Commercial funding and results of pediatric critical care randomized trials: A systematic review

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Background
Commercial funding of randomized controlled trials (RCTs) is associated with both positive results and favourable conclusions in other clinical areas. (1)

Objectives
1) To describe the funding sources of pediatric critical care RCTs.
2) To compare the characteristics, results and conclusions of RCTs reporting a commercial funding source with those that did not.

Methods
Searching: We used the Evidence in Pediatric Intensive Care database (epicc.mcmaster.ca) to identify RCTs (Oct 2013 update). This database uses comprehensive search strategies to find published pediatric critical care RCTs. The database includes RCTs reporting the effect of any intervention on children or their families in a pediatric intensive care unit. It excludes trials enrolling only preterm infants and crossover trials. (2)

Inclusion criteria: We included all RCTs when describing funding and comparing characteristics of trials with commercial funding to other trials. To compare the results and conclusions we included superiority RCTs comparing 2 groups, published in English and reporting a primary outcome.

Data extraction: Pairs of reviewers abstracted data and independently classified the results and conclusions as follows:
- Positive results: The results for the primary outcome were statistically significant and favoured the experimental group.
- Favourable conclusions: The trial authors stated that the intervention is preferred without any reservations or qualifications, should now be used in all patients, or similar.
- Analysis: We used Fisher’s Exact and Mann Whitney U tests and logistic regression to compare groups.

Funding sources
Included studies: We included 267 trials, enrolling 28,045 children, published between 1986 and Oct 2013.
Funding source: 148 (55%) of trials reported their source of funding. 36 (14%) trials reported 2 or more sources. 39 (15%) reported funding from a commercial source. For 23 (9%) this was the only reported funding.

RCT characteristics
Characteristics of pediatric critical care RCTs

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Commercial funding (n=267)</th>
<th>Other trials (n=228)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number randomized</td>
<td>45 (23, 110)</td>
<td>50 (30, 88)</td>
<td>0.97</td>
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<tr>
<td>Multi-centred</td>
<td>23 (59)</td>
<td>26 (11)</td>
<td>&lt;0.01</td>
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<tr>
<td>Studied medications</td>
<td>26 (67)</td>
<td>112 (49)</td>
<td>0.06</td>
</tr>
<tr>
<td>Blinding</td>
<td>31 (79)</td>
<td>105 (46)</td>
<td>&lt;0.01</td>
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<tr>
<td>Stopped early</td>
<td>9 (23)</td>
<td>23 (10)</td>
<td>0.03</td>
</tr>
<tr>
<td>High risk of bias</td>
<td>13 (33)</td>
<td>100 (44)</td>
<td>0.29</td>
</tr>
</tbody>
</table>

Data are reported as median (IQR) or number (%).

Results of included RCTs
155 (24 with commercial funding) were superiority RCTs that compared 2 groups and reported a primary outcome. 21% (5 of 24) of trials with commercial funding and 39% (55 of 131) of trials without commercial funding had positive results (p=0.07).

Using logistic regression, early stopping was independently associated with positive results (p=0.01) but commercial funding, year of publication, and use of a pharmaceutical intervention or blinding were not.

Conclusions
Almost half of RCTs in pediatric critical care do not disclose their funding source. Of RCTs that do report funding, noncommercial funding is 3 times more common than commercial funding.

Compared to other RCTs, commercially funded RCTs are more likely to be multicentered, blinded and stopped early. In adjusted analyses, only early stopping was significantly associated with positive results.

More transparent reporting of pediatric critical care RCTs is needed.

References: