Clinical question.
In term infants without a detectable heart rate and no other signs of life at birth (P) does ceasing resuscitation after 15 minutes or longer of effective resuscitation (I) as opposed to 10 minutes (O) result in better outcomes (lower incidence of abnormal neurological examination and/or death).

Is this question addressing an intervention/therapy, prognosis or diagnosis? Intervention/therapy

State if this is a proposed new topic or revision of existing worksheet: New topic

Conflict of interest specific to this question
Do any of the authors listed above have conflict of interest disclosures relevant to this worksheet? NO

Search strategy (including electronic databases searched).
1. MEDLINE; "detectable heart rate".ti,ab; 1 results.
2. MEDLINE; "asystole".ti,ab; 2066 results.
3. MEDLINE; exp HEART ARREST/; 24583 results.
4. MEDLINE; "no heart rate".ti,ab; 45 results.
5. MEDLINE; 1 OR 2 OR 3 OR 4; 25626 results.
6. MEDLINE; resuscitation.ti,ab; 27620 results.
7. MEDLINE; exp RESUSCITATION/; 57553 results.
8. MEDLINE; 6 OR 7; 68928 results.
9. MEDLINE; 5 AND 8; 8616 results.
10. MEDLINE; 9 [Limit to: Publication Year 1988-2008 and Humans and (Age Groups Newborn Infant birth to 1 month)]]; 241 results.
11. MEDLINE; death.ti,ab; 315945 results.
12. MEDLINE; exp DEATH/; 93691 results.
13. MEDLINE; 11 OR 12; 377524 results.
14. MEDLINE; handicap.ti,ab; 6078 results.
15. MEDLINE; "physical disability".ti,ab; 1843 results.
16. MEDLINE; exp DISABLED PERSONS/; 35676 results.
17. MEDLINE; exp MENTAL RETARDATION/; 68917 results.
18. MEDLINE; 14 OR 15 OR 16 OR 17; 108166 results.
19. MEDLINE; 13 OR 18; 483558 results.
20. MEDLINE; 10 AND 19 [Limit to: Publication Year 1988-2008 and Humans and (Age Groups Newborn Infant birth to 1 month)]]; 49 results.

Also:
Medline, Embase, CINAHL and Cochrane databases, and AHA/ECC Endnote library for the words:
Apgar score zero
Zero Apgar score
Withhold* resuscitat* and Apgar score
Withhold* resuscitat* limited to human and age group newborn infant
Resuscitat* and 10 minutes limited to human and age group newborn infant
(CPR or Cardiopulmonary resuscitat*) and 10 minutes limited to human and age group newborn infant
Resuscitat* and stillb*
Stillb* limited to human an age group newborn infant

Hand search of Pediatrics and Archives of Diseases of Childhood from 2005

• State inclusion and exclusion criteria
Excluded case reports, abstract only studies, none peer-reviewed studies and animal data.

• Number of articles/sources meeting criteria for further review:
9 in total
# Summary of evidence

## Evidence Supporting Clinical Question

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### Level of evidence

- **A** = Return of spontaneous circulation
- **B** = Survival of event
- **C** = Survival to hospital discharge
- **D** = Intact neurological survival
- **E** = Other endpoint

*Italics = Animal studies*
## Evidence Neutral to Clinical question

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<th>Good</th>
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A = Return of spontaneous circulation   C = Survival to hospital discharge   E = Other endpoint
B = Survival of event                   D = Intact neurological survival   *Italics* = *Animal studies*

## Evidence Opposing Clinical Question

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A = Return of spontaneous circulation   C = Survival to hospital discharge   E = Other endpoint
B = Survival of event                   D = Intact neurological survival   *Italics* = *Animal studies*
REVIEWER’S FINAL COMMENTS AND ASSESSMENT OF BENEFIT / RISK:

There are only 9 retrospective case series and in total only 130-140 babies and not all of these have full data available about whether Apgar score was 0 at 10 minutes or of follow up of all survivors. We know little of the cause for these babies being in poor condition at birth nor how heart rate was determined (auscultation or palpation), nor whether all eligible infants were resuscitated.

However there appears to be overwhelming evidence from these studies that an Apgar score of 0 at 10 minutes (as a proxy for no detectable heart rate) is associated with an 89% risk of death or a 97% risk of death or severe handicap. We do not know whether therapeutic hypothermia can alter these outcomes, but it would appear that the damage may be so overwhelming that it may have little or nothing to offer in this group (see summary table below).

<table>
<thead>
<tr>
<th>Author</th>
<th>Study years</th>
<th>Number</th>
<th>Death % (no)</th>
<th>Disability % (n)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Harrington et al</td>
<td>1994-2004</td>
<td>9</td>
<td>78 (7)</td>
<td>50 severe (1), 50 mild (1)</td>
<td>Death or severe disability in 89%</td>
</tr>
<tr>
<td>Berglund et al</td>
<td>1990-2005</td>
<td>8</td>
<td>87 (7)</td>
<td>100 moderate (1)</td>
<td>Apgar 0 at 15 mins, not 10</td>
</tr>
<tr>
<td>Patel and Beeby</td>
<td>1992-2002</td>
<td>29</td>
<td>69 (20)</td>
<td>89 severe (8), 11 moderate (1)</td>
<td>In total death or disability in 97%</td>
</tr>
<tr>
<td>Haddad et al</td>
<td>1986-1999</td>
<td>16</td>
<td>85 (14)</td>
<td>Unknown</td>
<td>(Only series with preterms (not included in figures): 100% mortality if BW&lt;1800g)</td>
</tr>
<tr>
<td>Casalaz et al</td>
<td>1986-1994</td>
<td>4</td>
<td>75(3)</td>
<td>100 severe (1)</td>
<td>100% risk of death or severe disability</td>
</tr>
<tr>
<td>Socol et al</td>
<td>1984-1994</td>
<td>1</td>
<td>0</td>
<td>100 moderate</td>
<td>Only 1 patient</td>
</tr>
<tr>
<td>Jain et al</td>
<td>1982-1986</td>
<td>58</td>
<td>98 957)</td>
<td>100 severe (1)</td>
<td>100% risk of death or severe disability</td>
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<tr>
<td>Koppe and Kleiverda</td>
<td>1969-1975</td>
<td>3</td>
<td>100 (3)</td>
<td>-</td>
<td>100% mortality</td>
</tr>
<tr>
<td>[Yeo and Tudehope]</td>
<td>8</td>
<td></td>
<td>100% death or severe disability</td>
<td>Breakdown of outcomes not specified</td>
<td></td>
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</table>

Summary of babies included in the analysis and their outcomes

Acknowledgements: Thank you to Catherine Richmond, Librarian at James Cook University Hospital for her help in formulating the search
Citation List

LOE 5 Supportive (retrospective cohort not directly related to the question and some selection bias)

Comment: This study was not directly related to the clinical question and its design (using only cases where there have been claims for financial compensation) must inevitably introduce significant selection bias. It was only possible to extract data for babies with continuing asystole at 15 rather than 10 minutes and of these 8, 7 died and the other has cerebral palsy (but there was no detail of type or severity). The findings that there were a significant number of cases where resuscitation may not have been carried out optimally was interesting, and reflects the fact that at least some of the babies included in these series may not have received “good quality resuscitation” throughout.

LOE 4 Supportive (Retrospective cohort)

Comment: A large series but only 4 babies fulfil the criteria of being still asystolic at 10 minutes, of which 3 died and 1 was severely disabled. The study was across 2 centres. Note that 93% of the total deliveries in the study were attended by a trained resuscitation team.

Haddad B, Mercer BM, Livingston JC, Talati A, Sibai BM  Outcome after successful resuscitation of babies born with Apgar scores of 0 at both 1 and 5 minutes. Am J Obstet Gynecol, 2000, 182(5), 1210-1214
LOE 4 Supportive (Retrospective cohort)

Comment: A series from one centre over a 14 year period. This is really the only series which includes significant numbers of preterm babies who had a 100% mortality. Again there are some problems, especially follow up of survivors. However, of the 16 who were still asystolic at 10 minutes, 14 died and we do not know about the neurological outcome of the other 2.

LOE 4 Supportive (retrospective cohort and review of the literature)

Comment: Much of the paper is related to a review of the literature and only 9 patients who directly answer this question are added to the numbers already reported in the literature. There is no information (as for most of these series) about the quality of the resuscitation and many go back for a long period (until 1991 in this case). Of 9 babies with Apgar zero at 10 minutes 8 died and/or had severe disability. Note that in the table the data for the Jain paper appears incomplete: 58 babies had Apgar of zero at ≥10 minutes.

LOE 4 Supportive (Retrospective cohort)

Comment: By far the largest group of patients pertinent to the question to be answered. Again, we do not know
how the absence of HR was determined (auscultation, palpation or ECG?), whether all eligible babies were included and what the quality of resuscitation provided was. Of 58 babies with an Apgar of zero at 10 minutes, 57 died and the other had severe disability.

LOE 5 Supportive (Retrospective cohort)

Comment: This study was actually designed to look at return of spontaneous respiration as a prognostic sign, but amongst the babies 3 were asystolic at 10 minutes and all of these died. Again, as in many other studies here were methodological concerns and little detail about the resuscitation given to these babies.

LOE 4 Supportive (Retrospective cohort)

Comment: This study looked at all babies admitted to 10 Level 3 NICU’s in NSW, Australia with Apgar scores of zero at 1 and 5 minutes. Local clinicians were then asked to determine which babies still had apgar scores of zero at 10 minutes. Inevitably there must have been selection bias as many babies may not have been born in or transferred into these units who may have been successfully resuscitated or died. Again, we do not know what resuscitation the included babies actually received.
Of 29 babies identified 20 died and 8 were severely handicapped. Interestingly 28 had an audible heart rate at 15 minutes but these data are very supportive of the very poor prognosis.

LOE 5 Supportive (Retrospective cohort)

Comment: Only 1 infant (who survived with moderate disability) with a HR of zero at 10 minutes was included in this study which was designed to look at umbilical cord gases in babies with lower Apgar scores.

Yeo CL and Tudehope DI  Outcome of resuscitated apparently stillborn infants: a ten year review. J Paediatr Child Health, 1994, 30(2), 129-133
LOE 5 Supportive (Retrospective cohort)

Comment: This study looked at outcome when 1 minute Apgar was zero. Unfortunately those with Apgar of zero at 10 minutes were not specified. 8 infants had Apgar scores of zero at 5 minutes and they all died or were severely handicapped, but it is not possible to determine the relative proportions of these outcomes. Again we have no data about possible selection bias or the resuscitation given to these babies.
Interestingly the authors concluded that resuscitation should be stopped if the Apgar score was zero at 5 minutes.