

## QUESTION

Should adults with cardiac arrest be cared for at cardiac arrest centers vs. non-cardiac arrest centers?	
POPULATION:	Adult non-traumatic in-hospital (IHCA) or out-of-hospital (OHCA) cardiac arrests
INTERVENTION:	Care at a specialized cardiac arrest center (CAC)
COMPARISON:	Care in an institute not designated as a specialized CAC
MAIN OUTCOMES:	Survival to 30 days with favorable neurological outcome (defined as cerebral performance category [CPC] 1 or 2, modified Rankin Scale [mRS] 0-3); Survival to hospital discharge with good neurological outcome; Survival to hospital discharge; Survival to 30 days; return of spontaneous circulation (ROSC) after hospital admission.
SETTING:	OHCA / IHCA
PERSPECTIVE:	Patient perspective
BACKGROUND:	<p>Post-resuscitation care is an important component in the chain of survival. There is a growing body of evidence that outcomes after cardiac arrest vary between hospitals, and that this variation is associated with a hospital's capacity to deliver evidenced-based post-resuscitation care (i.e. CACs versus non-CACs).</p> <p>The 2015 International Liaison Committee on Resuscitation (ILCOR) review, comparing patients transported to cardiac arrest centers to those transported to other centers, found low quality evidence and concluded with a weak recommendation ("We suggest that OHCA patients should be considered for transport to a specialist cardiac arrest center as part of wider regional system of care for management of patients with OHCA (weak recommendation, low-quality evidence)").</p>
CONFLICT OF INTERESTS:	Janet Bray (EIT Task Force Member) is a co-author on a paper included in this review.

## ASSESSMENT

Problem		
Is the problem a priority?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <li><input type="radio"/> No</li> <li><input type="radio"/> Probably no</li> <li><input type="radio"/> Probably yes</li> <li><input checked="" type="radio"/> Yes</li> <li><input type="radio"/> Varies</li> <li><input type="radio"/> Don't know</li> </ul>	<p>Post-resuscitation care, including percutaneous coronary intervention (PCI) and targeted temperature measurement (TTM), are important interventions to achieving good neurological outcome. In most countries, post-resuscitation care is not regionalized to specialized hospitals (i.e. CACs) and there is wide variation among hospitals in the availability and type of post-resuscitation care.</p> <p>Other time-sensitive illness (e.g. trauma, acute myocardial infarction and stroke services) use regional triage systems to direct patients according to clinical needs to specialist centers which offer concentration of services and greater provider experience. Centralizing specialized services or use of regional triage system to improve the provision of evidence-based post-resuscitation care may offer similar benefits.</p> <p>The ILCOR Education, Implementation and Teams (EIT) and Advance life Support (ALS) Task Forces have prioritized an updated review of this evidence following the publication of two large registry studies on this topic since the 2015 ILCOR review (Bhanji 2015 S242; Finn 2015 e203).</p>	<p>There is a lack of consensus on what defines a CAC.</p> <p>CACs are likely to differ between health systems, emergency care response systems and countries.</p>
Desirable Effects		
How substantial are the desirable anticipated effects?		
JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <li><input type="radio"/> Trivial</li> <li><input type="radio"/> Small</li> <li><input type="radio"/> Moderate</li> <li><input checked="" type="radio"/> Large</li> <li><input type="radio"/> Varies</li> <li><input type="radio"/> Don't know</li> </ul>	<p>The Task Forces placed high value on the availability of evidence-based post-resuscitation care. Structured post-resuscitation care is associated with both improved survival and neurologic recovery, which are outcomes valued by patients and their caregivers. (Haywood et al. Circulation. 2018)</p>	<p>Potential to maximize favorable neurological outcomes post-cardiac arrest.</p> <p>Transport to a CAC may provide the opportunity for organ donation.</p>

		<p>Direct transport has the potential to reduce treatment times (e.g. door-to-balloon times) due to secondary transfers.</p> <p>Patients who are admitted to CACs may not always receive evidence-based post-resuscitation care. Reasons behind this is likely multifactorial.</p> <p>Survival to hospital admission is not a relevant outcome since the majority of studies include patients with prehospital ROSC.</p> <p>To examine whether good outcomes are restricted to subgroups, we examined the commonly used subgroup of shockable versus nonshockable initial rhythm.</p>
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## Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <li><input type="radio"/> Large</li> <li><input type="radio"/> Moderate</li> <li><input type="radio"/> Small</li> <li><input type="radio"/> Trivial</li> <li><input type="radio"/> Varies</li> <li><input checked="" type="radio"/> Don't know</li> </ul>	<p>There is a lack of reporting in the published literature of:</p> <ul style="list-style-type: none"> <li>• adverse events (e.g. rearrest) in bypassing nearest facility;</li> <li>• the potential social impact for families or patients due to longer distance to travel;</li> <li>• whether an optimal transport time to maximize patient outcomes exists is unknown, and is likely to differ regionally. A recent systematic review (Geri 2017 96) of nine studies concluded that transport time was not associated with OHCA survival or good neurological outcome. We also acknowledge that total delay time may not be reflected in transport times.</li> </ul> <p>To examine whether good outcomes are restricted to those with primary transport to a CACs, we examined the subgroup of primary versus secondary transport to a CAC. But the evidence was limited and of very low quality.</p>	<p>We also considered:</p> <ul style="list-style-type: none"> <li>• The high resource costs to set up new CACs and support systems.</li> <li>• The impact for EMS, including the need for systems of transport to ensure regions are not left without EMS coverage during OHCA transport.</li> <li>• The pros and cons for non- CACs, including the potential for de-skilling, financial issues and resource reallocation.</li> <li>• The unnecessary transfer if patients are not going to survive.</li> <li>• Potential social impact for patients and families (e.g. removal from social supports, transport and accommodation costs).</li> </ul>

## Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <li><input checked="" type="radio"/> Very low</li> <li><input type="radio"/> Low</li> <li><input type="radio"/> Moderate</li> <li><input type="radio"/> High</li> <li><input type="radio"/> No included studies</li> </ul>	<p>The evidence is of non-randomized study designs and registry based cohort studies.</p> <p>Downgraded due to high heterogeneity, inconsistency and imprecision.</p>	<p>ARREST study A randomized trial of expedited transfer to a cardiac arrest center for non-ST elevation out of hospital cardiac arrest is underway. Due for completion in 2020 (ISRCTN96585404)</p> <p><a href="https://doi.org/10.1186/ISRCTN96585404">https://doi.org/10.1186/ISRCTN96585404</a></p>

## Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <li><input type="radio"/> Important uncertainty or variability</li> <li><input type="radio"/> Possibly important uncertainty or variability</li> <li><input type="radio"/> Probably no important</li> </ul>	<p>Measures to maximize favorable neurological outcomes are a research priority to both patients and clinicians.</p> <p>COSCA (Core Outcome Set for Cardiac Arrest) in Adults: An Advisory Statement From the International Liaison Committee on Resuscitation. Kirstie Haywood et al. Circulation. 2018;CIR.0000000000000562.</p>	<p>Even small improvements in outcomes are likely to be favored by patients and clinicians.</p> <p>There may be variation in cultural views towards the priority of outcome of survival and survival with favorable neurological outcomes in different</p>

uncertainty or variability ● No important uncertainty or variability		countries.
<b>Balance of effects</b> Does the balance between desirable and undesirable effects favor the intervention or the comparison?		
<b>JUDGEMENT</b>  <input type="radio"/> Favors the comparison <input type="radio"/> Probably favors the comparison <input type="radio"/> Does not favor either the intervention or the comparison <input checked="" type="radio"/> Probably favors the intervention <input type="radio"/> Favors the intervention <input type="radio"/> Varies <input type="radio"/> Don't know	<b>RESEARCH EVIDENCE</b>  The general direction of effect across most studies (adjusted and unadjusted results) favors care at CACs.  There is little direct evidence to suggest longer transfer time to get to CAC will lead to significant harm.  Survival to hospital discharge with good neurological outcome and survival to hospital are outcomes that are of critical importance to patients. These outcomes were significantly increased in patients cared for at CACs, therefore the balance between desirable and undesirable effects favors CACs.	<b>ADDITIONAL CONSIDERATIONS</b>  High resource costs to set up new CACs and support system especially in rural areas or low-density populations.  In healthcare systems where intensive care and interventional cardiology services are already well established, there is a potential that resources may be reallocated.  This solution should be balanced however by the potential for diverting vital resources from other patients and the potential impact on sustainability of other services.  Potential to facilitate the organization of organ donation.
<b>Resources required</b> How large are the resource requirements (costs)?		
<b>JUDGEMENT</b>  <input type="radio"/> Large costs <input type="radio"/> Moderate costs <input type="radio"/> Negligible costs and savings <input type="radio"/> Moderate savings <input type="radio"/> Large savings <input checked="" type="radio"/> Varies <input type="radio"/> Don't know	<b>RESEARCH EVIDENCE</b>  No studies examined costs for CACs.  In healthcare systems where intensive care and interventional cardiology services are already well established additional costs may be minimal.	<b>ADDITIONAL CONSIDERATIONS</b>  Resources are similar to those implemented for trauma, stroke, STEMI centers.  Some countries already have regionalized care in place and have established PCI and ICU services. Team work and co-ordination between EMS, EDs, cardiology, radiology, neurology and ICU are necessary.  Registries may be necessary to monitor and evaluate.  Implementation may be an issue in very remote regions and regions with less developed transport or emergency systems.  CACs need to be part of coordinated system of emergency medical response system.
<b>Certainty of evidence of required resources</b> What is the certainty of the evidence of resource requirements (costs)?		
<b>JUDGEMENT</b>  <input type="radio"/> Very low <input type="radio"/> Low <input type="radio"/> Moderate <input type="radio"/> High <input checked="" type="radio"/> No included studies	<b>RESEARCH EVIDENCE</b>  No studies examined resource use of costs for CACs.  Costs of transporting patients to CACs center may need to be weighed against setting up regional centers, such as in non-urban areas. A study examined costs of setting up a PCI center in non-urban areas in Canada compared with transporting patients to urban center. Constructing a new catheterization laboratory would cost \$7,667 per QALY gained over ambulance transport. Sensitivity analyses showed that building a new PCI center was robustly cost-effective as long as it operated at ≥30% maximum capacity and maintained a PCI transport time ≤70min (Potter B, Weinstein M C, Gaziano T A. Cost-Effectiveness of STEMI Management Strategies for Patients Presenting to Non-Urban Centers: A Model- Based Analysis Circulation. 2013;128: A15562).	<b>ADDITIONAL CONSIDERATIONS</b>
<b>Cost effectiveness</b> Does the cost-effectiveness of the intervention favor the intervention or the comparison?		

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <li><input type="radio"/> Favors the comparison</li> <li><input type="radio"/> Probably favors the comparison</li> <li><input type="radio"/> Does not favor either the intervention or the comparison</li> <li><input type="radio"/> Probably favors the intervention</li> <li><input type="radio"/> Favors the intervention</li> <li><input type="radio"/> Varies</li> <li>● No included studies</li> </ul>	<p>No studies examined the cost-effectiveness for CACs.</p> <p>Indirect evidence from stroke and STEMI centers report cost-effectiveness following the centralization of care (Guzauskas G et al. The Cost-Effectiveness of Primary Stroke Centers for Acute Stroke Care Stroke. 2012;43:1617-1623; Birkemeyer et al. Short-term cost effectiveness of a regional myocardial infarction network. Health Economics Review 2013, 3:10, Regueiro A, Bosch J, Martín-Yuste V, et al. Cost- effectiveness of a European ST-segment elevation myocardial infarction network: results from the Catalan Codi Infarct network. BMJ Open 2015;5:e009148).</p>	

## Equity

What would be the impact on health equity?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <li><input type="radio"/> Reduced</li> <li><input type="radio"/> Probably reduced</li> <li><input type="radio"/> Probably no impact</li> <li>● Probably increased</li> <li><input type="radio"/> Increased</li> <li><input type="radio"/> Varies</li> <li><input type="radio"/> Don't know</li> </ul>	<p>No studies examined health equity for CACs.</p>	<p>Likely to reduce regional variation in care but may come at a cost to other areas of health care systems (e.g. impact of removing emergency services during patient transports; diversion of funds from other areas).</p> <p>May not benefit countries where no infrastructure or resources are in place to support CACs.</p> <p>The impact of regionalization of care on health care providers is likely to vary widely. In some health care settings, regionalization of care generally may threaten the viability of bypassed hospitals. Whereas in other settings, dedicated centers may allow resources in bypassed hospitals to be used elsewhere.</p>

## Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <li><input type="radio"/> No</li> <li><input type="radio"/> Probably no</li> <li>● Probably yes</li> <li><input type="radio"/> Yes</li> <li><input type="radio"/> Varies</li> <li><input type="radio"/> Don't know</li> </ul>	<ul style="list-style-type: none"> <li>● No studies examined acceptability for cardiac arrest centers</li> </ul>	<p>Some countries already have cardiac arrest centers, regionalized emergency transport system and registry.</p> <p>The establishment of cardiac arrest center and emergency transport system needs to fit in with local health priorities and needs</p> <p>Further evidence may persuade others to fund and support cardiac arrest centers</p>

## Feasibility

Is the intervention feasible to implement?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <li><input type="radio"/> No</li> <li><input type="radio"/> Probably no</li> <li><input type="radio"/> Probably yes</li> <li><input type="radio"/> Yes</li> <li>● Varies</li> <li><input type="radio"/> Don't know</li> </ul>	<p>No studies examined the feasibility of CACs.</p>	<p>Feasible in regions with advanced emergency systems</p> <p>Similar systems in trauma, stroke and AMI are now standard practice.</p> <p>Feasibility maybe an issue in rural areas or low density population.</p>

## SUMMARY OF JUDGEMENTS

## JUDGEMENT

PROBLEM	No	Probably no	Probably yes	<b>Yes</b>		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	<b>Large</b>		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial		Varies	<b>Don't know</b>
CERTAINTY OF EVIDENCE	<b>Very low</b>	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	<b>No important uncertainty or variability</b>			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	<b>Probably favors the intervention</b>	Favors the intervention	Varies	Don't know
RESOURCES REQUIRED	Large costs	Moderate costs	Negligible costs and savings	Moderate savings	Large savings	<b>Varies</b>	Don't know
CERTAINTY OF EVIDENCE OF REQUIRED RESOURCES	Very low	Low	Moderate	High			<b>No included studies</b>
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	<b>No included studies</b>
EQUITY	Reduced	Probably reduced	Probably no impact	<b>Probably increased</b>	Increased	Varies	Don't know
ACCEPTABILITY	No	Probably no	<b>Probably yes</b>	Yes		Varies	Don't know
FEASIBILITY	No	Probably no	Probably yes	Yes		<b>Varies</b>	Don't know

## TYPE OF RECOMMENDATION

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  ○
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## CONCLUSIONS

### Recommendation

We suggest adult non-traumatic OHCA patients (P) be cared for in cardiac arrest centers (I) rather than non-cardiac arrest centers (C) in settings where this can be implemented (weak recommendation, very low certainty of evidence).

For patients with IHCA, we found no evidence to support an EIT and ALS Task Force recommendation for or against the intervention.

For patient subgroups with either shockable or non-shockable initial cardiac rhythm, the current evidence is inconclusive and confidence in the effect estimates is currently too low to support a separate EIT and ALS Task Force recommendation.

For regional triage of OHCA patients to a cardiac arrest center by primary EMS transport or secondary interfacility transfer subgroups, the current evidence is inconclusive and confidence in the effect estimates is currently too low to support a separate EIT and ALS Task Force recommendation.

### Justification

In making this suggestion, the EIT and ALS Task Forces considered that in settings where this can be implemented, the potential benefits in clinical outcomes may outweigh the logistical issues with implementation. We also considered the following:

- We considered the consistency of improved outcomes in patients treated at CACs across most studies; even though the certainty of the evidence is very low, studies were all observational and the heterogeneity of included studies was high.
- We placed a high value on the availability of evidence based post-resuscitation care where possible.
- We noted other evidence demonstrating benefits of specialized acute care for other emergency conditions such as trauma, stroke and ST-elevation myocardial infarction.
- We note the lack of evidence suggesting clinical harm due to longer transport time. (Geri 2017 96).
- We considered the limited available data on regional triage of OHCA patients to cardiac arrest centers via primary EMS transport or secondary inter-facility transfer. We considered the potential for referral bias (transporting patient likely to survive) in this evidence. The ideal regional triage scheme of OHCA patients to cardiac arrest centers is likely region-dependent based on resource allocation and logistical considerations. The impact of primary EMS transport or secondary inter-facility transfer is identified as a knowledge gap.
- We recognize that the implementation of this suggested recommendation may not be feasible in all regions due to resources, costs, and inherent differences in health care delivery.
- We recognize that regionalized cardiac arrest care may remove patients from their local social support networks.
- It remains unclear whether specific patient subgroups (e.g. shockable or non-shockable initial cardiac rhythm) benefit to a different extent from regionalized cardiac arrest care. This is identified as a knowledge gap.
- We did not find any studies on in-hospital cardiac arrest and have identified this as a knowledge gap.
- We recognize that this weak recommendation supports regional systems in areas with available resources. The very low certainty evidence does not necessarily support the creation of *de novo* systems.

## Subgroup considerations

Subgroup analyses in the observational studies were clinically heterogeneous and comprised both adjusted and unadjusted data. This limited our ability to pool data and make treatment recommendations about specific subgroups of OHCA patients.

The majority of the evidence is based on patients who achieved prehospital ROSC.

We excluded children from this study based on a recommendation from the Pediatric Task Force.

### Subgroups

#### Shockable versus non-shockable

There were 8 studies that reported outcomes in CACs versus non-CACs stratified by shockable or non-shockable rhythms (Chocron 2017, Cournoyer 2018 28, Elmer 2018 48, Lick 2018 26, Mumma 2015, Seiner 2018 e234, Spaite 2014 496, Tagami 2012 589).

In patients with shockable rhythm, 5 studies reported improved outcomes at CACs (Elmer 2018 48, Lick 2018 26, Mumma 2015, Spaite 2014 496, Tagami 2012 589), and three studies reported no difference (Chocron 2017, Cournoyer 2018 28, Seiner 2018).

In patients with non-shockable initial rhythms, CACs were associated with improved outcomes in one study (Mumma 2015) and no difference in two studies (Cournoyer 2018 28, Spaite 2014 496).

#### Primary versus secondary transfers

Only 4 studies examined outcomes in OHCA patients who were transferred to a CAC from a non-CAC (Elmer 2018 48, Lai 2018 e0191954, McKenzie 2018, Tagami 2012 589). Two studies reported no difference in (unadjusted) outcomes (Elmer 2018 48, Tagami 2012 589). One study (McKenzie 2018 76) reported higher (adjusted) survival in patients who were transferred directly to a CAC compared to secondary transfers, and another study (Lai 2018 e0191954) reports higher (adjusted) survival among patients secondarily transferred to a CAC compared to remaining at the original hospital.

## Implementation considerations

- We recognized that implementing this recommendation may be resource and cost intensive, and that it may not be feasible in all regions.
- We recognize that this weak recommendation supports regional systems in areas with available resources. The very low certainty evidence does not necessarily support the creation of *de novo* systems.
- We considered the successful implementation of regionalized care for trauma, stroke and STEMI.

## Monitoring and evaluation

- Registries are an effective method for monitoring the use and effectiveness of regionalized care.

## Research priorities

Current knowledge gaps include but are not limited to:

- There are currently no randomized data on this topic beyond a single, small, feasibility trial.
- There is no high-quality evidence surrounding primary EMS transport compared to secondary inter-facility transfer
- There is no evidence regarding IHCA.
- There is no universal definition of a cardiac arrest center. The precise aspects of post-cardiac arrest care that improve outcomes is unclear.
- Evidence of the impact on other clinical outcomes such as cognitive recovery and quality of life are lacking.
- Evidence in certain subgroups of cardiac arrest patients (e.g. cardiac etiology, shockable rhythm, witnessed collapse) is currently insufficient.
- There is no evidence of the cost-effectiveness of caring for OHCA patients at specialized cardiac arrest centers.
- More evidence is needed on the risks of bypassing a local hospitals and transferring patients to specialized cardiac arrest centers (e.g. re-arrest).
- More evidence is needed on whether OHCA subjects should be transported primarily to a specialized cardiac arrest center by prehospital services, or through secondary inter-facility transport after initial evaluation and stabilization at a local hospital.
- Studies are needed to assess the hospital- and clinician-level effects on bypassed hospitals (e.g. degrading skill set in post-resuscitation management and downgrading of services).
- The impact of transporting subjects away from their local social support networks is unknown.