to ethics/end-of-life guidelines published in 2014 and 2015 [5,7], changes in local legislation [25], and recall/social desirability bias [1].

5. Conclusions

There was a persisting, substantial variation in resuscitation/end-of-life practices across Europe in 2019, indicating a need for progress, preferably through harmonized legislations, governmental policies, and education/training. There was an overall improvement in emergency care organization from 2015 to 2019, driven by countries with “low” 2015 emergency care organization scores. Significant end-of-life practice changes were also noted in countries with “low” 2015 end-of-life practice scores. As in 2015, higher end-of-life practice scores were associated with better emergency care organization in 2019.

Supplementary Materials: The following supporting information can be downloaded at: <https://www.mdpi.com/article/10.3390/jcm11144005/s1>. Summary of results reported in supplemental Tables S1 to S3; Table S1: Country-specific, initial number of discrepancies in responses and/or missing responses, and outcome of efforts to resolve these issues; Table S2: Country-level domain A to D scores in 2015 and 2019, and corresponding summary results; Table S3: Results on domain scores, subscores and their components in all 25 countries; Table S4: Results on domain total scores and subscores and their components in countries with “low” 2015 domain total scores (as defined in main paper’s Methods) Table S5: Results on domain total scores and subscores and their components in countries with “high” 2015 domain total scores (as defined in main paper’s Methods); Summary of responses to questions included only in the 2019 survey; Exploratory analyses: summary of results reported in supplemental Figure S1; Figure S1: Graphs of linear relationships between 2019 domain A and domain D scores with (A) and without (B) the questions included only in the 2019 survey; Graphs of linear relationships between 2019 do-not-attempt cardiopulmonary resuscitation (DNACPR) and advance care planning (ACP) variable-specific scores (C), and between 2019 advance directives and ACP variable-specific scores (D); summary of results reported in Table S6; Table S6: Changes in responses to the 2019 questionnaire due to the coronavirus disease-19 (COVID-19) pandemic). Ethics Committee Approval; Study participant eligibility criteria; Compliance with the Checklist for Reporting Results of Internet E-surveys (CHERRIES); Statistical Analysis—additional details on linear regression.

Author Contributions: Study concept: L.B. and S.D.M. Study Design: S.D.M., K.C., V.R., J.D. and L.B. Acquisition of Data: L.B. and S.D.M. Drafting of the manuscript: S.D.M. Critical revision of the manuscript for important intellectual content: all authors. Statistical analyses: S.D.M., Study supervision: L.B. and S.D.M. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: The study protocol was approved by the Regional Ethics and Scientific Committee of Evaggelismos General Hospital of Athens, the Athens Eye Clinic, and the Athens Polyclinic (Approval No. 447/29/7/2019). The approval was used to support the conduct of the survey study in 32 European countries and Turkey.

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: “De-identified” datasets used and/or analyzed during the current study are available (in the form of Microsoft Excel Worksheets) from the corresponding author on reasonable request.

Acknowledgments: Support from Epidemiology team: Ingvild Tjelmeland, Jan Wnent.

Conflicts of Interest: The authors declare no conflict of interest.

Abbreviations

AED	automated external defibrillator
ACP	advance care planning
COVID-19	coronavirus disease 19
DCD	donation after circulatory death
DNACPR	do-not-attempt cardiopulmonary resuscitation
EMS	emergency medical services

References

1. Sprung, C.L.; Ricou, B.; Hartog, C.S.; Maia, P.; Mentzelopoulos, S.D.; Weiss, M.; Levin, P.D.; Galarza, L.; De La Guardia, V.; Schefold, J.C.; et al. Changes in End-of-Life Practices in European Intensive Care Units From 1999 to 2016. *JAMA* **2019**, *322*, 1692–1704. [[CrossRef](#)] [[PubMed](#)]
2. Avidan, A.; Sprung, C.L.; Schefold, J.C.; Ricou, B.; Hartog, C.S.; Nates, J.L.; Jaschinski, U.; Lobo, S.M.; Joynt, G.M.; Lesieur, O.; et al. Variations in end-of-life practices in intensive care units worldwide (Ethicus-2): A prospective observational study. *Lancet Respir. Med.* **2021**, *9*, 1101–1110. [[CrossRef](#)]
3. Mentzelopoulos, S.D.; Bossaert, L.; Raffay, V.; Askitopoulou, H.; Perkins, G.; Greif, R.; Haywood, K.; Van de Voorde, P.; Xanthos, T. A survey of key opinion leaders on ethical resuscitation practices in 31 European Countries. *Resuscitation* **2016**, *100*, 11–17. [[CrossRef](#)] [[PubMed](#)]
4. Mentzelopoulos, S.D.; Slowther, A.-M.; Fritz, Z.; Sandroni, C.; Xanthos, T.; Callaway, C.; Perkins, G.D.; Newgard, C.; Ischaki, E.; Greif, R.; et al. Ethical challenges in resuscitation. *Intensiv. Care Med.* **2018**, *44*, 703–716. [[CrossRef](#)]
5. Bossaert, L.L.; Perkins, G.D.; Askitopoulou, H.; Raffay, V.I.; Greif, R.; Haywood, K.L.; Mentzelopoulos, S.D.; Nolan, J.P.; Van de Voorde, P.; Xanthos, T.T.; et al. Ethics of resuscitation and end-of-life decisions section Collaborators. European Resuscitation Council Guidelines for Resuscitation 2015: Section 11. The ethics of resuscitation and end-of-life decisions. *Resuscitation* **2015**, *95*, 302–311. [[CrossRef](#)]
6. Mentzelopoulos, S.D.; Couper, K.; Van de Voorde, P.; Druwé, P.; Blom, M.; Perkins, G.D.; Lulic, I.; Djakow, J.; Raffay, V.; Lilja, G.; et al. European Resuscitation Council Guidelines for Resuscitation 2021: Section 11. The ethics of resuscitation and end-of-life decisions. *Resuscitation* **2021**, *161*, 408–432. [[CrossRef](#)] [[PubMed](#)]
7. Council of Europe. Guide on the Decision-Making Process Regarding Medical Treatment in End-of-Life Situations. *Bioethics.net website*. Available online: <http://www.bioethics.net/2014/05/council-of-europe-launches-guide-on-decision-making-process-regarding-medical-treatment-in-end-of-life-situations/> (accessed on 21 March 2019).
8. Davidson, J.E.; Aslakson, R.A.; Long, A.C.; Puntillo, K.A.; Kross, E.K.; Hart, J.; Cox, C.E.; Wunsch, H.; Wickline, M.A.; Nunnally, M.E.; et al. Guidelines for Family-Centered Care in the Neonatal, Pediatric, and Adult ICU. *Crit. Care Med.* **2017**, *45*, 103–128. [[CrossRef](#)]
9. Kon, A.A.; Davidson, J.E.; Morrison, W.; Danis, M.; White, D.B. American College of Critical Care Medicine; American Thoracic Society. Shared Decision Making in ICUs: An American College of Critical Care Medicine and American Thoracic Society Policy Statement. *Crit. Care Med.* **2016**, *44*, 188–201. [[CrossRef](#)]
10. Houben, C.H.; Spruit, M.A.; Groenen, M.T.; Wouters, E.F.; Janssen, D.J. Efficacy of Advance Care Planning: A Systematic Review and Meta-Analysis. *J. Am. Med. Dir. Assoc.* **2014**, *15*, 477–489. [[CrossRef](#)]
11. Brinkman-Stoppelenburg, A.; Judith, A.C.; Rietjens, J.A.C.; van der Heide, A. The effects of advance care planning on end-of-life care: A systematic review. *Palliat. Med.* **2014**, *28*, 1000–1025. [[CrossRef](#)]
12. Kernick, L.A.; Hogg, K.J.; Millerick, Y.; Murtagh, F.E.M.; Djahit, A.; Johnson, M. Does advance care planning in addition to usual care reduce hospitalisation for patients with advanced heart failure: A systematic review and narrative synthesis. *Palliat. Med.* **2018**, *32*, 1539–1551. [[CrossRef](#)] [[PubMed](#)]
13. El-Jawahri, A.; Paasche-Orlow, M.K.; Matlock, D.; Stevenson, L.W.; Lewis, E.F.; Stewart, G.; Semigran, M.; Chang, Y.; Parks, K.; Walker-Corkery, E.S.; et al. Randomized, Controlled Trial of an Advance Care Planning Video Decision Support Tool for Patients With Advanced Heart Failure. *Circulation* **2016**, *134*, 52–60. [[CrossRef](#)] [[PubMed](#)]
14. Chan, H.Y.-L.; Ng, J.S.-C.; Chan, K.-S.; Ko, P.-S.; Leung, D.Y.-P.; Chan, C.W.-H.; Chan, L.-N.; Lee, I.F.-K.; Lee, D.T.-F. Effects of a nurse-led post-discharge advance care planning programme for community-dwelling patients nearing the end of life and their family members: A randomised controlled trial. *Int. J. Nurs. Stud.* **2018**, *87*, 26–33. [[CrossRef](#)] [[PubMed](#)]
15. Cohen, S.M.; Volandes, A.E.; Shaffer, M.L.; Hanson, L.C.; Habtemariam, D.; Mitchell, S.L. Concordance Between Proxy Level of Care Preference and Advance Directives Among Nursing Home Residents With Advanced Dementia: A Cluster Randomized Clinical Trial. *J. Pain Symptom Manag.* **2019**, *57*, 37–46.e1. [[CrossRef](#)] [[PubMed](#)]
16. Green, M.J.; Van Scoy, L.J.; Foy, A.J.; Dimmock, A.E.; Lehman, E.; Levi, B.H. Patients With Advanced Cancer Choose Less Aggressive Medical Treatment on Vignettes After Using a Computer-Based Decision Aid. *Am. J. Hosp. Palliat. Care* **2020**, *37*, 537–541. [[CrossRef](#)]
17. Tolle, S.W.; Teno, J.M. Lessons from Oregon in Embracing Complexity in End-of-Life Care. *N. Engl. J. Med.* **2017**, *376*, 1078–1082. [[CrossRef](#)]
18. Fritz, Z.; Slowther, A.-M.; Perkins, G.D. Resuscitation policy should focus on the patient, not the decision. *BMJ* **2017**, *356*, j813. [[CrossRef](#)]
19. Hawkes, C.A.; Fritz, Z.; Deas, G.; Ahmedzai, S.H.; Richardson, A.; Pitcher, D.; Spiller, J.; Perkins, G.D.; ReSPECT Working Group Collaborators. Development of the Recommended Summary Plan for eEmergency Care and Treatment (ReSPECT). *Resuscitation* **2020**, *148*, 98–107. [[CrossRef](#)]
20. Sulmasy, D.P. Italy's New Advance Directive Law: When in Rome. *JAMA Intern. Med.* **2018**, *178*, 607–608. [[CrossRef](#)]
21. Danish Patient Safety Authority. A Guide on Withholding Life Support, Resuscitation and Withdrawing of Treatment. 2012. Available online: <https://stps.dk/da/udgivelser/2012/vejledning-om-forudgaende-fravalg-af-livsforlaengende-behandling-herunder-genoplivningsforsoeg-og-om-afbrydelse-af-behandling> (accessed on 21 June 2018).

22. The Norwegian Directorate of Health. Decision-Making Process when Limiting Life-Sustaining Treatment. 2013. Available online: <https://helsedirektoratet.no/retningslinjer/bslutningsprosesser-ved-begrensning-av-livsforlengende-behandling> (accessed on 21 June 2018).
23. Schulz-Quach, C.; Wenzel-Meyburg, U.; Fetz, K. Can elearning be used to teach palliative care?—Medical students' acceptance, knowledge, and self-estimation of competence in palliative care after elearning. *BMC Med. Educ.* **2018**, *18*, 82. [[CrossRef](#)]
24. Sandelowski, M.; Voils, C.L.; Knafl, G. On Quantitizing. *J. Mix Methods Res.* **2009**, *3*, 208–222. [[CrossRef](#)] [[PubMed](#)]
25. Ciliberti, R.; Gorini, I.; Gazzaniga, V.; De Stefano, F.; Gulino, M. The Italian law on informed consent and advance directives: New rules of conduct for the autonomy of doctors and patients in end-of-life care. *J. Crit. Care* **2018**, *48*, 178–182. [[CrossRef](#)] [[PubMed](#)]
26. Orsi, L.; Gristina, G.R. Palliative sedation: The position statement of the Italian National Committee for Bioethics. *Minerva Anesthesiol.* **2017**, *83*, 524–528. [[CrossRef](#)] [[PubMed](#)]
27. Cherny, N.I.; Radbruch, L. The Board of the European Association for Palliative Care European Association for Palliative Care (EAPC) recommended framework for the use of sedation in palliative care. *Palliat. Med.* **2009**, *23*, 581–593. [[CrossRef](#)]
28. Le Dorze, M.; Kandelman, S.; Veber, B.; SFAR's Ethics Committee. End-of-life care in the French ICU: Impact of Claeys-Leonetti law on decision to withhold or withdraw life-supportive therapy. *Anaesth. Crit. Care Pain Med.* **2019**, *38*, 569–570. [[CrossRef](#)] [[PubMed](#)]
29. Beller, E.M.; van Driel, M.L.; McGregor, L.; Truong, S.; Mitchell, G. Palliative pharmacological sedation for terminally ill adults. *Cochrane Database Syst. Rev.* **2015**, *1*, CD010206. [[CrossRef](#)]
30. Downar, J.; Delaney, J.W.; Hawryluck, L.; Kenny, L. Guidelines for the withdrawal of life-sustaining measures. *Intensiv. Care Med.* **2016**, *42*, 1003–1017. [[CrossRef](#)]
31. Mentzelopoulos, S.D.; Haywood, K.; Cariou, A.; Mantzanas, M.; Bossaert, L. Evolution of medical ethics in resuscitation and end of life. *Trends Anaesth. Crit. Care* **2016**, *10*, 7–14. [[CrossRef](#)]
32. Badarau, D.O.; De Clercq, E.; Elger, B.S. Continuous Deep Sedation and Euthanasia in Pediatrics: Does One Really Exclude the Other for Terminally Ill Patients? *J. Med. Philos.* **2019**, *44*, 50–70. [[CrossRef](#)]
33. Bhyan, P.; Pesce, M.B.; Shrestha, U.; Goyal, A. Palliative Sedation. 2 December 2020. In *StatPearls [Internet]*; StatPearls Publishing: Treasure Island, FL, USA, 2020; PMID: 29262025.
34. Benítez-Rosario, M.A.; Ascanio-León, B. Palliative sedation: Beliefs and decision-making among Spanish palliative care physicians. *Support. Care Cancer* **2020**, *28*, 2651–2658. [[CrossRef](#)]
35. Riisfeldt, T.D. Weakening the ethical distinction between euthanasia, palliative opioid use and palliative sedation. *J. Med. Ethic* **2019**, *45*, 125–130. [[CrossRef](#)] [[PubMed](#)]
36. Sulmasy, D.P. Sedation and care at the end of life. *Theor. Med. Bioeth.* **2018**, *39*, 171–180. [[CrossRef](#)]
37. Cohen-Almagor, R.; Ely, E.W. Euthanasia and palliative sedation in Belgium. *BMJ Support. Palliat. Care* **2018**, *8*, 307–313. [[CrossRef](#)] [[PubMed](#)]
38. Horn, R. The 'French exception': The right to continuous deep sedation at the end of life. *J. Med. Ethic* **2018**, *44*, 204–205. [[CrossRef](#)] [[PubMed](#)]
39. Kirby, J. Morally-Relevant Similarities and Differences Between Assisted Dying Practices in Paradigm and Non-Paradigm Circumstances: Could They Inform Regulatory Decisions? *J. Bioethical Inq.* **2017**, *14*, 475–483. [[CrossRef](#)]
40. den Hartogh, G. Continuous deep sedation and homicide: An unsolved problem in law and professional morality. *Med. Health Care Philos.* **2016**, *19*, 285–297. [[CrossRef](#)]
41. Raho, J.A.; Miccinesi, G. Contesting the Equivalency of Continuous Sedation until Death and Physician-assisted Suicide/Euthanasia: A Commentary on LiPuma. *J. Med. Philos.* **2015**, *40*, 529–553. [[CrossRef](#)]
42. Seale, C.; Raus, K.; Bruinsma, S.; van der Heide, A.; Sterckx, S.; Mortier, F.; Payne, S.; Mathers, N.; Rietjens, J.; Addington-Hall, J.; et al. The language of sedation in end-of-life care: The ethical reasoning of care providers in three countries. *Health* **2014**, *19*, 339–354. [[CrossRef](#)]
43. Ebell, M.H.; Vellinga, A.; Masterson, S.; Yun, P. Meta-analysis of the accuracy of termination of resuscitation rules for out-of-hospital cardiac arrest. *Emerg. Med. J.* **2019**, *36*, 479–484. [[CrossRef](#)]
44. Nas, J.; Kleinnibbelink, G.; Hannink, G.; Navarese, E.P.; van Royen, N.; de Boer, M.-J.; Wik, L.; Bonnes, J.L.; Brouwer, M.A. Diagnostic performance of the basic and advanced life support termination of resuscitation rules: A systematic review and diagnostic meta-analysis. *Resuscitation* **2020**, *148*, 3–13. [[CrossRef](#)]
45. Verhaert, D.; Bonnes, J.L.; Nas, J.; Keuper, W.; van Grunsven, P.M.; Smeets, J.L.; de Boer, M.J.; Brouwer, M.A. Termination of resuscitation in the prehospital setting: A comparison of decisions in clinical practice vs. recommendations of a termination rule. *Resuscitation* **2016**, *100*, 60–65. [[CrossRef](#)] [[PubMed](#)]
46. Eckstein, M.; Stratton, S.J.; Chan, L.S. Termination of Resuscitative Efforts for Out-of-hospital Cardiac Arrests. *Acad. Emerg. Med.* **2005**, *12*, 65–70. [[CrossRef](#)] [[PubMed](#)]
47. Hansen, C.; Lauridsen, K.G.; Schmidt, A.S.; Løfgren, B. Decision-making in cardiac arrest: Physicians' and nurses' knowledge and views on terminating resuscitation. *Open Access Emerg. Med.* **2018**, *11*, 1–8. [[CrossRef](#)]
48. Campwala, R.T.; Schmidt, A.R.; Chang, T.P.; Nager, A.L. Factors influencing termination of resuscitation in children: A qualitative analysis. *Int. J. Emerg. Med.* **2020**, *13*, 12–14. [[CrossRef](#)] [[PubMed](#)]

49. Long, A.C.; Brumback, L.C.; Curtis, J.R.; Avidan, A.; Baras, M.; De Robertis, E.; Efferen, L.; Engelberg, R.A.; Kross, E.K.; Michalsen, A.; et al. Agreement With Consensus Statements on End-of-Life Care: A Description of Variability at the Level of the Provider, Hospital, and Country. *Crit. Care Med.* **2019**, *47*, 1396–1401. [[CrossRef](#)] [[PubMed](#)]
50. Gardiner, D.; Charlesworth, M.; Rubino, A.; Madden, S. The rise of organ donation after circulatory death: A narrative review. *Anaesthesia* **2020**, *75*, 1215–1222. [[CrossRef](#)] [[PubMed](#)]
51. Ortega-Deballon, I.; Hornby, L.; Shemie, S.D. Protocols for uncontrolled donation after circulatory death: A systematic review of international guidelines, practices and transplant outcomes. *Crit. Care* **2015**, *19*, 1–15. [[CrossRef](#)]
52. Smith, M.; Dominguez-Gil, B.; Greer, D.M.; Manara, A.R.; Souter, M.J. Organ donation after circulatory death: Current status and future potential. *Intensiv. Care Med.* **2019**, *45*, 310–321. [[CrossRef](#)]
53. Hallstrom, A.P.; Ornato, J.P.; Weisfeldt, M.; Travers, A.; Christenson, J.; A McBurnie, M.; Zalenski, R.; Becker, L.B.; Schron, E.B.; Prochan, M.; et al. Public-Access Defibrillation and Survival after Out-of-Hospital Cardiac Arrest. *N. Engl. J. Med.* **2004**, *351*, 637–646. [[CrossRef](#)]
54. Kitamura, T.; Kiyohara, K.; Sakai, T.; Matsuyama, T.; Hatakeyama, T.; Shimamoto, T.; Izawa, J.; Fujii, T.; Nishiyama, C.; Kawamura, T.; et al. Public-Access Defibrillation and Out-of-Hospital Cardiac Arrest in Japan. *N. Engl. J. Med.* **2016**, *375*, 1649–1659. [[CrossRef](#)]
55. Baekgaard, J.S.; Viereck, S.; Møller, T.P.; Ersbøll, A.K.; Lippert, F.; Folke, F. Response by Baekgaard et al to Letters Regarding Article, “The Effects of Public Access Defibrillation on Survival After Out-of-Hospital Cardiac Arrest: A Systematic Review of Observational Studies”. *Circulation* **2017**, *137*, 954–965. [[CrossRef](#)] [[PubMed](#)]
56. Holmberg, M.J.; Vogensen, M.; Andersen, M.S.; Donnino, M.W.; Andersen, L.W. Bystander automated external defibrillator use and clinical outcomes after out-of-hospital cardiac arrest: A systematic review and meta-analysis. *Resuscitation* **2017**, *120*, 77–87. [[CrossRef](#)] [[PubMed](#)]
57. Pollack, R.A.; Brown, S.P.; Rea, T.; Aufderheide, T.; Barbic, D.; Buick, J.E.; Christenson, J.; Idris, A.H.; Jasti, J.; Kampp, M.; et al. Impact of Bystander Automated External Defibrillator Use on Survival and Functional Outcomes in Shockable Observed Public Cardiac Arrests. *Circulation* **2018**, *137*, 2104–2113. [[CrossRef](#)] [[PubMed](#)]
58. Kobayashi, D.; Sado, J.; Kiyohara, K.; Kitamura, T.; Kiguchi, T.; Nishiyama, C.; Okabayashi, S.; Shimamoto, T.; Matsuyama, T.; Kawamura, T.; et al. Public location and survival from out-of-hospital cardiac arrest in the public-access defibrillation era in Japan. *J. Cardiol.* **2020**, *75*, 97–104. [[CrossRef](#)]
59. Smith, C.M.; Keung, S.N.L.C.; Khan, M.O.; Arvanitis, T.N.; Fothergill, R.; Hartley-Sharpe, C.; Wilson, M.H.; Perkins, G. Barriers and facilitators to public access defibrillation in out-of-hospital cardiac arrest: A systematic review. *Eur. Heart J. Qual. Care Clin. Outcomes* **2017**, *3*, 264–273. [[CrossRef](#)]
60. Deakin, C.D.; Shewry, E.; Gray, H.H. Public access defibrillation remains out of reach for most victims of out-of-hospital sudden cardiac arrest. *Heart* **2014**, *100*, 619–623. [[CrossRef](#)]
61. Deakin, C.D.; Anfield, S.; Hodgetts, G.A. Underutilisation of public access defibrillation is related to retrieval distance and time-dependent availability. *Heart* **2018**, *104*, 1339–1343. [[CrossRef](#)]
62. Sun, C.L.F.; Karlsson, L.; Morrison, L.J.; Brooks, S.C.; Folke, F.; Chan, T.C.Y. Effect of Optimized Versus Guidelines-Based Automated External Defibrillator Placement on Out-of-Hospital Cardiac Arrest Coverage: An In Silico Trial. *J. Am. Heart Assoc.* **2020**, *9*, e016701. [[CrossRef](#)]
63. Zègre-Hemsey, J.K.; Grewe, M.E.; Johnson, A.M.; Arnold, E.; Cunningham, C.J.; Bogle, B.M.; Rosamond, W.D. Delivery of Automated External Defibrillators via Drones in Simulated Cardiac Arrest: Users’ Experiences and the Human-Drone Interaction. *Resuscitation* **2020**, *157*, 83–88. [[CrossRef](#)]
64. Von Vopelius-Feldt, J.; Powell, J.; Bengler, J.R. Cost-effectiveness of advanced life support and prehospital critical care for out-of-hospital cardiac arrest in England: A decision analysis model. *BMJ Open* **2019**, *9*, e028574. [[CrossRef](#)]
65. Baker, T.W.; King, W.; Soto, W.; Asher, C.; Stolfi, A.; Rowin, M.E. The Efficacy of Pediatric Advanced Life Support Training in Emergency Medical Service Providers. *Pediatr. Emerg. Care* **2009**, *25*, 508–512. [[CrossRef](#)] [[PubMed](#)]
66. Pilbery, R.; Teare, M.D.; Lawton, D. Do RATs save lives? A service evaluation of an out-of-hospital cardiac arrest team in an English ambulance service. *Br. Paramedic J.* **2019**, *3*, 32–39. [[CrossRef](#)] [[PubMed](#)]
67. Park, J.-H.; Moon, S.; Cho, H.; Ahn, E.; Kim, T.-K.; Bobrow, B.J. Effect of team-based cardiopulmonary resuscitation training for emergency medical service providers on pre-hospital return of spontaneous circulation in out-of-hospital cardiac arrest patients. *Resuscitation* **2019**, *144*, 60–66. [[CrossRef](#)] [[PubMed](#)]
68. Naito, H.; Yumoto, T.; Yorifuji, T.; Tahara, Y.; Yonemoto, N.; Nonogi, H.; Nagao, K.; Ikeda, T.; Sato, N.; Tsutsui, H. Improved outcomes for out-of-hospital cardiac arrest patients treated by emergency life-saving technicians compared with basic emergency medical technicians: A JCS-ReSS study report. *Resuscitation* **2020**, *153*, 251–257. [[CrossRef](#)]
69. Sato, N.; Matsuyama, T.; Akazawa, K.; Nakazawa, K.; Hirose, Y. Benefits of adding a physician-staffed ambulance to bystander-witnessed out-of-hospital cardiac arrest: A community-based, observational study in Niigata, Japan. *BMJ Open* **2019**, *9*, e032967. [[CrossRef](#)]
70. Gräsner, J.-T.; Lefering, R.; Koster, R.W.; Masterson, S.; Böttiger, B.W.; Herlitz, J.; Wnent, J.; Tjelmeland, I.B.; Ortiz, F.R.; Maurer, H.; et al. EuReCa ONE-27 Nations, ONE Europe, ONE Registry: A prospective one month analysis of out-of-hospital cardiac arrest outcomes in 27 countries in Europe. *Resuscitation* **2016**, *105*, 188–195. [[CrossRef](#)]
71. Gräsner, J.-T.; Masterson, S. EuReCa and international resuscitation registries. *Curr. Opin. Crit. Care* **2015**, *21*, 215–219. [[CrossRef](#)]

72. Donnino, M.W.; Saliccioli, J.D.; Howell, M.D.; Cocchi, M.N.; Giberson, B.; Berg, K.; Gautam, S.; Callaway, C. For the American Heart Association's Get With The Guidelines-Resuscitation Investigators Time to administration of epinephrine and outcome after in-hospital cardiac arrest with non-shockable rhythms: Retrospective analysis of large in-hospital data registry. *BMJ* **2014**, *348*, g3028. [[CrossRef](#)]
73. Gräsner, J.-T.; Wnent, J.; Herlitz, J.; Perkins, G.D.; Lefering, R.; Tjelmeland, I.; Koster, R.W.; Masterson, S.; Rossell-Ortiz, F.; Maurer, H.; et al. Survival after out-of-hospital cardiac arrest in Europe—Results of the EuReCa TWO study. *Resuscitation* **2020**, *148*, 218–226. [[CrossRef](#)]
74. Lim, Z.J.; Reddy, M.P.; Afroz, A.; Billah, B.; Shekar, K.; Subramaniam, A. Incidence and outcome of out-of-hospital cardiac arrests in the COVID-19 era: A systematic review and meta-analysis. *Resuscitation* **2020**, *157*, 248–258. [[CrossRef](#)]
75. Baert, V.; Jaeger, D.; Hubert, H.; Lascarrou, J.-B.; Debaty, G.; Chouihed, T.; Javaudin, F.; on behalf of the GR-RéAC. Assessment of changes in cardiopulmonary resuscitation practices and outcomes on 1005 victims of out-of-hospital cardiac arrest during the COVID-19 outbreak: Registry-based study. *Scand. J. Trauma Resusc. Emerg. Med.* **2020**, *28*, 119. [[CrossRef](#)] [[PubMed](#)]
76. Coleman, J.J.; Botkai, A.; Marson, E.J.; Evison, F.; Atia, J.; Wang, J.; Gallier, S.; Speakman, J.; Pankhurst, T. Bringing into focus treatment limitation and DNACPR decisions: How COVID-19 has changed practice. *Resuscitation* **2020**, *155*, 172–179. [[CrossRef](#)] [[PubMed](#)]
77. Heale, R.; Twycross, A. Validity and reliability in quantitative studies. *Évid. Based Nurs.* **2015**, *18*, 66–67. [[CrossRef](#)]
78. Taber, K.S. The Use of Cronbach's Alpha When Developing and Reporting Research Instruments in Science Education. *Res. Sci. Educ.* **2018**, *48*, 1273–1296. [[CrossRef](#)]
79. Bolarinwa, O.A. Principles and methods of validity and reliability testing of questionnaires used in social and health science researches. *Niger. Postgrad. Med. J.* **2015**, *22*, 195–201. [[CrossRef](#)] [[PubMed](#)]
80. WMA Declaration on Euthanasia and Physician-Assisted Suicide. Adopted by the 70 WMA General Assembly, Tbilisi, Georgia. October 2019. Available online: <https://www.wma.net/policies-post/declaration-on-euthanasia-and-physician-assisted-suicide/> (accessed on 23 May 2022).
81. American Medical Association. Ethics. *Euthanasia*. Available online: <https://www.ama-assn.org/delivering-care/euthanasia> (accessed on 23 May 2022).