|  |  |
| --- | --- |
| Question 2. | |
| **Should thermal mattress vs. thermal mattress be used for preterm neonates born at less than 34 weeks' gestation or equivalent birth weight, immediately after birth?** | |
| **Population:** | Preterm neonates born at less than 34 weeks' gestation or equivalent birth weight, immediately after birth |
| **Intervention:** | Thermal mattress |
| **Comparison:** | No thermal mattress |
| **Main outcomes:** | Primary outcomes   * Survival to hospital discharge (critical) * Rate of normothermia on admission to neonatal unit or postnatal ward (important)   Secondary outcomes:   * Body temperature (and rates of moderate hypothermia, cold stress and hyperthermia) on admission to neonatal unit or before transfer to neonatal unit or postnatal ward, or at times ≤ 1 hour of age (as defined by authors). * Response to resuscitation, e.g., need for assisted ventilation, highest FiO2 * Major morbidity: bronchopulmonary dysplasia (important), intraventricular hemorrhage all grades (important) and severe (critical), necrotising enterocolitis (important), respiratory distress syndrome (surfactant treatment for), late onset sepsis. |
| **Setting:** | Birth environment, in or out of hospital |
| **Perspective:** | Individual patients, their families and providers caring for those patients. |
| **Background:** | Thermal mattresses have been recommended by ILCOR for maintaining normal body temperature in preterm infants after birth, in order to prevent adverse outcomes including death. {Perlman 2015 S204} The systematic review of evidence for this intervention was updated to include studies published since the previous systematic review. Thermal mattresses may provide an external source of heat to augment or replace a radiant warmer. Note that the term ‘thermal mattress’ is used to describe self-heating gel mattresses designed to prevent hypothermia in newborn infants and is used synonymously with ‘exothermic mattress’, a term used in many of the included studies. |
| **Conflict of interests:** | Authors Trevisanuto and de Almeida wrote a recent review article on maintaining normothermia in newborn infants at birth. {Trevisanuto 2018 333}  Author Ramaswamy is an author of a network meta-analysis of methods to maintain normal temperature in infants in the delivery room {Abiramalatha e210775} |

# Assessment

|  |  |  |
| --- | --- | --- |
| Problem Is the problem a priority? | | |
| Judgement | Research evidence | Additional considerations |
| ○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know | A systematic review conducted for ILCOR concluded that "For the critical outcome of mortality, there is evidence from 36 observational studies of increased risk of mortality associated with hypothermia at admission (low-quality evidence but upgraded to moderate-quality evidence due to effect size, dose-effect relationship, and single direction of evidence)". {Perlman 2015 S204} The same systematic review concluded that "There is evidence of a dose effect on mortality, suggesting an increased risk of at least 28% for each 1° below 36.5°C body temperature at admission and dose-dependent effect size". {Perlman 2015 S204} In preterm infants it is common to measure a lower-than-normal body temperature. A systematic review from data collected for the EPICE European collaboration project estimated that hypothermia was common in infants born at hospitals (prevalence range, 32% to 85%) and homes (prevalence range, 11% to 92%), even in tropical environments. In a large cohort of 5697 infants < 32 weeks’ gestation Wilson et al. {Wilson 2016 61} showed that 53.4% of the cohort had a body temperature at admission less than 36.5°C, and 12.9% below 35.5°C. In their model adjusted for pregnancy complications, singleton or multiple pregnancy, antenatal corticosteroids, mode of delivery, gestational age, infant size and sex, and Apgar score <7 at 5 minutes, an admission temperature <35.5°C was associated with increased mortality at postnatal ages 1-6 days, (risk ratio 2.41; 95% CI 1.45-4.00), and 7-28 days (risk ratio 1.79; 1.15-2.78) but not after 28 days of age. {Wilson 2016 61} A recent network meta-analysis examining benefit and safety of interventions to reduce mortality and morbidity from hypothermia reported that various interventions aimed at improving thermoregulation can improve body temperature at admission and are associated with a lower risk of mortality and major brain injury. {Abiramalatha 2021 e210775} |  |
| Desirable Effects How substantial are the desirable anticipated effects? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Trivial ○ Small ○ Moderate ○ Large ● Varies ○ Don't know | Two different types of studies were available for this comparison:  Two randomized controlled trials (RCTs) compared a thermal mattress to no thermal mattress. Infants in both groups received the same cointerventions (such as radiant warmer, hat and plastic bag or wrap) in each arm of the study. {Chawla 2011 780, McCarthy 2013 e135} These two studies were considered to have no serious indirectness with respect to the comparison of thermal mattress to no thermal mattress and yielded low to moderate certainty evidence.  Two RCTs compared a thermal mattress without a plastic barrier (bag or wrap) to a plastic barrier without a thermal mattress. {Mathew 2013 317, Simon 2011 33} These two studies were meta-analysed separately and were considered to have very serious indirectness with respect to the comparison of thermal mattress to no thermal mattress and yielded very low certainty evidence.  Meta analysis of the two pairs of studies is shown separately.  **Primary outcomes:**  In the two studies that compared thermal mattress to no thermal mattress, for the important primary outcome **survival to hospital discharge, clinical benefit or harm cannot be excluded** (relative risk (RR) 1.02 95% confidence intervals (CI) 0.98 to 1.06, absolute risk difference (ARD) 19 more infants per 1000, 95% CI 19 fewer to 56 more per 1000) **low certainty evidence** downgraded for risk of bias and imprecision from two RCTs enrolling 174 participants. {Chawla 2011 780, McCarthy 2013 e135}  There were similar findings in the two studies comparing thermal mattress to a plastic bag or wrap; **clinical benefit or harm cannot be excluded** (RR 0.96 95%CI 0.87 to 1.05, ARD 35 fewer per 1000, 95% CI 114 fewer to 44 more per 1000) **very low certainty evidence,** downgraded for indirectness and imprecision from two RCTs enrolling 77 participants. {Mathew 2013 317, Simon 2011 33}  In a study that compared use of a thermal mattress to no thermal mattress, for the second primary outcome **normothermia on admission** there was **possible clinical harm** (RR 0.53, 95% CI 0.34 to 0.81, ARD 363 fewer infants per 1000 were normothermic on admission with use of a thermal mattress, 95% CI 147 fewer to 509 fewer per 1000) **moderate certainty evidence**, downgraded for imprecision from 1 RCT enrolling 72 participants. {McCarthy 2013 e135} This study compared thermal mattress with no thermal mattress.   | **Primary outcomes** | **№ of participants (studies)** | **Certainty of the evidence (GRADE)** | **Relative effect (95% CI)** | **Anticipated absolute effects\* (95% CI)** | | | --- | --- | --- | --- | --- | --- | | **Risk with thermal mattress** | **Risk difference with thermal mattress** | | Survival – control group no thermal mattress | 174 (2 RCTs)1,2 | ⨁⨁◯◯ Lowa,b | **RR 1.02** (0.98 to 1.06) | 929 per 1,000 | **19 more per 1,000** (19 fewer to 56 more) | | Survival – control group plastic bag or wrap | 77 (2 RCTs)3,4 | ⨁◯◯◯ Very lowa,c,d | **RR 0.96** (0.87 to 1.05) | 875 per 1,000 | **35 fewer per 1,000** (114 fewer to 44 more) | | Normothermia on admission (36.5-37.5ºC)  – control group no thermal mattress | 72 (1 RCT)2 | ⨁⨁⨁◯ Moderatea,e | **RR 0.53** (0.34 to 0.81) | 771 per 1,000 | **363 fewer per 1,000** (509 fewer to 147 fewer) |  1. {Chawla 2011 780} 2. {McCarthy 2013 e135} 3. {Simon 2011 33} 4. {McCarthy 2013 e135} 5. Optimal information size (OIS) criterion not satisfied 6. One included study that contributed a large proportion of the participants was at high risk of bias 7. Study(ies) compared a thermal mattress with use of a plastic bag or wrap 8. Both studies were at low risk of bias 9. The only included study was at low risk of bias   **Secondary Outcomes**  For **mean body temperature on admission**, there was **possible clinical benefit.** The mean difference (MD) in temperature was 0.46°C higher in the thermal mattress group (95% CI 0.22 to 0.69°C) **low certainty evidence,** downgraded for risk of bias and imprecision from two RCTs enrolling 174 participants that compared thermal mattress to no thermal mattress {Chawla 2011 780, McCarthy 2013 e135}  However, the two studies that compared thermal mattress with a plastic bag or wrap found a minimal MD in temperature: The mean temperature was 0.09°C higher in the thermal mattress group 95% CI 0.59 lower to 0.77°C higher), **low certainty evidence** downgraded for indirectness and imprecision from two RCTs enrolling 77 participants. {Mathew 2013 317, Simon 2011 33} This lack of improvement in temperature in most infants, which may be because two measures to maintain normal temperature were being compared with each other, should be taken into account when considering other outcome data for these studies.  For **hypothermia < 36.5°C on admission to the NICU, clinical benefit or harm cannot be excluded** RR 2.58 (95% CI 0.47 to 14.26), **moderate certainty evidence** downgraded for indirectness and imprecision from one RCT enrolling 49 participants. {McCarthy 2013 e135}  For **IVH > Grade 2, clinical benefit or harm cannot be excluded** (RR 4.62, 95% CI 0.56 to 38.19, ARD 74 more per 1000 infants, 95% CI 9 fewer to 759 more), **very low certainty evidence** downgraded for risk of bias and imprecision from one RCT enrolling 102 participants that compared thermal mattress with no thermal mattress. {Chawla 2011 780} and (RR 0.94, 95% CI 0.24 to 3.57, ARD 118 fewer infants per 1000, 95% CI 219 fewer to 75 more infants per 1000), **very low certainty evidence** downgraded for indirectness and imprecision from two RCTs enrolling 77 participants that compared thermal mattress to plastic bag or wrap. {Mathew 2013 317, Simon 2011 33}  For **NEC**, **clinical benefit or harm cannot be excluded** (RR0.642, 95% CI 0.33 to 1.23, ARD 118 fewer infants per 1000, 95% CI 219 fewer to 75 more infants per 1000), **very low certainty evidence** downgraded for risk of bias an imprecision from one RCT enrolling 102 participants that compared thermal mattress to no thermal mattress {Chawla 2011 780} and (RR 1.83, 95% CI 0.58 to 5.76, ARD 83 more infants per 1000, 95% CI 42 fewer to 476 more per 1000), **very low certainty evidence** downgraded for indirectness and imprecision from two RCTs enrolling 77 participants that compared thermal mattress with plastic bag or wrap. {Mathew 2013 317, Simon 2011 33} and  For **BPD, clinical benefit or harm cannot be excluded** RR 1.59(95% CI 0.94 to 2.66, ARD 119 more infants per 1000, 95% CI 12 fewer to 336 more infants per 1000), **low certainty evidence** downgraded for risk of bias and imprecision from two RCTs enrolling 174 participants that compared thermal mattress to no thermal mattress {Chawla 2011 780, McCarthy 2013 e135} and RR 0.75,( 95% CI 0.40 to 1.3), very low certainty evidence downgraded for indirectness and imprecision from one RCT enrolling 36 participants that compared thermal mattress with plastic bag or wrap. {Simon 2011 33}  For the outcome **late onset sepsis** **clinical benefit or harm cannot be excluded** (RR 0.90 95% CI 0.37 to 2.19, ARD 27 fewer infants per 1000, (95% CI 167 fewer to 316 more per 1000), **very low certainty evidence** downgraded for risk of bias and imprecision from one RCT enrolling 102 participants that compared thermal mattress to no thermal mattress {Chawla 2011 780}  For the other secondary outcomes intubation in the delivery room and serious haemorrhage (e.g., pulmonary, subgaleal) there were no data.   | **Secondary outcomes** | **№ of participants (studies)** | **Certainty of the evidence (GRADE)** | **Relative effect (95% CI)** | **Anticipated absolute effects\* (95% CI)** | | | --- | --- | --- | --- | --- | --- | | **Risk with thermal mattress** | **Risk difference with thermal mattress** | | Mean body temperature –control group no thermal mattress | 174 (2 RCTs)1,2 | ⨁⨁◯◯ Lowa,b | Not applicable | The mean mean body temperature was **36.3**°C | MD **0.46°C higher** (0.22 higher to 0.69 higher) | | Mean body temperature – control group plastic bag or wrap | 77 (2 RCTs)3,4 | ⨁◯◯◯ Very lowb,c,d | Not applicable | The mean mean body temperature Simon and Mathew was **36.1**°C | MD **0.09°C higher** (0.59 lower to 0.77 higher) | | Admission temp <36.5ºC (control group no thermal mattress) | 36 (1 RCT)2 | ⨁⨁⨁◯ Moderateb,e | **RR 2.58** (0.47 to 14.26) | 684 per 1,000 | **1,081 more per 1,000** (363 fewer to 9,073 more) | | IVH > Grade 2 (control group no thermal mattress) | 102 (1 RCT)1 | ⨁◯◯◯ Very lowb,f,g | **RR 4.62** (0.56 to 38.19) | 20 per 1,000 | **74 more per 1,000** (9 fewer to 759 more) |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | | IVH > Grade 2 (control group plastic bag or wrap) | 77 (2 RCTs) 3,4 | ⨁◯◯◯ Very lowb,c,d | **RR 0.64** (0.33 to 1.23) | 327 per 1,000 | **118 fewer per 1,000** (219 fewer to 75 more) |  |  |  |  |  |  |  | | --- | --- | --- | --- | --- | --- | | NEC  (control group no thermal mattress) | 102 (1 RCT)1 | ⨁⨁◯◯ Lowa,b | **RR 0.64** (0.33 to 1.23) | 327 per 1,000 | **118 fewer per 1,000** (219 fewer to 75 more) | | NEC – studies comparing with plastic bag or wrap | 77 (2 RCTs)3,4 | ⨁◯◯◯ Very lowb,d,f | **RR 1.83** (0.58 to 5.76) | 100 per 1,000 | **83 more per 1,000** (42 fewer to 476 more) | | BPD (author defined) – studies comparing with no thermal mattress | 174 (2 RCTs)1,2 | ⨁⨁◯◯ Lowa,b | **RR 1.59** (0.94 to 2.66) | 202 per 1,000 | **119 more per 1,000** (12 fewer to 336 more) | | BPD (author defined) (control group plastic bag or wrap) | 36 (1 RCT)3 | ⨁◯◯◯ Very lowb,d,f | **RR 0.75** (0.40 to 1.37) | 632 per 1,000 | **158 fewer per 1,000** (379 fewer to 234 more) | | Late onset sepsis  (control group no thermal mattress) | 102 (1 RCT)1 | ⨁◯◯◯ Very lowb,f,g | **RR 0.90** (0.37 to 2.19) | 265 per 1,000 | **27 fewer per 1,000** (167 fewer to 316 more) |   1 {Chawla 2011 780}  2 {McCarthy 2013 e135}   1. 3 {Simon 2011 33} 2. 4 {Mathew 2013 317} 3. One included study that contributed a large proportion of the participants was at high risk of bias 4. OIS criterion not satisfied 5. Both studies were at low risk of bias 6. Study(ies) compared a thermal mattress with use of a plastic bag or wrap 7. The only included study was at low risk of bias 8. Low event rate and wide CIs   For beneficial outcomes, the observational studies did not change the outcomes of the review, so they are not described further.  **The rationale for considering the effect varies** is that there was moderate certainty evidence for a small decreasein the number of normothermic participants with use of a thermal mattress compared to no thermal mattress, and yet very low certainty evidence for a small improvement in mean body temperature. From studies comparing thermal mattress to a plastic bag or wrap, there was minimal benefit for temperature. | We do not know the effect size in the presence of additional or fewer co-interventions. Infants in both the thermal mattress and no thermal mattress groups were equally exposed to additional thermoregulation measures, for example radiant warmer and plastic bag for infants < 28 weeks’ gestation. |
| Undesirable Effects How substantial are the undesirable anticipated effects? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Large ○ Moderate ● Small ○ Trivial ○ Varies ○ Don't know | For the important adverse outcome **hyperthermia** (temp on admission >37.5°C) there was evidence of **possible harm** (RR 2.77 95% CI 1.24 to 6.17, ARD 126 more infants were hyperthermic per 1000, 95% CI 17 more to 369 more) **low certainty evidence**, downgraded for risk of bias and imprecision from two RCTs enrolling 174 participants that compared thermal mattress to no thermal mattress {Chawla 2011 780, McCarthy 2013 e135}. In RCTs comparing a thermal mattress without a plastic barrier (bag or wrap) to a plastic barrier without a thermal mattress, one reported this outcome; (RR 12.29 95% CI 0.02 to 77700.79) **very low certainty evidence** downgraded for indirectness and imprecision from one RCT enrolling 36 participants. {Simon 2011 33}  The systematic review also found 5 observational studies that examined use of a thermal mattress combined with use of a plastic bag or wrap compared to use of a plastic bag or wrap alone (no thermal mattress) in a total of 1027 infants. {Ibrahim 2010 795, Lewis 2011 160, McCarthy 2011 1534, Pinheiro 2011 357, Singh 2010 45}  For the important adverse outcome of **hyperthermia** on admission the observational studies that reported this outcome also suggested **evidence of possible harm** (RR 3.44 95% CI 1.91 to 6.20, ARD 113 more infants were hyperthermic per 1,000, 95% CI from 42 more to 241 more infants per 1000), **moderate certainty evidence** downgraded for risk of bias from 4 observational studies including 703 infants. {Ibrahim 2010 795, McCarthy 2011 1534, Pinheiro 2011 357, Singh 2010 45}   | **Outcomes** | **№ of participants (studies) Follow-up** | **Certainty of the evidence (GRADE)** | **Relative effect (95% CI)** | **Anticipated absolute effects\* (95% CI)** | | | --- | --- | --- | --- | --- | --- | | **Risk with thermal mattress** | **Risk difference with thermal mattress** | | Temperature > 37.5°C | 174 (2 RCTs)1,2 | ⨁⨁◯◯ Lowa,b | **RR 2.77** (1.24 to 6.17) | 71 per 1,000 | **126 more per 1,000** (17 more to 369 more) | | Temperature >37.5°C Simon | 36 (1 RCT)3 | ⨁◯◯◯ Very lowb,c,d | **RR 12.29** (0.02 to 7700.79) | 0 per 1,000 | **0 fewer per 1,000** (0 fewer to 0 fewer) |   1 {Chawla 2011 780}  2 {McCarthy 2013 e135}  3 {Simon 2011 33}   1. One included study that contributed a large proportion of the participants was at high risk of bias 2. OIS criterion not satisfied 3. Study(ies) compared a thermal mattress with use of a plastic bag or wrap 4. Low event rate and wide CIs   **The rationale for considering the effect small** was because the effect size was considered to be possibly clinically important. The outcome of temperature >38°C was considered more likely to cause harm, but it was not reported by most studies. | Note that the McCarthy 2013 study stopped recruitment after enrolling 58 infants following a pre-planned review by an external data safety monitoring committee (DSMC). {McCarthy 2013 e135} The DSMC identified that a significant difference between groups for the primary outcome had been determined. It is not clear if the study was stopped early mainly for concerns about efficacy or concerns about safety.  In both the McCarthy 2013 and Chawla 2011 studies, infants in both the thermal mattress and control groups were equally exposed to additional thermoregulation measures, for example radiant warmer. Some {Chawla 2011 780} or all {McCarthy 2013 e135} infants in each group were managed with a plastic bag. These additional measures may have affected body temperatures.  The effect size (for benefit or harm) may be different in the presence of additional or fewer co-interventions, and caution is warranted to ensure that the target of normal temperature is being met.  To underscore the importance for careful monitoring when a thermal mattress is used in conjunction with a radiant warmer the British Association of Perinatal Medicine (BAPM) has warned users to be aware of the risk of hyperthermia and skin burns. ( [Safety Issue - Transwarmer Mattresses | British Association of Perinatal Medicine (bapm.org)](https://www.bapm.org/articles/44-safety-issue-transwarmer-mattresses) ww.bapm.org/articles/44-safety-issue-transwarmer-mattresses. Manufacturer’s instructions also advise against the use of any other heat source while using the Transwarmer®mattress. <https://www.coopersurgical.com/product-resources/ef950206-9f7e-4dcf-a3d7-cb79379ed189_TransWarmer-Infant-Transport-Matterss-Instructions-for-Use.pdf> |
| 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 | The certainty of evidence for the two primary outcomes was very low to moderate and for secondary outcomes was very low to moderate. |  |
| 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 | The outcome of survival to hospital discharge (or its converse, mortality) have been judged by both care givers and parents to be the highest ranked outcomes of importance. {Strand 2020 F328, Webbe 2020 425} | Cold stress and hypothermia are common particularly among preterm infants and has been associated with increased mortality and morbidity {de Almeida 2014 271, Perlman 2015 S204} |
| 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 | The review found evidence of possible clinical benefit for mean temperature on admission to the NICU, however there was an increased rate of hyperthermia. | Recent observational studies have confirmed an association between hyperthermia on admission and adverse outcomes. {Brophy 2022 1706, Wilson 2016 61}  A thermal mattress might be useful to prevent hypothermia when other forms of thermal support (radiant warmer, plastic bag/wrap) are not available in out of hospital settings. |
| 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 | Among included studies, estimates of cost were $46.50 (US) {McCarthy 2013 e135}; $14.52 (US ) {Simon 2011 33} and $17(US) per unit. {Lewis 2011 160} | The cost of a thermal mattress differs between brands. Regardless, the cost may make the device unaffordable in middle or low resource settings.  The devices are marketed as single use. |
| 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 | Two of the included RCTs and one observational study provided an estimate of cost of a thermal mattress. There may be variation between brands and locations. |  |
| 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 | No studies investigated cost-effectiveness. | Single use thermal mattresses are a relatively expensive intervention compared with some other interventions to maintain normal temperature in the delivery room, but they may be cost-effective where devices such as radiant warmers are unavailable (such as for out-of-hospital births). Accurate estimates of cost effectiveness would need to include studies large enough to estimate effects on survival and major neonatal morbidities. All included studies were well below the OIS for these outcomes. |
| 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 cost of providing a thermal mattress is likely to be unaffordable in low-income and some middle-income countries. |  |
| Acceptability Is the intervention acceptable to key stakeholders? | | |
| Judgement | Research evidence | Additional considerations |
| ○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know | There were no data available from studies in this review. However, using a thermal mattress to promote thermoregulation is already standard care in some high resource settings described in publications reporting quality improvement activities. {Aley-Raz 2020 476, Billimoria 2013 455, Croop 2020 530, Frazer 2018 520, Harer 2017 1242, Harriman 2018 462, Lee 2008 754, Manani 2013 8, Russo 2014 31055} | Many neonatal retrieval/transport services use thermal mattresses to maintain normal temperature during inter-hospital transport. {L'Herault 2001 210, LeBlanc 1984 593} |
| Feasibility Is the intervention feasible to implement? | | |
| Judgement | Research evidence | Additional considerations |
| ○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know | Using a thermal mattress to promote thermoregulation is already standard care in some high resource settings described in publications describing quality improvement activities. {Aley-Raz 2020 476, Billimoria 2013 455, Croop 2020 530, Frazer 2018 520, Harer 2017 1242, Harriman 2018 462, Lee 2008 754, Manani 2013 8, Russo 2014 31055} | In one study using a thermal mattress was described as technically easy to use. {McCarthy 2013 e135}  Where a radiant warmer is not available a thermal mattress might be a useful alternative. |

# 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

|  |
| --- |
| Recommendation |
| In preterm infants, born at less than 34 weeks’ gestation, where hypothermia on admission is identified as a problem, it is reasonable to consider addition of a thermal mattress, but there is a risk of hyperthermia. (Conditional recommendation, low certainty evidence). |

|  |
| --- |
| Justification |
| The effect of a thermal mattress varied between studies. There was an increased risk of hyperthermia on admission. The combined studies did not meet the optimal information size to confirm other benefits or harms. |

|  |
| --- |
| Subgroup considerations |
| Subgroups identified a priori for this review were gestational age (< 28 weeks’ compared with ≥ 28 weeks’ gestation, inborn compared with outborn births, high resource compared with low resource settings, and the effect of early or delayed cord clamping   * Outcomes for the subgroup gestational age < 28 weeks’ compared with ≥28 weeks’ gestation were reported in two studies.   Two studies reported data for infants <28 weeks' gestation and found conflicting results: Chawla et al found no difference in admission temperatures in infants <28 weeks' gestation exposed to a thermal mattress vs no thermal mattress, whereas McCarthy et al found larger increases in body temperature in infants <28 weeks' gestation and no difference for those ≥ 28 weeks' gestation. McCarthy et al found more hyperthermic infants in the lower gestational age group. {Chawla 2011 780, McCarthy 2013 e135}  One study reported data for 21 infants <750 g compared with infants ≥750 g. The mean (±SD) admission temperature was significantly lower in the group of infants <750 grams exposed to a thermal mattress compared with the no thermal mattress group 35 (±1.3)ºC and 36 (±0.4)ºC respectively. {Mathew 2013 317}   * For inborn compared with outborn births, there were no data. * All studies reported outcomes from births in high resource settings. * No studies reported the effect of umbilical cord clamping on outcomes. |

|  |
| --- |
| Implementation considerations |
| Thermal mattresses are relatively simple to use and require only a few minutes of preparation time to reach effective temperatures. Care needs to be taken to use a barrier layer of towelling or sheeting between the mattress and the infant in order to prevent skin burns and hyperthermia, because they can reach temperatures of at least 42°C.{McCarthy 2013 e135} When using a thermal mattress frequent temperature monitoring is recommended (Good practice statement). |

|  |
| --- |
| Monitoring and evaluation |
| Preterm neonates' temperatures on admission to neonatal intensive care units should continue to be monitored as important indicators of quality of care. {Perlman 2015 S204} |

|  |
| --- |
| Research priorities |
| * Studies are needed comparing specific bundles of interventions to maintain normal temperature vs other specific bundles. * What is the balance of risks and benefits when using a thermal mattress for preterm infants in the birthing room when other combinations of thermoregulation interventions (ambient temperature, plastic bag or wrap, thermal mattress, cap, servo-controlled radiant warmer) are applied? * Cost effectiveness of thermal mattresses. * Safety and effectiveness for various subgroups. * Role of thermal mattresses during delayed cord clamping. * Role of thermal mattresses in pre-hospital settings. |

|  |  |
| --- | --- |
| Question 3. | |
| **Should a plastic bag or wrap vs. standard care be used for preterm infants < 34 weeks’ gestation or equivalent birth weight, immediately after birth ?** | |
| **Population:** | Preterm infants < 34 weeks’ gestation or equivalent birth weight, immediately after birth |
| **Intervention:** | Plastic bag or wrap |
| **Comparison:** | Standard care |
| **Main outcomes:** | Primary outcomes   * Survival to hospital discharge (critical) * Rate of normothermia on admission to neonatal unit or postnatal ward (important)   Secondary outcomes:   * Body temperature (and rates of moderate hypothermia, cold stress and hyperthermia) on admission to neonatal unit or before transfer to neonatal unit or postnatal ward, or at times ≤ 1 hour of age (as defined by authors). * Response to resuscitation, e.g., need for assisted ventilation, highest FiO2 * Major morbidity: bronchopulmonary dysplasia (important), intraventricular hemorrhage all grades (important) and severe (critical), necrotising enterocolitis (important), respiratory distress syndrome (surfactant treatment for), late onset sepsis. |
| **Setting:** | Birth environment, in or out of hospital |
| **Perspective:** | Individual patients, their families and providers caring for those patients. |
| **Background:** | Plastic bags or wraps have been recommended by ILCOR for maintaining normal body temperature in preterm infants after birth, in order to prevent adverse outcomes including death. {Perlman 2015 S204} The systematic review of evidence for this intervention was updated to include studies published since the previous systematic review. Plastic bags or wraps may prevent heat loss by reducing evaporative or convective heat losses. |
| **Conflict of interests:** | Authors Ramaswamy and Trevisanuto were co-authors of a previous network metaanalysis of delivery room interventions for hypothermia in neonates. {Abiramalatha 2021 e210775} Author Trevisanuto was author of a study included in the systematic review, but was excluded from decisions about inclusion or risk of bias assessment for this study. {Trevisanuto 2010 914} |

# Assessment

|  |  |  |
| --- | --- | --- |
| Problem Is the problem a priority? | | |
| Judgement | Research evidence | Additional considerations |
| ○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know | A systematic review conducted for ILCOR concluded that "F*or the critical outcome of mortality, there is evidence from 36 observational studies of increased risk of mortality associated with hypothermia at admission (low-quality evidence but upgraded to moderate-quality evidence due to effect size, dose-effect relationship, and single direction of evidence)*". {Perlman 2015 S204} The same systematic review concluded that "*There is evidence of a dose effect on mortality, suggesting an increased risk of at least 28% for each 1° below 36.5°C body temperature at admission and dose-dependent effect size*").  In preterm infants it is common to measure body temperatures in the cold stress or hypothermic range. A systematic review estimated that hypothermia was common in infants born at hospitals (prevalence range, 32% to 85%) and homes (prevalence range, 11% to 92%), even in tropical environments. In a large cohort of 5697 infants < 32 weeks’ gestation, 53.4% of the cohort had a body temperature at admission less than 36.5°C, and 12.9% below 35.5°C. {Wilson 2016 61} After adjustment for pregnancy complications, singleton or multiple pregnancy, antenatal corticosteroids, mode of delivery, gestational age, infant size and sex, and Apgar score <7 at 5 minutes, an admission temperature <35.5°C was associated with increased mortality at postnatal ages 1-6 days, (risk ratio 2.41; 95% CI 1.45-4.00), and 7-28 days (risk ratio 1.79; 1.15-2.78) but not after 28 days of age. )  A recent network meta-analysis examining benefit and safety of interventions to reduce mortality and morbidity from hypothermia reported that various interventions aimed at improving thermoregulation can improve body temperature at admission and are associated with a lower risk of mortality and major brain injury. {Abiramalatha 2021 e210775} |  |
| Desirable Effects How substantial are the desirable anticipated effects? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know | This systematic review found that for a **plastic bag or wrap when compared to standard care** for preterm infants (<34 weeks' gestation):  For the critical primary outcome of **survival to hospital discharge,** there was **probable clinical benefit** (relative risk (RR) 1.05 95% CI 1.00 to 1.10), **high certainty evidence** from 11 RCTs enrolling 1419 infants. {Ahmed 2013 169, Chantaroj 2011 S32, Farhadi 2012 19, Knobel 2005 304, Reilly 2015 262, Reilly 2019 37, Smith 2013 235, Trevisanuto 2010 914, Vohra 1999 547, Vohra 2004 750}  For the important primary outcome of **normothermia on admission** to a neonatal unit, there was **possible clinical benefit** (RR 2.86 95% CI 1.66 to 4.91), **low certainty evidence** downgraded for risk of bias and imprecision from 5 RCTs enrolling 449 infants. {Chantaroj 2011 S32, Knobel 2005 304, Nimbalkar 2019 122, Rohana 2011 468, Trevisanuto 2010 914}   | **Outcomes** | **№ of participants (studies) Follow-up** | **Certainty of the evidence (GRADE)** | **Relative effect (95% CI)** | **Anticipated absolute effects\* (95% CI)** | | | --- | --- | --- | --- | --- | --- | | **Risk with standard care** | **Risk difference with a plastic bag or wrap** | | Survival | 1419 (11 RCTs)1-11 | ⨁⨁⨁⨁ Higha,b,c,d | **RR 1.05** (1.00 to 1.10) | Study population | | | 816 per 1,000 | **41 more per 1,000** (0 fewer to 82 more) | | Normothermia | 449 (5 RCTs)2,4,5,9,12 | ⨁⨁◯◯ Lowa,d,e,f | **RR 2.86** (1.66 to 4.91) | Study population | | | 128 per 1,000 | **238 more per 1,000** (85 more to 501 more) |  1. {Ahmed 2013 169} 2. {Chantaroj 2011 S32} 3. {Farhadi 2012 19} 4. {Knobel 2005 304} 5. {Nimbalkar 2019 122} 6. {Reilly 2015 262} 7. {Reilly 2019 37} 8. {Smith 2013 235} 9. {Trevisanuto 2010 914} 10. {Vohra 1999 547} 11. {Vohra 2004 750} 12. {Rohana 2011 468} 13. The PICO was similar in the included trials 14. Narrow 95% confidence interval with optimal information size criterion (OIS) satisfied for sample size and event rates as calculated for relative risk reduction of 25% 15. For this outcome, most of the trials with higher weightage contributing to the meta-analysis had a low risk of bias or some concerns. 16. The test for heterogeneity was not significant 17. For this outcome, with a control group event rate of 12.8%, for a RRR of 25% an approximate sample size of 2500 is required. Hence the OIS criterion was not satisfied 18. For this outcome, most of the trials with higher weightage in the meta-analysis had a high overall risk of bias   Among important secondary outcomes  For **mean body temperature on admission** to a neonatal unit, **there was possible clinical benefit .** Mean temperaturemeasured by axilla was 0.65°C higher (95% CI 0.44 to 0.86 °C ), and measured by the rectum was 0.77 °C (95% CI 0.44 to 0.86 °C ), **low certainty evidence** downgraded due to serious risk of bias and possible publication bias from 12 RCTs enrolling 821 infants. {Chantaroj 2011 S32, Farhadi 2012 19, Knobel 2005 304, Nimbalkar 2019 122, Reilly 2015 262, Reilly 2019 37, Rohana 2011 468, Smith 2013 235, Trevisanuto 2010 914, Vohra 1999 547, Vohra 2004 750}  For **any hypothermia < 36.5°C on admission** to a neonatal unit **there was probable clinical benefit** (RR 0.64, 95% CI 0.50 to 0.82), **moderate certainty evidence** downgraded for risk of bias from 6 RCTs enrolling 489 infants. {Chantaroj 2011 S32, Farhadi 2012 19, Knobel 2005 304, Nimbalkar 2019 122, Rohana 2011 468, Trevisanuto 2010 914}  For **moderate hypothermia on admission** to a neonatal unit there was **possible clinical benefit** (RR 0.40 ,95% CI 0.19 to 0.81), **very low certainty evidence** downgraded for risk of bias, indirectness and imprecision from 4 RCTs enrolling 1055 infants. {Ahmed 2013 169, Bhavsar 2015 23, Reilly 2015 262, Rohana 2011 468}  For **IVH >grade 2, clinical benefit or harm could not be excluded** (RR 0.99 95% CI 0.69 to 1.41), **moderate certainty evidence** downgraded for imprecision from 4 RCTs enrolling 972 infants. {Knobel 2005 304, Reilly 2015 262, Reilly 2019 37, Rohana 2011 468}  For **NEC, clinical benefit or harm could not be excluded** (RR 0.95, 95%CI 0.61 to 1.50), **low certainty evidence** downgraded for indirectness, and imprecision from 3 RCTs enrolling 935 infants. {Reilly 2015 262, Reilly 2019 37, Rohana 2011 468}  For **late onset sepsis**, **clinical benefit or harm could not be excluded** (RR 0.92, 95%CI 0.76 to 1.11), **low certainty evidence** downgraded for inconsistency and imprecision from 3 RCTs enrolling 853 infants. {Reilly 2015 262, Reilly 2019 37, Smith 2013 235}  For **intubation in the delivery room,** **benefit or harm could not be excluded** (RR 1.02, 95%CI 0.82 to 1.26), **low certainty evidence** downgraded for risk of bias and imprecision from 3 RCTs enrolling 174 infants. {Rohana 2011 468, Trevisanuto 2010 914}   | **Outcomes** | **№ of participants (studies) Follow-up** | **Certainty of the evidence (GRADE)** | **Relative effect (95% CI)** | **Anticipated absolute effects\* (95% CI)** | | | --- | --- | --- | --- | --- | --- | | **Risk with standard care** | **Risk difference with a plastic bag or wrap** | | Mean body temperature (Axillary) | 821 (12 RCTs) | ⨁⨁◯◯ Lowa,b,c,d | n/a | The mean body temperature (axillary) was **35.52** °C | MD **0.65 °C higher** (0.44 higher to 0.86 higher) | | Mean body temperature (Rectal) | 348 (7 RCTs) | ⨁⨁◯◯ Lowa,d | n/a | The mean body temperature (Rectal) was **35.86** °C | MD **0.77 °C higher** (0.5 higher to 1.04 higher) | | Hypothermia < 36.5 degree °C | 489 (6 RCTs)1,2,3,4,5,6 | ⨁⨁⨁◯ Moderateb,e,f,g | **RR 0.64** (0.50 to 0.82) | 870 per 1,000 | **313 fewer per 1,000** (435 fewer to 157 fewer) | | IVH any grade | 836 (2 RCTs)7,8 | ⨁⨁⨁◯ Moderatef,h,i,j | **RR 0.91** (0.72 to 1.14) | 372 per 1,000 | **34 fewer per 1,000** (104 fewer to 52 more) | | IVH > grade 2 | 972 (4 RCTs)1,6,7,9 | ⨁⨁⨁◯ Moderatec,f,h,i | **RR 0.99** (0.69 to 1.41) | 113 per 1,000 | **1 fewer per 1,000** (35 fewer to 46 more) | | NEC | 935 (3 RCTs)6,7,9 | ⨁⨁◯◯ Lowc,h,i,k | **RR 0.95** (0.61 to 1.50) | 77 per 1,000 | **4 fewer per 1,000** (30 fewer to 38 more) | | Late onset neonatal sepsis | 853 (3 RCTs)7,8,9 | ⨁⨁◯◯ Lowf,h,i,j | **RR 0.92** (0.76 to 1.11) | 332 per 1,000 | **27 fewer per 1,000** (80 fewer to 36 more) | | Intubation in the delivery room | 174 (2 RCTs)2,6 | ⨁⨁◯◯ Lowe,f,i,j | **RR 1.02** (0.82 to 1.26) | 511 per 1,000 | **10 more per 1,000** (92 fewer to 133 more) |  1. {Knobel 2005 304} 2. {Trevisanuto 2010 914} 3. {Chantaroj 2011 S32} 4. {Farhadi 2012 19} 5. {Nimbalkar 2019 122} 6. {Rohana 2011 468} 7. {Reilly 2015 262} 8. {Smith 2013 235} 9. {Reilly 2019 37} 10. Overall, most of the trials had similar weightage in the meta-analysis. Amongst them there were a significant number of trials which either had some concerns or a high risk of overall bias 11. Though I2 was high, this was attributed to difference between small and large magnitude of effect estimate 12. The 95% confidence interval did not cross the line of no effect and OIS criterion satisfied 13. Egger's test showed a possibility of publication bias with a p-value of 0.002 14. For this outcome, most of the trials with higher weightage in the meta-analysis had a high risk of overall bias 15. The PICO was similar in the included trials 16. 95% CI did not cross the line of no effect; OIS criterion satisfied for a control group event rate of 87% for RRR of 25% 17. For this outcome, the trial with the highest weightage had low risk of overall bias 18. The test for heterogeneity was not significant 19. The 95% CI cross the line of no effect 20. Two studies did not specified the staging of NEC and hence indirectness related to the outcome was adjudged.   The reason to consider the **overall effect size as moderate** was because there was possible or probable benefit for both primary outcomes and three secondary outcomes. | We do not know the effect size in the presence of additional co-interventions.    Infants in these studies were generally stabilized in the delivery room under radiant warmers set to manual mode.    A majority of studies reported axillary temperatures. A small number of studies only measured rectal temperatures. Axillary temperatures are reported as lower than rectal temperature. {Cho 2021 180, McCarthy 2021 509} This difference could be important when comparing results between studies. |
| Undesirable Effects How substantial are the undesirable anticipated effects? | | |
| Judgement | Research evidence | Additional considerations |
| ○ Large ● Moderate ○ Small ○ Trivial ○ Varies ○ Don't know | For **hyperthermia (> 38.0°C** ) there was **probable harm** (RR 3.73 95%CI 1.81 to 7.69), **moderate certainty evidence** downgraded for risk of bias from 12 RCTs enrolling 1652 infants.) {Bhavsar 2015 23, Farhadi 2012 19, Gathwala 2010 24, Knobel 2005 304, Lyu 2015 e150277, Nimbalkar 2019 122, Reilly 2015 262, Rohana 2011 468, Smith 2013 235, Trevisanuto 2010 914, Vohra 2004 750}   | **Outcomes** | **№ of participants (studies) Follow-up** | **Certainty of the evidence (GRADE)** | **Relative effect (95% CI)** | **Anticipated absolute effects\* (95% CI)** | | | --- | --- | --- | --- | --- | --- | | **Risk with standard care** | **Risk difference with a plastic bag or wrap** | | Hyperthermia | 1652 (12 RCTs)1,10,11,12,2,3,4,5,6,7,8,9 | ⨁⨁⨁◯ Moderatea,b,c,d | **RR 3.73** (1.81 to 7.69) | 11 per 1,000 | **29 more per 1,000** (9 more to 72 more) |  1. {Bhavsar 2015 23} 2. {Farhadi 2012 19} 3. {Gathwala 2010 24} 4. {Knobel 2005 304} 5. {Lyu 2015 e150277} 6. {Nimbalkar 2019 122} 7. {Reilly 2015 262} 8. {Rohana 2011 468} 9. {Smith 2013 235} 10. {Trevisanuto 2010 914} 11. {Vohra 2004 750} 12. There were two trials that had contributed significant weightage in the meta-analysis. While one had some concerns, the other had a high risk of overall bias. 13. The test for heterogeneity was not significant 14. The PICO was similar across trials 15. Though the event rate is low, this is a scenario where the presence of large sample size may override the OIS criterion   **The reason to consider the effect as moderate** is because hyperthermia has been associated with adverse outcomes. | Measures to prevent hypothermia may increase the risk for hyperthermia. Preterm neonates may have deficient thermoregulation and their capacity to maintain normothermia is limited.  The risk of hyperthermia was identified in the 2015 COSTR stated that; "*A by-product of [these] interventions to prevent hypothermia is more-frequent hyperthermia ( temperature greater than 37.5°C). Hyperthermia ( temperature greater than 37.5°C) also increases the risk for neonatal mortality and morbidiy in both term and preterm infants*". {Perlman 2015 S204}  Recent observational studies have also reported an association between high admission temperatures and adverse outcomes including death. {Brophy 2022 1706, Cavallin 2020 } |
| 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 | The certainty of evidence for the primary outcome survival was high. For the second primary outcome; rate of normothermia, the certainty was low.  Certainty for the secondary outcomes varied from very low (moderate hypothermia) or low certainty (mean body temperature measured by axilla or rectal route, NEC, late onset sepsis, intubation in the delivery room) to moderate certainty (hyperthermia, and hypothermia < 36.5°C ). |  |
| 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 | The outcome of survival to hospital discharge (or its converse, mortality) has been judged by both care givers and parents to be the highest ranked outcomes of importance {Strand 2020 F328, Webbe 2020 425} | Other outcomes such as admission temperatures or presence of hypothermia have not been ranked. However, they are likely to be ranked as important because of their potential effect on mortality. |
| 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 | The review found evidence of benefit for some outcomes (survival, temperatures on admission) with the use of a plastic bag or wrap. However, there was some evidence of harm from an increased risk of hyperthermia. | The risk of hyperthermia could be mitigated by regular temperature monitoring |
| 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 | No studies provided sufficient detail about the costs of universal of plastic bags or wraps for all preterm infants <34 weeks' gestation. | Plastic bags or wraps are likely to be an inexpensive method to improve thermoregulation in very preterm infants. However, the costs depend on whether bags or wraps specifically marketed for newborn care are used, or widely available products such as those used for food storage.  The Task Force also considered the environmental impacts of recommending widespread use of plastic caps. However, this must be weighed against benefits, and also compared with the widespread use of other disposables in clinical care. |
| 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 studies provided sufficient detail about costs to determine the certainty of evidence for required resources. |  |
| 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 | Studies included in the review did not measure cost-effectiveness. However, studies did make recommendations regarding cost-effectiveness of the intervention. Two studies described the use of a plastic bag as inexpensive {Chantaroj 2011 S32, Knobel 2005 304}, low cost {Nimbalkar 2019 122} or a cost effective intervention {Bhavsar 2015 23} |  |
| 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 | Plastic bags or wraps are likely to be an intervention that could be applied easily in low-resource setting or in high- resource settings.  The included studies were undertaken in high-income countries (USA, Canada(4), Australia, Italy) and middle income countries (India (3), Turkey, Thailand, Malaysia, Egypt, Iran). (Ref https://blogs.worldbank.org/opendata/new-world-bank-country-classifications-income-level-2022-2023) |  |
| Acceptability Is the intervention acceptable to key stakeholders? | | |
| Judgement | Research evidence | Additional considerations |
| ○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know | No studies in this review included information about acceptability regarding use of plastic bag or wrap in the delivery room.  Within quality improvement studies assessed for this systematic review there was almost universal use of the plastic bag or wrap, suggesting a high level of acceptability. {Aley-Raz 2020 476, Ashmeade 2016 73, Billimoria 2013 455, Caldas 2018 368, Choi 2018 239, Cleator 2022 75, Croop 2020 530, DeMauro 2013 e1018, Ferretti 2021 e240, Frazer 2018 520, Frazer 2022 99, Godfrey 2013 311, Harer 2017 1242, Harriman 2018 462, Keir 2021 375, Lee 2008 754, Manani 2013 8, Peleg 2019 387, Pinheiro 2014 e218, Reuter 2014 397, Russo 2014 31055, Sharma 2020 1851, Sivanandan 2016 39, Sprecher 2021 270, Vinci 2018 e125, Wlodaver 2016 182, Yip 2017 922, Young 2021 2745} | The plastic bag does not hinder auscultation of an infant's heart rate, application of electrocardiogram or pulse oximeter sensors.    The use of a plastic bag or wrap is considered standard of care in many neonatal services. |
| Feasibility Is the intervention feasible to implement? | | |
| Judgement | Research evidence | Additional considerations |
| ○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know | Use of a plastic bag or wrap appeared feasible in the middle and high income countries in which the included studies were performed.  Quality improvement studies assessed for this systematic review resulted in almost universal use of the plastic bag or wrap, suggesting a high level of feasibility | Barriers to implementing plastic bag or wrap in the birthing room could be related to the cost and availability of the intervention.    It is important to ensure that the plastic bag or wrap is opened or lifted as infrequently as possible, until the baby is transferred to a prewarmed, humidified incubator. Otherwise the benefits of the plastic bag or wrap are likely to be reduced. |

# 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

|  |
| --- |
| Recommendation |
| In newborn preterm infants (<34 weeks’ gestation) immediately after birth we recommend the use of plastic bag or wrap to maintain normal temperature. (Strong recommendation, moderate certainty of evidence).  The risk of hyperthermia should be carefully monitored and managed (Good practice statement). |
| Justification |
| **Overall justification**  Plastic bag or wrap to maintain normal temperature in the delivery room is feasible.  **Detailed justification**  *Problem*  Hypothermia is a common problem in preterm infants (<34 weeks’ gestation) has been associated with increased mortality and morbidity.  *Desirable Effects*  Plastic bag or wrap compared with standard care reduced the risk of hypothermia and improved mean temperature on admission, and may improve survival  *Undesirable Effects*  There was an increased risk of hyperthermia in infants in the plastic bag or wrap group  *Certainty of evidence*  The evidence was variable from low to high certainty  *Cost effectiveness*  There were no studies on cost effectiveness |
| Subgroup considerations |
| * *For subgroup analysis by gestational age groups: (<28 weeks vs 28-33+6 weeks)* a plastic bag or wrap was more efficacious in preventing moderate hypothermia in the lower gestation subgroup (test for subgroup differences (random effects): χ2 = 5.27, df = 1 (p = 0.02)). For all other outcomes results of tests for subgroup differences were not statistically significant. * *For subgroup analysis high income vs middle income country setting* a plastic bag or wrap was more efficacious in preventing moderate hypothermia inhigh income countries, (test for subgroup differences (random effects): χ2 = 5.20, df =1 (p =0.02)). For all other outcomes results of tests for subgroup differences were not statistically significant. * *For subgroup analysis by setting high resource vs low resource setting* there were no data. * *For subgroup analysis by site (inborn vs outborn)* the tests for subgroup differences were not statistically significant. |
| Implementation considerations |
| Plastic bag or wrap for thermoregulation in the delivery room has been shown to be feasible in any resource setting. Practice change would be required to implement the intervention. |
| Monitoring and evaluation |
| Preterm neonate's temperature on admission to neonatal intensive care units should continue to be monitored asan important indicator of the quality of care. {Perlman 2015 S204} |
| Research priorities |
| * What is the balance of risks and benefits when using a plastic bag or wrap for preterm infants in the birthing room when other combination of thermoregulation interventions (ambient temperature, heated and humidified gases, exothermic mattress, head covering, servo-controlled radiant warmer) are applied? * What is the evidence for cost effectiveness when using a plastic bag or wrap for preterm infants in the birthing room? * More information is needed about the gestation-specific effects of plastic bags or wraps, especially in the context of numerous other interventions to maintain normothermia.  |  |  | | --- | --- | | Question 4. | | | **Should plastic cap vs. no plastic cap be used for in preterm neonates born at less than 34 weeks’ gestation or equivalent birth weight immediately after birth?** | | | **Population:** | in preterm neonates born at less than 34 weeks’ gestation or equivalent birth weight immediately after birth | | **Intervention:** | Plastic cap | | **Comparison:** | No plastic cap | | **Main outcomes:** | Primary outcomes   * Survival to hospital discharge (critical) * Rate of normothermia on admission to neonatal unit or postnatal ward (important)   Secondary outcomes:   * Body temperature (and rates of moderate hypothermia, cold stress and hyperthermia) on admission to neonatal unit or before transfer to neonatal unit or postnatal ward, or at times ≤ 1 hour of age (as defined by authors). * Response to resuscitation, e.g., need for assisted ventilation, highest FiO2 * Major morbidity: bronchopulmonary dysplasia (important), intraventricular hemorrhage all grades (important) and severe (critical), necrotising enterocolitis (important), respiratory distress syndrome (surfactant treatment for), late onset sepsis. | | **Setting:** | Birth environment, in or out of hospital | | **Perspective:** | Individual patients, their families and providers caring for those patients. | | **Background:** | A head covering (cap or bonnet) has been recommended by ILCOR for maintaining normal body temperature in preterm infants after birth, in order to prevent adverse outcomes including death. {Perlman 2015 S204} The systematic review of evidence for this intervention was updated to include studies published since the previous systematic review. The scalp is a large proportion of body surface area in a preterm infant and hence is considered likely make a large contribution to evaporative, radiant, conductive or convective heat loss. The review intended to consider head coverings made from a variety of materials, but the only study that provided evidence of sufficient certainty to contribute to development treatment recommendation examined use of a double-layered plastic cap. | | **Conflict of interests:** | Author Trevisanuto was lead author on the only study eligible for this comparison, and was excluded from assessment of the study for inclusion, risk of bias assessment and certainty of evidence assessment. {Trevisanuto 2010 914}  Author de Almeida was lead author on an observational study which examined the effects of a bundle of interventions including a cloth cap, and was excluded from assessment of the study for inclusion, risk of bias assessment and certainty of evidence assessment. {de Almeida 2014 271}  Authors Trevisanuto and de Almeida wrote a recent review article on maintaining normothermia in newborn infants at birth. {Trevisanuto 2018 333}  Author Ramaswamy is an author of a network meta-analysis of methods to maintain normal temperature in infants in the delivery room {Abiramalatha 2021 e210775} |  Assessment  |  |  |  | | --- | --- | --- | | Problem Is the problem a priority? | | | | Judgement | Research evidence | Additional considerations | | ○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know | A systematic review conducted for ILCOR concluded that "For the critical outcome of mortality, there is evidence from 36 observational studies of increased risk of mortality associated with hypothermia at admission (low-quality evidence but upgraded to moderate-quality evidence due to effect size, dose-effect relationship, and single direction of evidence)". {Perlman 2015 S204} The same systematic review concluded that "There is evidence of a dose effect on mortality, suggesting an increased risk of at least 28% for each 1° below 36.5°C body temperature at admission and dose-dependent effect size". In preterm infants it is common to measure body temperatures in the cold stress or hypothermic range. A systematic review estimated that hypothermia was common in infants born at hospitals (prevalence range, 32% to 85%) and homes (prevalence range, 11% to 92%), even in tropical environments. In a large cohort of 5697 infants < 32 weeks’ gestation, 53.4% of the cohort had a body temperature at admission less than 36.5°C, and 12.9% below 35.5°C. {Wilson 2016 61} After adjustment for pregnancy complications, singleton or multiple pregnancy, antenatal corticosteroids, mode of delivery, gestational age, infant size and sex, and Apgar score <7 at 5 minutes, an admission temperature <35.5°C was associated with increased mortality at postnatal ages 1-6 days, (risk ratio 2.41; 95% CI 1.45-4.00), and 7-28 days (risk ratio 1.79; 1.15-2.78) but not after 28 days of age. {Wilson 2016 61} A recent network meta-analysis examining benefit and safety of interventions to reduce mortality and morbidity from hypothermia reported that various interventions aimed at improving thermoregulation can improve body temperature at admission and are associated with a lower risk of mortality and major brain injury. {Abiramalatha 2021 e210775} |  | | Desirable Effects How substantial are the desirable anticipated effects? | | | | Judgement | Research evidence | Additional considerations | | ○ Trivial ○ Small ● Moderate ○ Large ○ Varies ○ Don't know | For the primary outcomes:  For the critical primary outcome of **survival**, **clinical benefit or harm could not be excluded** for the use of a plastic cap compared to no plastic cap. (RR 0.97 95% CI 0.84 to 1.12), **moderate certainty evidence** from 1 RCT enrolling 64 participants. {Trevisanuto 2010 914}  For the important primary outcome of **normothermia on admission** to a neonatal unit, there was **possible clinical benefit** with the use of a plastic cap compared to no plastic cap (RR 6.00 95% CI 1.96 to 18.38, ARD 469 more infants per 1000 were normothermic, 95% CI 90 more to 1000 infants more, NNTB 2 infants), **moderate certainty evidence** from 1 RCT enrolling 64 participants. {Trevisanuto 2010 914}   | **Outcomes** | **№ of participants (studies) Follow-up** | **Certainty of the evidence (GRADE)** | **Relative effect (95% CI)** | **Anticipated absolute effects\* (95% CI)** | | | --- | --- | --- | --- | --- | --- | | **Risk with no plastic cap** | **Risk difference with plastic cap** | | Survival | 64 (1 RCT)1 | ⨁⨁⨁◯ Moderatea | **RR 0.97** (0.84 to 1.12) | 938 per 1,000 | **28 fewer per 1,000** (150 fewer to 113 more) | | Normothermia | 64 (1 RCT)1 | ⨁⨁⨁◯ Moderateb | **RR 6.00** (1.96 to 18.38) | 94 per 1,000 | **469 more per 1,000** (90 more to 1,629 more) |   1 {Trevisanuto 2010 914}   1. Single study, 95% CI crossing line of no effect 2. Single study, Optimal information size (OIS) not satisfied   For secondary outcomes:  For **mean body temperature** there was **probable clinical benefit** (MD 0.8°C higher (0.41 to 1.19°C higher with the use of a plastic cap compared to no plastic cap), **moderate certainty evidence** downgraded for imprecisionfrom 1 RCT with 64 participants {Trevisanuto 2010 914}  For **hypothermia < 36.5 C** there was **probable clinical benefit** (RR 0.48 95%CI 0.32 to 0.73, ARD 471 fewer infants were hypothermic per 1,000 95% CI 616 fewer to 245 fewer per 1000 infants) **moderate certainty evidence** downgraded for imprecisionfrom 1 RCT with 64 participants (RR 0.48 95%CI 0.32 to 0.73) {Trevisanuto 2010 914}  For the **outcome of delivery room intubation clinical benefit or harm cannot be excluded, (**RR 0.82 95% CI 0.49 to 1.37, ARD 96 fewer infants were intubated per 1000, 95% CI 271 fewer to 197 more per 1000), **moderate certainty evidence** downgraded for imprecisionfrom 1 RCT with 64 participants. {Trevisanuto 2010 914}   | **Outcomes** | **№ of participants (studies) Follow-up** | **Certainty of the evidence (GRADE)** | **Relative effect (95% CI)** | **Anticipated absolute effects\* (95% CI)** | | | --- | --- | --- | --- | --- | --- | | **Risk with no plastic cap** | **Risk difference with plastic cap** | | Mean body temperature | 64 (1 RCT)1 | ⨁⨁⨁◯ Moderatea | - | The mean mean body temperature was **35.30°C** | MD **0.8°C** **higher** (0.41 higher to 1.19 higher) | | Hypothermia < 36.5 C | 64 (1 RCT) | ⨁⨁⨁◯ Moderatea,b | **RR 0.48** (0.32 to 0.73) | 906 per 1,000 | **471 fewer per 1,000** (616 fewer to 245 fewer) | | Delivery room intubation | 64 (1 RCT)1 | ⨁⨁⨁◯ Moderateb | **RR 0.82** (0.49 to 1.37) | 531 per 1,000 | **96 fewer per 1,000** (271 fewer to 197 more) |   1 {Trevisanuto 2010 914}   1. Single study, OIS not satisfied 2. Single study, 95% CI crossing line of no effect   **The rationale for considering the effect moderate was that** although no difference was found in the primary outcomes, hypothermia was avoided more often with a large absolute benefit. For the important secondary outcomes of **mean body temperature and hypothermia** < **36.5°C** there was **probable clinical benefit.**  ***Cloth cap compared to no cap:***  An observational study compared the use of various interventions that included use of a plastic bag or wrap; use of a linen or woolen cap; use of heated gases for ventilation; and use of a transport incubator. All infants were cared for under radiant heaters in the DR, and exothermic mattresses were not used. Using logistic regression, the effects of a **cloth cap** (used in in 894 infants vs no cap in 870 infants) were estimated, with adjustment for maternal and neonatal characteristics at birth and variables related to neonatal thermal care in the DR and variables related to thermal care during transport from the DR to the NICU.  For consistency with presentation of other data from the review, we have calculated an adjusted relative risk and adjusted absolute risk difference from the odds ratios reported in the paper. These results suggest that use of a **cloth cap** was associated with **lower rates of moderate hypothermia**(RR 0.84 95% CI 0.79 to 0.90, ARD 123 fewer infants were moderately hypothermic on admission with use of a cloth cap, 95% CI 77 fewer to 162 fewer infants per 1000) **low certainty evidence** downgraded for very serious risk of bias from one observational study including 1764 infants for this comparison. {de Almeida 2014 271} | We do not know the effect size in the presence of additional or fewer co-interventions. Infants in both groups were equally exposed to additional thermoregulation measures, for example radiant warmer.    Additional measures may affect infant thermoregulation. We do not know the effect size in the presence of additional or fewer co-interventions.    Other types of caps might also be effective. There is indirect evidence from the companion review in Late preterm and term infants: For the comparison woollen vs cotton cap, the review found one RCT enrolling 126 participants that examined two outcomes relevant to the review and found small differences in mean temperature and the rate of moderate hypothermia favouring the woollen cap group. {Lang 2004 843, Ramaswamy 2022 81} | | Undesirable Effects How substantial are the undesirable anticipated effects? | | | | Judgement | Research evidence | Additional considerations | | ○ Large ○ Moderate ○ Small ○ Trivial ○ Varies ● Don't know | In this review the one RCT did not report any episodes of hyperthermia in either group. {Trevisanuto 2010 914} | The one RCT in this review was small and did not satisfy the OIS for uncommon outcomes. | | 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 | The certainty of evidence for the primary outcomes, survival and normothermia and for the important secondary outcome measures of body temperature, hypothermia < 36.5°C, and delivery room intubation was moderate. The certainty of evidence for moderate hypothermia was very low. |  | | 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 | The outcome of survival to hospital discharge (or its converse, mortality) have been judged by both care givers and parents to be the highest ranked outcomes of importance. {Strand 2020 F328, Webbe 2020 425} |  | | 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 | The review found evidence of probable clinical benefit for two important secondary outcomes (any hypothermia < 36.5°C, and mean body temperature on admission to the NICU with MD 0.8°C higher temperature with the intervention.  There was no evidence of harm. However, the single RCT was of insufficient size to measure uncommon effects. |  | | 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 | The study included in this review did not provide an estimate of costs to determine the certainty of evidence for required resources. | The Task Force also considered the environmental impacts of recommending widespread use of plastic caps. However, this must be weighed against benefits, and also compared with the widespread use of other disposables in clinical care. | | 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 | The study provided in this review did not provide sufficient detail about costs to determine the certainty of evidence for required resources. |  | | 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 | No studies in the review examined cost effectiveness of the plastic cap. | The Task Force considered that the effects of use of a plastic cap in decreasing rates of hypothermia on admission to a neonatal unit may offset the minimal cost of the plastic caps themselves. | | 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 one RCT identified in this review took place in a high resource setting. In high resource settings it may be relatively easy to introduce plastic caps in the delivery room. In low and middle resource settings plastic caps may be unavailable or unaffordable. | Alternatives to plastic caps that might be more readily available include woven or knitted hats made of various fibres. | | Acceptability Is the intervention acceptable to key stakeholders? | | | | Judgement | Research evidence | Additional considerations | | ○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know | The study included in this review did not report did not report any concerns about acceptability of plastic caps in the delivery room. | The ILCOR NLS Task Force has recommended the use of a cap as one of several measures to maintain normal temperature for preterm infants in the delivery room since 2015, (1) and this recommendation is reflected in many regional and national guidelines. | | Feasibility Is the intervention feasible to implement? | | | | Judgement | Research evidence | Additional considerations | | ○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know | Use of a plastic cap appeared feasible in the setting in the study identified in this review.  In addition, quality improvement studies identified for this systematic review commonly used some type of head covering for maintaining normal temperature in preterm infants, suggesting feasibility and acceptability | Some of the plastic wraps purpose-designed for maintaining normal infant temperatures at birth now incorporate a head covering, obviating the need for a separate cap. |  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  |  | | --- | | Recommendation | | In preterm infants (<34 weeks’ gestation) immediately after birth we suggest the use of a head covering to maintain normal temperature. (Strong recommendation, moderate certainty evidence).  In preterm infants (<34 weeks’ gestation) we recommend any head covering is preferable to no head covering (Good practice point)  In preterm infants (<34 weeks’ gestation) it is reasonable to consider the use of a plastic cap as a head covering. (Conditional recommendation, moderate certainty evidence).  There is currently little published evidence that head coverings of other materials are effective in preterm infants (< 34 weeks’ gestation), but they may also help maintain normothermia based on an observational study and studies in infants ≥ 34 weeks’ gestation. | | Justification | | **Overall justification**  Applying a plastic cap to prevent heat loss from the head of a newly born preterm infant is feasible and effective.  **Detailed justification**  *Problem*  Hypothermia is a common problem in preterm infants (< 34 weeks’ gestation) and has been associated with increased mortality and morbidity.  *Desirable Effects*  A plastic cap compared to no plastic cap increased mean body temperature and the proportion of infants who were hypothermic on admission to the NICU.  *Undesirable Effects*  No undesirable effects were identified. The study was of insufficient size to measure uncommon adverse outcomes including hyperthermia.  *Certainty of evidence*  The evidence was moderate for most outcomes reported  *Cost effectiveness*  There were no data to determine cost effectiveness | | Subgroup considerations | | In the single study identified in this review there were no data on the pre-specified subgroups analyses; inborn vs. outborn, by resources of setting, by gestational age or by effect of delayed cord clamping. | | Implementation considerations | | Covering the head of preterm infants (<34 weeks’ gestation) in the delivery room is common practice in high-income countries. In low resource settings practice change might be required to implement the intervention. | | Monitoring and evaluation | | Preterm neonate's temperatures on admission to neonatal intensive care units should continue to be monitored as important indicators of the quality of care. {Perlman 2015 S204} | | Research priorities | | * What is the balance of risks and benefits when using head covering composed of different materials? * We do not know if caps made from other materials, might be more, or less effective in maintaining normal temperature. * What is the balance of risks and benefits of a plastic head covering for preterm infants when receiving other combinations of interventions to promote thermoregulation (heating and humidifying gases for positive pressure ventilation in the birthing room; ambient temperature, plastic bag or wrap, exothermic mattress, servo-controlled radiant warmer) are applied? * Can plastic caps be used in the setting of delayed cord clamping? * We do not know the costs and environmental impact of plastic caps.  |  |  | | --- | --- | | Question 5. | | | **Should heated and humidified gas vs. non-heated non-humidified gases be used for resuscitation in the delivery room for preterm neonates born at less than 34 weeks' gestation or equivalent birth weight immediately after birth?** | | | **Population:** | Resuscitation in the delivery room for preterm neonates born at less than 34 weeks' gestation or equivalent birth weight immediately after birth | | **Intervention:** | Heated and humidified gas | | **Comparison:** | Non-heated non-humidified gases | | **Main outcomes:** | Primary outcomes   * Survival to hospital discharge (critical) * Rate of normothermia on admission to neonatal unit or postnatal ward (important)   Secondary outcomes:   * Body temperature (and rates of moderate hypothermia, cold stress and hyperthermia) on admission to neonatal unit or before transfer to neonatal unit or postnatal ward, or at times ≤ 1 hour of age (as defined by authors). * Response to resuscitation, e.g., need for assisted ventilation, highest FiO2   Major morbidity: bronchopulmonary dysplasia (important), intraventricular hemorrhage all grades (important) and severe (critical), necrotising enterocolitis (important), respiratory distress syndrome (surfactant treatment for), late onset sepsis. | | **Setting:** | Birth environment, in hospital | | **Perspective:** | Individual patients, their families and providers caring for those patients. | | **Background:** | Use of warmed and humidified gases is regarded as routine in mechanically ventilated patients in intensive care units, to prevent damage to the lungs. {Sottiaux 2006 } Heating and humidification may also play a key role in maintaining normal body temperature, {Gillies 2017 Cd004711} particularly in preterm infants. However, clinical trials of the use of heated and humidified gases during initial resuscitation at birth have only been published recently. | | **; (; Conflict of interests:** | Lead author J Dawson was a co-author of one of the trials included for this comparison, {McGrory 2018 47} and was excluded from decisions about inclusion and risk of bias assessment for this article. |  Assessment  |  |  |  | | --- | --- | --- | | Problem Is the problem a priority? | | | | Judgement | Research evidence | Additional considerations | | ○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know | A systematic review conducted for ILCOR concluded that "For the critical outcome of mortality, there is evidence from 36 observational studies of increased risk of mortality associated with hypothermia at admission (low-quality evidence but upgraded to moderate-quality evidence due to effect size, dose-effect relationship, and single direction of evidence)". {Perlman 2015 S204} The same systematic review concluded that "There is evidence of a dose effect on mortality, suggesting an increased risk of at least 28% for each 1° below 36.5°C body temperature at admission and dose-dependent effect size". {Perlman 2015 S204} In preterm infants it is common to measure a lower than normal body temperature. A large cohort study of 5697 infants < 32 weeks’ gestation in 19 regions in 11 European countries found that hypothermia was common in infants born in hospitals (prevalence range, 32% to 85%) and homes (prevalence range, 11% to 92%), even in warm climates. {Wilson 2016 61} In this cohort, 53.4% had a body temperature at admission below 36.5°C, and 12.9% below 35.5°C. After adjusting for pregnancy complications, singleton or multiple pregnancy, antenatal corticosteroids, mode of delivery, gestational age, infant size and sex, and Apgar score <7 at 5 minutes, an admission temperature <35.5°C was associated with increased mortality at postnatal ages 1-6 days, (risk ratio 2.41; 95% CI 1.45-4.00), and 7-28 days (risk ratio 1.79; 1.15-2.78) but not after 28 days of age. {Wilson 2016 61} A recent network meta-analysis examining benefit and safety of interventions to reduce mortality and morbidity from hypothermia reported that various interventions aimed at improving thermoregulation can improve body temperature at admission and are associated with a lower risk of mortality and major brain injury. {Abiramalatha 2021 e210775} |  | | Desirable Effects How substantial are the desirable anticipated effects? | | | | Judgement | Research evidence | Additional considerations | | ○ Trivial ● Small ○ Moderate ○ Large ○ Varies ○ Don't know | This systematic review found that for the use of heated and humidified gases, when compared to non-heated and non-humidified gases for resuscitation in the delivery room for preterm infants:  For **survival to hospital discharge**, the first primary outcome for the review **clinical benefit or harm cannot be excluded** (RR 1.00 95% CI 0.94 to 1.05), **very** **low certainty evidence** downgraded for risk of bias and imprecision, from 2 RCTs enrolling 476 participants. {McGrory 2018 47, Meyer 2015 245} This result was supported by an observational study enrolling 112 participants, which also produced evidence of very low certainty. {te Pas 2010 e1427}  For **normothermia on admission** to a neonatal unit (the second primary outcome) **clinical benefit or harm cannot be excluded** (RR 1.23 95% CI 0.93 to 1.62), **very low certainty evidence** downgraded for risk of bias and imprecision from 2 RCTs enrolling 476 participants. {McGrory 2018 47, Meyer 2015 245} However, an observational study of 112 infants found **possible clinical benefit** (RR 3.53, 95% CI 1.65 to 7.55) **low certainty evidence** downgraded for risk of bias and imprecision. {te Pas 2010 e1427}   | **Primary Outcomes** | **№ of participants (studies) Follow-up** | **Certainty of the evidence (GRADE)** | **Relative effect (95% CI)** | **Anticipated absolute effects\* (95% CI)** | | | --- | --- | --- | --- | --- | --- | | **Risk with non-heated non-humidified gases** | **Risk difference with heated and humidified gas** | | Survival | 476 (2 RCTs)1,2 | ⨁◯◯◯ Very lowa,b,c | **RR 1.00** (0.94 to 1.05) | 918 per 1,000 | **0 fewer per 1,000** (55 fewer to 46 more) | | Survival | 112 (1 observational study)3 | ⨁◯◯◯ Very lowc,d | **RR 1.01** (0.92 to 1.12) | 931 per 1,000 | **9 more per 1,000** (74 fewer to 112 more) | | Normothermia | 476 (2 RCTs)1,2 | ⨁◯◯◯ Very lowa,b,c,e | **RR 1.23** (0.93 to 1.62) | 471 per 1,000 | **108 more per 1,000** (33 fewer to 292 more) | | Normothermia | 112 (1 observational study)3 | ⨁⨁◯◯ Lowd,f | **RR 3.53** (1.65 to 7.55) | 121 per 1,000 | **305 more per 1,000** (78 more to 791 more) |  1. {Meyer 2015 245} 2. {McGrory 2018 47} 3. {te Pas 2010 e1427} 4. Of the two trials, one had some concerns for risk of bias 5. In the trials, plastic bag or wrap was used <28 weeks, <30 weeks or for all infants, according to each hospital’s protocol 6. Optimal information size (OIS) criterion not satisfied and 95% CI crosses line of no effect 7. The study had a moderate risk of bias 8. I2=52% 9. OIS criterion not satisfied   For secondary outcomes:  For **mean body temperature on admission**, there was **possible benefit but the clinical significance is uncertain** (mean body temperature was 0.15°C higher 95% CI 0.03 to 0.26°C higher), **moderate certainty evidence** from 2 RCTs enrolling 476 participants. {McGrory 2018 47, Meyer 2015 245}  For **any hypothermia <36.5 °C** there was **possible clinical benefit** (RR 0.67 95% CI 0.51 to 0.87), **low certainty evidence** downgraded for risk of bias and imprecision from 2 RCTs enrolling 476 participants. {McGrory 2018 47, Meyer 2015 245}  For **mild hypothermia clinical benefit or harm cannot be excluded** (RR 0.61 95% CI 0.35 to 1.05), **low certainty evidence** downgraded for risk of bias and imprecision from 2 RCTs enrolling 476 participants. {McGrory 2018 47, Meyer 2015 245}  For **moderate hypothermia** there was **possible clinical benefit** (RR 0.58 95% CI 0.36 to 0.94), **low certainty evidence** downgraded for risk of bias and imprecision from 2 RCTs enrolling 476 participants. {McGrory 2018 47, Meyer 2015 245}  For **RDS requiring surfactant clinical benefit or harm cannot be excluded** (RR 0.91 95%CI 0.76 to 1.09), **low certainty evidence** downgraded for risk of bias, and imprecision from 2 RCTs enrolling 476 participants. {McGrory 2018 47, Meyer 2015 245}  For **delivery room intubation clinical benefit or harm cannot be excluded** (RR 1.10 95%CI 0.88 to 1.39), **low certainty evidence** downgraded for risk of bias, indirectness and imprecision from 2 RCTs enrolling 476 participants. {McGrory 2018 47, Meyer 2015 245}  For **BPD** **clinical benefit or harm cannot be excluded** (RR 0.89 95%CI 0.70 to 1.13), **very low certainty evidence** downgraded for risk of bias, indirectness and imprecision from 2 RCTs enrolling 476 participants. {McGrory 2018 47, Meyer 2015 245}  For **IVH >Grade 2,** there was **probable clinical benefit** (RR 0.39 95% CI 0.17 to 0.91), **moderate certainty evidence** downgraded for imprecision from 2 RCTs enrolling 476 participants. {McGrory 2018 47, Meyer 2015 245}  For **NEC** **clinical benefit or harm cannot be excluded** (RR1.55 CI 95% 0.45 to 5.31), **very low certainty evidence** downgraded for risk of bias, and imprecision from 2 RCTs enrolling 476 participants. {McGrory 2018 47, Meyer 2015 245}   | **Secondary Outcomes** | **№ of participants (studies) Follow-up** | **Certainty of the evidence (GRADE)** | **Relative effect (95% CI)** | **Anticipated absolute effects\* (95% CI)** | | | --- | --- | --- | --- | --- | --- | | **Risk with non-heated non-humidified gases** | **Risk difference with heated and humidified gas** | | Mean body temperature | 476 (2 RCTs)1,2 | ⨁⨁⨁◯ Moderatea,b | - | The mean body temperature was **36.59°C** | MD **0.15°C higher** (0.03°C higher to 0.26°C higher) | | Hypothermia < 36.5 C | 476 (2 RCTs)1,2 | ⨁⨁◯◯ Lowb,c,d | **RR 0.67** (0.51 to 0.87) | 389 per 1,000 | **128 fewer per 1,000** (191 fewer to 51 fewer) | | Mild hypothermia | 476 (2 RCTs)1,2 | ⨁⨁◯◯ Lowb,c,d,e | **RR 0.61** (0.35 to 1.05) | 234 per 1,000 | **91 fewer per 1,000** (152 fewer to 12 more) | | Moderate hypothermia | 476 (2 RCTs)1,2 | ⨁⨁◯◯ Lowc,d | **RR 0.58** (0.36 to 0.94) | 172 per 1,000 | **72 fewer per 1,000** (110 fewer to 10 fewer) | | IVH > grade 2 | 476 (2 RCTs)1,2 | ⨁⨁⨁◯ Moderatea,b,d | **RR 0.39** (0.17 to 0.91) | 82 per 1,000 | **50 fewer per 1,000** (68 fewer to 7 fewer) | | RDS requiring surfactant therapy | 476 (2 RCTs)1,2 | ⨁◯◯◯ Very lowb,c,f | **RR 0.91** (0.76 to 1.09) | 500 per 1,000 | **45 fewer per 1,000** (120 fewer to 45 more) | | NEC | 203 (1 RCT)1 | ⨁◯◯◯ Very lowb,c,f,g | **RR 1.55** (0.45 to 5.31) | 39 per 1,000 | **21 more per 1,000** (21 fewer to 167 more) | | Late onset neonatal sepsis | 476 (2 RCTs)1,2 | ⨁◯◯◯ Very lowb,c,f | **RR 1.07** (0.75 to 1.54) | 213 per 1,000 | **15 more per 1,000** (53 fewer to 115 more) | | BPD | 476 (2 RCTs)1,2 | ⨁◯◯◯ Very lowb,c,f | **RR 0.89** (0.70 to 1.13) | 377 per 1,000 | **41 fewer per 1,000** (113 fewer to 49 more) | | Delivery room intubation | 476 (2 RCTs)1,2 | ⨁⨁◯◯ Lowa,b,f | **RR 1.10** (0.88 to 1.39) | 344 per 1,000 | **34 more per 1,000** (41 fewer to 134 more) |   1 {Meyer 2015 245}  2 {McGrory 2018 47}   1. The trial with greatest weightage had a low risk of overall bias 2. In the trials, plastic bag or wrap was used <28 weeks, <30 weeks or for all infants, according to each hospital’s protocol 3. Of the two trials, one had some concerns for risk of bias 4. Optimal information size (OIS) criterion not satisfied 5. 95% CI crosses line of no effect 6. OIS criterion not satisfied and 95% CI crosses line of no effect 7. Very low event rates with wide 95% CI   We found one before and after study enrolling 112 infants. This observational study provided moderate certainty evidence for each of the secondary outcomes, but none of the findings were statistically significant except for a lower risk of moderate hypothermia (RR 0.58 95% CI 0.36 to 0.94). {te Pas 2010 e1427}  **The rationale for considering the effect small** was that little difference was found in the primary outcomes. However, for the important secondary outcome **IVH > Grade 2** there was probable clinical benefit, albeit in two RCTs for which the combined number of participants fell well below the optimal information size (OIS) for this (and most other outcomes). The result of reduced IVH>grade 2 could easily be a type I error and would need to be replicated in larger studies. For the important secondary outcome **moderate hypothermia** there was **possible clinical benefit.** For the secondary outcome, **mean temperature on admission** infants in the heated and humidified gas group achieved a higher temperature by 0.15°C (0.03°C higher to 0.26°C higher) a difference that may not be clinically significant, because this increase and its confidence intervals did not cross a threshold of treatment effect. In the included studies, other measures to maintain normal temperature were used for both intervention and control arms, including plastic bags or wraps (either for all infants or for all infants <28 weeks’ gestation) and a radiant warmer. It is possible that in the presence of fewer other measures, the effect size for heated and humidified gases may be larger, or in the presence of more measures (e.g., increased ambient room temperature or addition of a thermal mattress) the effect may be smaller. | We do not know the effect size in the presence of additional or fewer co-interventions. Infants in both the heated and humidified gas and the non-heated and humidified gas group were equally exposed to additional thermoregulation measures, for example radiant warmer. Additionally, the least mature infants were managed with a plastic bag or wrap.  These additional measures may have affected infant thermoregulation. We do not know the effect size in the presence of additional or fewer co-interventions. | | Undesirable Effects How substantial are the undesirable anticipated effects? | | | | Judgement | Research evidence | Additional considerations | | ○ Large ○ Moderate ○ Small ○ Trivial ○ Varies ● Don't know | This systematic review found that when heated humidified gas compared to non-heated and humidified gas for resuscitation in the delivery room for preterm infants:   * For **hyperthermia (> 37.5°C**) **clinical benefit or harm could not be excluded** (RR 1.46 95% CI 0.60 to 3.52), **very low certainty evidence**, downgraded for risk of bias, inconsistency, and imprecision from 2 RCTs enrolling 476 infants. {McGrory 2018 47, Meyer 2015 245} * The observational study provided low certainty evidence also supporting that clinical benefit or harm could not be excluded. {te Pas 2010 e1427}  | **Outcomes** | **№ of participants (studies) Follow-up** | **Certainty of the evidence (GRADE)** | **Relative effect (95% CI)** | **Anticipated absolute effects\* (95% CI)** | | | --- | --- | --- | --- | --- | --- | | **Risk with non-heated non-humidified gases** | **Risk difference with heated and humidified gas** | | Hyperthermia (> 37.5 C) | 476 (2 RCTs)1,2 | ⨁◯◯◯ Very lowa,b,c,d | **RR 1.46** (0.60 to 3.52) | 90 per 1,000 | **41 more per 1,000** (36 fewer to 227 more) | | Hyperthermia | 112 (1 observational study)3 | ⨁⨁◯◯ Lowe,f | **RR 2.15** (0.20 to 23.02) | 17 per 1,000 | **20 more per 1,000** (14 fewer to 380 more) |  1. {Meyer 2015 245} 2. {McGrory 2018 47} 3. {te Pas 2010 e1427} 4. Of the two trials, one had some concerns for risk of bias 5. I2=55% 6. Amongst the extremely preterm subgroup of neonates included in both trials, plastic bag or wrap was used as a co-intervention in neonates <28 weeks’ gestation in one trial and <30 weeks at one site in the other trial 7. OIS criterion not satisfied and 95% CI crosses line of no effect 8. The trial had a moderate risk of bias 9. 95% CI crosses line of no effect   The reason for concluding that the effect on hyperthermia is not known is that although the point estimates suggested a greater likelihood of clinical harm, the confidence intervals were wide and crossed the line of no effect. The evidence was of very low certainty. Furthermore, in the included studies, other measures to maintain normal temperature were used for both intervention and control arms. The number and type of other measures used could affect the risk of hyperthermia. | Infants in both the heated and humidified gas and the non-heated and humidified gas group were equally exposed to additional thermoregulation measures, for example radiant warmer. Additionally, the least mature infants were managed with a plastic bag or wrap. These additional measures may have affected infant thermoregulation.  In one study infants were exposed to delayed cord clamping for 40 seconds. The effect of delayed cord clamping on thermoregulation in very and extremely preterm infants is unclear.  We do not know the effect size in the presence of additional or fewer co-interventions. | | 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 | The certainty of evidence for the primary outcomes (survival and normothermia) was very low. For the important secondary outcomes relating to body temperature the certainty of evidence was low, except for mean temperature on admission and IVH > grade 2, for which the certainty of evidence was moderate. For the remaining secondary outcomes, the certainty of evidence was very low. |  | | 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 | The outcome of survival to hospital discharge (or its converse, mortality) have been judged by both care givers and parents to be the highest ranked outcomes of importance. {Strand 2020 F328, Webbe 2020 425} | Cold stress and hypothermia are common particularly among preterm infants and are associated with increased mortality and morbidity. {de Almeida 2014 271} | | 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 | The review found evidence of possible clinical benefit for three outcomes (any hypothermia < 36.5°C, moderate hypothermiaand IVH >Grade 2) with heated and humidified gases for resuscitation in the delivery room. None of the remaining outcomes suggested increased likelihood of harm. | The mean temperature of piped wall air has been measured as 23.4°C and mean relative humidity 5.4%. {Dawson 2014 24} Exposure to cold dry gas in preterm lambs has shown a trend to increased proinflammatory interleukin-1Beta messenger RNA when compared to heated and humidified gas. {Greenspan 1991 , Pillow 2009 } Although these results have not been confirmed in studies of human preterm infants, the effects are likely to be similar.  The additional potential benefits of using heated and humidified gas for resuscitation in the delivery room on biomarkers of lung injury were not measured specifically in trials included in this review. Warmed, humidified gases are considered mandatory for all subsequent respiratory support in all age groups. {Sottiaux 2006 } | | 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 | The two studies included in the review took place in high resource settings. One of the studies estimated that the additional equipment required to provide heated humidified gas in the delivery room could cost US$50 for the single-use humidification circuit and chamber. {McGrory 2018 47} The true cost is likely to be higher as this estimate did not include the cost of the heater, temperature probes and sterile water required to provide the intervention. | It is possible that the circuit used in the delivery room to provide respiratory support could "travel" with the baby to the NICU when ongoing respiratory support is required.  Nevertheless, there is likely to be considerable expense to purchase and maintain equipment to safely heat and humidify gases in all locations where preterm infants are born.  The costs of the additional devices and disposable components may well be unaffordable where resources are limited. | | 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 studies provided sufficient detail about costs to determine the certainty of evidence for required resources. |  | | 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 | No studies in the review examined cost effectiveness for use of heated and humidified gas for resuscitation in the delivery room. |  | | 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 studies addressed impact on health equity. In high resource settings, the equipment for heated and humidified gases for resuscitation in the delivery room is likely to be accessible because of routine use during subsequent NICU care. In low and middle resource settings, and especially where resources for subsequent respiratory support are limited, it may be unavailable or unaffordable. | Where resources are limited, providing heated and humidified gases in the delivery room could divert resources away from the NICU.  Any potential harmful effect of using non-heated and non-humidified gases for resuscitation in the delivery room may be limited if respiratory support is only required for a short time. However, it is not established whether there is a safe duration for ventilation using non-heated and non-humidified gases before admission to a NICU.  It is very unlikely that heated and humidified gases would be available in an out-of-hospital setting. | | Acceptability Is the intervention acceptable to key stakeholders? | | | | Judgement | Research evidence | Additional considerations | | ○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know | The two studies included in this review did not include information about acceptability of heating and humidifying gases for resuscitation in the delivery room. In the NICU it is considered mandatory to heat and humidify gases used for ventilation and CPAP. |  | | Feasibility Is the intervention feasible to implement? | | | | Judgement | Research evidence | Additional considerations | | ○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know | Use of heating and humidification appeared feasible in the included studies. | Barriers to implementing heated and humidify gases in the birthing room are likely to be related to the cost of the intervention, and training requirements. |  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  |  | | --- | | Recommendation | | In newborn preterm infants (<34 weeks’ gestation) receiving ventilatory support immediately after birth, we suggest heated and humidified gases for respiratory support in the delivery room can be used where audit shows that admission hypothermia is a problem and resources allow. (Conditional recommendation, very low certainty evidence) . | | Justification | | **Overall justification**  The evidence from this systematic review indicated that heating and humidifying gases for respiratory support in the delivery room is safe, feasible and confers a small clinical benefit for several secondary outcomes.  **Detailed justification**  *Problem*  Hypothermia is a common problem in preterm infants (<34 weeks gestation) and has been associated with increased mortality and morbidity.  *Desirable Effects*  The systematic review found 2 RCTs and 1 observational study that found improvements in some secondary outcomes of the review. For the important secondary outcome IVH > Grade 2 there was probable clinical benefit, albeit in two RCTs for which the combined number of participants fell well below the optimal information size (OIS) for this (and most other outcomes). The result of reduced IVH>grade 2 could easily be a type I error and would need to be replicated in larger studies. Any potential harmful effect of using non-heated and non-humidified gases for resuscitation in the delivery room may be limited if respiratory support is only required for a short time before heating and humidification can be provided. However, the safe upper limit of duration for ventilation using non-heated and non-humidified gases before admission to a NICU is not established.  *Undesirable Effects*  No undesirable effects (including risk of hyperthermia) were confirmed (although the evidence was of low to very low certainty).  *Certainty of evidence*  The evidence for various outcomes ranged from very low to moderate certainty. It should be noted that in the combined studies, the optimal information size was not met for most outcomes.  *Cost effectiveness and equity*  There were no data to determine cost effectiveness or effects on equity. However, there will be expense to purchase and maintain equipment to safely heat and humidify gases in all locations where preterm infants are born. In low- and middle-income countries and other low resource settings, the costs are likely to be unaffordable, or providing heated and humidified gases in the delivery room could divert resources away from the NICU. To mitigate this, it is possible that the circuit used in the delivery room to provide respiratory support could "travel" with the baby to the NICU when ongoing respiratory support is required. | | Subgroup considerations | | Predefined subgroup analyses for this review were by gestation groups (or approximate birth weight equivalent), by location of birth and resources of setting and by early vs later cord clamping.  There were insufficient data to perform formal analysis of interaction.  One study reported outcomes for the **subgroup of infants < 26 weeks’ gestation**, (but not other gestation subgroups).  Primary outcome:   * For **normothermia on admission to a neonatal unit** (the second primary outcome) **clinical benefit or harm** cannot be excluded (RR 0.80 95% CI 0.48 to 1.34) (low certainty evidence from 1 RCT enrolling 69 participants < 26 weeks gestation. {McGrory 2018 47}   For important secondary outcomes:   * For **mean body temperature on admission**, there was **possible clinical benefit** (MD 0.40°C higher with use of heated and humidified gases, 95% CI 0.02 to 0.82°C higher) (moderate certainty evidence from 1 RCT enrolling 69 participants in this gestation group) * For **any hypothermia <36.5 °C clinical benefit or harm cannot be excluded** (RR 0.79 95% CI 0.40 to 1.56) (low certainty evidence downgraded for risk of bias and imprecision from 1 RCT enrolling 69 participants). {McGrory 2018 47} * For **moderate hypothermia** there was possible clinical benefit (RR 0.37 95% CI 0.13 to 1.06) (low certainty evidence downgraded for risk of bias and imprecision from 1 RCT enrolling 69 participants). {McGrory 2018 47} * For **hyperthermia (> 37.5°C ) clinical benefit or harm could not be excluded** (RR 2.57 95% CI 0.89 to 7.42)(very low certainty evidence, downgraded for risk of bias, inconsistency, and imprecision) from 1 RCT enrolling 69). {McGrory 2018 47}   Thus, the findings were similar for the <26-week gestation infants as for the study as a whole. However, the study did not report a test for interaction.  One study specified that delayed cord clamping was routinely performed for all study infants. {Meyer 2015 245} All infants in included studies were born in hospital and the studies were conducted in high income countries. {McGrory 2018 47, Meyer 2015 245, te Pas 2010 e1427} | | Implementation considerations | | Heating and humidifying gases used for respiratory support is standard care in NICUs in high-income countries. Depending on location, purchase, supply and maintenance of equipment and practice changes would be required to implement the intervention. | | Monitoring and evaluation | | Preterm neonates’ temperatures on admission to neonatal intensive care units should continue to be monitored as important indicators of the quality of care. {Perlman 2015 S204} | | Research priorities | | * What is the balance of risks and benefits when heating and humidifying gases for preterm infants receiving positive pressure ventilation in the birthing room when other combinations of thermoregulation interventions (ambient temperature, plastic bag or wrap, exothermic mattress, cap, servo-controlled radiant warmer) are applied? * What is the evidence for cost effectiveness when using heated and humidified gases in the delivery room when providing respiratory support? * Can heating and humidifying gases be used in the setting of delayed cord clamping? * Does use of heated and humidified gases during resuscitation reduce lung injury? * Does use of heated and humidified gases from birth reduce the risk of severe IVH in studies that meet the optimal information size for this outcome, and if so, what is the mechanism?  |  |  | | --- | --- | | Question 6. | | | **Should servo controlled radiant warmer mode vs. manual mode radiant warmer be used for preterm neonates born at less than 34 weeks' gestation or equivalent birth weight, immediately after birth?** | | | **Population:** | Preterm neonates born at less than 34 weeks' gestation or equivalent birth weight immediately after birth | | **Intervention:** | Servo controlled mode radiant warmer | | **Comparison:** | Manual mode radiant warmer | | **Main outcomes:** | Primary outcomes   * Survival to hospital discharge (critical) * Rate of normothermia on admission to neonatal unit or postnatal ward (important)   Secondary outcomes:   * Body temperature (and rates of moderate hypothermia, and hyperthermia) on admission to neonatal unit or before transfer to neonatal unit or postnatal ward, or at times ≤ 1 hour of age (as defined by authors). * Response to resuscitation, e.g., need for assisted ventilation, highest FiO2 * Major morbidity: bronchopulmonary dysplasia (important), intraventricular hemorrhage all grades (important) and severe (critical), necrotising enterocolitis (important), respiratory distress syndrome (surfactant treatment for), late onset sepsis. | | **Setting:** | Birth environment, in hospital | | **Perspective:** | Individual patients, their families and providers caring for those patients. | | **Background:** | Infants in the neonatal intensive care unit are generally nursed under a radiant warmer or in an incubator. The temperature of the incubator or radiant warmer can be adjusted manually or by servo controlling heater output to achieve a set neonatal body temperature measured at the site of a skin sensor. The previous ILCOR systematic review of Warming Adjuncts (and a subsequent evidence update NLS 599: EvUp) made no comment regarding use of manual or servo mode to control warmers used in the delivery room. {Perlman 2015 S204} | | **Conflict of interests:** | Author Trevisanuto was an author of the study of use of servo-control mode during newborn resuscitation included in this review, {Cavallin 2021 572} and was excluded from decisions about inclusion or bias assessment for this study. |  Assessment  |  |  |  | | --- | --- | --- | | Problem Is the problem a priority? | | | | Judgement | Research evidence | Additional considerations | | ○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know | A systematic review conducted for ILCOR concluded that *"For the critical outcome of mortality, there is evidence from 36 observational studies of increased risk of mortality associated with hypothermia at admission (low-quality evidence but upgraded to moderate-quality evidence due to effect size, dose-effect relationship, and single direction of evidence)*". {Perlman 2015 S204} The same systematic review concluded that "*There is evidence of a dose effect on mortality, suggesting an increased risk of at least 28% for each 1° below 36.5°C body temperature at admission and dose-dependent effect size*". {Perlman 2015 S204}  In preterm infants it is common to measure body temperatures in the cold stress or hypothermic range. A systematic review estimated that hypothermia was common in infants born at hospitals (prevalence range, 32% to 85%) and homes (prevalence range, 11% to 92%), even in tropical environments. In a large cohort of 5697 infants < 32 weeks’ gestation, 53.4% of the cohort had a body temperature at admission less than 36.5°C, and 12.9% below 35.5°C. {Wilson 2016 61} After adjustment for pregnancy complications, singleton or multiple pregnancy, antenatal corticosteroids, mode of delivery, gestational age, infant size and sex, and Apgar score <7 at 5 minutes, an admission temperature <35.5°C was associated with increased mortality at postnatal ages 1-6 days, (risk ratio 2.41; 95% CI 1.45-4.00), and 7-28 days (risk ratio 1.79; 1.15-2.78) but not after 28 days of age. {Wilson 2016 61}  A recent network meta-analysis examining benefit and safety of interventions to reduce mortality and morbidity from hypothermia reported that various interventions aimed at improving thermoregulation can improve body temperature at admission and are associated with a lower risk of mortality and major brain injury. {Abiramalatha 2021 e210775} |  | | Desirable Effects How substantial are the desirable anticipated effects? | | | | Judgement | Research evidence | Additional considerations | | ○ Trivial ○ Small ○ Moderate ○ Large ○ Varies ● Don't know | This systematic review found that when a radiant warmer in servo controlled mode was used compared to using a radiant warmer in manual mode for preterm infants in the delivery room:  For the critical primary outcome of **survival to hospital discharge**, **clinical benefit or harm could not be excluded** (RR 1.05, 95% CI 0.99 to 1.11), **moderate certainty evidence** downgraded for imprecision from 1 RCT enrolling 450 participants. {Cavallin 2021 572}  For the important primary outcome of **normothermia on admission to a neonatal unit**, **clinical benefit or harm could not be excluded** (RR 0.94, 95% CI 0.75 to 1.17), **moderate certainty evidence** downgraded for imprecision from 1 RCT enrolling 450 participants. {Cavallin 2021 572}   | **Primary Outcomes** | **№ of participants (studies) Follow-up** | **Certainty of the evidence (GRADE)** | **Relative effect (95% CI)** | **Anticipated absolute effects\* (95% CI)** | | | --- | --- | --- | --- | --- | --- | | **Risk with manual mode radiant warmer** | **Risk difference with servo controlled radiant warmer** | | Survival | 450 (1 RCT)1 | ⨁⨁⨁◯ Moderatea | **RR 1.05** (0.99 to 1.11) | 884 per 1,000 | **44 more per 1,000** (9 fewer to 97 more) | | Normothermia | 450 (1 RCT)1 | ⨁⨁⨁◯ Moderatea | **RR 0.94** (0.75 to 1.17) | 422 per 1,000 | **25 fewer per 1,000** (106 fewer to 72 more) |  1. {Cavallin 2021 572} 2. 95% CI crossing line of no effect   For secondary outcomes:  For **mean body temperature on admission, there was probable clinical harm** (temperature 0.2°C lower, 95% CI 0.33 to 0.07 lower), **moderate certainty evidence** downgraded for imprecision from 1 RCT enrolling 450 participants) {Cavallin 2021 572}  For **hypothermia < 36.5** **there was probable clinical harm** (RR1.20 95% CI 1.01 to1.42), **moderate certainty evidence** downgraded for imprecision from 1 trial enrolling 450 infants. {Cavallin 2021 572}  For **mild hypothermia** **(36.0 to 36.4°C )** there was **probable clinical harm** (RR 1.48 (95% CI 1.09 to 2.01), **moderate certainty evidence** downgraded for imprecision from 1 RCT enrolling 450 infants. {Cavallin 2021 572}  For **moderate to severe hypothermia < 36.0**°C **clinical benefit or harm cannot be excluded** (RR 0.97 95% CI 0.71 to 1.31), **moderate certainty evidence** downgraded for imprecision from 1 RCT enrolling 450 infants. {Cavallin 2021 572}  For **IVH (>grade 2)** **clinical benefit or harm cannot be excluded** (RR 0.87 95% CI 0.42 to 1.78 ), moderate certainty evidence downgraded for imprecision from 1 RCT enrolling 450 infants. {Cavallin 2021 572}  For l**ate onset sepsis** **clinical benefit or harm cannot be excluded** (RR 1.39 95% CI 0.89 to 2.18), **moderate certainty evidence** downgraded for imprecision from 1 RCT enrolling 450 infants. {Cavallin 2021 572}  For b**ronchopulmonary dysplasia clinical benefit or harm cannot be excluded** (RR 0.98 95%CI 0.68 to 1.41), **moderate certainty evidence** downgraded for imprecision from 1 RCT enrolling 450 infants. {Cavallin 2021 572}  For **delivery room intubation** there was **possible clinical benefit**(RR 0.67 95%CI 0.46 to 0.97), **moderate certainty evidence** downgraded for imprecision from 1 RCT enrolling 450 infants. {Cavallin 2021 572}  For **delivery room nasal positive pressure ventilation, clinical benefit or harm cannot be excluded** (RR 1.06 95%CI0.90 to 1.23), **moderate certainty evidence** downgraded for imprecision from 1 RCT enrolling 450 infants. {Cavallin 2021 572}  For other secondary outcomes, (RDS requiring surfactant, NEC) outcome data were not reported.   | **Secondary Outcomes** | **№ of participants (studies) Follow-up** | **Certainty of the evidence (GRADE)** | **Relative effect (95% CI)** | **Anticipated absolute effects\* (95% CI)** | | | --- | --- | --- | --- | --- | --- | | **Risk with manual mode radiant warmer** | **Risk difference with servo controlled radiant warmer** | | Mean body temperature | 450 (1 RCT)1 | ⨁⨁⨁◯ Moderatea | - | The median mean body temperature was **36.5°C** | MD **0.2**°C **lower** (0.33°C lower to 0.07°C lower) | | Hypothermia < 36.5 C | 450 (1 RCT)1 | ⨁⨁⨁◯ Moderatea | **RR 1.20** (1.01 to 1.42) | 498 per 1,000 | **100 more per 1,000** (5 more to 209 more) | | Mild hypothermia 36.0-36.4 | 450 (1 RCT)1 | ⨁⨁⨁◯ Moderatea | **RR 1.48** (1.09 to 2.01) | 222 per 1,000 | **107 more per 1,000** (20 more to 224 more) | | Moderate hypothermia < 36.0C | 450 (1 RCT)1 | ⨁⨁⨁◯ Moderateb | **RR 0.97** (0.71 to 1.31) | 276 per 1,000 | **8 fewer per 1,000** (80 fewer to 85 more) | | IVH > grade 2 | 450 (1 RCT)1 | ⨁⨁⨁◯ Moderateb,c | **RR 0.87** (0.42 to 1.78) | 67 per 1,000 | **9 fewer per 1,000** (39 fewer to 52 more) | | Late onset neonatal sepsis | 450 (1 RCT)1 | ⨁⨁⨁◯ Moderateb,c | **RR 1.39** (0.89 to 2.18) | 124 per 1,000 | **49 more per 1,000** (14 fewer to 147 more) | | BPD | 450 (1 RCT)1 | ⨁⨁⨁◯ Moderateb,c | **RR 0.98** (0.68 to 1.41) | 209 per 1,000 | **4 fewer per 1,000** (67 fewer to 86 more) | | Delivery room intubation | 450 (1 RCT)1 | ⨁⨁⨁◯ Moderatec | **RR 0.67** (0.46 to 0.97) | 240 per 1,000 | **79 fewer per 1,000** (130 fewer to 7 fewer) | | Delivery room nasal positive pressure ventilation | 450 (1 RCT)1 | ⨁⨁⨁◯ Moderateb,c | **RR 1.06** (0.90 to 1.23) | 564 per 1,000 | **34 more per 1,000** (56 fewer to 130 more) |   1 {Cavallin 2021 572}   1. Single study, though optimal information size (OIS) satisfied 2. 95% CI crossing line of no effect 3. OIS not satisfied   We considered **the effect of servo control mode uncertain** because there were no important differences in the rates of primary outcomes. Among secondary outcomes, the mean difference in temperature was only 0.2°C lower in the servo control group, although this difference did cross a line of treatment effect, in that the mean temperature in the servo control group was in the cold stress (mild hypothermia) range. The proportion of infants who were mildly hypothermic was higher in the group exposed to servo control, but the confidence interval was wide. | We do not know the effect size in the presence of additional or fewer co-interventions. Infants in both the servo controlled and the manual warmer group were equally exposed to additional thermoregulation measures.  The servo control system was set at 37°C, we do not know the effect of different set temperatures on the outcomes of interest. Manual mode was set at maximum output for ten minutes before the birth of an infant. We do not know the effect of specific manual mode settings other than those used in the studies. Also, if there was less time for the heater to warm up in manual mode before the birth of a baby, this could alter the difference between servo and manual modes (effect size). | | Undesirable Effects How substantial are the undesirable anticipated effects? | | | | Judgement | Research evidence | Additional considerations | | ○ Large ○ Moderate ○ Small ○ Trivial ○ Varies ● Don't know | This systematic review found that when a servo controlled radiant warmer was used in the delivery room compared to using a radiant warmer in manual mode for preterm infants:  For **Hyperthermia (> 38.0°C** **), clinical benefit or harm cannot be excluded** (RR 0.02 95% CI 0.00 to 8.46), **low certainty evidence** downgraded for imprecision from 1 RCT enrolling 450 infants. {Cavallin 2021 572}   | **Outcomes** | **№ of participants (studies) Follow-up** | **Certainty of the evidence (GRADE)** | **Relative effect (95% CI)** | **Anticipated absolute effects\* (95% CI)** | | | --- | --- | --- | --- | --- | --- | | **Risk with manual mode radiant warmer** | **Risk difference with servo controlled radiant warmer** | | Hyperthermia | 450 (1 RCT)1 | ⨁⨁◯◯ Lowa | **RR 0.02** (0.00 to 8.46) | 27 per 1,000 | **26 fewer per 1,000** (27 fewer to 199 more) |  1. {Cavallin 2021 572} 2. Single study with low event rates, 95% CI crossing line of no effect | The single study in this review also used a plastic bag or wrap plus a hat for a similar proportion of infants in each group. Additionally, delayed cord clamping, or thermal mattress or heated humidified gases were used in a proportion of infants in each group.  We do not know the effect size in the presence of fewer or more co-interventions.  Radiant warmers in servo control mode require a sensor to adhere to the infant’s skin or a probe inserted into the neonate's rectum. Both methods have some potential to cause harm.  Tape used to secure the temperature sensor could cause skin damage in preterm infants due to their fragile, underdeveloped skin. {Mishra 2021 1627}  Damage to the rectum from rectal temperature probes is possible but rare. {Morley 1992 122} | | 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 | The certainty of evidence for all outcomes was moderate except, **"**hyperthermia**"** which was low. |  | | 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 | The outcome of survival to hospital discharge (or its converse, mortality) have been judged by both care givers and parents to be the highest ranked outcomes of importance. {Strand 2020 F328, Webbe 2020 425} | Cold stress and hypothermia are common, particularly among preterm infants and are associated with increased mortality and morbidity {de Almeida 2014 271} | | 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 | The review found evidence from a single study that it was improbable that there was benefit or harm for the two primary outcomes. The review found possible evidence of harm for three secondary outcomes measuring temperature on admission to the neonatal unit (mean temperature on admission, hypothermia < 36.5°C, mild hypothermia (36.0°C to 36.4°C)) for infants exposed to a servo controlled radiant warmer. In this study, servo control did not cause hyperthermia. | The single study did not present data in a form that enabled analysis by birthweight categories. It is possible that the balance of benefits and harms varies by birthweight or gestation subgroups. | | 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 | The one study included in the review was conducted in a high resource setting. No estimates of costs or resources required were provided in this, or other studies considered for inclusion. | Additional equipment expenses include a radiant warmer capable of servo control, disposable or reusable sensors or probes. | | 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 | The review found no specific information about required resources. |  | | 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 study included in the review did not provide information on cost effectiveness. |  | | 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 | In high resource settings, radiant warmers capable of being used in either servo or manual mode are likely to be available for resuscitation of preterm infants in the delivery room. In low and middle resource settings, radiant warmers may be unavailable or unaffordable or capable of use only in manual mode. However, since the intervention (servo control) did not appear to be beneficial, the net effects on equity are unknown. | Servo controlled radiant warmers are likely to be more expensive than manual mode radiant warmers. In addition to the cost of the device there is an additional cost for the sensors that need to be applied to an infant's skin. In a low resource setting the need for additional servo control may be unaffordable.  Servo control is not possible for all models of radiant warmer used in delivery rooms, particularly in low- or middle-income countries. | | Acceptability Is the intervention acceptable to key stakeholders? | | | | Judgement | Research evidence | Additional considerations | | ○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know | In the one study included in this review the study protocol was followed for all infants, suggesting that both servo control and manual mode were acceptable in the context of the study. After NICU admission, it is standard practice in countries where suitable equipment is available, to use servo control for thermoregulation. |  | | Feasibility Is the intervention feasible to implement? | | | | Judgement | Research evidence | Additional considerations | | ○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know | Use of servo or manual control appeared feasible in the setting in the study. | Barriers to implementing servo-controlled heating in the delivery room are likely to be related to the cost of the intervention. |  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 | | ○ | ○ **○p** | ○ | ○ | ○ |  Conclusions  |  | | --- | | Recommendation | | In preterm infants (<34 weeks’ gestation) immediately after birth there is insufficient published human evidence to suggest for or against the use of a radiant warmer in servo-controlled mode compared to manual mode for maintaining normal temperature. (Weak recommendation, moderate certainty evidence).  In preterm infants (<34 weeks’ gestation) immediately after birth a radiant warmer is recommend (Good practice statement) | | Justification | | **Overall justification**  Use of servo control mode for radiant warmers did not affect primary outcomes of the systematic review but did result in lower body temperatures and more infants with temperatures in the mildly hypothermic range.  **Detailed justification**  *Problem*  Hypothermia is a common problem after birth in preterm infants and is associated with increased morbidity and mortality.  *Desirable Effects*  The effects of servo control compared with manual control were small but favoured use of manual control.  *Undesirable Effects*  Use of servo control did not affect rates of hyperthermia (the undesirable outcome examined in this review).  *Certainty of evidence*  The evidence is low or moderate certainty.  *Balance of effects and Cost effectiveness*  No evidence was found.  *Equity*  The additional cost of servo controlled radiant warmers and associated consumables is likely to preclude use in low resource settings. | | Subgroup considerations | | There were insufficient data from the single included study to undertake meaningful sub group analyses by gestational age, location of birth or effect of deferred cord clamping. | | Implementation considerations | | Servo controlled radiant warmers are widely used in neonatal units for thermoregulation. Manual mode radiant warmers are cheaper, depending on location the additional cost for servo controlled radiant warmers might be an unacceptable expense. | | Monitoring and evaluation | | Neonate's temperatures on admission to neonatal units should continue to be monitored as an important indicator of care. {Perlman 2015 S204} | | Research priorities | | * The role of servo control in maintaining normal temperature in preterm infants requiring prolonged resuscitation * The balance of risks and benefits of servo controlled radiant warmers in the setting of various levels of ambient temperature and humidity. * The balance of risks and benefits of servo control when there is variation in the co-interventions to prevent hypothermia (e.g. plastic bag of wrap, skin-to-skin care, thermal mattress, warmed and humidified resuscitation gases) are used in conjunction with a radiant warmer. * Are there servo-controlled devices that could be adapted for use during deferred cord clamping? * Does position of the temperature sensor probe affect the outcomes? |  References Summary | | |

Abiramalatha T, Ramaswamy VV, Bandyopadhyay T, Pullattayil AK, Thanigainathan S, Trevisanuto D, et al. Delivery Room Interventions for Hypothermia in Preterm Neonates: A Systematic Review and Network Meta-analysis. JAMA Pediatr. 2021;175(9)e210775.

Ahmed BT, Hussein MA, Monir H. Effect of Plastic Bag (Vinyl Bags) on Prevention of Hypothermia in Preterm Infants. Med J Cairo Univ. 2013;81(1)169-173.

Aley-Raz ES, Talmon G, Peniakov M, Hasanein J, Felszer-Fisch C, Weiner SA. Reducing neonatal hypothermia in premature infants in an israeli neonatal intensive care unit. Israel Medical Association Journal. 2020;22(9)476-480.

Ashmeade TL, Haubner L, Collins S, Miladinovic B, Fugate K. Outcomes of a Neonatal Golden Hour Implementation Project. Am J Med Qual. 2016;31(1)73-80.

Bhavsar S, Kabra N, Avasthi B, Sharma S, Dash S, Tali S, et al. Efficacy and safety of Polythene Wrap in Preventing Hypothermia in Preterm and Low Birth Weight Neonates During Transport: A Randomized Controlled Trial. Perinatology. 2015;1623-30.

Billimoria Z, Chawla S, Bajaj M, Natarajan G. Improving admission temperature in extremely low birth weight infants: a hospital-based multi-intervention quality improvement project. J Perinat Med. 2013;41(4)455-60.

Brophy H, Tan GM, Yoxall CW. Very Low Birth Weight Outcomes and Admission Temperature: Does Hyperthermia Matter? Children (Basel). 2022;9(11).

Caldas JPS, Millen FC, Camargo JF, Castro PAC, Camilo A, Marba STM. Effectiveness of a measure program to prevent admission hypothermia in very low-birth weight preterm infants. J Pediatr (Rio J). 2018;94(4)368-373.

Cavallin F, Calgaro S, Brugnolaro V, Wingi OM, Muhelo AR, Da Dalt L, et al. Non-linear association between admission temperature and neonatal mortality in a low-resource setting. Sci Rep. 2020;10(1)20800.

Cavallin F, Doglioni N, Allodi A, Battajon N, Vedovato S, Capasso L, et al. Thermal management with and without servo-controlled system in preterm infants immediately after birth: a multicentre, randomised controlled study. Arch Dis Child Fetal Neonatal Ed. 2021;106(6)572-577.

Chantaroj S, Techasatid W. Effect of polyethylene bag to prevent heat loss in preterm infants at birth: a randomized controlled trial. J Med Assoc Thai. 2011;94 S32-7.

Chawla S, Amaram A, Gopal SP, Natarajan G. Safety and efficacy of Trans-warmer mattress for preterm neonates: results of a randomized controlled trial. J Perinatol. 2011;31(12)780-4.

Cho M, Kim CY, Lee J, Lee Y, Park M, Bae S, et al. Comparing Axillary and Rectal Temperature Measurements in Very Preterm Infants: A Prospective Observational Study. Neonatology. 2021;118(2)180-186.

Choi HS, Lee SM, Eun H, Park M, Park KI, Namgung R. The impact of a quality improvement effort in reducing admission hypothermia in preterm infants following delivery. Korean J Pediatr. 2018;61(8)239-244.

Cleator AJ, Coombe E, Alexopoulou V, Levingston L, Evans K, Hurst JC, et al. Maintaining Normothermia in Preterm Babies during Stabilisation with an Intact Umbilical Cord. Children (Basel). 2022;9(1).

Croop SEW, Thoyre SM, Aliaga S, McCaffrey MJ, Peter-Wohl S. The Golden Hour: a quality improvement initiative for extremely premature infants in the neonatal intensive care unit. J Perinatol. 2020;40(3)530-539.

Dawson JA, Owen LS, Middleburgh R, Davis PG. Quantifying temperature and relative humidity of medical gases used for newborn resuscitation. J Paediatr Child Health. 2014;50(1)24-6.

de Almeida MF, Guinsburg R, Sancho GA, Rosa IR, Lamy ZC, Martinez FE, et al. Hypothermia and early neonatal mortality in preterm infants. J Pediatr. 2014;164(2)271-5.e1.

DeMauro SB, Douglas E, Karp K, Schmidt B, Patel J, Kronberger A, et al. Improving delivery room management for very preterm infants. Pediatrics. 2013;132(4)e1018-25.

Farhadi R, Naderi M, Rahmani Z, Ghaffari V, Khalilian A. Effect of "ZIPKIF" plastic bag on prevention of hypothermia in preterm infants: A randomized controlled trial. Journal of Mazandaran University of Medical Sciences. 2012;22(93)19-26.

Ferretti E, Daboval T, Rouvinez-Bouali N, Lawrence SL, Lemyre B. Extremely low gestational age infants: Developing a multidisciplinary care bundle. Paediatr Child Health. 2021;26(6)e240-e245.

Frazer M, Ciarlo A, Herr J, Briere CE. Quality Improvement Initiative to Prevent Admission Hypothermia in Very-Low-Birth-Weight Newborns. J Obstet Gynecol Neonatal Nurs. 2018;47(4)520-528.

Frazer M, Ciarlo A, Hinderer KA, Briere CE. Reducing Admission Hypothermia in Neonates Born at Less Than 32 Weeks or 1500 g. Adv Neonatal Care. 2022;22(2)99-107.

Gathwala G, Singh G, Kunal, Agrawal N. Safety and efficacy of vinyl bags in prevention of hypothermia of preterm neonates at birth. Indian J Public Health. 2010;54(1)24-6.

Gillies D, Todd DA, Foster JP, Batuwitage BT. Heat and moisture exchangers versus heated humidifiers for mechanically ventilated adults and children. Cochrane Database Syst Rev. 2017;9(9)Cd004711.

Godfrey K, Nativio DG, Bender CV, Schlenk EA. Occlusive bags to prevent hypothermia in premature infants: a quality improvement initiative. Adv Neonatal Care. 2013;13(5)311-6.

Greenspan JS, Wolfson MR, Shaffer TH. Airway responsiveness to low inspired gas temperature in preterm neonates. J Pediatr. 1991;118(3)443-5.

Harer MW, Vergales B, Cady T, Early A, Chisholm C, Swanson JR. Implementation of a multidisciplinary guideline improves preterm infant admission temperatures. J Perinatol. 2017;37(11)1242-1247.

Harriman TL, Carter B, Dail RB, Stowell KE, Zukowsky K. Golden Hour Protocol for Preterm Infants: A Quality Improvement Project. Adv Neonatal Care. 2018;18(6)462-470.

Ibrahim CP, Yoxall CW. Use of self-heating gel mattresses eliminates admission hypothermia in infants born below 28 weeks gestation. Eur J Pediatr. 2010;169(7)795-9.

Keir AK, Cavallaro A. Improving the admission temperatures of preterm infants in the neonatal unit. Archives of Disease in Childhood: Education and Practice Edition. 202110.1136/archdischild-2020-321226375-378.

Knobel RB, Wimmer JE, Jr., Holbert D. Heat loss prevention for preterm infants in the delivery room. J Perinatol. 2005;25(5)304-8.

L'Herault J, Petroff L, Jeffrey J. The effectiveness of a thermal mattress in stabilizing and maintaining body temperature during the transport of very low-birth weight newborns. Appl Nurs Res. 2001;14(4)210-9

Lang N, Bromiker R, Arad I. The effect of wool vs. cotton head covering and length of stay with the mother following delivery on infant temperature. Int J Nurs Stud. 2004;41(8)843-6.

LeBlanc MH. Evaluation of two devices for improving thermal control of premature infants in transport. Crit Care Med. 1984;12(7)593-5.

Lee HC, Ho QT, Rhine WD. A quality improvement project to improve admission temperatures in very low birth weight infants. J Perinatol. 2008;28(11)754-8.

Lewis DA, Sanders LP, Brockopp DY. The effect of three nursing interventions on thermoregulation in low birth weight infants. Neonatal Netw. 2011;30(3)160-4.

Lyu Y, Shah PS, Ye XY, Warre R, Piedboeuf B, Deshpandey A, et al. Association between admission temperature and mortality and major morbidity in preterm infants born at fewer than 33 weeks' gestation. JAMA Pediatr. 2015;169(4)e150277.

Manani M, Jegatheesan P, DeSandre G, Song D, Showalter L, Govindaswami B. Elimination of admission hypothermia in preterm very low-birth-weight infants by standardization of delivery room management. Perm J. 2013;17(3)8-13.

Mathew B, Lakshminrusimha S, Sengupta S, Carrion V. Randomized controlled trial of vinyl bags versus thermal mattress to prevent hypothermia in extremely low-gestational-age infants. Am J Perinatol. 2013;30(4)317-22.

McCarthy LK, Molloy EJ, Twomey AR, Murphy JF, O'Donnell CP. A randomized trial of exothermic mattresses for preterm newborns in polyethylene bags. Pediatrics. 2013;132(1)e135-41.

McCarthy LK, O'Donnell CP. Warming preterm infants in the delivery room: polyethylene bags, exothermic mattresses or both? Acta Paediatr. 2011;100(12)1534-7.

McCarthy LK, O'Donnell CPF. Comparison of rectal and axillary temperature measurements in preterm newborns. Arch Dis Child Fetal Neonatal Ed. 2021;106(5)509-513.

McGrory L, Owen LS, Thio M, Dawson JA, Rafferty AR, Malhotra A, et al. A Randomized Trial of Conditioned or Unconditioned Gases for Stabilizing Preterm Infants at Birth. J Pediatr. 2018;19347-53

Meyer MP, Hou D, Ishrar NN, Dito I, te Pas AB. Initial respiratory support with cold, dry gas versus heated humidified gas and admission temperature of preterm infants. J Pediatr. 2015;166(2)245-50.e1.

Mishra U, Jani P, Maheshwari R, Shah D, D'Cruz D, Priyadarshi A, et al. Skincare practices in extremely premature infants: A survey of tertiary neonatal intensive care units from Australia and New Zealand. J Paediatr Child Health. 2021;57(10)1627-1633.

Morley CJ, Hewson PH, Thornton AJ, Cole TJ. Axillary and rectal temperature measurements in infants. Arch Dis Child. 1992;67(1)122-5.

Nimbalkar SM, Khanna AK, Patel DV, Nimbalkar AS, Phatak AG. Efficacy of Polyethylene Skin Wrapping in Preventing Hypothermia in Preterm Neonates (<34 Weeks): A Parallel Group Non-blinded Randomized Control Trial. J Trop Pediatr. 2019;65(2)122-129.

Peleg B, Globus O, Granot M, Leibovitch L, Mazkereth R, Eisen I, et al. "Golden Hour" quality improvement intervention and short-term outcome among preterm infants. J Perinatol. 2019;39(3)387-392.

Perlman JM, Wyllie J, Kattwinkel J, Wyckoff MH, Aziz K, Guinsburg R, et al. Part 7: neonatal resuscitation: 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. Circulation. 2015;132(suppl 1)(16)S204‒S241.

Pillow JJ, Hillman NH, Polglase GR, Moss TJ, Kallapur SG, Cheah FC, et al. Oxygen, temperature and humidity of inspired gases and their influences on airway and lung tissue in near-term lambs. Intensive Care Med. 2009;35(12)2157-63.

Pinheiro JM, Boynton S, Furdon SA, Dugan R, Reu-Donlon C. Use of chemical warming packs during delivery room resuscitation is associated with decreased rates of hypothermia in very low-birth-weight neonates. Adv Neonatal Care. 2011;11(5)357-62.

Pinheiro JM, Furdon SA, Boynton S, Dugan R, Reu-Donlon C, Jensen S. Decreasing hypothermia during delivery room stabilization of preterm neonates. Pediatrics. 2014;133(1)e218-26.

Ramaswamy VV, de Almeida MF, Dawson JA, Trevisanuto D, Nakwa FL, Kamlin CO, et al. Maintaining normal temperature immediately after birth in late preterm and term infants: A systematic review and meta-analysis. Resuscitation. 2022;18081-98.

Reilly MC, Vohra S, Rac VE, Dunn M, Ferrelli K, Kiss A, et al. Randomized trial of occlusive wrap for heat loss prevention in preterm infants. J Pediatr. 2015;166(2)262-8.e2.

Reilly MC, Vohra S, Rac VE, Zayack D, Wimmer J, Vincer M, et al. Parallel Exploratory RCT of Polyethylene Wrap for Heat Loss Prevention in Infants Born at Less than 24 Weeks' Gestation. Neonatology. 2019;116(1)37-41.

Reuter S, Messier S, Steven D. The neonatal Golden Hour--intervention to improve quality of care of the extremely low birth weight infant. S D Med. 2014;67(10)397-403.

Rohana J, Khairina W, Boo NY, Shareena I. Reducing hypothermia in preterm infants with polyethylene wrap. Pediatr Int. 2011;53(4)468-74.

Russo A, McCready M, Torres L, Theuriere C, Venturini S, Spaight M, et al. Reducing hypothermia in preterm infants following delivery. Pediatrics. 2014;133(4)e1055-62.

Sharma D, Murki S, Kulkarni D, Pawale D, Vardhelli V, Anne RP, et al. The impact of a quality improvement project to reduce admission hypothermia on mortality and morbidity in very low birth weight infants. Eur J Pediatr. 2020;179(12)1851-1858.

Simon P, Dannaway D, Bright B, Krous L, Wlodaver A, Burks B, et al. Thermal defense of extremely low gestational age newborns during resuscitation: exothermic mattresses vs polyethylene wrap. J Perinatol. 2011;31(1)33-7.

Singh A, Duckett J, Newton T, Watkinson M. Improving neonatal unit admission temperatures in preterm babies: exothermic mattresses, polythene bags or a traditional approach? J Perinatol. 2010;30(1)45-9.

Sivanandan S, Sankar MJ, Deorari A. Quality Improvement Initiative to Prevent Hypothermia at Admission in Neonatal Intensive Care Unit Among Preterm Neonates < 32 Weeks' Gestation. Journal of Neonatology. 2016;30(4)39-49.

Smith J, Usher K, Alcock G, Buettner P. Application of plastic wrap to improve temperatures in infants born less than 30 weeks gestation: a randomized controlled trial. Neonatal Netw. 2013;32(4)235-45.

Sottiaux TM. Consequences of under- and over-humidification. Respir Care Clin N Am. 2006;12(2)233-52.

Sprecher A, Malin K, Finley D, Lembke P, Keller S, Grippe A, et al. Quality Improvement Approach to Reducing Admission Hypothermia Among Preterm and Term Infants. Hosp Pediatr. 2021;11(3)270-276.

Strand ML, Simon WM, Wyllie J, Wyckoff MH, Weiner G. Consensus outcome rating for international neonatal resuscitation guidelines. Arch Dis Child Fetal Neonatal Ed. 2020;105:F328–F330.

te Pas AB, Lopriore E, Dito I, Morley CJ, Walther FJ. Humidified and heated air during stabilization at birth improves temperature in preterm infants. Pediatrics. 2010;125(6)e1427-32.

Trevisanuto D, Doglioni N, Cavallin F, Parotto M, Micaglio M, Zanardo V. Heat loss prevention in very preterm infants in delivery rooms: a prospective, randomized, controlled trial of polyethylene caps. J Pediatr. 2010;156(6)914-917.e1.

Trevisanuto D, Testoni D, de Almeida MFB. Maintaining normothermia: Why and how? Semin Fetal Neonatal Med. 2018;23(5)333-339.

Vinci A, Islam S, Quintos-Alegheband L, Hanna N, Nayak A. A Quality Improvement Intervention to Decrease Hypothermia in the Delivery Room Using a Checklist. Pediatr Qual Saf. 2018;3(6)e125.

Vohra S, Frent G, Campbell V, Abbott M, Whyte R. Effect of polyethylene occlusive skin wrapping on heat loss in very low birth weight infants at delivery: a randomized trial. J Pediatr. 1999;134(5)547-51.

Vohra S, Roberts RS, Zhang B, Janes M, Schmidt B. Heat Loss Prevention (HeLP) in the delivery room: A randomized controlled trial of polyethylene occlusive skin wrapping in very preterm infants. J Pediatr. 2004;145(6)750-3.

Webbe JWH, Duffy JMN, Afonso E, Al-Muzaffar I, Brunton G, Greenough A, et al. Core outcomes in neonatology: development of a core outcome set for neonatal research. Arch Dis Child Fetal Neonatal Ed. 2020;105(4)425-431.

Wilson E, Maier RF, Norman M, Misselwitz B, Howell EA, Zeitlin J, et al. Admission Hypothermia in Very Preterm Infants and Neonatal Mortality and Morbidity. J Pediatr. 2016;17561-67.e4.

Wilson E, Maier RF, Norman M, Misselwitz B, Howell EA, Zeitlin J, et al. Admission Hypothermia in Very Preterm Infants and Neonatal Mortality and Morbidity. J Pediatr. 2016;17561-67 e4.

Wlodaver A, Blunt M, Satnes K, Escobedo M, Hallford G, Szyld E. A retrospective comparison of VLBW outcomes before and after implementing new delivery room guidelines at a regional tertiary care center. J Perinatol. 2016;36(3)182-5.

Yip WY, Quek BH, Fong MCW, Thilagamangai, Ong SSG, Lim BL, et al. A quality improvement project to reduce hypothermia in preterm infants on admission to the neonatal intensive care unit. Int J Qual Health Care. 2017;29(7)922-928.

Young A, Azeez F, Godad SP, Shetty P, Sharma A. A multimodal quality improvement approach to promote normothermia in very preterm infants. Acta Paediatr. 2021;1102745-2752.