A systematic review of cost-effectiveness research of cardiac arrest treatment

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Running title: Costs related to cardiac arrest management
Key words: out-of-hospital cardiac arrest, costs, cost-effectiveness, outcome

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Background

Each year, about 320,000 people in the US, and up to 40,000 people in France and Canada will suffer an out-of-hospital cardiac arrest (OHCA).[1, 2, 3] The two major systems of emergency care delivery used in OHCA in these countries are the Anglo-American system, which “brings the patient to the hospital” and the French-German system, which “brings the hospital to the patient”. [4, 5, 6] The strategy used in France (as well as in other European countries) involves the presence of an emergency physician at the scene, while the strategy used in Canada and the US relies on paramedics to treat OHCA patients at the scene and then transport them to hospital. Even if designation differs between Canada and the US, both prehospital health care delivery systems are very similar regarding the occupational titles for EMS providers as well as the meanings of these titles. [6, 5] Moreover, in-hospital management of successfully resuscitated OHCA patients nowadays requires multifaceted interventions as therapeutic hypothermia or immediate coronary angiography with percutaneous coronary intervention. Such an invasive strategy has been associated with improved short- and long-term survival [7, 8, 9, 10] and an organized regional system of care for OHCA is recommended. [11] Whereas this has not been officially implemented in Canada and in France, their system focuses on delivering patients the highest level of care available even if variables rates of immediate coronary angiography and variable and targeted temperature management have been reported. [12, 13, 7, 14, 15]

Although the systems are different, overall survival to hospital discharge is similar across these three countries.[12, 16] This observation raises a question about the economics of the respective OHCA management strategies. To date, the published economic data are not applicable to a “real-life” daily practice in OHCA management. Indeed, previously reported works have specifically focused on the incremental cost-effectiveness ratio of public access defibrillation [17, 18, 19, 20, 21, 22], of AEDs location [23, 24] or lay responders’ training [25]. Although published data exits on cost-effectiveness of a specific part of OHCA management as targeted temperature management [26] or in subgroups defined by age cohorts [27], no data has been previously published regarding the costs of a “bottom-up” strategy from arrival on scene to hospital discharge. Moreover, few data included cost retrieval at an individual patient level.

Measuring the costs associated with OHCA resuscitation (prehospital and in-hospital) is essential in order to evaluate the economic effects of different delivery strategies in prehospital and in-hospital management of OHCA patients.[28] That’s why we aimed in the present systematic review of literature at screening and selecting all the studies, which reported costs of pre-hospital and in-hospital care of out-of-hospital cardiac arrest.
Methods

PICO question

The PICO question is the following:

- **P**: cardiac arrest patients (i.e. in-hospital and out-of-hospital cardiac arrest, both adult and pediatrics)
- **I**: any intervention to do with cardiac arrest will be taken into consideration in this systematic review: public access defibrillation, bystander CPR, dispatcher assisted CPR, therapeutic hypothermia and coronary angiography (and percutaneous coronary intervention), post arrest bundles of care
- **C**: patients who do not have the intervention
- **O**: cost-effectiveness ratio, cost identification, cost-benefit ratio, cost evaluation

Literature search

The databases included in the literature search will be: PubMed, Embase, Web of Science and Medline.

The following keywords will be used:

- out-of-hospital cardiac arrest AND
- costs OR cost-effectiveness AND
- public access defibrillation OR
- dispatcher assisted CPR OR bystander CPR OR chest compression OR
- therapeutic hypothermia OR targeted temperature management OR
- coronary angiography OR percutaneous coronary intervention

Studies will be included if they performed a comparative analysis of both costs and effects of at least 2 competing strategies and provided an incremental analysis of cost per effect. All treatment strategies for cardiac arrest (including public access defibrillation, dispatcher assisted CPR, therapeutic hypothermia and coronary angiography) will be eligible.
To determine the cost-effectiveness of a particular intervention, we will rely on the authors’ conclusions in the primary publication. A cost-effectiveness ratio of less than $50,000 to $100,000 per QALY is usually considered to be cost-effective. In addition to the ratios reported in the primary publication, we will calculate and report the ratios inflated to 2015 US dollars using the medical component of the consumer price index.

**Evidence appraisal**

Based on GRADE, the level of evidence (LOE) will be evaluated by two authors:

- **LOE 1**: randomized controlled trial or meta-analysis of randomized controlled trials
- **LOE 2**: studies using concurrent controls without randomization for comparison
- **LOE 3**: studies using retrospective controls for comparison
- **LOE 4**: studies without a control group for comparison
- **LOE 5**: studies not directly related to the specific population

Comparison studies without matched concurrent controls will be classified as LOE 4. The studies will be categorised as prospective or retrospective as a simple evaluation of quality.

**Evaluation of risk of bias**

The ROBINS-I tool (Risk Of Bias In Non-randomized Studies of Interventions) (Cochrane Methods) will be used to evaluate the risk of bias of the selected paper.

**PROSPERO registry registration**

The present systematic review will registered to the PROSPERO registry.

**Planned presentation of the results**

The following tables/figures will be drawn to present the results of the present systematic review:

- **Figure 1**: Flow diagram of the selection of included studies
• **Table 1**: Attributes of included studies

• **Table 2**: Cost-effectiveness analyses of cardiac arrest treatments: intervention, alternative and patient population

• **Table 3**: Cost-effectiveness of public access defibrillation

• **Table 4**: Cost-effectiveness of dispatcher-assisted bystander CPR

• **Table 5**: Cost-effectiveness of targeted temperature management

• **Table 6**: Cost-effectiveness of coronary angiography

• **Supplementary material** including detailed literature search algorithm and kappa coefficients for titles/abstracts and full-paper review steps.

**Targeted journals**

The following journals will be considered for submission of the paper:

• Resuscitation journals
  – Resuscitation
  – Critical Care Medicine
  – Annals of Emergency Medicine

• Public Health journals
  – Circulation, Quality and Outcomes
  – International Journal of Public Health
  – Journal of Public Health
  – American Journal of Public Health

**Timeline and authors’ contribution**

GG, LJM and CZ will design the literature search.

CZ will perform the literature search and draft the literature search section.

GG and JG will review the retrieved titles/abstracts and full-papers as well as will extract the data. GG will draft the paper.

LJM will review the paper.
Table 1: Time line

<table>
<thead>
<tr>
<th>Literature search</th>
<th>mid-May mid-June 2016</th>
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<tbody>
<tr>
<td>Abstracts and titles review</td>
<td>July 2016</td>
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<tr>
<td>Full-paper review</td>
<td>August 2016</td>
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<tr>
<td>Data extraction</td>
<td>August 2016</td>
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<tr>
<td>Draft redaction</td>
<td>September 2016</td>
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<tr>
<td>Draft submission to co-authors</td>
<td>Early days of October 2016</td>
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<td>Manuscript modifications and finalization</td>
<td>End of October 2016</td>
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<td>Manuscript submission</td>
<td>November 2016</td>
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