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European Resuscitation Council Guidelines 2021: Ethics of resuscitation and end of life decisions

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Abstract

These European Resuscitation Council Ethics guidelines provide evidence-based recommendations for the ethical, routine practice of resuscitation and end-of-life care of adults and children. The guideline primarily focus on major ethical practice interventions (i.e. advance directives, advance care planning, and shared decision making), decision making regarding resuscitation, education, and research. These areas are tightly related to the application of the principles of bioethics in the practice of resuscitation and end-of-life care.

Introduction and scope

The purpose of the current European Resuscitation Council Guideline chapter is to provide evidence-based recommendations for the ethical, routine practice of resuscitation and end-of-life care of adults and children. This means maximising the benefit of life-sustaining treatments, while concurrently preventing pertinent harm, and promoting equitable access to best-quality resuscitation care. The chapter should be read in conjunction with other chapters that focus on specific relevant topics; information on e.g. epidemiology, education, post-resuscitation care and on the ethics of resuscitation of newly born babies (transition at birth), can be found in the dedicated chapters within these guidelines.

We primarily focus on major ethical practice interventions (i.e. advance directives, advance care planning, and shared decision making), decision making regarding resuscitation, education, and research. These areas are tightly related to the application of the principles of bioethics in the practice of resuscitation and end-of-life care. Consensus definitions of core bioethical principles and relevant key terms are included in the online supplement.

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We also refer to emerging ethical challenges that resulted from the societal and legal changes associated with the coronavirus disease-19 (COVID-19) pandemic.[1] These changes include new social norms (e.g. social distancing), potential exacerbation of healthcare inequalities, and dissemination of public health misinformation.[1,2]

The chapter content is based on scoping reviews of 22 research questions, and expert opinion. Reviews were originally completed in 2019. Due to the COVID-19 crisis and the postponement of the publication of the 2020 guidelines, we updated each scoping review in mid-2020. Full details of each scoping review, including search strategies, included studies, and study findings are included in the electronic supplement.

Key messages from this chapter are summarised in Fig. 1.

These guidelines were drafted and agreed by the Ethics Writing Group members. The methodology used for guideline development is presented in the Executive summary.[2a] The guidelines were posted for public comment in October 2020. The feedback was reviewed by the writing group and the guidelines was updated where relevant. The Guidelines were presented to and approved by the ERC General Assembly on 10th December 2020.

Concise guidelines for clinical practice

Major interventions aimed at safeguarding autonomy

Patient preferences and treatment decisions

Clinicians should:

- Use advance care planning that incorporates shared decision making to improve consistency between patient wishes and treatment.
- Offer advance care planning to all patients at increased risk of cardiac arrest or poor outcome in the event of cardiac arrest.
- Support advance care planning in all cases where it is requested by the patient.

Fig. 1 – Key messages relating to ethics in Guidelines 2021.

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- Record advance care plans in a consistent manner (e.g. electronic registries, documentation templates etc.).
- Integrate resuscitation decisions with other treatment decisions, such as invasive mechanical ventilation, in overarching advance emergency care treatment plans to increase clarity of treatment goals and prevent inadvertent deprivation of other indicated treatments.
- Clinicians should not offer CPR in cases where resuscitation would be futile.

Improving communication

- Clinicians should use evidence-based communication interventions to improve end-of-life discussions and support completion of advance directives/advance care plans.
- Clinicians should combine structured end-of-life discussions with video decision aids for shared decision making about end-of-life hospital transfer from nursing homes in systems where this technology is available.
- Clinicians should consider inviting a communication facilitator to join discussions with patients and/or their family when making advance care plans about the appropriateness of life sustaining treatments. This refers to systems where communication facilitators are available.
- Healthcare systems should provide clinicians with communication skills training interventions to improve clinicians' skill and comfort in delivering bad news or supporting patients to define care goals.
- Clinicians should integrate the following patient/family support elements with shared decision making:

1. Provide information about the patient's status and prognosis in a clear and honest manner. This may be supported by use of a video-support tool.
2. Seek information about the patient's goals, values, and treatment preferences.
3. Involve patients/family members in discussions about advance care plans.
4. Provide empathic statements assuring non-abandonment, symptom control, and decision-making support.
5. Provide the option of spiritual support.
6. Where appropriate, explain and apply protocolised patient-centred procedures for treatment withdrawal with concurrent symptom control and patient/family psychological support.
7. Consider recording meetings with family for the purpose of audit/quality improvement.

Deciding when to start and when to stop cardiopulmonary resuscitation (CPR)

Withholding and Withdrawing CPR

- Systems, clinicians, and the public should consider cardiopulmonary resuscitation (CPR) a conditional therapy.
- Systems should implement criteria for the withholding and termination of CPR for both in-hospital cardiac arrest (IHCA) and out-of-hospital cardiac arrest (OHCA), taking into consideration the specific local legal, organisational, and cultural context.
- Systems should define criteria for the withholding and termination of CPR, and ensure criteria are validated locally. The following criteria may be considered:
  - Unequivocal criteria:
    - When the safety of the provider cannot be adequately assured
    - When there is obvious mortal injury or irreversible death
    - When a valid and relevant advance directive becomes available that recommends against the provision of CPR.
  - Further criteria to inform decision making:
    - Persistent asystole despite 20 minutes of advanced life support (ALS) in the absence of any reversible cause.
    - Unwitnessed cardiac arrest with an initial non-shockable rhythm where the risk of harm to the patient from ongoing CPR likely outweighs any benefit e.g. absence of return of spontaneous circulation (ROSC), severe chronic co-morbidity, very poor quality of life prior to cardiac arrest.
    - Other strong evidence that further CPR would not be consistent with the patient's values and preferences, or in their best interests.
  - Criteria that should not alone inform decision-making e.g.
    - Pupil size
    - CPR duration
    - End-tidal carbon dioxide (CO_2) value
    - Co-morbid state
    - Initial lactate value
    - Suicide attempt
- Clinicians should clearly document reasons for the withholding or termination of CPR, and systems should audit this documentation.
- Systems should implement criteria for early transport to hospital in cases of OHCA, taking into account the local context, if there are no criteria for withholding/terminating CPR. Transfer should be considered early in the CPR attempt and incorporate patient, event (e.g. distance to hospital, risk of high-priority transport for those involved), and treatment (e.g. risk of suboptimal CPR) factors. Patients who may particularly benefit from early transport include emergency medical services (EMS) witnessed arrest [or by bystander performing high quality basic life support (BLS)] with either ROSC at any moment or ventricular fibrillation/tachycardia (VT/VF) as presenting rhythm and a presumed reversible cause (e.g. cardiac, toxic, hypothermia).
- Systems should implement criteria for inter-hospital transfer of IHCA patients in hospitals where advanced CPR techniques are not offered.
- Clinicians should start CPR in patients who do not meet local criteria for withholding CPR. Treatments may then be tailored as more information becomes available.
- Clinicians should not partake in 'slow codes'.
- During a pandemic, resource demand (e.g. critical care beds, ventilators, staffing, drugs) may significantly exceed resource availability. Healthcare teams should carefully assess each patient's likelihood of survival and/or good long-term outcome and their expected resource use to optimise allocation of resources. Clinicians should not use categorical or blanket criteria (e.g. age thresholds) to determine the eligibility of a patient to receive treatment.
- In systems that offer uncontrolled donation after circulatory death and other systems of organ donation, transparent criteria should be developed for the identification of candidates and process for obtaining consent and organ preservation.

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Bystander CPR

Systems should:

- Recognise the importance of bystander CPR as a core component of the community response to OHCA.
- Recognise bystander CPR as a voluntary act, with no perceived moral or legal obligation to act.
- Support bystanders in minimising the impact on their own health of performing bystander CPR. In the context of transmissible disease (such as COVID-19), bystanders also have a responsibility of preventing further disease transmission to other individuals in the immediate vicinity and the wider community.
- Aim to identify cases where bystander CPR is likely to be beneficial and cases where it is unlikely to be beneficial.
- Never evaluate the value of (bystander) CPR in isolation but as part of the whole system of healthcare within their region. (Bystander) CPR seems feasible in settings where resources and organisation support the integrity of the chain of survival.

Family presence during resuscitation

Resuscitation teams should offer family members of cardiac arrest patients the opportunity to be present during the resuscitation attempt in cases where this opportunity can be provided safely, and a member of the team can be allocated to provide support to the patient's family. Systems should provide clinicians with training on how best to provide information and support to family members during resuscitation attempts.

Patient outcomes and ethical considerations

- When making decisions about CPR, clinicians should explore and understand the value that a patient places on specific outcomes.
- Health systems should monitor outcomes following cardiac arrest, and identify opportunities to implement evidence-based interventions to reduce variability in patient outcome.
- Cardiac arrest research should collect core outcomes, as described in the cardiac arrest core outcome set.

Ethics and emergency research

- Systems should support the delivery of high-quality emergency, interventional and non-interventional research, as an essential component of optimising cardiac arrest outcomes.
- Researchers should involve patients and members of the public throughout the research process, including design, delivery and dissemination of the research.
- For observational research (e.g. in the context of registry data collection and/or DNA biobank data sampling and analyses) we suggest consideration of a deferred and broad consent model, with concurrent implementation of appropriate safeguards aimed at preventing data breaches and patient re-identification.
- Communities or population in which research is undertaken and who bear the risk of research-related adverse events, should be given the opportunity to benefit from its results.
- Researchers must ensure that research has been reviewed and approved by an independent ethical review committee, in line with local law, prior to it being commenced.
- Researchers must respect the dignity and privacy of research subjects and their families.
- Researchers should comply with best practice guidance to ensure transparency of research, including study protocol registration, prompt reporting of results, and data sharing.
- Systems should ensure that funding for cardiac arrest research is proportionate to the societal burden caused by cardiac arrest-associated morbidity and mortality.

Evidence informing the guidelines

For ethics in relation to the COVID-19 pandemic see ″Ethical considerations on resuscitation during the COVID-19 pandemic″.[3]

Major interventions aimed at safeguarding autonomy

The key interventions for safeguarding patient autonomy are advance directives and advance care planning. These interventions should be underpinned by a shared decision-making process.

Variability in terminology, definitions, type and delivery of interventions, and outcome choice makes it challenging to identify and assimilate research evidence in this area.[4,5] In view of this, the writing group developed consensus definitions and statements for advance directives, advance care planning, and shared decision making, which are summarised in Tables 1–3 and the online supplement.

In developing treatment guidelines, we drew on core ethical principles, 29 systematic/scoping reviews, and 49 recent primary research papers. Key systematic reviews and studies are summarised in the supplementary text and Tables S2 and S3. The corresponding rapid reviews 1.1–1.4 are summarised in the respective appendices.

Advance directives

Effective use of advance directives relies on the accurate and efficient exchange of information about patient values, goals, and preferences, and available treatment options.[4] Consequently, several, structured communication tools (e.g. paper, video, or computer decision aids, and educational interventions) have been developed to facilitate end-of-life decision-making.[4] Evidence from meta-analyses of randomised controlled trials (RCTs), systematic reviews, and recent studies suggests that structured communication tools aid in the completion of advance directives and may increase concordance of end-of-life care with the care desired by the patient.[4,6–12]

Do not attempt CPR (DNACPR) decisions seek to protect patients from receiving invasive treatments they have declined, they have considered futile, or from treatments that are not aligned with the patient's values and preferences.[13] Evidence from 13 RCTs and from 8 nonrandomised studies included in 3 systematic reviews suggests associations of communication interventions with an increased frequency of DNACPR orders.[4,7,8,10]

Four systematic reviews reported mixed findings regarding the impact of advance directives on the documentation of patient's wishes about treatment escalation and resuscitation decision-making.[5,9,10,14] These reviews also highlighted that, in some studies, the making of a DNACPR decision may confer benefit as regards the patient's quality of care through, for example, more adequate pain relief and hydration, and improved response of healthcare providers to clinical deterioration.

Recent evidence from RCTs supports the use of informational video decision support tools in both the nursing home and the in-

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Table 1 – Consensus definition and statements for advance directives.

Advance directives *

- An advance directive is an instrument that relays information concerning an individual's preferences and goals regarding medical procedures and treatments, especially those used for end-of-life care.
- Advance directives intend to extend the patient's autonomy to situations in which he/she is unable to express his/her preferences regarding treatment decisions. They reflect a patient's individual moral, cultural, and religious attitudes. They are represented in three formats: Living Will (or instruction directive), Appointment of a Healthcare Proxy (or proxy directive), and Legal Status of Preferences.
- In principle, advance directives (ADs) must fulfil the following 3 criteria: Existence, Validity (partly realised through periodic review), and Applicability.
- Health care professionals should determine whether their patients have ADs.
- Physicians should respect their patient's ADs and incorporate them into their decision making.
- Physicians should discuss advance directives with their patients.
- Attempts should be made to ascertain patient's wishes (especially patients with terminal diseases) concerning life-sustaining treatments when they are capable of making decisions or, alternatively, from their surrogates when they are not capable of making decisions.
- There are times when advance directives should not be followed. These include situations when the advance directive calls for an action that is prohibited by the country's laws and/or regulations, where there is compelling evidence that the patient may have changed his/her mind since completing the advance directive, when there is compelling evidence suggesting that the patient did not understand the nature of the advance directive he/she completed, or when there is evidence that the patient did not have freedom of choice at the time of drafting.
- If advance directives concern the refusal of a specific treatment, careful interpretation should be made as to whether this should concern similar (but still alternative) treatments or not. For example, a patient may refuse a specific medical or surgical treatment due to certain rare but severe side effects. In such a case, it may not be appropriate to exclude alternative treatments that may exhibit a more favourable safety profile and comparable efficacy relative to the refused treatment.
- Reasons for refusal of standard treatments of a specific disease may not apply after the introduction of new interventions with more favourable safety profiles and increased efficacy. Given the fact of the continuous and rapid progress in clinical practice, old (e.g. >5 years) and non-updated advance directives should be cautiously interpreted in the context of availability of new, safer, and potentially more effective therapies.
- Nonstandard advance directives (e.g. tatoos indicating do-not-attempt cardiopulmonary resuscitation - DNACPR) should not be immediately perceived as legally valid, unless designated so by local law. In countries where the presence of nonstandard advance directives is considered legally valid, CPR administered in conditions where resuscitation is likely to be futile can lead to legal prosecution of the healthcare professional. Concurrently, every effort should be promptly undertaken to clarify whether a valid, pertinent advance directive exists.

*, Consensus definitions and statements were based on 7 references.[5a–5g]

Table 2 – Consensus definition and statements for advance care planning.

Advance care planning *

- A process that enables individuals to define goals and preferences for future medical treatment and care, to thoroughly discuss these goals and preferences with family and health-care professionals, and to record and review these preferences if appropriate. The main objective of advance care planning is to help ensure that people receive medical care that is consistent with their values, goals and preferences during serious, chronic and/or acute/life-threatening illness.
- Advance care planning elements may include communication interventions such as information brochures or pamphlets, and video decision support tools.
- Regarding specific population subgroups with morbidity-related decisional incapacity (e.g. patients with dementia, or children with intellectual disability and a life-limiting illness): due to very limited or even completely lacking, relevant evidence, it is still unclear whether advance care planning (based on surrogate decision-making) can positively impact their health-related quality of end-of-life, and also ameliorate the surrogates' psychological burden, symptoms, and distress. In the meantime, advance care planning should still be considered for such patients.
- Advance care plans that are not updated or re-reviewed should be cautiously interpreted in the context of availability of new and improved therapies that might potentially affect patient preferences; patient preferences may also evolve with time independently of available treatment options.
- Patient's cultural background, religious beliefs/religiosity, and associated, possible spiritual needs, should be taken into account/respected in the course of development and reviewing of advance care planning.
- Regarding treatment limitation directives, a recent multicenter observational study suggested that end-of-life treatment limitation practices may be affected both by patients and physician religion.

*, Consensus definitions and statements were based on 3 references.[5a,5g,64]

hospital setting by reducing the frequency of delivery of interventions that are unlikely to be beneficial.[15–18] Four recent retrospective studies and a point-prevalence review suggest that advance directives and/or DNACPR decisions are associated with reduced use of life-sustaining treatments.[19–24]

Evidence from two systematic reviews suggests that the use of advance directives is associated with reductions in emergency room visits, hospital admissions, health care costs, and more preference for comfort care as opposed to life-sustaining treatments.[4,8] The effect on outcomes such as hospital/ICU length of stay, and patient preference for end-of-life care is less clear. These mixed findings may be partly attributed to heterogeneity across studies in relation to population, interventions, and the comparator group. Despite study limitations, findings of studies of advance directives generally support the use of structured communication tools.[4]

Symptom control is key to improving the end-of-life experiences of a dying patient.[25] However, 15 RCTs included in a systematic review failed to determine any advance directive benefit on patients' anxiety, depression, pain, psychological well-being and health.[8]

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Table 3 – Consensus definition and statements for shared decision making.

Shared decision making *

- Shared decision making is a collaborative process that allows patients, or their surrogates, and a possibly/preferably multidisciplinary team of healthcare professionals to reach consensus on which treatment strategies and interventions - including life-support limitation and palliative care- accord with the patient's values, goals, and preferences. Healthcare decisions should take the best available scientific evidence into account. Honest exchange of information should foster the development of trust/partnership between patient/surrogate(s) and clinician(s). Clinicians should be trained in communication skills. Shared decision making practices should be evaluated by research using patient-/surrogate-reported outcomes.
- The shared decision making process should include information exchange, deliberation, and decisions relating to a treatment.
- Shared decision making should preferably be part of the application of current guidelines on family-centred care.
- Shared decision making should take into account any pre-existing, documented patient goals, values, and preferences in the form of either ″isolated″ advance directives, or advance directives completed in the context of advance care planning.

*, Consensus definitions and statements were based on 3 references.[4a,5h,64]

In recent guidelines, patient/family satisfaction was considered as a core outcome.[26] Data from eight RCTs included in three systematic reviews indicated that communication interventions aiding the completion of advance directives had no significant effect on patient/family satisfaction with end-of-life care.[4,7,8] However, another 4 RCTs included in one of these reviews, reported an increase in patient/family satisfaction with care associated with a communication intervention.[8]

Advance care planning

Advance care planning may be regarded as the state-of-the art procedure for ensuring respect for patient autonomy. It is a dynamic process based on effective and honest communication between the patient and their family, and healthcare professionals (Table 2).

Most studies support the use of advance care planning as a strategy to ensure that end-of-life care is in line with the patient's values and preferences, although there is some inconsistency across the available evidence.[9,27–32] Video-based information and other types of interventions may support the development of advance care plans and thereby increase the concordance between care desired and care received. How effective interventions are in achieving concordance may depend on their nature and on the context in which they are used.[33–36]

Documenting a person's or a patient's updated preferences about end-of-life treatments (including life-sustaining treatments and CPR) is a major objective of advance care planning (Table 2); documented preferences may then be accessed by healthcare professionals to potentially inform treatment decisions. Evidence from six systematic reviews indicates that advance care planning increases documentation of patient preferences.[27,30,32,37–39] Recent studies also reported positive results.[40–42]

We identified mainly positive results on the effect of advance care planning (with or without the aid of communication tools) on the preference for and/or actual use of life-sustaining treatments at the end-of-life. In a meta-analysis of seven RCTs, a video intervention reduced the likelihood of indicating a preference for CPR relative to control.[43] Another systematic review concluded that advance care planning was associated with a reduction in the use of life-sustaining treatments.[9] In contrast, two RCTs and four observational studies included in another systematic review did not report any significant association between communication tools for end-of-life decision making and DNACPR status.[44] Nevertheless, four recent RCTs[45–48] and a cross-sectional survey[49] suggest that advance care planning is associated with less frequent preferences for CPR and/or use of life-sustaining treatments at the end-of-life.

We identified limited supporting evidence for the use of communication tools in the context of advance care planning, to reduce hospitalisations, ICU admissions, and hospital/ICU utilisation among patients who are unlikely to obtain any benefit. Indeed, in meta-analyses that included five RCTs and eight observational studies, communication tools had no effect on ICU length of stay.[44] In addition, although a meta-analysis of three observational studies suggested that communication tools are associated with reduced ICU length of stay of non-survivors, this was not confirmed in one RCT.[44] A meta-analysis of five observational studies suggested that communication tools may be associated with reduced hospital costs. However, one RCT and another two observational studies did not report any effect of communication tools on hospital costs in ICU non-survivors. One RCT reported a reduction in the duration of mechanical ventilation with the use of communication tools, but another two RCTs and two observational studies failed to confirm such benefit.[44]

The effects of advance care planning on hospital/ICU admissions, healthcare resource utilisation, death at preferred location, hospice use, palliative care referrals, healthcare costs, and quality of dying and death are inconsistent between studies.[9,27,30,31,36,38,43,49–58]

Evidence from systematic reviews suggests that advance care planning is associated with improvements in symptom control and quality of life.[9,30,31,37,38,50,59] However, three recent RCTs found no benefit with respect to patients' health-related quality-of-life, physical/functional outcomes, and anxiety or depression.[53,60,61]

A recent cluster RCT in nursing homes reported an advance care planning-associated decrease in family carers' decisional conflict.[62] A cross-sectional survey,[49] and a historically controlled, prospective study[57] reported associations of advance care planning with good quality of end-of-life and decreased suffering in children/adolescents,[49,57] or adults[49] with complex chronic conditions; advance care planning was also associated with reduced parental decisional regret, or lower caregiver burden.

Evidence from five systematic reviews suggests that advance care planning may improve patient/family satisfaction with care.[9,31,37,38,44] However, a recent, multicenter RCT of advanced cancer patients reported that consultation plus early palliative care did not affect family satisfaction with care.[53]

Specific and adequate training of healthcare professionals is key to improving the quality of end-of-life care.[63] The results of 21 studies (RCT, $n=3$) included in a systematic review suggested that communication skills training interventions increase comfort, self-efficacy, and preparedness of healthcare professionals in the delivery of end-of-life care.[37] In an interview-based study included in a systematic review, advance care planning discussions increased

healthcare professionals' confidence in their dealings with the patient.[29]

Shared decision making

Shared decision making is an individualised, collaborative, multistep process aimed at reaching major and preference-sensitive treatment decisions (Table 3).[64] The concept underpins all patient-focused healthcare decision-making.

Effective communication about end-of-life care relies on a shared decision-making process. Its use has been shown to improve end-of-life care, particularly in relation to concordance between care desired and care received, in a systematic review[65] and most recent studies.[60,66–70] However, studies reporting the effect on quality of care and symptom control have produced conflicting findings.[65]

From a health service perspective, shared decision-making may support the appropriate allocation of resources by ensuring that patient treatment aligns with their values and preferences. Use of interventions based on the concept of effective shared decision-making may be associated with shorter ICU/hospital length-of-stay, selection of palliative care pathways in nursing homes, and reduced health care costs and fewer in-hospital deaths, although evidence from systematic reviews and recent studies is inconsistent.[65,67,69,71–79]

Family members of patients may be impacted by the illness of their loved ones. Up to 50% of family members of critically ill patients experience psychological symptoms, such as acute stress, post-traumatic stress disorder, anxiety, depression, and decisional conflict/regret.[26,80–82] Family support interventions may help to reduce these psychological impacts, as suggested by four systematic reviews,[37,71,72,83] and two recent studies.[84,85] However, some recent studies found that family support interventions did not reduce psychological symptoms in family members.[66,67,75,79]

Patient and family satisfaction is a key objective of patient- and family centred communication and care. Communication in the context of shared decision-making is associated with higher patient/family satisfaction and increased decisional confidence, as suggested by four systematic reviews.[65,71,72,74] Key components of this approach include open, honest, clear, and frequent communication and inclusion of family members in discussions with healthcare professionals.[83] Recordings of clinician-family conferences suggest that communication is often sub-optimal, such that the patient's values and preferences are infrequently elicited.[86] The use of structured communication tools may help to improve communication with families, as suggested by two systematic reviews.[37,44] Furthermore, according to recent studies, communication supported by other strategies such as video decision aids may be associated with improved family satisfaction.[67,75,78]

Major interventions aimed at safeguarding autonomy and COVID-19

During periods of public health disaster, such as the COVID-19 pandemic, the importance of pre-existing documentation of patient's wishes regarding life-sustaining treatments, including mechanical ventilation and CPR, may increase, especially for overstretched healthcare systems with limited resources.[87–89] In the absence of advance directives, healthcare professionals should actively seek to engage in treatment escalation decisions with patients, especially those at high-risk of death.[90] Ideally, this should apply to all healthcare settings, using digital communications as appropriate and feasible.[87–89] Discussions should focus on eliciting an individual's values and preferences, rather than asking them to choose a treatment option.[91] Treatment escalation decision-making, such as DNACPR, should be based on an individualised patient assessment that draws upon clinical and scientific evidence,[92] the patient's values and preferences, and the local context, such as resource availability. Decision-making based on single factors such as age, sex, race, religion/ethnicity, intellectual disability, and socioeconomic status is not ethically justifiable.[87,88,92,93] Discrimination according to a patient's COVID-19 status must also be avoided.[94]

Structured advance care planning interventions may include face-to-face conversations between the patient and a healthcare professional over a specified time interval, often with family members present.[46] Clearly, such interventions may be hindered by the need for physical distancing due to healthcare catastrophes like the COVID-19 pandemic. Although digital telecommunication technology may obviate the need for physical presence during a discussion, its availability and the patient's/proxy's capability of adequate use should not always be taken for granted. Concurrently, there may be a perceived need for augmented dissemination and even acceleration of the advance care planning processes to prevent the waste of potentially scarce resources on disproportionate and/or unwanted, aggressive end-of-life treatments.[89] Such upscaling process should be achieved solely through improvements in system organisation and infrastructure, public communication and education, and effective suppression of health misinformation.[1,2] Any form of psychological pressure in the context of categorical discrimination of frail people should be regarded as ethically unacceptable.[92] For emergency department patients at high risk of severe COVID-19 and without advance care plans, a viable alternative may comprise the implementation of an emergency department-based palliative care team committed to high-quality goals of care discussions with the patient and/or proxy. Such interventions may increase the rates of time-sensitive decisions about CPR and other life-sustaining treatments, and comfort care.[95]

Shared decision-making becomes more challenging in situations where face-to-face communication is not feasible. In the context of COVID-19, visiting has been limited in many hospitals and the burden on hospital services may have limited the time available to healthcare professionals to engage in detailed discussions with patients and their families. In these circumstances, use of teleconferences may be an acceptable and feasible approach to maintain patient-centred communication with families and integrate shared decision-making in routine clinical practice.

Deciding when to start and when to stop CPR

The corresponding rapid reviews 2.1–2.7 are summarised in the respective appendices (pages 167–310 of the online supplement).

Termination of resuscitation

The 2020 International Liaison Committee on Resuscitation (ILCOR) Consensus on Science and Treatment Recommendation conditionally supported the use of termination of resuscitation (ToR) rules (very-low certainty evidence).[96] In making the recommendation, the ILCOR Education Implementation and Teams task force acknowledged variation in patient values, resources available, and performance of ToR rules across settings. The task force sought to balance the risk that implementation might result in missed survivors, against current variation in practice and improve termination decisions more generally. ToR may also reduce demand on hospital resources and

increase rescuer safety by reducing the number of patients transported to hospital in cardiac arrest.

It is generally agreed that CPR should not be provided to all patients. This viewpoint reflects both medical and ethical perspectives, including the potential harm of CPR (in terms of dignity, victim awareness, deception of relatives, etc.), and the risks of unfavourable outcome in survivors (and likewise burden for caregivers, risks to healthcare providers, medical costs, and preservation of medical resources). Many authors strongly defend the individual's right to die in a society where more and more advanced medical techniques can lengthen life at the potential cost of quality of life and palliative comfort.[97,98] Prolongation of an inevitable dying process should be considered harm (dysthanasia). In practice, it is often challenging to reliably identify which individuals will have a poor outcome in the event of cardiac arrest.[99–103]

Futility has traditionally been described as a likelihood of survival of less than 1%.[104] More recently, this concept has been challenged for not considering either neurological and functional outcome of survivors or broader societal considerations opinions (e.g. utility trade-off).[104–106] Importantly, Van Norman et al. posed relevant questions about fairness of the concept when there is a potential for unconscious bias based on socioeconomic and demographic factors like social status, fear of litigation or the patient gestalt.[107–109] The appreciation of futility is timely and contextual in nature and often also incorporating religious or spiritual beliefs.[110,111] Patients and families may define futility very differently than medical providers. Marked differences are also observed between different providers. Many clinicians lack confidence in making ToR decisions and some report using non-validated or controversial factors as a single reason for terminating CPR.[106,107,112–122] Decision-making becomes even more complex in the context of newer advanced resuscitation technologies.

Defining an unfavourable outcome is challenging. The cut-off of a cerebral performance category (CPC) of 2 may translate to a spectrum of functional outcomes. Moreover, the value of an outcome to an individual will likely be specific to that person.[105] Defining –as a society, healthcare provider or even as a relative– that a certain life no longer is worth living, especially when this becomes balanced against cost or societal interaction, should only be done with the greatest caution as it incorporates a great inherent risk of quickly crossing acceptable ethical boundaries.[123,124] As such, there has been a shift from futility to considering the broader concept of best interests, which rather evaluates burden versus benefit.

Decision-making regarding the withholding or termination of resuscitation exists in a legal framework, which will have primacy over ethical concepts.[125] The ILCOR Education, Implementation, and Teams (EIT) taskforce in their insights highlighted the need to consider local legislation.[96]

There are important differences between the withholding or termination of resuscitation between the in-hospital and out-of-hospital setting. In the out-of-hospital setting, EMS teams often arrive at a scene where CPR is in progress, and then can only decide to withdraw (not withhold) resuscitation efforts. They often have limited information on the patient's previous medical history and their values and preferences, and may be unable to discuss treatment options with family members. As such, where there is uncertainty about the appropriateness of terminating resuscitation, the focus should be on patient treatment with a view to reconsidering the appropriate treatment once the patient's values and preferences, and clinical trajectory are known.[98,102]

The ILCOR COSTR recommends that none of the existing ToR rules should be the sole determinant of when to discontinue resuscitation.[96] ToR rules will inevitably introduce a self-fulfilling prophecy and should be reviewed periodically as new treatments evolve. Intra-arrest factors are not sufficiently reliable to be used in isolation for terminating resuscitation.[126–135] Examples of factors that should not be used alone include serum potassium, end-tidal CO_2, cardiac standstill on ultrasound, pupillary response/size, temperature, co-morbid status, cause of arrest, no-flow time, low-flow time, and absence of ROSC.

The ILCOR CoSTR summarises several ToR rules.[136,137] Some factors are consistent across tools, such as whether the arrest was witnessed. A key challenge in operationalising these rules stems from uncertainty as to the applicability of rules to other healthcare settings and the challenge in reliably estimating the number of missed potential survivors when applying the rule.[103,104,138–144]

There are specific guidelines for specific subpopulations, such as children.[145] Despite differences in pathophysiology and aetiology, the ethical framework in paediatric cardiac arrest is otherwise similar, although many clinicians may be more cautious in terminating the resuscitation of a child.[99,146,147]

Typical, but not only important for children, is the mandate and role of surrogate decision makers. Time is often limited to come to shared decision-making during cardiac arrest. Moreover, the likelihood of truly informed unbiased consent is low, and it is unclear whether the best interest of the patient might not conflict with the rights and interests of the relatives.[148] Importantly, putting for instance parents in the position to forgo CPR may intensify parental grief and helplessness.[148] Therefore, clinicians should carry the primary professional and moral responsibility for the decision and use a model of informed assent from parents, allowing for respectful disagreement. Nevertheless, local regulation and laws might demand actual guardian's consent.

Slow code

A 'slow code' is slang for the deceptive practice of purposely delivering sub-optimal CPR with the pretence of attempting to save the patient's life. There is evidence that slow codes continue to be performed both in IHCA and OHCA, even when CPR is considered of no benefit to the patient.[149–151]

Use of the slow code is extremely ethically problematic, although some have advocated for it in certain circumstances.[152,153] Several alternatives have been described that are ethically more acceptable, such as informed non-dissent, tailored code or early advance care planning with open communication. More education on ethics in resuscitation might positively affect this.

Extracorporeal (E)-CPR

The European Resuscitation Council (ERC) ethics writing group acknowledges the ALS and paediatric life support 2020 ILCOR COSTRs that support the use of E-CPR as a rescue therapy for selected cardiac arrest patients when conventional CPR has failed in settings where E-CPR can be implemented (weak recommendation, very-low certainty of evidence).[154,155] To inform our insights, we further identified 6 systematic reviews,[156–161] four narrative reviews[162–165] and 13 observational studies[68,140,160,166–175] on this topic. Other sources, such as commentaries and ethical dissertations, were considered as indirect information.

The evidence base for the cost-effectiveness and ethical framework of E-CPR is limited. For IHCA, E-CPR may be cost-

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effective, provided the programme is limited to specific patient groups. The incremental cost-effectiveness ratio is mainly influenced by the probability of survival, although large variations in in-hospital cost estimates have been reported. Physicians involved should be knowledgeable and provide proper stewardship of available resources. Across 224 North American hospitals that participate in the American Heart Association (AHA) Get-with-the-Guidelines-Resuscitation-registry, fewer than 1% patients received E-CPR between 2000 and 2018, indicating a further need for optimised patient selection and E-CPR implementation strategies.[170,171] One systematic review examined E-CPR in refractory adult OHCA of cardiac origin.[157] They suggested that it is feasible and may increase both neurologically intact survival and organ donation in non-survivors. Implementation in existing EMS systems is challenging and requires detailed protocols for patient selection and transportation.[160,173–175] The Ethics writing group identified an urgent need for more research on patient selection, modifiable outcome variables, risk-benefit, and cost-effectiveness of E-CPR. Such data are crucial for E-CPR programme implementation.

Organ donation

Patients who sustain a cardiac arrest are an important source of donor organs, mainly because severe neurological injury is a common mode of death.[176–178] There are three pathways by which cardiac arrest patients might donate organs: following confirmation of brainstem death, following withdrawal of life-sustaining treatment leading to circulatory death (controlled donation after circulatory death) or donation where resuscitation attempts to achieve ROSC have been unsuccessful (uncontrolled donation after circulatory death). The Post-Resuscitation Care and ALS sections of the guidelines provide further details on these pathways. This section focuses on the ethics of organ donation.

We included two systematic reviews,[178,179] four narrative reviews,[180–183] five observational studies[184–188] and some additional editorials and ethical dissertations.

Across Europe, there is variability in organ donor rates, availability of organ donation pathways, and law and policy regulating organ donation (World Health Organization Collaborating Centre on Organ Donation and Transplantation 2019). Shortage of available donor organs is an ongoing challenge across Europe and contributes to premature morbidity and mortality in individuals with organ failure. Organ donation provides an opportunity following a tragic event to respect the donor's wish to benefit wider society. For relatives of the donor, consenting to organ donation may provide comfort that their grief has given life to others.[188] Organ donation is generally supported by society, although levels of support vary by cultural group and between individuals.[181,186]

A key issue is the need for both family members and society to maintain trust that donation is considered only when ongoing treatment will not achieve an outcome important to the patient. Examples of safeguards to maintain this trust include respect for the dead-donor rule, a clear division between the clinical and transplantation team, and transparent communication with family members before organ retrieval. A review of attitudes towards organ donation concluded that both general and ethical education may serve to guide policy and to facilitate family member requests and informed consent dialogues.[180] Helping families to understand and accept not only medical and legal criteria for determining death, but also ethical criteria for withdrawing life support, may help them be more comfortable with their decisions.

Uncontrolled donation after circulatory death raises ethical challenges.[185,189] In particular, the time-critical nature of the process usually requires the initiation of organ preservation processes prior to family consultation to maintain organ viability.[186,190,191] Cardiac arrest patients may meet criteria for both uncontrolled donation and E-CPR programmes.[157,159,179] In centres that offer both modalities, uncontrolled donation should be considered only in patients who do not meet clinical criteria for E-CPR, in order to prevent the loss of potentially saveable life.[163] For a more in-depth discussion see the supplement (pages 255–259).

Importantly, several authors suggest that organ-preserving CPR should be considered only for patients who are brain-dead, or in those with evidence of futility, a known wish for organ donation and a specific informed consent from a next of kin.[163,190,192,193]

Family presence during resuscitation

In our literature search we did not specifically address parental presence during the resuscitation of a child as this is expected to be topic of a specific COSTR from the ILCOR paediatric Taskforce; however, our findings apply equally to this context and we also refer to the 2015 ERC guidelines.[194,195] For family presence during resuscitation, we identified one guideline,[196] two systematic reviews,[197,198] five narrative reviews,[199–203] one RCT,[204] and three observational studies,[205–207] as well as several ethical dissertations and opinion pieces.

The available evidence indicates that family presence during resuscitation does not affect patient outcome but may improve family member psychological outcomes. On this basis, teams should offer family members the option to be present during resuscitation in situations where it is safe, and when the family can be adequately supported.

CPR after attempted suicide

This guidance is based on one narrative review[208] and on an observational study,[209] with other sources included as indirect evidence.

The 2015 ERC ethics chapter highlighted the challenge of determining whether the patient who has attempted suicide had mental capacity at the time of the suicide attempt.[195] On this basis, the guidance recommended that treatment be started because of the risk of harm if treatment is delayed. Crucial to the decision making is the appreciation of mental capacity. This is defined as sufficient understanding of the nature, purpose and effects of the proffered treatment, and able to comprehend and retain the treatment information; believe the information; and weigh it among other factors to reach a decision.[210] The patient must also be able to communicate and substantiate the decision (see also supplement for our consensus definition of decisional incapacity). Sufficiency of capacity is seen as a spectrum, and the more profound the consequences of the decision, the higher the level of capacity that must be demonstrated.[210]

A specific complex situation is when the patient is not considered competent but has a valid advance directive.[211] A decision to withhold treatment might be viewed as abetting a suicide attempt, but it is reasonable to continue to honour a valid and applicable advance directive. This is because the test of capacity is based on when the advance directive was made, rather than at the time of the suicide attempt.[212] An alternative perspective is that there are competing rights that are sufficient to override a competent decision to refuse treatment. These may include the state's interests in preventing

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suicide and the need to protect innocent third parties, such as dependent children and even foetuses.

If the treating healthcare professional is uncertain about the patient's capacity or validity of an advance directive, it is reasonable to provide lifesaving treatment and simultaneously seek urgent ethical or legal advice. Sufficient time should be taken to consider contextual evidence relating to the suicidal behaviour, the nature of the treatment decision and the verification of any documentation.[208]

It is difficult to rapidly judge the context of an attempted suicide and it is suggested that the default should be to initiate life–sustaining treatment.[213] Surrogate decision makers may be unable to represent the views of patients, especially in the setting of attempted suicide. If the patient is stabilised, the quality of ongoing life may not be in line with their values and preferences. The response to the clinical situation should not be dogmatic but proportional to the individual case.[214]

Some authors have suggested that a suicide attempt is not as important as the underlying (disease) process that led to the attempt. In other words, it may be ethical to withhold or withdraw life–sustaining treatment in case of suicide when there is an underlying serious medical condition.[215]

The ethical framework of bystander CPR

Early bystander CPR improves patient outcomes in OHCA.[216–221] In many countries, systems of trained volunteers and/or first responders, in addition to dispatcher-assisted CPR by lay people, have been implemented. The crucial role of this community response to OHCA is incorporated in the chain of survival and in the ERC guidelines.[222] There are important differences in rates of bystander CPR between countries, regions and even in circumstances or victim characteristics.[217,223–226]

A 2020 ILCOR scoping review explored the individual's willingness to perform bystander CPR.[227] Factors influencing bystander willingness or actual delivery of bystander CPR include emotional factors, patient status (e.g. vomiting), socioeconomic status of the patient, patient sex, physical challenges (e.g. patient positioning, bystander age), and lack of knowledge or confidence.[228,229] Rescuers are more willing to perform compression-only CPR compared to CPR with rescue breaths. Some authors also identified fear of legal consequences as a potential barrier.[230,231] Older bystanders are less likely to start CPR, despite a higher chance of being bystanders to cardiac arrest. Important facilitators include prior knowledge and training, and feeling a moral obligation to act.[232–235]

There are ethical aspects concerning the ILCOR-supported use of smartphone-apps or text- messaging to alert trained lay rescuers to OHCA (strong recommendation, very low-certainty evidence).[236] Regional systems of alerting lay volunteers and/or first responders have many common characteristics but still may vary depending on the local context. [224,225,237–256] Some systems a priori exclude (young) children, traumatic cardiac arrest, intoxication, drowning and/or suicide, unsafe or inaccessible settings and/or nursing homes. Such exclusions are most often not further explained and/or defined. The low sensitivity and specificity of current dispatcher protocols for cardiac arrest recognition results in a high percentage of false positive and false negatives. We identify this as a major issue and consider better case selection a priority. In up to 30% of OHCAs, the attending EMS team will not start CPR. A priori identifying these cases is very difficult but might limit a subsequent ethical conflict between the lay rescuers and the arriving EMS team.

Further key ethical issues in relation to the establishment of these systems include the potential psychological impact on the bystander of attending a cardiac arrest, the potential variability in the skills and competence of volunteers dispatched to OHCA, and the potential impact on the patient's privacy of treatment by a non-professional rescuer. Most authors put higher value on the potential of saving a life than on the possible breach of privacy associated. A survey of North Americans found that most did not object to the implementation of an app-alerted volunteer system in their community nor to receiving crowdsourced help.[249]

An ILCOR review identified only limited evidence of harm to rescuers of performing CPR and/or using an AED. However, in the context of the COVID-19 pandemic, there is a risk of infection transmission to the rescuer. Whilst not performing CPR (or with substantial delay) will reduce the likelihood of a good outcome for many victims, bystanders should try to limit the associated risk of disease transmission by doing CPR.[3,257] The specific risk-benefit will be a function of factors such as the current regional COVID-19 prevalence, the victim's presentation (presumed COVID-19 status), the likelihood that CPR would be effective, the availability of personal protective equipment, and whether the bystander already had previous contact with the victim.

CPR training should better prepare lay rescuers for the various logistical, conceptual, and emotional challenges of resuscitation.[105,258,259] This includes limiting self-doubt, improving knowledge of the exact impact of performing or not performing certain actions and correcting certain misbeliefs.

CPR is promoted as a highly effective treatment both in the popular press and in dedicated media campaigns.[260] Only recently, more discussion about indications and limitations of CPR has started to take place in the public domain.[106] Such discussions, although from a patient and healthcare provider perspective very relevant, are difficult to appreciate for the lay rescuer. The Ethics writing group continues to support the emphasis on bystander CPR as a key link in the chain of survival.

Improved public information about the situations where CPR has a reasonable likelihood of providing clinical benefit and those where not, may be helpful.[105] EMS dispatch centre protocols should seek to better identify patients for whom bystander CPR might be beneficial but also try to identify those for whom it is not. Bystander CPR should never be considered a moral or judicial obligation.

Providing CPR is emotionally challenging for lay rescuers and first responder and, for some, has consequences in terms of family and work life.[253,261,262] The role undertaken by the lay bystander should be acknowledged by both the EMS dispatch centre and the EMS team.[263]

Finally, the ILCOR EIT Taskforce looked at OHCA in resource-limited environments, as many of the statements related to CPR might not be applicable in resource-limited settings.[264] They acknowledged that the feasibility and cost-effectiveness of CPR in OHCA in these settings can be challenged. One could argue that CPR is only ethically acceptable in settings where resources are such that other fundamental parts of the healthcare system are already sufficiently developed. CPR, as with many other healthcare choices, should never be evaluated in isolation but as part of the whole system of healthcare within a country or region. The role and remit of bystander CPR within such a context is obviously far less clear.

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Education, communication and system organisation

Education of lay persons, persons at risk of cardiac arrest and family

Education about patient's right of autonomy

Advance care planning discussions led by trained nurse facilitators or social workers are associated with an increase in patient knowledge about advance care planning, significantly more advance care planning discussions with physicians and a higher likelihood to agree to a DNACPR decision.[10,265–268] A patient-centred advance care planning approach increases the congruence in decision-making for future medical treatment between patients and their surrogate, improves satisfaction with the decision-making process and decreases the decisional conflict.[269] A pilot RCT addressing specific cultural factors by a tailored intervention using a bilingual, bicultural patient navigator suggests improved palliative care outcomes for minority groups facing advanced medical illness.[270] A controlled randomised intervention study in the US exploring peer mentoring by patients trained to help other patients with end-of-life planning had a significant influence on the completion of advance directives and the effect was also most prominent among African Americans.[271]

Education about CPR indications, procedures and outcome

Video decision support tools depicting CPR, resuscitation preference options and different levels of care are associated with higher rates of understanding of the purpose of CPR and resuscitation options.[4,17,272] Educational CPR videos and structured patient-centred interviews can be helpful in decision making with more patients likely to forgo CPR and focus on comfort.[4,45,70,273,274]

Education of healthcare professionals

DNACPR orders and advance care planning

More complex interventions involving education of healthcare professionals, education of patients and their caregivers as well as involvement of special teams seem to have greater impact at least on the effectiveness of DNACPR discussions. It is preferable to have these discussions as part of a broader approach such as advance care planning.[275] Some of the background evidence suggests that discrepant interpretations of DNACPR discussion occur with a concerning frequency between physicians and their hospitalised patients.[276] However, there is no direct evidence whether education (and in what form) changes this phenomenon.

Family presence during resuscitation

A presentation reviewing the literature supporting family presence during resuscitation, open discussion about family presence and a script that could be used to support families during resuscitation are all effective at improving attitudes of nurses and physicians towards family presence.[277–279] The presence of a trained support person may further increase staff comfort with family presence during resuscitation.[196]

Communication

Advance care planning

Advance care planning discussions with a trained nurse facilitator, structured nurse-led advance care planning discussions with long-term care residents of a nursing home and their proxies, and a physician and clinical nurse specialist team processing medical information of the primary physician all improved the consensus about care between patients, their families and the healthcare professionals.[37,265,267,280]

Termination of resuscitation and breaking bad news

Ambulance personnel feel particularly concerned about the skills required to deliver death notification and communicate with family and bystanders. This unpreparedness is associated with avoidance and distress. Ambulance personnel use distancing and detachment as a coping mechanism and focus on rational or structured behaviours of resuscitation to avoid interaction or empathetic engagement with family and bystanders.[281]

Patient outcomes and ethical considerations

The outcome of a cardiac arrest can be defined in several ways. Outcomes may be measured at multiple time points from during the cardiac arrest (e.g. end-tidal CO_2) to hospital discharge (e.g. survival, neurological outcome) and beyond (e.g. survival, neurological outcome, health-related quality of life).[282] A successful resuscitation may be characterised as survival with an acceptable quality of life. This means that long-term outcomes are of particular interest to patients and the resuscitation community.[283,284]

Valuing outcomes

Traditionally, cardiac arrest outcomes have been clinician-reported, and often dichotomised as good or poor.[283] This dichotomisation often attempts to separate individuals that are functionally independent from those with ongoing dependency or death.

Today, it is understood that cardiac arrest outcome is multifactorial and may include long-term changes in functional, emotional, physical, cognitive and social domains, all associated with health-related quality of life.[283] To make patient-centred decisions about the appropriateness of resuscitation requires clinicians and patients to have a shared understanding of how the patient defines a good outcome. The patient's perspective on outcome may be influenced by factors such as age, religion, societal values, and personal experiences. This should inform decisions about treatments, such as CPR.

Epidemiological data provides information on outcome at the population level.[217,285,286] Outcome for an individual is influenced by patient-level factors such as age, co-morbid status, and aetiology of cardiac arrest. As such, predicting outcome at an individual patient level is challenging. Key challenges for clinicians are effective communication of uncertainty about the likely outcome if an individual has a cardiac arrest, and to ensure that their personal values and preferences do not influence the patient.

Individual autonomy gives individuals the right to decline a treatment but does not obligate a health system to provide a treatment that is either futile or not cost-effective. Publicly funded healthcare systems have limited resources with an expectation that systems use funding in the most effective way. Treatments that do not meet predefined cost-effectiveness thresholds may not be made available. To date, few cardiac arrest interventions have been subjected to a health economic evaluation.[287–289]

In recent years organ donation has been highlighted as an important outcome following cardiac arrest.[290] Organ donation provides benefit to the wider health system and society as a clinical and cost-effective treatment for organ failure.

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In some cases, eliciting how an individual values a particular outcome may not be possible, such as in the context of young children or individuals with severe cognitive dysfunction. In these circumstances, clinicians should discuss treatment decisions with those close to the individual. Society often places particular value on the life of a child. Clinicians must take care to ensure that any decision is in the individual's best interests. In rare cases where the clinical team and other parties hold discordant views that cannot be reconciled, parties may need to defer decision-making to the legal system.

Variability in outcome

Variability in outcome following cardiac arrest has been described in both IHCA and OHCA.[217,285,286,291,292] This variability may be between locality, EMS systems, hospitals, regions, and countries. Variation may reflect differences at several levels, including data collection methods, case-mix, and treatment.[293,294] From an ethical perspective, the key concern occurs when variability is caused by differences in treatment or processes of care.

Observational data suggest that females and individuals from socially deprived and ethnic minority groups are less likely to receive bystander CPR and key post-arrest interventions.[295,296] Survey data indicates that both in-hospital systems of care and long-term follow up and rehabilitation differ markedly between hospitals.[291,297–299]

One strategy proposed to improve patient outcomes is centralisation of hospital services across a range of conditions including cardiac arrest.[300,301] This enables the development of clinical expertise and facilitates delivery of specialist interventions, such as primary percutaneous coronary intervention and extracorporeal CPR. There is a concern that centralisation may disadvantage individuals that live in rural areas.

Research and registry outcomes

Utstein statements describe the outcomes that should be collected by registries. Core outcomes are identified as ROSC, survival at hospital discharge/30-days, and neurological outcome at hospital discharge.[302,303] The inclusion of health-related quality of life and 12-month survival as supplementary outcomes reflects the balance between the importance of these outcomes, and the challenges of collection, such as the associated resource requirement.

In the context of research, differences in the way that outcomes are measured or reported by studies may preclude comparison of results between studies, and limit opportunities for meta-analysis.[304] A systematic review of cardiac arrest literature identified variability in the outcomes reported, differences in outcome definitions, and differences in the timepoint and method used to record outcomes.[282] The patient's perspective on outcome was rarely included.

To address this issue, ILCOR developed a cardiac arrest core outcome set (COSCA) in a process that involved patients, their partners, clinicians and researchers.[305] Core outcome sets describe the key outcomes that should be reported in all clinical trials, thereby ensuring consistency in outcome reporting.[306,307] COSCA identified three outcomes: survival at discharge/30-days; modified Rankin score at discharge/30-days; and health-related quality of life at 180-days/1-year. COSCA supports the collection of detailed measures of specific problems experienced by cardiac arrest survivors, such as fatigue, anxiety and societal participation. These data may improve our knowledge of cardiac arrest survivorship and patient support and rehabilitation in the post-acute phase.

An important challenge for both registries and clinical trials is ensuring a high level of data completeness for outcomes that rely on patient or proxy engagement, such as health-related quality of life. Response rates vary markedly across trials.[288,308,309] A key concern is that respondents may be systematically different to non-respondents.[310] In cardiac arrest research, survivors with poor outcome are less likely to respond, leading to bias.[311–313] The SPIIRT (Standard Protocol Items: Recommendations for Interventional Trials) PRO (Patient-reported outcome) extension guidelines provide information on including patient reported outcomes in clinical trials.[310]

Ethics and emergency research

Right to self-determination vs. scientific progress

The prognosis after cardiac arrest remains poor.[314–316] Therefore, there is a need for interventional, multicentre, randomised, controlled clinical research aimed at reliably assessing the effects of new and potentially beneficial treatments or validating empirical routine practice treatments of uncertain efficacy.[63,195,317,318] Striking the best balance between respect for autonomy (i.e. the right to self-determination) and beneficence (i.e. improving patient outcomes) or even non-maleficence (i.e. avoiding patient exposure to unproven treatments) has been recognised as one of the greatest challenges of emergency research conduct.[63,195,317,319]

The new European Union Clinical Trials Regulation No. 536/2014. permits the use of deferred consent in drug trials under clearly specified conditions. Tested interventions should be considered of minimal risk/burden for the subject in comparison with the standard treatment for the subject's condition.[317] Thus, the new regulation enables potentially beneficial, low-risk, multicentre, and multinational cardiac arrest research.[195,317,320] Nevertheless, regulatory improvements are still needed as the new regulation does not concern clinical trials evaluating devices.[317] Notably, device-related emergency research may confer considerable benefit in terms of leading to improvements in clinical practice and patient outcomes.[321]

Deferred consent (i.e. obtaining consent from a surrogate and/or patient as soon as possible after enrolment) may be necessary because the therapeutic window is too narrow to obtain a valid pre-enrolment consent.[63,317,322–324] This is considered as an ethically acceptable alternative for low-risk research, ensuring both the possibility of research benefit and respect for patient/family autonomy.[325,326] In contrast, a strict requirement for pre-enrolment consent may delay the initiation of an experimental intervention, thereby hampering its potential benefit to the patient.[327] Another ethically acceptable and legally supported consent model comprises exception to informed consent (EIC) with prior community consultation (and a possibility of prospective opt out for community members).[328–335] The EIC model also mandates obtaining post-enrolment consent.[317]

Both deferred consent and EIC models are limited by the patient's and or next-of-kin's right for consent withdrawal later on, as this may introduce bias in trial results by excluding the data from patients with a more complicated clinical course.[63] This might be partly addressed by regulatory provisions aimed at preventing the exclusion of patient data recorded until the time point of consent revocation.[63]

A recent pragmatic trial of adrenaline (epinephrine) in OHCA used a combination of a deferred consent model with informative press releases before and throughout the study period, a constantly updated trial website during the study period, an electronically supported opt-out option (which requires further evaluation), a pre-specified and realistic approach to inform the patient and request their consent after regaining their decisional capacity, a pre-specified and clear definition of personal and professional legal

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representative for patients lacking decisional capacity, a pre-specified method of approach and communication with the legal representative, a clearly specified procedure for consent refusal or revocation, and a pre-specified approach for passive provision of trial information (e.g. through websites or newsletters) to the families of patients who died before their relatives could be contacted.[318] Future research should compare the relative potential benefits (i.e. less emotional stress) and harms (i.e. limited or no knowledge of the patient's trial participation details) of passive versus active provision of information (i.e. more stress but also more knowledge about the patient's trial participation).

During the design phase of the pragmatic adrenaline trial, the main outcomes were specified in collaboration with patient and public representatives.[318] Involvement of all major stakeholders (including patients and representatives of the public) in the iterative development of core outcome sets during study design, as well as conduct and delivery of the research and dissemination of its results is an emerging and promising practice. Indeed, this practice has already been adopted in several fields of research and may comprise patient-centric initiatives such as advocacy group support and involvement, patient advisory panels, and focus groups, interviews with trial participants and staff, questionnaires and Delphi surveys/consensus processes, and consensus meetings.[336–344]

The EIC model is based on the 1996 United States Food and Drug Administration regulation 21 CFR 50.24.[345] Although this regulation seems to provide clearly defined guidance for the conduct of emergency research, several authors have previously attributed to it significant procedural impediments.[346,347] For instance, if a family member is present in an emergency, it may not be feasible for the researcher to explain to them the research protocol, or even the concept of informed consent.[348] Furthermore, a survey with 530 respondents from a community participating in EIC research projects revealed that only 5% of the respondents were aware of ongoing research protocols despite pre-study community consultation. This casts doubt upon the feasibility of adequate dissemination of research information among research-participating communities.[349]

A worrying reduction of cardiac arrest trials of 15% per year between 1992 and 2002 was documented in the United States.[350] Similar worries were articulated for steep reductions of 30–50% in European trials submitted for grants or ethical approval by the end of 2005[351–353]; at that time, European Union Directive 2001/20/EC was in force and its strict interpretation mandated pre-enrolment consent for all types of drug clinical trials.[63,354]

The literature cited above highlights the inherent perplexity of respecting autonomy of patients lacking decisional capacity when enrolling them in emergency clinical research protocols aimed at improving their outcomes. This ongoing ethical dilemma could be partly addressable by advance care planning specifically pertaining to participation in emergency research. However, such care plans should also be immediately accessible by emergency healthcare staff and researchers, even in the setting of OHCA; this may still prove electronic resource-demanding or even impossible in many situations/settings.[355]

Large, national and international registries enable the recording of general population data on the incidence, presumed cause, and outcomes of cardiac arrest. Information about whether a patient collapse was witnessed or not, cardiac arrest location, certain aspects of emergency care organisation (e.g. availability of dispatcher-assisted bystander CPR), patient characteristics (e.g. age, sex, race, and comorbidities), treating hospital characteristics (e.g. bed size and teaching status), downtimes (e.g. time from collapse to first shock), and treatments administered may also be collected.[356,357] Registry data can be analysed to (1) study regional variation, temporal trends, and predictors of patient outcomes; (2) compare propensity score matched patient subgroups receiving different treatments; and (3) gain insights into the implementation of published evidence and guidelines in routine clinical practice.[316,356,358–361] In addition, DNA biobanks have been established for DNA sequencing in the context of genomic research in sudden cardiac arrest.[362]

Big observational registry/biobank data originate from multiple sources. Such data may have to be linked for the detection of associations between potential predictor variables and patient outcomes.[363] The resulting production of high-quality evidence informing personalised prevention and treatment may contribute to improved outcomes and reduction of healthcare costs.[364] However, these beneficial processes are not free of ethical issues pertaining to privacy (i.e. risk of patient re-identification), genetic discrimination, and moral obligation for disclosure of findings to high-risk patients who decline becoming aware of their genetic test results. There are also challenges around observational data quality and potentially biased results leading to creation of incorrect risk profiles, obtaining consent for data use in an emergency research setting, and use of appropriate safeguards for data protection.[362,365–374]

The current European Union General Data Protection Regulation (GDPR) 2016/680 mandates that specific appropriate safeguards (e.g. safe data storage and encryption, access logging, data enclaves, etc.) be in place for the scientific processing of the data of a natural person. Records of processing activities must be kept by data controllers. A data protection impact assessment may be required to determine and confirm the risks relative to the subject's rights. GDPR compliance of research institutions must be monitored by a designated data protection officer.[362]

The GDPR does not concern anonymous data and data from deceased persons. Nevertheless, there are also stronger conditions concerning consent for the inclusion of personal patient data in research. Notably, a strict requirement for prospective (or pre-collection) informed consent would exclude collection of data from most sudden cardiac arrest patients. This would result in consent bias, skewing of the data, and compromised reliability of research results, with consequent societal harm. Furthermore, excluding collection of data from some incapacitated patients could potentially violate their preference to act in favour of the common good.[362] Therefore, for observational emergency research we suggest that local/regional supervising authorities consider allowing deferred and broad (i.e. for the overall research topic) consent, while concurrently ensuring the implementation of safeguards aimed at preventing data breaches and patient re-identification.[362,375–377] Lastly, and regarding both observational and interventional research, sometimes, it may not be possible to obtain even deferred consent, e.g. the patient dies and no surrogate decision maker can be located, or two surrogates of equal legal standing disagree. In such cases, we suggest consideration of permitting the use of the data collected until the time point of confirmation of the inability to obtain the consent.

Equal distribution of research benefits and risks

Whenever certain communities or societal groups bear the burden of the risk of research-associated adverse events, they should also have the possibility of enjoying any benefits arising from the research results.[63] Indeed, the use of relevant scientific achievements should not be confined to other privileged populations not participating in the research protocol(s).[63]

Access to best possible care and respect for patient/family dignity

Enrolment in a research protocol should in no way be linked to the quality or intensity of care. For instance, obtainment of deferred surrogate consent for a given patient's continued participation in a cardiac arrest trial evaluating therapeutic hypothermia should not result in preferential ICU admission of that patient over another patient whose proxy has refused consent.[63]

Researchers should also ensure that the dignity and privacy of the research participant and their family are respected. For example, enrolees in a cardiac arrest trial should be referred to as post cardiac arrest patients rather than cardiac arrests or cardiac arrest victims.[63]

Study design issues, and transparency of study conduct and reporting of results

Previously identified ethical issues concerning mainly commercial research have prompted the requirement for pre-enrolment registration of trial protocols,[63,378] reporting of any protocol and trial status changes (e.g., temporary suspension) throughout the period of trial conduct, and posting of main results to the trial registry within 12 months of study completion and publication in a peer-reviewed journal after another 12 months.[63,379] At the time of paper submission to a peer-reviewed journal, authors are normally obliged to report on the sponsor's role as well as on their own contributions to the study, and also approve the submission.[63] Furthermore, data sharing policies could be adopted to further enhance research transparency.[63,380]

Another concern pertains to the substantially disproportionate funding favouring commercial research evaluating the efficacy of high-cost, patent protected drugs or devices over the undoubtedly necessary, non-commercial, academic resuscitation research on patent-unprotected, low-cost, widely used drugs of potentially uncertain efficacy, such as adrenaline (epinephrine), or antiarrhythmics.[63,318,381,382] This may partly explain the fact that BLS/ALS guidelines are based on 35–53-fold fewer RCTs/10,000 deaths/year relative to guidelines for acute cardiovascular events and heart failure.[63,381] Governmental, or non-profit organisation, or even mixed public and private/industrial funding of resuscitation research needs therefore to be increased.[63,383] Furthermore, such funding should be fairly and proportionately distributed between studies of in-hospital and pre-hospital interventions, preferably also according to their estimated effect(s) on patient outcomes.[384]

Emergency research and the COVID-19 mass casualty crisis.

COVID-19 case surges may cause disruption over a wide spectrum of societal and healthcare system activities.[1,385–387] Accordingly, processes and procedures primarily related to interventional research may be hindered or halted. The need for physical distancing may cause cancellation of face-to-face meetings concerning study design (see also above), study protocol approval, and evaluation of the progress of study conduct (by investigators, and data monitoring committees); nevertheless, physical meeting issues can be at least partly addressed by using digital telecommunication technology. Delays in CPR initiation due to donning of personal protective equipment may impact patient outcomes,[385,386,388] and thereby modify the measured effect of concurrent or subsequent, investigational, resuscitative interventions, such as new drug therapies, or temperature/ventilatory management during and/or after resuscitation. In OHCA, increases in the volume of emergency calls in the context of a saturated healthcare system may prolong arrival times of emergency medical services, whereas the potential risk of contracting the disease while performing chest compressions may reduce bystander CPR rates.[3,389] Again, both latter factors may impact patient outcomes, and ultimately, the results of any ongoing emergency research. Fear of contracting the infection and/or excessive workload may discourage healthcare professionals from participating in research teams or initiating and leading a research project.[89,390–392] Lastly, increases in DNACPR decisions and especially use of blanket CPR exclusion criteria such as age[87,88,385,390,393] may introduce selection bias and hamper the generalisability of the research results, as well as their applicability to normal conditions. Such challenges may be addressable solely through effective governmental policies limiting viral spread and preventing healthcare system overload.

Future directions

The evidence supporting autonomy-safeguarding interventions exhibits several limitations, such as diversity/variability in definitions of key terms (see also Tables 1–3 and online supplement), evaluated intervention type/design, geographical distribution of studies and characteristics of participating populations (e.g. type of life-limiting illness, religion/religiosity, ethnicity, etc.) specified outcomes and methods of their determination, and reliability of reported results (further details provided in the supplement).

These weaknesses have either precluded the conduct of meta-analyses or increased the heterogeneity of reported meta-analyses results. Accordingly, the certainty of existing evidence has been judged most frequently as low to very low by authors of systematic reviews.[7–10,28,38,39,43,44,72]

As a result, scientific gaps exist regarding the actual effects of advance directives, advance care planning, and shared decision making on patient outcomes. These gaps range from uncertainty about the effect estimates of meta-analyses (in the presence of substantial pertinent literature), to very limited data from nonrandomised studies, and/or even the absence of relevant studies (e.g. the case of healthcare-related quality of life after cardiac arrest; see also online supplement).

Therefore, new, high-quality, and preferably multinational RCTs, based on clear and wide consensus-based definitions of interventions and outcomes are warranted. Observational big data potentially matching the strength of RCT data[394,395] and qualitative research identifying key issues that need to be addressed are also needed.[28,29,59,71,83,396] Further study is also warranted to establish the effectiveness of inter-professional shared decision making, which has been recently recommended by experts for important clinical decisions. Inter-professional shared decision making takes into account the available evidence, the expertise of involved clinicians, and the patient's values goals, and preferences.[397]

Despite the limitations of the currently available, substantial but still heterogenous, body of evidence, the presence of either positive or neutral RCTs on structured communication tools aimed at facilitating the completion of advance care directives and plans suggests a class effect and increased likelihood of benefit compared with usual care.[4,7] Structured, complex, multifaceted interventions in the context of advance care planning and shared decision making may effectively prevent disproportionate/unwanted end-of-life care and accordingly reduce use of healthcare resources.[4,7,44,72,355,398] Future pertinent research should primarily be guided by scientific evidence.

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Potentially successful, organisational interventions include: (1) structural educational initiatives of the public (e.g. informational videos, media coverage, and patient-public involvement workshops); (2) systematic training of healthcare professionals in ethics and communication skills[355]; (3) infrastructural initiatives enabling emergency healthcare providers to instantly access and honour the patient's recorded wishes (e.g. establishment of electronic registries/health records and appropriate regulatory provisions[355,398]; (4) public involvement to ensure clarity and acceptability of electronic documents used for the recording of treatment options; (5) immediate availability of adequate palliative care services upon patient/family request – this pertains to paediatric palliative care as well[399]; and (6) continuous monitoring of the quality of care supporting relevant improvement efforts/initiatives.

During a pandemic such as COVID-19, patient/family engagement in advance care planning and shared decision-making should still be feasible as part of remote clinical monitoring and care models (ClinicalTrials.gov NCT04425720).

The Ethics writing group emphasises the importance of thorough societal consultation and debate to provide a context-specific ethical framework for many of the complex resuscitation decisions such as use of extracorporeal CPR or uncontrolled donation after circulatory death.

Systems should continue to evaluate the performance of their decision making with regard to withdrawing or withholding life support, including the potential use of specific ToR rules, the degree of implementation of advance directives, and the number of advanced CPR cases. As technology progresses, it is likely that these concepts will evolve as well.

Systems should try and better define the place and remit of bystanders and first responders, as well as the ethical challenges around bystander CPR particularly in respect of the balance between benefit for the victim and harm to the rescuer.

There is a need to measure and track outcomes that are meaningful to both patients generally and the specific patient being treated.

Future, high-quality research should identify the optimal educational method for healthcare professionals on standardised patient outcome sets, and also evaluate its effect on healthcare professional's understanding of patient's preferences.

Systems should consider educational interventions to introduce the concept of family presence during resuscitation. Future research projects should consider the identification of healthcare personnel best suited to guide families through the resuscitation, and also being able to provide comfort, recognise family distress and participate in debriefing sessions after resuscitation.

More research is needed to determine how best to prepare and support ambulance personnel for the challenges of resuscitation decision-making and patient death, acknowledging the unique contextual demands of the prehospital setting.

We suggest the broadest possible/multinational establishment of harmonised regulations for emergency research aimed at fostering interventional drug and device trials as well as observational studies, while concurrently safeguarding participants' autonomy and protection/integrity of their personal data.

Conclusions

The Ethics writing group has provided sets of simple and clear recommendations supported by a wealth of systematic reviews, recent RCTs and nonrandomised studies. Despite the generally low certainty about the precision of the effect estimates of several evaluated meta-analyses, the directions of the effects on patient outcomes clearly favour the use of interventions such as advance care planning, shared decision making, and ToR rules. The writing group also produced three narrative reviews to summarise the existing key evidence/knowledge/issues on education/system organisation, patient outcomes, and ethics of emergency research. Lastly, the writing group has provided a set of consensus definitions of key terms, which could potentially prove useful in both routine clinical practice and the design of future research protocols.

Conflict of interest

MB declares her role of co-coordinator EU project ESCAPE-NET. GDP reports funding from Elsevier for his role as an editor of the journal Resuscitation. He reports research funding from the National Institute for Health Research (NIHR) in relation to the PARAMEDIC2 trial and the RESPECT project.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.resuscitation.2021.02.017.

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