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| Question | |
| **Among adults and children who are receiving solid organ transplantation in any setting (P), does an organ retrieved from a donor who has had CPR (e.g. donor dies in ICU after initial successful CPR, or donation after unsuccessful CPR) (I), compared with an organ retrieved from a donor who did not have CPR (C), change graft or recipient survival (O)?** | |
| **Population:** | Adults and children who are receiving solid organ transplantation in any setting |
| **Intervention:** | Transplantation of an organ retrieved from a donor who, following cardiac arrest, received cardiopulmonary resuscitation (e.g., donation after initial successful cardiopulmonary resuscitation or after unsuccessful cardiopulmonary resuscitation). |
| **Comparison:** | Transplantation of an organ retrieved from a donor who did not receive cardiopulmonary resuscitation. |
| **Main outcomes:** | Primary outcome: graft function or recipient survival at the longest follow-up available. Secondary outcomes: graft function or recipient survival at 30 days and 1 year. |
| **Setting:** | In-hospital or out-of-hospital cardiac arrest |

# Assessment

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| Problem Is the problem a priority? | | |
| Judgement | Research evidence | Additional considerations |
| ○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know | There is currently a mismatch between organ availability and demand worldwide. Only a minority of this demand can be met by donations from living donors, and only for some organs, such as kidneys. Therefore, the contribution from deceased donors is crucial. Patients who do not recover after cardiac arrest represent a potential source of organ donation. This can occur when patients die after initial successful resuscitation from cardiac arrest because of brain death (donors after death by neurological criteria, DBD) or following withdrawal of life-sustaining treatment (WLST) because of predicted poor outcome (controlled donors after cardiac death, cDCD)1. In other patients, cardiac death is pronounced at the end of an unsuccessful resuscitation attempt (uncontrolled donors after cardiac death uDCD). With organs from donors who have had cardiopulmonary resuscitation, there is concern that whole-body ischemia-reperfusion injury can result in significant extracerebral organ damage, making organs unsuitable for transplantation or at risk of worse outcomes and complications for the recipient.  Given the important worldwide implications, we aim to assess whether organs retrieved from donors who died after sudden cardiac arrest and received cardiopulmonary resuscitation (i.e., donation after initial successful cardiopulmonary resuscitation or after unsuccessful cardiopulmonary resuscitation) have comparable outcomes compared to organs retrieved from donors who did not suffer a cardiac arrest (i.e., living donors or DBD donors).  This topic had previously been reviewed for the 20102and 20153 ILCOR COSTR. However, a recent ILCOR nonsystematic review1 showed that a considerable amount of evidence needing assessment has been accumulated since then, and a new systematic review is desirable.  The systematic review included evidence from studies conducted in adults or children. No date or language limits were imposed.  The primary outcome measure was graft function or recipient survival at the longest available follow-up. The secondary outcome measures were graft function or recipient survival at 1 month and 1 year. Subgroup analyses were conducted based on the type or organ, outcome measure, and donor pathway (DBD or DCD). DCDs were further divided into uDCD (also classified as Maastricht category II donors) and cDCD (also classified as Maastricht category III) donors. |  |
| Desirable Effects How substantial are the desirable anticipated effects? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Trivial  ○ Small ● Moderate ○ Large ○ Varies ○ Don't know | A total of 35 observational studies (28 retrospective and 7 prospective) were identified. Of these, 12 reported on heart donation, 10 on kidney donation, 9 on liver donation, 4 on pancreas donation, 2 on lung donation, and 1 on intestine donation. Twenty-three studies included adults, six included children, and six included a mix of adult and children.  **Heart**  For the critical outcome of **graft function or recipient survival at the longest available follow-up**, we identified very low certainty of evidence (downgraded for inconsistency and indirectness) from 12 studies4-15 (63,805 patients; 8 enrolling 48,371 adults and 4 enrolling 15,349 children), which showed no statistically significant difference in graft or recipient survival in organ recipients from donors who received CPR versus donors who did not receive CPR in all studies (OR, 1.07 [95% CI, 0.86 to 1.33]), in adults-only studies (OR 1.25 [95% CI, 0.93 to 1.68], and in children studies (OR 0.86 [95% CI, 0.63 to 1.17]).  For the critical outcome of **graft function or recipient survival at 1 year**, we identified very low certainty of evidence (downgraded for inconsistency and indirectness) from 9 studies4, 5, 7-11, 13, 15 (57,393 patients; 7 enrolling 47,864 adults and 2 enrolling 9,529 children), which showed no statistically significant difference in graft or recipient survival in organ recipients from donors who received CPR versus donors who did not receive CPR in all studies (OR, 1.09 [95% CI, 0.98 to 1.22]), in adults-only studies (OR 1.09 [95% CI, 0.96 to 1.23], and in children studies (OR 1.07 [95% CI, 0.97 to 1.21]).  For the critical outcome of **graft function or recipient survival at 30 days**, we identified very low certainty of evidence (downgraded for inconsistency and indirectness) from 11 studies4-11, 13-15 (63,720 patients; 7 enrolling 48,371 adults and 2 enrolling 15,349 children), which showed no statistically significant difference in graft or recipient survival in organ recipients from donors who received CPR versus donors who did not receive CPR in all studies (OR, 1.05 [95% CI, 0.87 to 1.25]), in adults-only studies (OR 1.10 [95% CI, 0.91 to 1.31], and in children studies (OR 1.02 [95% CI, 0.69 to 1.48]).  **Kidney**  For the critical outcome of **graft function or recipient survival at the longest available follow-up**, we identified very low-certainty evidence (downgraded for inconsistency and indirectness) from 10 studies10, 16-24 (16,405 patients; 8 studies enrolling 2,794 adults and 2 studies enrolling 13,611 adults and children), which showed no statistically significant difference in graft or recipient survival in organ recipients from donors who received CPR versus donors who did not receive CPR in all studies (OR, 0.98 [95% CI, 0.73 to 1.30]), in adults-only studies (OR 0.93 [95% CI, 0.73 to 1.30], and in mixed adults and children studies (OR 1.13 [95% CI, 0.78 to 1.63]).  For the critical outcome of **graft function or recipient survival at 1 year**, we identified very low certainty of evidence (downgraded for inconsistency and indirectness) from 6 studies4, 5, 7-11, 13, 15 (15,494 patients; 4 studies enrolling 1,883 adults and 2 studies enrolling 13,611 adults and children), which showed no statistically significant difference in graft or recipient survival in organ recipients from donors who received CPR versus donors who did not receive CPR in all studies (OR, 0.86 [95% CI, 0.62 to 1.18]) and in mixed adults and children studies (OR, 1.13 [95% CI, 0.78 to 1.62]), and worse graft or recipient survival in adults-only studies (OR, 0.70 [95% CI, 0.53 to 0.92]). However, this was observed only when the comparison was made between uDCDs vs. DBDs, while it was not observed when the comparison was made between uDCDs vs. cDCDs or DBDs after CPR vs. DBDs without CPR.  For the critical outcome of **graft function or recipient survival at 30 days**, we identified very low certainty of evidence (downgraded for inconsistency and indirectness) from 7 studies17-21, 23, 24 (2,686 adult patients). These studies showed worse graft or recipient survival in organ recipients from donors who received CPR versus donors who did not (OR, 0.22 [95% CI, 0.08 to 0.65]). However, this was observed only when the comparison was made between uDCDs vs. DBDs, while it was not observed when it was made between uDCDs vs. cDCDs or DBDs after CPR vs. DBDs without CPR.  **Liver**  For the critical outcome of **graft function or recipient survival at the longest available follow-up**, we identified very low certainty of evidence (downgraded for inconsistency and indirectness from 9 studies16, 25-32 (6,714 patients; 5 enrolling 5954 adults, 2 enrolling 510 adults and children, and 1 enrolling 240 children), which showed no statistically significant difference in graft or recipient survival in organ recipients from donors who received cardiopulmonary resuscitation versus donors who did not receive cardiopulmonary resuscitation in all studies (OR, 0.90 [95% CI, 0.70 to 1.16]), in adults-only studies (OR 0.82 [95% CI, 0.55 to 1.21], in mixed adults and children studies (OR 1.15 [95% CI, 0.30 to 4.43]), and in children studies (OR 0.95 [95% CI, 0.36 to 2.47]).  However, in the subgroup analysis, we observed a worse outcome when comparing uDCDs to DBDs, while this was not observed when comparing DBDs after CPR to DBDs without CPR.  For the critical outcome of **graft function or recipient survival at 1 year**, we identified very low certainty of evidence (downgraded for inconsistency and indirectness) from 3 studies16, 26, 27 in 839 adult patients, showing no statistically significant difference in graft or recipient survival in organ recipients from donors who received cardiopulmonary resuscitation versus donors who did not (OR, 0.52 [95% CI, 0.25 to 1.07]). However, in the subgroup analysis, we observed a worse outcome when the comparison was made between uDCDs vs. DBDs, while this was not observed when the comparison was made between DBDs after CPR vs. DBDs without CPR.  For the critical outcome of **graft function or recipient survival at 30 days**, we identified very low certainty of evidence (downgraded for inconsistency and indirectness) from 8 studies25-32 (6674 patients; 5 enrolling 5954 adults, 2 enrolling 510 adults and children, and one enrolling 210 children), which showed no statistically significant difference in graft or recipient survival in organ recipients from donors who received cardiopulmonary resuscitation versus donors who did not receive cardiopulmonary resuscitation in all studies (OR 0.79 [95% CI, 0.42 to 1.46]), in adults-only studies (OR 0.45 [95% CI, 0.18 to 1.14]), and in mixed adults and children studies (OR 1.15 [95% CI, 0.30 to 4.43]), and better in 1 pediatric study (OR 2.23 [95% CI, 1.07 to 4.67]).  **Lung**  For the critical outcome of **graft function or recipient survival at the longest available follow-up**, we identified very low certainty of evidence (downgraded for inconsistency and indirectness) from 2 studies enrolling 1,194 adult patients, which showed no statistically significant difference in graft or recipient survival in organ recipients from donors who received CPR versus donors who did not receive CPR in all studies (OR, 1.82 [95% CI, 0.37 to 9.11]). We found no studies reporting this outcome in children.  We found no studies reporting the critical outcome of **graft function or recipient survival at 1 year**,  For the critical outcome of **graft function or recipient survival at 30 days**, we identified very low certainty of evidence (downgraded for inconsistency and indirectness) from 2 studies enrolling 1,150 adult patients, which showed no statistically significant difference in graft or recipient survival in organ recipients from donors who received CPR versus donors who did not receive CPR in all studies (OR, 0.74 [95% CI, 0.48 to 1.12]). We found no studies reporting this outcome in children.  **Pancreas**  For the critical outcome of **graft function or recipient survival at the longest available follow-up**, we identified very low certainty of evidence (downgraded for indirectness) from 4 studies (14,559 patients; 2 enrolled 948 adults and 2 enrolled 13,611 adults and children). The studies showed no statistically significant difference in graft or recipient survival in organ recipients from donors who received CPR versus donors who did not receive CPR in all studies (OR, 1.04 [95% CI, 0.87 to 1.25]), in adults-only studies (OR 1.03 [95% CI, 0.62 to 1.72], and in mixed adults and children studies (OR 1.04 [95% CI, 0.86 to 1.27]). We found no studies reporting this outcome in children.  For the critical outcome of **graft function or recipient survival at 1 year**, we identified very low certainty of evidence (downgraded for indirectness) from one study enrolling 13,095 adults and children, which showed no statistically significant difference in graft or recipient survival in organ recipients from donors who received CPR versus donors who did not receive CPR in all studies (OR, 1.01 [95% CI, 0.81 to 1.25]). We found no studies reporting this outcome in adults only or in children.  For the critical outcome of **graft function or recipient survival at 30 days**, we identified very low certainty of evidence (downgraded for indirectness) from 1 study enrolling 606 adults, which showed no statistically significant difference in graft or recipient survival in organ recipients from donors who received CPR versus donors who did not receive CPR in all studies (OR, 0.60 [95% CI, 0.24 to 1.50]). We found no studies reporting this outcome in children.  **Intestine**  For the critical outcome of **graft function or recipient survival at the longest available follow-up**, we identified very low certainty of evidence (downgraded for imprecision and indirectness) from one study enrolling 67 adults, which showed no statistically significant difference in graft or recipient survival in organ recipients from donors who received CPR versus donors who did not receive CPR in all studies (OR, 1.11 [95% CI, 0.21 to 5.88]). | Most of the evidence was on heart, liver and kidney transplantation. Limited evidence was available for lung, pancreas and intestine.  Evidence for kidney and liver transplants showed worse 30-day and 1-year function or survival for grafts transplanted from uDCD donors compared to DBD donors who did not undergo CPR. However, we did not observe significant differences in organ function or survival at the longest available follow-up.  Only 7/35 studies were conducted in DCD donors, Of these, five were conducted in kidney donors, and two were conducted in liver donors. All donors were uDCDs.  No comparative studies on cDCD after CPR were found. |
| Undesirable Effects How substantial are the undesirable anticipated effects? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know | We could not identify any remarkable undesirable effect for organ donation from DBDs. For organ donation from uDCD donors, there is potentially an increased risk of graft failure. | Given the alternatives of not having a solid organ transplant, i.e., lifelong dialysis or death from liver failure, a donation from a uDCD donor is probably still preferable. |
| Certainty of evidence What is the overall certainty of the evidence of effects? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Very low ● Low ○ Moderate ○ High ○ No included studies | The certainty of the evidence was very low because:   1. All studies were observational 2. We found inconsistencies in the timing of the longest follow-up (from 7 days to 15 years) and the variables considered for adjustment. 3. There was indirectness:    1. in most studies on organs retrieved from DBD donors, the timing of cardiac arrest and CPR was unclear (i.e., before vs. after death by neurological criteria), so we cannot exclude that in some patients, cardiac arrest and resuscitation may have followed, rather than preceded, death by neurological criteria (cardiac arrest in a brain-dead donor, Maastricht category IV).    2. in some studies on organs retrieved from uDCD donors, the witnessed status of the original cardiac arrest was not specified. Therefore, we cannot exclude that in some patients, CPR was performed on a patient who would not be otherwise resuscitated (found dead and resuscitated solely for the purpose of organ donation; Maastricht I donor). |  |
| Values Is there important uncertainty about or variability in how much people value the main outcomes? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability ○ No important uncertainty or variability | Organ shortage is an important problem worldwide. We assume that the community puts a high value on ensuring that those waiting for a donated organ can benefit from organs donated by those who die after CPR.  The results of our review’s subgroup analysis showed that short- or middle-term outcomes of organs donated by uDCD donors could be worse than those of organs donated by DBDs. However, long-term outcomes were not significantly different, although this might be due to the smaller number of long-term survivors. In addition, the advantage of increasing the number of available organs for patients who need transplants may overcome the increased risk of short- and long-term failure of grafts from DCD donors. |  |
| Balance of effects Does the balance between desirable and undesirable effects favor the intervention or the comparison? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Favors the comparison ○ Probably favors the comparison ● Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ○ Don't know | Our review showed no significant overall differences in graft survival or function between organs retrieved from donors with and without CPR. Therefore, patients who die after CPR can be considered suitable organ donors. |  |
| Resources required | | |
| Judgement | Research evidence | Additional considerations |
| ○ Large costs ○ Moderate costs ○ Negligible costs and savings ●  Moderate savings ○ Large savings ○ Varies ○ Don't know | Organ donation results in a reduction of costs associated with morbidity of patients with end-stage organ failure. In a substudy of the PARAMEDIC2 trial, incorporating the indirect economic effects of transplanted organs substantially altered the cost-effectiveness of epinephrine administered to patients in cardiac arrest in favor of the drug.33 In that study, the authors did not investigate what donor type (i.e., DBD or cDCD) contributed to the result. |  |
| Certainty of evidence of required resources What is the certainty of the evidence of resource requirements (costs)? | | |
| Judgement | Research evidence | Additional considerations |
| ● Very low ○ Low ○ Moderate ○ High ○ No included studies | Because our review's overall certainty of evidence of effects is very low, the certainty of evidence regarding the required resources is also very low. | Given organ retrieval processes are already in place for donors who have not had CPR, the additional resources for donation after DBD or cDCD would be limited. Significant additional resource and ethical issues would need to be overcome to develop a uDCD program. |
| Cost effectiveness Does the cost-effectiveness of the intervention favor the intervention or the comparison? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Favors the comparison ● Probably favors the comparison ● Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ○ No included studies | Donation after cardiac arrest results in similar rates of graft function or survival compared with donation in patients who did not have cardiac arrest. We conclude that the increased availability of organs from donors after cardiac arrest is cost-effective. |  |
| Equity What would be the impact on health equity? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Reduced ○ Probably reduced ○ Probably no impact ●  Probably increased ○ Increased ○ Varies ○ Don't know | In some healthcare systems, As a result of organ shortage, some patients may consider traveling abroad to receive the organs they need, which may result in considerable additional costs for those patients. Reducing organ shortage can result in increased equity and access to transplantation- |  |
| Acceptability Is the intervention acceptable to key stakeholders? | | |
| Judgement | Research evidence | Additional considerations |
| ○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know | The intervention appears acceptable to the stakeholders. However, the practice of uDCD may raise ethical concerns in some countries or communities because of concern that patients with cardiac arrest are resuscitated for the sole purpose of organ donation. |  |
| Feasibility Is the intervention feasible to implement? | | |
| Judgement | Research evidence | Additional considerations |
| ○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know | Donation of organs after CPR probably does not require special resources in healthcare systems where organ donation is already implemented. However, the implementation of uDCD requires an efficient organization to ensure that the process of consent, diagnosis and organ retrieval is implemented rapidly after an unsuccessful resuscitation attempt. Donations from DBDs after CPR require that healthcare professionals are aware of the possibility that patients with acute hypoxic-ischemic brain injury (HIBI) evolve to brain death 2-3 days after CPR. Implementing cDCD after CPR requires that all the necessary procedures to ascertain poor outcome with a high degree of certainty are conducted. |  |

# Summary of judgements

|  | **Judgement** | | | | | | |
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| **Problem** | No | Probably no | Probably yes | **Yes** |  | Varies | Don't know |
| **Desirable Effects** | Trivial | Small | **Moderate** | Large |  | Varies | Don't know |
| **Undesirable Effects** | Trivial | Small | **Moderate** | Large |  | Varies | Don't know |
| **Certainty of evidence** | **Very low** | Low | Moderate | High |  |  | No included studies |
| **Values** | Important uncertainty or variability | Possibly important uncertainty or variability | **Probably no important uncertainty or variability** | No important uncertainty or variability |  |  |  |
| **Balance of effects** | Favors the comparison | Probably favors the comparison | **Does not favor either the intervention or the comparison** | Probably favors the intervention | Favors the intervention | Varies | Don't know |
| **Resources required** | Large costs | Moderate costs | Negligible costs and savings | **Moderate savings** | Large savings | Varies | Don't know |
| **Certainty of evidence of required resources** | Very low | **Low** | Moderate | High |  |  | No included studies |
| **Cost effectiveness** | Favors the comparison | Probably favors the comparison | Does not favor either the intervention or the comparison | **Probably favors the intervention** | Favors the intervention | Varies | No included studies |
| **Equity** | Reduced | Probably reduced | Probably no impact | **Probably increased** | Increased | Varies | Don't know |
| **Acceptability** | No | Probably no | **Probably yes** | Yes |  | Varies | Don't know |
| **Feasibility** | No | Probably no | **Probably yes** | Yes |  | **Varies** | Don't know |

# Type of recommendation

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| Strong recommendation against the intervention | Conditional recommendation against the intervention | Conditional recommendation for either the intervention or the comparison | **Conditional recommendation for the intervention** | Strong recommendation for the intervention |
| ○ | ○ | ○ | ● | ○ |

# Conclusions

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| Recommendation |
| We recommend that all patients who have restoration of circulation after cardiopulmonary resuscitation and who subsequently progress to death be evaluated for organ donation (strong recommendation, low-certainty evidence). |
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| Justification |
| The major concern with organ donation from patients who have undergone CPR is damage to their organs from ischemia and reperfusion injury. However, the suitability of organs for donation is based on criteria established by the transplantation team. This review suggests that, once these criteria are met, transplant organ outcomes are similar regardless of whether the organs come from donors who have had CPR or not before donation.  We have used the term ‘restoration of circulation’ to include patients who become potential organ donors after ECPR and are stabilized on VA-ECMO but do not have spontaneous circulation.  Despite the low-certainty evidence, the TF has made a strong recommendation. This is because the TF values ensuring that those waiting for a donated organ can benefit from organs donated by those who die after CPR, given that a large number of studies show organ function and recipient outcomes are similar in CPR+ and CPR- groups. |

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| Subgroup considerations |
| Seven of the 35 studies in this review compared the outcomes of kidneys and livers transplanted from patients who died after unsuccessful resuscitation (uncontrolled donors after cardiac death [uDCDs]; Maastricht category II) with those of organs transplanted from donors after death by neurological criteria (donors after brain death [DBDs]; six studies17, 18, 20, 24, 26, 27) or from donors who die by cardiac criteria after life-sustaining treatment is suspended because of futility (controlled donors after cardiac death [cDCDs]: Maastricht category III; one study).23 In these studies, the outcomes of organs transplanted from uDCDs at one month and one year were significantly worse than in the comparator group.  In uDCD studies, the donors’ witnessed status was not always explicitly reported. Consequently, there was a chance that some donors were unrecoverable at the arrival of the treating team (found dead) and that resuscitation was started only with the aim of potential donation (Maastricht category I).  Because of these inconsistencies, the Task Force decided not to make any recommendation regarding uncontrolled organ donors. |

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| Implementation considerations |
| Donation of organs after CPR probably does not require special resources in healthcare systems where organ donation is already implemented. However, the implementation of uDCD requires efficient organization to ensure that the process of consent, diagnosis and organ retrieval is implemented rapidly after an unsuccessful resuscitation attempt.  Donations from DBDs after CPR require that healthcare professionals are aware of the possibility that patients with acute hypoxic-ischemic brain injury (HIBI) evolve to brain death 2-3 days after CPR34.  Implementing cDCD after CPR requires that all the necessary procedures be conducted to ascertain a poor outcome with a high degree of certainty35. |

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| Monitoring and evaluation |
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| Research priorities |
| * Future studies on DBDs who underwent CPR should clearly identify those who evolved towards death by neurological criteria after resuscitation, to avoid confusion with DBDs who had cardiac arrest before organ retrieval. * Comparative studies are needed to investigate cDCD donation after CPR * Future studies should investigate the utilization rate of donors who underwent CPR vs those who did not. * There are no established criteria to identify the potential for donation in patients who die after CPR. |

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