**Appendix 1 – Updated ALS EtD**

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| Question | |
| **Should ALS vs. no ALS be used for health problem or population?** | |
| **Population:** | Adult in-hospital patients who have a cardiac arrest |
| **Intervention:** | Prior participation of one or more members of the resuscitation team in an accredited advanced cardiac life support course (e.g. AHA ACLS, RC(UK)/ERC ALS) |
| **Comparison:** | No such participation |
| **Main outcomes:** | ROSC; Survival to Discharge or 30-day survival; 1 year survival; |
| **Setting:** | **In-hospital** |
| **Perspective:** |  |
| **Background:** |  |
| **Conflict of interests:** | Janet Bray is a member of the Australian Resuscitation Council – who provide ALS training.  Andy Lockey is a Trustee of the Resuscitation Council UK – who provide ALS training. |

# 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 | Attendance of participants on an advanced cardiac life support course comes at a cost - both financial and time - to stakeholders including participants themselves and their institutions. It is therefore important to show whether this participation has any meaningful impact upon patient outcomes. | Likely to be a lack of recent data as advanced cardiac life support training is generally widespread. |
| Desirable Effects How substantial are the desirable anticipated effects? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know | The original systematic review, with a search date of 6 March 2018, identified 8 studies (Lowenstein 1986 512, Sanders 1994 56, Makker 1995 116, Camp 1997 529, Pottle 2000 45, Dane 2000 83, Moretti 2007 458, Sodhi 2011 209).  One additional study was identified in an updated search run in May and October 2021 (Pareek et al., 2018),  For the critical outcome of “return of spontaneous circulation” we have identified very low quality evidence (downgraded for risk of bias, inconsistency, indirectness and imprecision) from seven observational studies (Lowenstein, Sabyan, Lassen, & Kern, 1986; Makker, Gray-Siracusa, & Evers, 1995; Moretti et al., 2007; Pareek et al., 2018; Pottle & Brant, 2000; Sanders et al., 1994; Sodhi, Singla, & Shrivastava, 2011) enrolling 2093 patients showing benefit for advanced cardiac life support training (OR 1.66 95% CI 1.24 – 2.21).  For the critical outcome of “survival to hospital discharge” or “survival to 30 days” we have identified very low quality evidence (downgraded for risk of bias, inconsistency, indirectness and imprecision) from eight (Camp, Parish, & Andrews, 1997; Dane, Russell-Lindgren, Parish, Durham, & Brown Jr, 2000; Lowenstein et al., 1986; Moretti et al., 2007; Pareek et al., 2018; Pottle & Brant, 2000; Sanders et al., 1994; Sodhi et al., 2011) observational studies (Lowenstein 1986 512, Sanders 1994 56, Camp 1997 529, Pottle 2000 45, Dane 2000 83, Moretti 2007 458, Sodhi 2011 209) enrolling 1667 patients showing possible benefit for advanced cardiac life support training (OR 2.48 95% CI 1.21 – 5.09).  For the critical outcome of “survival to 1 year” we have identified very low quality evidence (downgraded for risk of bias, inconsistency, and imprecision) from two observational studies (Pottle 2000 45, Moretti 2007 458) enrolling 455 patients showing no benefit (OR 3.61 95% CI 0.11 – 119.42). One study had very high loss to followup (25%) in the ALS training period (Pottle 2000 46). | No studies were found that examined the impact of advanced cardiac life support training on good neurological outcomes.  All except the latest study (Pareek et al., 2018) were conducted prior to the current available evidence for post-resuscitation care (e.g. targetted temperature management).  More contemporary studies found consistently better outcomes for the intervention (Pareek et al., 2018; Sodhi et al., 2011).  One study reported a statistically significant improvement in time to ROSC following the introduction of advanced cardiac life support training (mean 11.5 minutes vs 30.0 minutes). This study reported no change in duration of attempted resuscitation in patients who did not achieve ROSC (Moretti 2007 458)  One study reported the probablity of achieving ROSC was associated with number of resuscitating team members who were trained in ACLS (Moretti 2007 458).  One study reported a decrease treatment errors, such as incorrect rhythm assessment, in IHCA following the implementation of ALS training (Makker 1995, 116).  Studies were not able to identify which components of training contributed to outcomes.  Advanced cardiac life support training provides the opportunity to update health care professionals on changes in resuscitation practice as new evidence emerges and is integrated into resuscitation guidelines and algorhythms. |
| Undesirable Effects How substantial are the undesirable anticipated effects? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Large ○ Moderate ○ Small ● Trivial ○ Varies ○ Don't know | Some studies reported increased rates of attempted resuscitation following the introduction of advanced cardiac life support training, but do not report on the appropriateness of this change. [Lowenstein 1986 512, Camp 1997 529] |  |
| 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 | ROSC (7 studies - (Lowenstein et al., 1986; Makker et al., 1995; Moretti et al., 2007; Pareek et al., 2018; Pottle & Brant, 2000; Sanders et al., 1994; Sodhi et al., 2011)) & Survival to discharge and 30 days (8 studies - (Camp et al., 1997; Dane et al., 2000; Lowenstein et al., 1986; Moretti et al., 2007; Pareek et al., 2018; Pottle & Brant, 2000; Sanders et al., 1994; Sodhi et al., 2011)) - downgraded for risk of bias, inconsistency, indirectness and imprecision  1 year survival (2 studies - Pottle 2000 45, Moretti 2007 458) - downgraded for risk of bias, inconsistency and imprecision  The certainty of evidence is very low. Existing evidence is old and of very poor quality –mostly retrospective, single-centre studies, using historical controls, with poor reporting on patient characteristics. Only one study adjusted outcomes for possible confounding –but only adjusted for rhythm (Dane 2000 83). Some studies were conducted with small sample sizes, and are likely to be underpowered.  The most recent studies reporting data post-2000 which is when international guidelines were first introduced, ((Pareek et al., 2018; Sodhi et al., 2011)) showed a significant benefit to the addition of advanced cardiac life support training to staff already trained in basic life support. One study is subject to significant confounding, as the authors only reported unadjusted outcomes and provided very limited data on patient and arrest characteristics between the two periods (Sodhi et al., 2011). The other study was limited to nursing staff in one institution in India (Pareek et al., 2018).  Most effect estimates favoured advanced cardiac life support training. | Advanced cardiac life support courses have evolved over time. |
| 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 | Patients value survival with good neurological outcome (Haywood 2018 e783). It is expected that health care professionals are trained to treat medical emergencies. Standardised advanced cardiac life support training is likely to improve the care provided during cardiac arrest, and thus improve outcomes for patients. | No studies examined the critical outcome of good neurological function. |
| 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 | Whilst the positive effects are presented with very low evidence, they likely offset the potential negative effect of inappropriate attempted resuscitations. |  |
| Resources required How large are the resource requirements (costs)? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Large costs ● Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know | There has been no formal cost effectiveness analysis in the studies identified. | The costs of running advanced life support courses include:  1) costs to the overseeing Resuscitation Council (e.g. manual production, e-learning platforms)  2) costs to the course centre (e.g. faculty costs, facility costs, equipment purchase and maintenance)  3) costs to the employers (e.g. course fees, covering study and professional leave time for candidates and faculty)  4) costs to the employees (e.g. course fees in some cases)  These costs can be mitigated by alternative methods of course delivery, including hybrid courses consisting of e-learning modules.  There may also be costs incurred in low resource settings in terms of other educational interventions that may suffer if advanced cardiac life support training were to be prioritised. |
| 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 | Costs are likely to vary between different health care settings. |  |
| 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 | The potential for lives saved by health care professional’s participation in these courses outweighs the costs of candidates attending these courses. |  |
| 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 | The associated resources and costs may prohibit advanced cardiac life support training in some health care settings. If advanced cardiac life support courses were to be prioritised, this may come at the expense of other healthcare educational interventions in low resource settings. |  |
| Acceptability Is the intervention acceptable to key stakeholders? | | |
| Judgement | Research evidence | Additional considerations |
| ○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know | The potential for lives saved by participation in these courses outweighs the costs of candidates attending these courses.  There is an expectation from the public and healthcare institutions that employees will be trained to deal with this important critical condition, so this evidence supports the fact that these courses are fit for purpose. |  |
| Feasibility Is the intervention feasible to implement? | | |
| Judgement | Research evidence | Additional considerations |
| ○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know | This is an intervention that has been well established in healthcare education in high resource settings. But its provision may not be feasible or appropriate in in some health care settings. |  |

# Summary of judgements

|  | **Judgement** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Problem** | No | Probably no | **Probably yes** | Yes |  | Varies | Don't know |
| **Desirable Effects** | Trivial | **Small** | Moderate | Large |  | Varies | Don't know |
| **Undesirable Effects** | Large | Moderate | Small | **Trivial** |  | 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 recommend the provision of accredited adult advanced cardiac life support training for health care professionals who provide advanced life support care for adults (strong recommendation, very low quality of evidence). |
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| Justification |
| Adult advanced cardiac life support training improves resuscitation knowledge and skills and it is likely to ensure best practice is applied in these emergency situations.  We recognize that the evidence in support of this recommendation comes from observational studies of very low quality. However, pooling of the available evidence consistently favours advanced cardiac life support training, and having advanced cardiac life support trained staff present during an attempted adult resuscitation has been found to reduce treatment errors such as incorrect rhythm assessment (Makker 1995, 116) and time to ROSC (Moretti 2007 458). We recognise that the provision of accredited adult advanced cardiac life support training may not be feasible or appropriate in low resource settings. |

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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 |
| Similar review needed for other life support courses (e.g. PALS).  Recommended CoSTR:   * + We recommend the provision of accredited adult advanced cardiac life support training for health care professionals who provide advanced life support care for adults (strong recommendation, very low quality of evidence).   + Values and preferences statement: In making this recommendation we recognize that the evidence comes from observational studies of very low certainty. However pooling of the available evidence consistently favours ACLS/ALS training.   + The provision of accredited ACLS/ALS training may not be feasible or appropriate in some low resource settings.   + Knowledge gaps: impact of blended learning approaches, ideal recertification intervals, impact of modifications necessitated by COVID pandemic. |

**Appendix 2 – NRT EtD**

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| Question | |
| **Are cardiac arrest outcomes improved as a result of a member of the resuscitation team attending an accredited advanced life support course?** | |
| **Population:** | Patients requiring in-hospital cardiac arrest resuscitation of any age - NEWBORN |
| **Intervention:** | Prior participation of one or more members of the resuscitation team in an accredited advanced life support course NEONATAL RESUSCITATION TRAINING (NRT) |
| **Comparison:** | No such participation |
| **Main outcomes:** | ROSC; Survival to Discharge or 30-day survival; 1 year survival; survival with favourable neurological outcome; stillbirth rate; neonatal mortality; perinatal mortality |
| **Setting:** | **hospital setting** |
| **Conflict of interests:** | Andy Lockey is a Trustee of Resuscitation Council UK – who provide NLS training. |

# 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 | Neonatal survival rates are globally poor, in particular in low and middle income settings. The potential for number of lives saved is more impactful for newborn than it is with adults. | Attendance of participants on an NRT course comes at a cost - both financial and time - to stakeholders including participants themselves and their institutions. It is therefore important to show whether this participation has any meaningful impact upon patient outcomes.  All studies were from low-income or middle-income countries. |
| Desirable Effects How substantial are the desirable anticipated effects? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Trivial ○ Small ○ Moderate •Large ○ Varies ○ Don't know | The systematic review identified 20 studies. 2 studies were RCTs (Bang 1999, Gill 2011) and the remainder were pre-post studies.  4 studies covered community settings (Bang 1999, Ariawan 2006, Carlo 2010, Gill 2011), and the remainder covered hospital settings.  **NRT verses control**  All stillbirths: RR 0.79, 95% CI 0.44 to 1.41; participants=5661; studies=2; I2=67%  7-day neonatal deaths: RR 0.53, 95% CI 0.38 to 0.73; participants=5518; studies=2; I2=0%  28-day neonatal deaths: RR 0.50, 95% CI 0.37 to 0.68; participants=5442; studies=2; I2=0%  perinatal deaths: RR 0.63, 95% CI 0.42 to 0.94; participants=5584; studies=2; I2=68%  The effect was significant for 7-day neonatal mortality , 28-day neonatal mortality and perinatal mortality. Significant heterogeneity was observed in analysis of total stillbirths and perinatal mortality.  **Post-NRT verses pre-NRT**  All stillbirths: RR 0.88, 95% CI 0.83 to 0.94; participants=1 425 540; studies=12; I2=47%  Fresh stillbirths: RR 0.74, 95% CI 0.61 to 0.90; participants=296 819; studies=8; I2=84%  1-day neonatal mortality: RR 0.58, 95% CI 0.42 to 0.82; participants=280 080; studies=6; I2=89%  7-day neonatal mortality: RR 0.82, 95% CI 0.73 to 0.93; participants= 360 383; studies=7; I2=71%  28-day neonatal mortality: RR 0.86, 95% CI 0.65 to 1.13; participants=1 116 463; studies=7; I2=95%  Perinatal mortality: RR 0.82, 95% CI 0.74 to 0.91; participants=1 243 802; studies=6; I2=90%  The changes were significant in all the outcomes; except 28-day neonatal mortality. Heterogeneity was significant in all outcomes except all stillbirths. A funnel plot for all stillbirths showed asymmetry, thereby indicating a publication bias.  **Extracting and analysing data for hospital based studies only gives the following results:**  All studies were Post-NRT verses pre-NRT (no RCTs containing hospital data)  All Stillbirths: RR 0.88, 95% CI 0.82-0.94; participants 1 334 307; 9 studies; I2=48%  Fresh Stillbirths: RR 0.71, 95% CI 0.54-0.93; participants 231 455; 6 studies; I2=88%  1-day neonatal mortality: RR 0.58, 95% CI 0.38-0.90; participants 216 373; 5 studies; I2=89%  7-day neonatal mortality: RR 0.78, 95% CI 0.63-0.97; participants 296 300; 5 studies; I2=79%  28-day mortality: RR 0.89, 95% CI 0.65-1.22; participants 1 090 594; 6 studies; I2=96%  Perinatal mortality: RR 0.78, 95% CI 0.70-0.87; participnts1 178 446; 4 studies; I2=83%  The changes were significant in all the outcomes; except 28-day neonatal mortality. Statistical and clinical heterogeneity was significant in all outcomes except all stillbirths. Hospital based studies only therefore showed even more consistency in direction of effect. | No evidence presented for high-income settings.  Hospital based studies show more consistency in direction of effect. This may be due to more consistent implementation of training and more accurate data acquisition when compared with community settings.  Pre-post studies lack concurrent control group, therefore confounding factors are present.  Lack of consistency of settings, duration of training, varying study designs, and lack of consistent outcomes contribute to substantial heterogeneity.  Despite the heterogeneity of evidence, all analyses show a coniststent treatment effect for this training with potential for many lives saved. |
| Undesirable Effects How substantial are the undesirable anticipated effects? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Large ○ Moderate ○ Small •Trivial ○ Varies ○ Don't know | Nil identified. | Potential for diverting resource away from other public health initiatives in low income settings |
| 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 | **Post-NRT verses pre-NRT (Hospital settings only)**  The quality of evidence for post-NRT verses pre-NRT was very low for all outcomes.  Downgraded for risk of bias, indirectness, and inconsistency. |  |
| 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 | Patients value survival with good neurological outcome (Haywood 2018 e783). It is expected that health care professionals are trained to treat medical emergencies. Standardised NRT training is likely to improve the care provided during cardiac arrest, and thus improve outcomes for patients. | No studies examined the critical outcome of longer term outcomes or good neurological function.  No studies explored the values of key stakeholders or family members. |
| 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 | Yes - no undesirable effects identified. |  |
| Resources required How large are the resource requirements (costs)? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Large costs •Moderate costs ○ Negligible costs and savings ○ Moderate savings ○ Large savings ○ Varies ○ Don't know | There has been no formal cost effectiveness analysis. | All studies covered low-income and middle-income countries only. There may be significant resource implications if manikins are required for training. |
| 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 | No evidence was identified | Costs are likely to vary between different health care settings. |
| 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 | There is no evidence surrounding the actual costs, although the cost-benefit analysis is likely to favour the intervention | The potential for lives saved by health care professional’s participation in these courses outweighs the costs of providing these courses. |
| 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 | Variable evidence. | The associated resources and costs may prohibit NRT training in some health care settings, although some kind of training may be provided at low costs. If advanced NRT courses were to be prioritised, this may come at the expense of other healthcare educational interventions in low resource settings. However this should be balanced against the benefits of improving patient outcomes with potentially very little cost or resource needed. |
| Acceptability Is the intervention acceptable to key stakeholders? | | |
| Judgement | Research evidence | Additional considerations |
| ○ No ○ Probably no • Probably yes ○ Yes ○ Varies ○ Don't know | Whilst there is no evidence surrounding the acceptability for key stakeholders, it is reasonable to expect that it would be an acceptable intervention. | The potential for lives saved by participation in these courses outweighs the costs of candidates attending these courses.  There is an expectation from the public and healthcare institutions that employees will be trained to deal with this important critical condition, so this evidence supports the fact that these courses are fit for purpose. |
| Feasibility Is the intervention feasible to implement? | | |
| Judgement | Research evidence | Additional considerations |
| ○ No ○ Probably no ○ Probably yes • Yes ○ Varies ○ Don't know | This is an intervention that has been well established in healthcare education in low-income and middle-income settings. |  |

# Summary of judgements

|  | **Judgement** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Problem** | No | Probably no | **Probably yes** | **Yes** |  | Varies | Don't know |
| **Desirable Effects** | Trivial | **Small** | Moderate | **Large** |  | Varies | Don't know |
| **Undesirable Effects** | Large | Moderate | Small | **Trivial** |  | 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

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| 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 recommend the provision of accredited NRT life support training for health care professionals who provide advanced life support care for newborns and babies (strong recommendation, very low-certainty evidence).   |  | | --- | | Justification | | * A quarter of global neonatal deaths are due to birth asphyxia. The majority of these deaths occur in low-resource settings and are preventable. * Neonatal resuscitation training (NRT) of birth attendants using mannequins result in improved knowledge and skills needed for resuscitation. * Translation of NRT into improved neonatal outcomes and the effect estimates of improvements are important factors to be re-evaluated and updated. * NRT resulted in significant reduction in stillbirths and early neonatal mortality. However, continuum of care is needed for mortality reduction from day 7 to 28 | |
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| Subgroup considerations |
| * HBB addressed in separate ETD. |

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| Implementation considerations |
| * Published evidence only covers low and middle income settings. * This provides evidence of where the impact of this intervention is particularly beneficial |

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| Monitoring and evaluation |
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| Research priorities |
| * Future studies need to establish the best combination of settings, trainee charecteristics and training frequency to sustain the existing effect on perinatal mortality reduction. * Studies addressing longer term outcomes including favourable neurological outcomes * Studies of courses in high income settings needed as well   **NRT recommendation:**   * + We recommend the provision of accredited NRT life support training for health care professionals who provide advanced life support care for newborns and babies (strong recommendation, very low-certainty evidence).   + Values and preferences statement: In making this recommendation we recognize that the evidence in support of this recommendation comes from studies of very low quality and relate to a range of NRT courses run in different low and middle resource settings around the world over a large time period.   + The provision of accredited NRT training is feasible in low and middle resource settings.   + Knowledge gaps: best combination of settings, trainee charecteristics and training frequency to sustain the existing effect on perinatal mortality reduction. |

**Appendix 3 – HBB EtD**

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| Question | |
| **Is perinatal mortality reduced as a result of a member of the resuscitation team attending a helping babies breathe (HBB) course?** | |
| **Population:** | Newborns in low-income settings requiring in-hospital cardiac arrest resuscitation |
| **Intervention:** | Prior participation of one or more members of the resuscitation team in a Helping Babies Breathe (HBB) intervention |
| **Comparison:** | No such participation |
| **Main outcomes:** | ROSC; Survival to Discharge or 30-day survival; 1 year survival; survival with favourable neurological outcome; stillbirth rate; neonatal mortality; perinatal mortality |
| **Setting:** | **hospital setting** |
| **Perspective:** | Data on the effectiveness of a certified teaching program to improve survival might justify allocation of resources and stimulate further dissemination. |
| **Background:** | In 2015, a UN-inter-agency group for child mortality estimated about 2.6 million neonates die each year in their first month of life, 98% in low-resource settings. The American Academy of Pediatrics initiated the “Helping Baby Breath” program in 2010 as an evidence-based neonatal resuscitation program to save newborns’ lives in resource limited settings. This simulation-based training of healthcare providers in postnatal resuscitation and care was adopted by WHO and implemented in a variety of countries. |
| **Conflict of interests:** | none |

# Assessment

|  |  |  |
| --- | --- | --- |
| Problem Is the problem a priority? | | |
| Judgement | Research evidence | Additional considerations |
| ○ No ○ Probably no ○ Probably yes • Yes ○ Varies ○ Don't know | Neonatal survival rates are globally poor, in particular in low income settings. The potential for number of lives saved is more impactful for newborn than it is with adults. | Attendance of participants on an HBB course comes at a cost - both financial and time - to stakeholders including participants themselves and their institutions. It is therefore important to show whether this participation has any meaningful impact upon patient outcomes.  All studies were from low-income countries. |
| Desirable Effects How substantial are the desirable anticipated effects? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Trivial ○ Small ○ Moderate •Large ○ Varies ○ Don't know | The systematic review by Versantvoort 2020 identified 7 studies. All studies were pre/post studies.  Our search identified one additional study (Innerdal 2020)  All studies were conducted in low-resource settings focusing on the association between HBB and intrapartum related stillbirths and/or neonatal mortality.  **Post-HBB versus pre-HBB**  No meta-analysis was performed  Significant decreases were found after the implementation of HBB in  one of two studies describing **perinatal mortality (all dealths in the first week after birth including intrapartum still births)** (n=25 108, RR 0.75 p<0.001)  one study described a reduction in **perinatal mortality (FSR + 1 day neonatal mortality**) (n=9769, RR 0.27 p<0.0001)  four out of six studies related to **intrapartum still births (fresh still births)** (n=135 489, RR 0.31-0.76)  five out of six studies focusing on **1 day neonatal mortality** (n=121 058, RR 0.12-0.67)  one out of three studies regarding **7 day neonatal mortality** (n=4 390, RR 0.32)  The changes were significant in all outcomes. No changes were seen in the late (28-day neonatal mortality. All included studies were predominantly of moderate quality. There was a single high quality study (Arabi 2018) | No evidence presented for middle or high-income settings.  Pre-post studies lack concurrent control group, therefore confounding factors are present.  Lack of consistency of settings, duration of training, varying study designs, and lack of consistent outcomes contribute to substantial heterogeneity.  Despite the heterogeneity of evidence, all analyses show a coniststent treatment effect for this training with potential for many lives saved. |
| Undesirable Effects How substantial are the undesirable anticipated effects? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Large ○ Moderate ○ Small •Trivial ○ Varies ○ Don't know | Nil identified. | Potential for diverting resource away from other public health initiatives in low income settings.  Teaching material developed in high income countries and supported by charities and international health organisations |
| 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 | HBB training was performed differently in the selected studies eg. duration of training and follow-up was not identical.  Because of clinical and statistical heterogeneity, meta-analysis was not performed.  Downgraded for risk of bias and inconsistency. |  |
| 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 | No studies examined the critical outcome of longer term outcomes or good neurological function.  No studies explored the values of key stakeholders or family members. | Patients value longterm survival with good neurological outcome (Haywood 2018 e783).  It is expected that health care professionals are trained to treat medical emergencies. Additional interventions in the postnatal period that focus on other causes of mortality such as neonatal infections, convulsions, hypothermia and feeding difficulties may be needed to increase overall neonatal survival rate. |
| 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 | Yes - no undesirable effects identified. |  |
| Resources required How large are the resource requirements (costs)? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Large costs ○Moderate costs ○ Negligible costs and savings • Moderate savings ○ Large savings ○ Varies ○ Don't know | There has been no formal cost effectiveness analysis in the included studies.  A separate cost effectiveness analysis was conducted at the Haydom Luteran Hospital in rural Tazania (Vossius 2014), this was based on the Msemo 2013 included in the systematic review  Costs per life saved were USD 233, while they were USD 4.21 per life year gained. Costs for maintaining the program were USD 80 per life saved and USD 1.44 per life year gained. Costs per disease adjusted life year (DALY) averted ranged from International Dollars (ID; a virtual valuta corrected for purchasing power world-wide) 12 to 23, according to how DALYs were calculated. | Cost effectiveness analysis including government owned institutions, urban hospitals and district facilities would be desirable for a more diverse analysis to explore cost-driving factors and predictors of enhanced cost-effectiveness.  All studies covered low-income countries only. |
| 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 | A cost-effectiveness analysis was conducted on the Msemo 2013 study in Tanzania. |  |
| 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 | The potential for lives saved by birth attendents’ participation in these courses outweighs the costs of providing these courses. |  |
| 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 | No evidence identified. | The associated resources and costs may prohibit HBB training in some health care settings. If HBB were to be prioritised, this may come at the expense of other healthcare educational interventions in low resource settings. However this should be balanced against the benefits of improving patient outcomes with potentially very little cost or resource needed. |
| Acceptability Is the intervention acceptable to key stakeholders? | | |
| Judgement | Research evidence | Additional considerations |
| ○ No ○ Probably no • Probably yes ○ Yes ○ Varies ○ Don't know | No evidence identified. | Whilst there is no evidence surrounding the acceptability for key stakeholders, it is reasonable to expect that it would be an acceptable intervention.  The potential for lives saved by participation in HBB outweighs the costs of candidates attending these courses.  There is an expectation from the public and healthcare institutions that employees will be trained to deal with this important critical condition, so this evidence supports the fact that these courses are fit for purpose. |
| Feasibility Is the intervention feasible to implement? | | |
| Judgement | Research evidence | Additional considerations |
| ○ No ○ Probably no ○ Probably yes • Yes ○ Varies ○ Don't know | This is an intervention that has been well established in healthcare education in low-income settings. |  |

# Summary of judgements

|  | **Judgement** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Problem** | No | Probably no | **Probably yes** | **Yes** |  | Varies | Don't know |
| **Desirable Effects** | Trivial | **Small** | Moderate | **Large** |  | Varies | Don't know |
| **Undesirable Effects** | Large | Moderate | Small | **Trivial** |  | 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

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| 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 recommend the provision of Helping Babies Breath support training for healthcare providers who provide advanced life support care for newborns and babies (strong recommendation, very low-certainty evidence).   |  | | --- | | Justification | | * A quarter of global neonatal deaths are due to birth asphyxia. The majority of these deaths occur in low-resource settings and are preventable. * HBB resulted in significant reduction in stillbirths and early neonatal mortality. However, continuum of care is needed for mortality reduction at or beyond 28 days. | |

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| Subgroup considerations |
| * NRT addressed in separate ETD. |

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| Implementation considerations |
| * Published evidence only covers low income settings. * This provides evidence of where the impact of this intervention is particularly beneficial |

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| Research priorities |
| * Future studies need to establish the best combination of settings, trainee charecteristics and training frequency to sustain the existing effect on perinatal mortality reduction. * Further cost-effectiveness analyses * Studies addressing longer term outcomes including favourable neurological outcomes   **HBB recommendation:**   * + We recommend the provision of Helping Babies Breath support training for healthcare providers who provide advanced life support care for newborns and babies (strong recommendation, very low-certainty evidence).   + Values and preferences statement: In making this recommendation we recognize that the evidence in support of this recommendation comes from studies of very low quality and relate to a range of HBB implementations run in different low resource settings around the world over a large time period.   + The provision of HBB training is feasible in low resource settings.   + Knowledge gaps: best combination of settings, trainee charecteristics and training frequency to sustain the existing effect on perinatal mortality reduction. |