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| Question | |
| **Should Intraosseous vs. intravenous be used for Cardiac arrest?** | |
| **Population:** | Cardiac arrest |
| **Intervention:** | Intraosseous |
| **Comparison:** | intravenous |
| **Main outcomes:** | 30-day survival; Return of spontaneous circulation (any); Return of spontaneous circulation (sustained); Survival (30-day/ discharge) with favourable neurological outcome; Survival at hospital discharge; Survival at 3-months; Survival at 6-months; Survival with favourable neurological outcome at 3-months; Survival with favourable neurological outcome at 6-months; Health-related quality of life at 3-months; Health-related quality of life at 6-months; |
| **Setting:** |  |
| **Perspective:** |  |
| **Background:** |  |
| **Conflict of interests:** |  |

# 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 | Drug therapy is a core component of Advanced Life Support. Current resuscitation guidelines recomend that drugs during cardiac arrest are given via the peripheral intravenous route, wherever feasible. The intraosseous route is recomended only when intravenous access cannot be rapidly achieved. Observational studies suggest the intraosseous route may facilitate more rapid drug administration. Over recent years, several studies have reported increased use of intraosseous access in adult cardiac arrest. |  |
| Desirable Effects How substantial are the desirable anticipated effects? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know | Drug therapy, particularly epinephrine, has been shown to have a large effect on return of spontaneous circulation and small-moderate effect on 30-day survival. The effect of a different drug route for administering cardiac arrest drugs is likely to be small.    In our systematic review, point-estimate of each meta-analysis varied between favouring the intravenous or intraosseous route, but the findings were typically not statistically significant. The point estimate typically suggested a small effect. |  |
| Undesirable Effects How substantial are the undesirable anticipated effects? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know | In our systematic review, point-estimate of each meta-analysis varied between favouring the intravenous or intraosseous route, but the findings were typically not statistically significant. The point estimate typically suggested a small effect. For sustained return of spontanous circulation, we found a statistically significant small effect in favour of the intravenous route. |  |
| 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 | Across all outcomes (including the three critical outcomes), the certainty of evidence was ranked as low or moderate. |  |
| 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 | Our list of incomes comprise all outcomes that were included in the Core Outcome Set for Cardiac Arrest, namely survival, survival with favourable neurological outcome, and health-related quality of life. These were outcomes that were prioritised by members of the public, cardiac arrest survivors, researchers and clinicians and are categorised as critical outcomes. |  |
| 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 | In our systematic review, point-estimate of each meta-analysis varied between favouring the intravenous or intraosseous route, but the findings were typically not statistically significant. The point estimate typically suggested a small effect. For sustained return of spontanous circulation, we found a statistically significant small effect in favour of the intravenous route. |  |
| Resources required | | |
| Judgement | Research evidence | Additional considerations |
| ○ Large costs ○ Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ● Varies ○ Don't know | There may be variability across settings.    Across the world, intravenous vascular access is typically routinely available and is the default access route in emergency care.    In many settings, clinicians will be skilled in securing intraosseous access and equipment will be routinely available. In these setting, a key consideration will be consumables required to secure intravenous and intraosseous access. An intraosseous needle is markedly more expensive than an intravenous cannula.  In other settings, intraosseous equipment may not be available to clinicians. In these settings, there would be a need to provide training and purchase equipment and consumables. |  |
| 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 | We did not specifically search for studies on costs. One trial (Couper et al 2024) will undertake a health economic analysis. |  |
| 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 | We did not specifically search for studies on costs. One trial (Couper et al 2024) will undertake a health economic analysis. |  |
| 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 none of the included trials (or in our meta-analysis) did we identify any evidence that the effectiveness of the intervention might vary across population sub-groups. |  |
| Acceptability Is the intervention acceptable to key stakeholders? | | |
| Judgement | Research evidence | Additional considerations |
| ○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know | Both intravenous and intraosseous access are already used frequently in emergency care. |  |
| Feasibility Is the intervention feasible to implement? | | |
| Judgement | Research evidence | Additional considerations |
| ○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know | Intraosseous and intravenous access are already routinely available in many emergency care systems.    There may be systems in which intraosseous has not yet been implemented and there may be some financial barriers that influence its implementation. |  |

# 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 suggest IV access, as compared to IO access, as the first attempt for vascular access during adult cardiac arrest (weak recommendation, XXXXXX certainty evidence).    If IV access cannot be rapidly achieved within two attempts, it is reasonable to consider IO access as an alternative route for vascular access during adult cardiac arrest (good practice statement). |
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| Justification |
| This topic was prioritized by the ALS Task Force based on the publication (or forthcoming publication) of three large randomised controlled trials evaluating the clinical effectiveness of an intraosseous vascular access strategy compared with an intravenous vascular access strategy in adult out-of-hospital cardiac arrest since the last ILCOR systematic review and CoSTR in 2020.    In considering the importance of this topic, the task force noted that several observational studies have reported marked increases in the use of the intraosseous route in adult out-of-hospital cardiac arrest over recent years, despite council guidelines continuing to recommend that the peripheral intravenous route should be the primary route for drug administration in adult cardiac arrest.    Given the availability of data from large RCTs and challenges in interpreting observational studies due to confounding and resuscitation time bias, the task force chose to consider only randomized controlled trials.    *In making these recommendations, the ALS Task Force considered the following:*   * The expected mechanism through which intraosseous drug administration might improve clinical outcomes is by facilitating faster administration of time-critical cardiac arrest drugs. However, whilst this effect was observed in an early randomized controlled trial, time to drug administration was similar between the intraosseous and intravenous groups in all three recent trials. * The use of intraosseous access did not result in a statistically significant improvement in survival, survival with favourable neurological outcome, or health-related quality of life at any time-point, in comparison to intravenous access. * The three trials were all superiority trial aiming to test the superiority of one group compared with the other group, such that the absence of an observed effect should not be interpreted as indicating that an intraosseous vascular access strategy is equivalent to an intravenous vascular access strategy. * There was evidence that the use of intraosseous access reduced the odds of achieving sustained return of spontaneous circulation. * In emergency care throughout the world, the intravenous route is the standard approach for administering drugs and fluid. * There are important cost implications in relation to intraosseous access, both in terms of training and equipment. Even in settings where intraosseous access is routinely available, the costs of a single intraosseous needle is markedly higher than a peripheral intravenous cannula. * Animal data provide some evidence that the pharmacokinetics of drugs administered via the intraosseous route may be influenced by insertion site (proximal humerus v proximal tibia). The findings of the systematic review sub-group analyses showed no evidence of an interaction between site and clinical outcome, with point estimates favoring the proximal tibial route, albeit with very wide confidence intervals. * Previous data suggests that the benefit of amiodarone may be enhanced when given through the intravenous route. Experts have expressed concern that absorption of lipophilic drugs, such as amiodarone, may be particularly influenced by intraosseous administration. However, this effect has not been observed in animal studies. * Trial sequential analyses suggest that the optimal information size has been reached for small sized effects (absolute difference of 2%), but not for very small effects. * The good practice statement reflects the approach taken in two of the included trials, whereby patients in the intravenous group were protocolized to receive two intravenous vascular access attempts, and then the route for subsequent vascular access attempts was at the discretion of the attending clinician. * There may be patients where IV access is not feasible due to specific patient factors (e.g. the patient is known to be very difficult to secure IV access) or environmental factors (e.g. very poor lighting; space constraints). For this small group of patients, it may be reasonable to attempt IO access first. * There was an absence of direct evidence for the in-hospital setting, but it was noted that the question is likely of less relevance to the hospital setting as: 1) A high proportion of patients will likely have established intravenous access at the time of cardiac arrest, and,  2) For the minority of patients without established intravenous access, environmental conditions (e.g. space/ lighting) and the higher number of staff members would likely lead to a high rate of successful intravenous access attempts. |

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| Subgroup considerations |
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| Implementation considerations |
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| Monitoring and evaluation |
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| Research priorities |
| Where there is a need for intraosseous access, there are limited data on the optimum anatomical site for insertion.    There are limited data on patient outcome beyond hospital discharge/ 30-days. |

# References Summary