Impact of neonatal resuscitation trainings on neonatal and perinatal mortality: a systematic review and meta-analysis

Archana Patel,1 Mahalaqua Nazli Khatib,2 Kunal Kurhe,1 Savita Bhargava,1 Akash Bang3

ABSTRACT

Background Training of birth attendants in neonatal resuscitation is likely to reduce birth asphyxia and neonatal mortality. We performed a systematic review and meta-analysis to assess the impact of neonatal resuscitation training (NRT) programme in reducing stillbirths, neonatal mortality, and perinatal mortality

Methods We considered studies where any NRT was provided to healthcare personnel involved in delivery process and handling of newborns. We searched MEDLINE, CENTRAL, ERIC and other electronic databases. We also searched ongoing trials and bibliographies of the retrieved articles, and contacted experts for unpublished work. We undertook screening of studies and assessment of risk of bias in duplicates. We performed review according to Cochrane Handbook. We assessed the quality of evidence using the GRADE approach.

Results We included 20 trials with 1 653 805 births in this meta-analysis. The meta-analysis of NRT versus control shows that NRT decreases the risk of all stillbirths by 21% (RR 0.79, 95% CI 0.44 to 1.41), 7-day neonatal mortality by 47% (RR 0.53, 95% CI 0.38 to 0.73), 28-day neonatal mortality by 50% (RR 0.50, 95% CI 0.37 to 0.68) and perinatal mortality by 37% (RR 0.63, 95% CI 0.42 to 0.94). The meta-analysis of pre-NRT versus post-NRT showed that post-NRT decreased the risk of all stillbirths by 12% (RR 0.88, 95% CI 0.83 to 0.94), fresh stillbirths by 26% (RR 0.74, 95% CI 0.61 to 0.90), 1-day neonatal mortality by 42% (RR 0.58, 95% CI 0.42 to 0.82), 7-day neonatal mortality by 18% (RR 0.82, 95% CI 0.73 to 0.93), 28-day neonatal mortality by 14% (RR 0.86, 95% CI 0.65 to 1.13) and perinatal mortality by 18% (RR 0.82, 95% CI 0.74 to 0.91).

Conclusions Findings of this review show that implementation of NRT improves neonatal and perinatal mortality. Further good quality randomised controlled trials addressing the role of NRT for improving neonatal and perinatal outcomes may be warranted.

Trial registration number PROSPERO 2016:CRD42016043668

INTRODUCTION

Approximately a quarter of 1 million neonatal deaths worldwide are as a result of birth asphyxia.1 A large majority of these deaths occur in low-resource settings and are preventable. Approximately 5%–10% of newborns require some support to adapt to the extrauterine environment and to establish regular respiration.1 2 Simple resuscitative measures are often enough to resuscitate newborns that may even appear to be lifeless at birth. Studies have shown that essential newborn care has been effective in reducing stillbirths (SB).3

In developing countries, measures to improve resuscitative efforts through training of basic steps of neonatal resuscitation are expected to reduce birth asphyxia and neonatal mortality. Numerous studies
have suggested that imparting neonatal resuscitation training (NRT) to healthcare providers involved in delivery process and handling of newborns has the potential to save newborn lives in low-income and middle-income settings.4–10 Improvements in knowledge and skills of trainees following training programme in resource-limited settings have been reviewed. However, the impact on perinatal mortality outcomes has not been updated in last 5 years.9 The effect estimates of mortality reduction as a result of training of healthcare providers involved in delivery process and handling of newborns needs to be updated to inform hospital administrators and policy-makers the importance of investing in NRT to sustain and improve neonatal survival. A previous systematic review and meta-analysis11 assessed knowledge, skills, neonatal morbidity, neonatal mortality in first 7 days after birth and from day 8 to 28. However, it did not include outcomes of stillbirth, 1-day neonatal mortality or perinatal mortality which has been included in our review.

The objective of this review is to assess the impact of NRT programme in reducing stillbirths, 1-day neonatal mortality, 7-day neonatal mortality, 28-day neonatal mortality and perinatal mortality.

MATERIALS AND METHODS

Inclusion criteria

Types of studies

We included relevant randomised, quasi-randomised controlled trials, interrupted time series studies and before–after studies regardless of language or publication status.

Types of participants (population) trained

We considered studies where NRT was provided to healthcare providers (including neonatologists, physicians, nurses, interns, midwives, traditional/community birth attendants, auxiliary nurse midwives, village health workers, paramedics) involved in delivery process and handling of newborns in a community (home-based, rural and village clusters) or a hospital (including district hospitals, health centres, dispensaries, teaching/university hospitals, regional hospital, delivery/health centres, local hospitals and tertiary care hospital) setting.

Types of interventions and comparison

Studies in which any NRT was compared with a control group (that received no NRT) or compared with data before the study (pre-NRT vs post-NRT) were included. For this purpose, we considered any NRT programme of healthcare professionals, including the American Academy of Pediatrics’ (AAP) Neonatal Resuscitation Program (NRP), Helping Babies Breathe (HBB) or any other training programme that had NRP or HBB as a clearly mentioned component of training methodology.

Types of outcomes measures

We included following outcomes in the review:

1. Stillbirths: defined as number of deaths prior to complete expulsion or extraction of products of conception from its mother.
2. Fresh stillbirths: clinically defined as those deaths with no signs of life at any time after birth and without any signs of maceration.
3. 1-day neonatal mortality: defined as number of deaths in first 24 hours of life
4. 7-day neonatal mortality: defined as number of deaths in first 7 days of life
5. Perinatal mortality: defined as number of stillbirths and deaths in the first week of life.
6. 28-day neonatal mortality: defined as number of deaths in the first 28 days of life.

Search strategy

We searched following electronic databases from inception to July 2016: MEDLINE (PubMed), The Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library); Education Resources Information Centre (ERIC), Web of Science, Science Citation Index and Scientific Electronic Library Online. The search strategies for PubMed and CENTRAL can be found in supplementary files S1 and S2 respectively. We also searched for ongoing trials at www.clinicaltrials.gov and www.controlled-trials.com. We searched published abstracts of conferences and examined bibliographies of retrieved articles for additional studies. We contacted and requested experts and authors in this field to provide possible unpublished work.

Study selection and data extraction

Screening of studies

Two reviewers (MNK and AB) independently examined studies identified by literature search; discarded articles that did not fulfill the inclusion criteria and assessed full texts of all relevant articles for inclusion. A third reviewer (AP) resolved disagreement among the primary reviewers.

Data extraction and management

For all studies that fulfilled the inclusion criteria, two reviewers (KK, SB) extracted data (table 1 and 2). Third review author (AP) cross-checked the data and resolved discrepancies. For studies where required data was lacking or could not be calculated, we requested the corresponding author for details.

Assessment of risk of bias in included studies

Two authors (SB, KK) independently assessed risk of bias for each study using criteria suggested by Cochrane Effective Practice and Organization of Care (EPOC)12 and using criteria outlined in Chapter 8 of Cochrane Handbook for Systematic Reviews of Interventions.13 Disagreements were resolved by discussion with the third reviewer (MNK).
<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>Author</th>
<th>Country</th>
<th>Study design</th>
<th>Study period</th>
<th>Funding</th>
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</thead>
<tbody>
<tr>
<td>2</td>
<td>Ariawan et al¹⁸</td>
<td>Indonesia</td>
<td>Pre–Post training</td>
<td>NR</td>
<td>NR</td>
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<tr>
<td>5</td>
<td>Gill et al¹¹</td>
<td>Zambia</td>
<td>Prospective, cluster randomised and controlled effectiveness study</td>
<td>30 months (Jun 2006–Nov 2008)</td>
<td>Boston University and The Office of Health and Nutrition of The United State Agency for International Development, AAP, Unicef</td>
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<td>6</td>
<td>Zhu et al¹⁶</td>
<td>China</td>
<td>Perspective study, pre–post training (traditional resuscitation vs NRPG)</td>
<td>24 months (1993–1995)</td>
<td>NR</td>
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<td>7</td>
<td>Deorari et al¹⁴</td>
<td>India</td>
<td>Pre–post training (</td>
<td>NR</td>
<td>Laerdal Foundation Norway</td>
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<td>8</td>
<td>Jeffery et al²⁸</td>
<td>Macedonia</td>
<td>Pre–Post training</td>
<td>60 months (1997–2001)</td>
<td>International Project Unit, Ministry of Health, Macedonia, IDA Credit, World Bank</td>
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<td>10</td>
<td>O’Hare et al²⁵</td>
<td>Uganda</td>
<td>Pre–Post training (historic group vs NRP pilot)</td>
<td>1 month (Dec 2001–Jan 2002)</td>
<td>Child Advocacy International</td>
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<td>11</td>
<td>Opiyo et al¹⁹</td>
<td>Kenya</td>
<td>Pre–Post training</td>
<td>NR</td>
<td>Laerdal Foundation for Acute Medicine, Wellcome Trust Senior Research Fellowship Award</td>
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<tr>
<td>12</td>
<td>Boo³¹</td>
<td>Malaysia</td>
<td>Pre–Post training, prospective observational study</td>
<td>100months (Sep 1996–Dec 2004)</td>
<td>Perinatal Society of Malaysia</td>
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<td>13</td>
<td>Sorensen et al²⁹</td>
<td>Tanzania</td>
<td>Prospective study, Pre–Post training</td>
<td>14 weeks (Jul 2008–Nov 2008)</td>
<td>Danish Society of Obstetrics and Gynecology</td>
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<td>14</td>
<td>Hole et al¹²</td>
<td>Malawi, Africa</td>
<td>Pre–Post training</td>
<td>30 months (Jun 2007–Dec 2009)</td>
<td>Stanford University School of Medicines, Medical Scholars Research Program, Department of Community Relations at Lucil Packard Children’s Hospital</td>
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<td>16</td>
<td>Goudar et al³³</td>
<td>India</td>
<td>Pre–Post training (pretraining vs post HBB)</td>
<td>12 months (Oct 2009–Sep 2010)</td>
<td>AAP, Global Implementation Task Force HBB Program, Laerdal Foundation for Acute Medicine, Stavanger Norway</td>
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Table 1 Continued

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<tr>
<th>Sr. No.</th>
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<th>Study period</th>
<th>Funding</th>
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</table>
| 17      | Vossius et al     | Tanzania                    | Pre-Post training (pretraining vs post HBB) | 24 months (Feb 2010–Jan 2012) | Laerdal Foundation for Acute Medicine and Municipality of Stavanger Norway  
SWedish Society of Medicine Research Department of HLH, Tanzania |
| 18      | Ashish et al      | Nepal                       | Pre-Post training (pretraining vs post HBB) | 15 months (Jul 2012–Sep 2013) | Laerdal Foundation for Acute Medicine  
Swedish Society of Medicine |
| 19      | Bellad et al      | Kenya, India (Belgaum, Nagpur) | Pre-Post training (pretraining vs post HBB) | 24 months (Nov 2011–Oct 2013) | NORAD  
Laerdal Foundation and NICHD |
| 20      | Patel et al       | India (Nagpur)              | Pre-Post training (pre-training vs post HBB) | 24 months (Nov 2011–Oct 2013) | NORAD  
Laerdal Foundation and NICHD |

*Data for this study has been taken from Lee et al. *  
**Data for very low birth weight (<1500 g).  
***Unpublished data obtained via personal communication with the author.

AAP, American Academy of Pediatrics; ENC, essential newborn care; HBB, helping babies breathe; NICHD, National Institute of Child and Human Development; NR, not reported; NRPG, Neonatal Resuscitation Program Guidelines; RCT, randomised control trial.

RESULTS

We identified 148 records through database searching and 11 records through other sources. After initial screening on the basis of title and abstract, we assessed 47 full-text articles for eligibility and finally included 20 articles in the meta-analysis. The screening details are presented in a Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram (figure 1).

We conducted meta-analysis and reported pooled statistics as risk ratios (RR) with 95% confidence interval (CI) for dichotomous data. We followed the Cochrane Handbook for Systematic Reviews of Interventions Sections 9.2 and 9.4 for measuring the effects.

**Measures of treatment effect**

We conducted meta-analysis and reported pooled statistics as risk ratios (RR) with 95% confidence interval (CI) for dichotomous data. We followed the Cochrane Handbook for Systematic Reviews of Interventions Sections 9.2 and 9.4 for measuring the effects.

Assessment of heterogeneity

We assessed heterogeneity amongst studies by inspecting forest plots for the overlap of confidence intervals. We interpreted I² values as follows: 0% to 40% as possibly unimportant, 30% to 60% as possibly significant, 50% to 90% as possibly substantial and 75% to 100% as possibly considerable.

**Assessment of reporting bias**

We used funnel plots for assessment of publication bias. We did not pool randomised and non-randomised (pre–post NRT) studies in the same meta-analysis.

**Summary of findings table**

We created the summary of findings (SoF) table using five GRADE considerations (study limitations, consistency of evidence, indirectness, imprecision, publication bias) to assess the quality of a body of evidence. We used methods and recommendations described in Chapter 12 of the Cochrane Handbook for Systematic Reviews of Interventions (GRADE Working Group grades of evidence were used in the SoF). We used GRADEpro software. We used GRADEpro software.

We interpreted the value of 50% as medium, 75% as high and 90% as very high. We assessed the overlap of confidence intervals (CI) and interpreted the value of 50% as medium and 90% as very high. We interpreted values between 15% and 25% as possibly important, 30% as possibly substantial and 50% as possibly considerable.

**Data synthesis and analysis**

We used funnel plots for assessment of publication bias. We conducted meta-analysis to compare the effect of training on the incidence of various outcomes. We explored possible clinical and methodological reasons for heterogeneity and carried out sensitivity analysis and meta-regression. We employed inverse variance method with random-effects model.

**We interpreted I² values as follows:**

0% to 40% as possibly unimportant, 30% to 60% as possibly significant, 50% to 90% as possibly substantial and 75% to 100% as possibly considerable.
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<tr>
<th>Sr. No.</th>
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<th>Trainees</th>
<th>Assessment</th>
<th>No. of births</th>
<th>Outcomes</th>
</tr>
</thead>
</table>
| 1      | Bang et al     | NR       | Community (86 villages) | A package of home-based neonatal care, health education including ENC, Suction, stimulation, Artificial respiration by mouth to mask and tube and mask | Community birth attendants, Village health workers                         | NR                                                      | A: 1159    | B: 1005       | 1. SB  
2. NMR: day 7  
3. Perinatal mortality | A: NR  
B: NR |
| 2      | Ariawan et al  | NR       | Community (7 sites)     | NRT including Use of tube mask, Refresher training at 3, 6 and 9months, use of video, Post resuscitation care | Midwives                                                                  | NR                                                      | A: 9816    | B: 16053      | 1. SB  
2. NMR: day 28 | A: NR  
B: NR |
| 3      | Carlo et al    | 3 days   | Rural communities (7 sites in 6 countries for ENC; 88 for NRP)      | ENC sensitisation followed by in-depth NRT including Initial resuscitation steps BMV | AAP-trained trainer, Research staff, either a physician or nurse           | Community birth attendants                                              | NR         | A: 35917      | 1. SB  
2. FSB  
3. NMR: day 1  
4. NMR: day 7  
5. PMR | A: BW <1500 g  
B: NR |
| 4      | Carlo et al    | 3 days   | Rural communities (7 sites in 6 countries for ENC; 88 for NRP)      | ENC sensitisation followed by in-depth NRT including Initial resuscitation steps BMV | AAP-trained trainer, Research staff, either a physician or nurse           | Community birth attendants                                              | NR         | A: 35017      | 1. SB  
2. FSB  
3. NMR: day 1  
4. NMR: day 7  
5. PMR | A: BW >1500 g  
B: NR |
| 5      | Gill et al     | 2 weeks  | Community (rural district setting)                                  | NRT modified from AAP/AHA including Initial steps, PPV Use of manikins to demonstrate and practice skills | 60 Community birth attendants/ TBAs One to one skills assessment | NR                                                      | A: 536     | B: 1961       | 1. SB  
2. NMR: day 7  
3. NMR: day 28  
4. PMR | A: NR  
B: NR |
| 6      | Zhu et al      | NR       | Hospital (1 hospital)                                              | NRPG curriculum established from AAP and AHA including Suction BMV or ET ventilation Intubation | Hospital birth attendants                                               | NR                                                      | A: 1722    | B: 4751       | 1. NMR: day 1  
2. NMR: day 7 | A: NR  
B: NR |
| 7      | Deorari et al  | NR       | Hospital (14 teaching hospitals)                                   | AAP/AHA-modified NRT with TOT approach 2 Faculty member trainer per facility | Hospital-based birth attendants No skills assessment                      | NR                                                      | A: 7070    | B: 25713      | 1. NMR: day 7  
2. NMR: day 28 | A: NR  
B: NR |
| 8      | Jeffery et al  | 9 weeks  | Hospital (3 tertiary care, 13 district hospitals)                   | A package of perinatal practices with NRT Australian-trained Macedonian teachers, OB/GYN Medical Education              | Doctors and nurses MOQ, SAQ and OSCE (practical test)                    | NR                                                      | A: 69840   | B: 45458      | 1. SB  
2. NMR: day 7  
3. PMR | A: NR  
B: NR |
| 9      | Valkilova et al| NR       | Hospital (delivery rooms of city hospitals)                        | French-Bulgarian Program on NRT                                        | Neonatologist Obstetrician Midwives                                      | NR                                                      | A: 67948   | B: 67647      | 1. NMR: day 7 | A: NR  
B: NR |
| 10     | O’Hare et al   | 10 days  | Hospital (5 days classroom+5 days delivery suite)                   | NRT including Airway management BMV Cardiac massage Use of manikins to demonstrate and practice skills | 5 members of nursing staff                                              | NR                                                      | A: 1296    | B: 1046       | 1. SB  
2. NMR: day 28 | A: NR  
B: NR |
| 11     | Opiyo et al    | 1 day    | Hospital (1 maternity hospital)                                     | NRT including Initial steps BMV (use of bag valve mask device) OC Use of manikins to demonstrate and practice skills | Instructor completed Kenya Resuscitation Council Advanced Life Support Generic Instructor Course Nurse/midwives | NR                                                      | A: 4084    | B: 4302       | 1. SB  
2. NMR: day 28 | A: NR  
B: NR |

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<tr>
<th>Sr. No.</th>
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<th>Trainees</th>
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<th>Assessment</th>
<th>Outcomes</th>
<th>Criteria for delivery outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>Boo et al</td>
<td>NR</td>
<td>Hospital</td>
<td>AAP-NRT tailored to local needs including</td>
<td>► 37 Core instructors&lt;br&gt; ► Doctors and nurses</td>
<td>14,575</td>
<td>A: 5,417,21</td>
<td>B: 465,140</td>
<td>1. SB</td>
<td>A: NR&lt;br&gt; B: NR</td>
</tr>
<tr>
<td>13</td>
<td>Sorensen et al</td>
<td>2 days</td>
<td>Hospital (1 referral hospital)</td>
<td>ALSO a widespread EmONC Use of manikins to demonstrate and practice skills</td>
<td>NR</td>
<td>1,577</td>
<td>B: 565</td>
<td>1. SB</td>
<td>A: NR</td>
<td>B: BW &gt; 1,000 g</td>
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<tr>
<td>14</td>
<td>Hole et al</td>
<td>1 day</td>
<td>Hospital (1 university hospital and 1 referral hospital)</td>
<td>AAP modified NRT to include Initial steps BMV CC and special consideration Use of manikins to demonstrate and practice skills</td>
<td>Paediatrics residents from Stanford University&lt;br&gt; ► Physician&lt;br&gt; ► Clinical officers&lt;br&gt; ► Midwives</td>
<td>145</td>
<td>B: 3515</td>
<td>1. NMR: day 28</td>
<td>A: NR</td>
<td>B: NR</td>
</tr>
<tr>
<td>15</td>
<td>Msemo et al</td>
<td>1 day</td>
<td>Hospital (3 referral hospitals, 4 regional hospitals and 1 district hospital)</td>
<td>HBB training including Initial steps BMV Face and mask ventilation ToT approach Use of simulators for hands on practice FBO training—reported by 1 site</td>
<td>40 Trainers</td>
<td>8124</td>
<td>B: 78,500</td>
<td>1. SB</td>
<td>A: NR</td>
<td>B: BW &gt; 750 g for live birth BW &gt; 1,000 g for FSB</td>
</tr>
<tr>
<td>16</td>
<td>Goudar et al</td>
<td>1 day</td>
<td>Hospital (primary health centres and rural and urban hospitals)</td>
<td>HBB-AAP-based NRT Initial steps Simulation Suctioning BMV ToT model Paired teaching Use of manikins to demonstrate and practice skills</td>
<td>18 Master trainers trained by AAP&lt;br&gt; ► Physicians and nurses</td>
<td>599</td>
<td>B: 5411</td>
<td>1. NMR: day 28</td>
<td>A: GA &gt; 28 wks</td>
<td>B: NR</td>
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<tr>
<td>17</td>
<td>Voossus et al</td>
<td>1 day</td>
<td>Hospital (1 tertiary hospital)</td>
<td>HBB-AAP-based NRT including BNC and resuscitation Simulation-based training using manikins ToT approach</td>
<td>40 Master trainers</td>
<td>4,876</td>
<td>B: 4734</td>
<td>1. FSB</td>
<td>A: NR</td>
<td>B: NR</td>
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<tr>
<td>18</td>
<td>Ashish et al</td>
<td>2 days</td>
<td>Hospital (1 tertiary hospital)</td>
<td>HBB-AAP-based NRT with QIC train the trainer model, paired teaching Skills and practice ToT model Use of manikins to demonstrate and practice skills</td>
<td>NR</td>
<td>9588</td>
<td>B: 55520</td>
<td>1. SB</td>
<td>A: GA &gt; 22 wks</td>
<td>B: NR</td>
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<td>Sr. No.</td>
<td>Author</td>
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<td>Outcomes</td>
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<td>19</td>
<td>Bellad et al a</td>
<td>3 days</td>
<td>Hospital (39 primary, 21 secondary and 11 tertiary facilities)</td>
<td>HBB-AAP-based NRT including initial steps, stimulation, suctioning, BMV, refresher training, QI activities, ToT model, paired teaching, use of manikins to demonstrate and practice skills</td>
<td>Neonatologists, Paediatricians, Obstetricians, Nurses</td>
<td>Hospital-based birth attendants, Paediatricians, Obstetricians, Physicians, Residents, Nursing staff, Medical assistants</td>
<td>MCQ, OSCE for skills assessment</td>
<td>A: 15232</td>
<td>1. FSB</td>
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<td>B: 15965</td>
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<td>5. PNMR</td>
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<td>20</td>
<td>Patel et al **</td>
<td>3 days</td>
<td>Hospital (2 primary, 4 secondary HTML validation and 7 tertiary facilities)</td>
<td>HBB-AAP-based NRT including initial steps, stimulation, suctioning, BMV, refresher training and QI activities, ToT model, paired teaching, use of manikins to demonstrate and practice skills</td>
<td>Neonatologists, Paediatricians, Obstetricians, Nurses</td>
<td>Hospital-based birth attendants, Paediatricians, Obstetricians, Physicians, Residents, Nursing staff, Medical assistants</td>
<td>MCQ, OSCE for skills assessment</td>
<td>A: 38078</td>
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</table>

*Data for this study has been taken from Lee et al.
**Data for very low-birth weight (<1500 g).
***Unpublished data obtained via personal communication with the author.

AAP, American Academy of Pediatrics; AHA, American Heart Association; ALSO, Advanced Life Support in Obstetrics; BMV, bag and mask ventilation; BW, birth weight; CC, chest compression; EmONC, Emergency Obstetrics & Neonatal Care; ENC, essential newborn care; ET, endotracheal tube; FBOS, frequent brief onsite simulation; FSB, fresh stillbirth; GA, gestational age; HBB, helping babies breathe; MCQ, multiple choice questions; NICHD, National Institute of Child and Human Development; NMR, neonatal mortality rate; NORT, Norwegian Agency for Development Cooperation; NR, not reported; NRPO, Neonatal Resuscitation Program Guidelines; NRT, neonatal resuscitation training; OSCE, objective structured clinical evaluation; PNMR, perinatal mortality rate; PPV, positive pressure ventilation; QI, quality improvement; QAQ, quality improvement cycle; RCT, randomised control trial; SAQ, short answer questions; SB, stillbirth; TBA, traditional birth attendants; ToT, training of trainer; wks, weeks.
Amongst included studies, two randomised trials addressed the efficacy of NRT in improving neonatal and perinatal outcomes, whereas 18 were pre–post studies. A full description of each study is included in Table 3 and 2. All studies were from low-income and middle-income countries. Four studies were done in community setting, whereas 16 studies were carried out in hospital setting. Four studies were from low-income and middle-income countries. Two studies were done in community setting, whereas 18 studies were carried out in hospital setting.

Table 3 Risk of bias assessment across studies

<table>
<thead>
<tr>
<th>Adequate sequence generation?</th>
<th>High risk</th>
<th>Low risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment?</td>
<td>High risk</td>
<td>Low risk</td>
</tr>
<tr>
<td>Incomplete outcome data</td>
<td>High risk</td>
<td>Low risk</td>
</tr>
<tr>
<td>Free of selective reporting?</td>
<td>Low risk</td>
<td>Low risk</td>
</tr>
<tr>
<td>Free of other bias?</td>
<td>Unclear risk</td>
<td>Low risk</td>
</tr>
<tr>
<td>Baseline outcomes similar?</td>
<td>Low risk</td>
<td>Low risk</td>
</tr>
<tr>
<td>Free of contamination?</td>
<td>Low risk</td>
<td>Low risk</td>
</tr>
</tbody>
</table>
| Baseline characteristics similar? | Unclear risk | Unclear risk | Unclear risk | Unclear risk | Unclear risk | Low risk | Unclear risk | Low risk | Low risk | Unclear risk | Low risk | Unclear risk | Low risk | Low risk | Low risk | Low risk
and compared them to outcomes of those clusters that received ENC + post ENC in-depth NRT. We therefore did not include this study in the NRT versus control analysis because the control group had also received NRT as a part of ENC training.

The study from Kenya had a complex design of randomisation of health workers to two groups—early training (phase I) or late training (phase II) and did not include a control group without training. Therefore, we analysed this study as before-after study where the rate of stillbirths prior to any training were compared with the rate of stillbirths after all phases of training.

Participants of the NRT programme differed across studies and included village health workers, community birth attendants,17 19 21 hospital-based birth attendants,17 22–26 or hospital-based birth attendants including high-level and mid-level staff/specialists.27–34

Different types of training employed by studies included AAP, HBB or NRP curricula,23 24 27 31 32 34 35 AAP/AHA,21 24 26 basic neonatal resuscitation and ENC,17–19 25 home-based neonatal care, basic training with mouth to mask or mask to mask resuscitation,35 Advanced Life Support in Obstetrics (ALSO),29 Bulgarian program on NRT.30 The duration of NRT also differed across studies.

We also included two unpublished trials after permission from authors (tables 1 and 2).

**Excluded studies**

Studies that included interventions that did not qualify as NRT were excluded from the review. These included trainings in safe birthing techniques,36 Emergency Obstetric and Neonatal Care (EmONC),37 38 ENC,39–41 promotion of antenatal care and maternal health education,42 and newborn care intervention package.43

Other interventions that did not qualify as NRT or included interventions like neonatal intensive care unit/special neonatal care unit training51 52 were also excluded.

Studies in which desired outcomes (fetal and neonatal outcome) were not assessed,53–58 or only trainees/training outcomes were assessed,59–73 were also excluded from the analysis.

Some studies that were subgroups of larger studies like Ersdal et al.74 75 (subgroup of Msemo et al.22), Matendo et al.76 (subgroup of Carlo et al.18), Matendo et al.76 and Vossius et al.77 (subgroup of Msemo et al.22) were also not included. However, Vossius et al.77 was included

---

**Figure 2** Forest plot comparing all SB between the NRT and the control groups. NRT, neonatal resuscitation training; SB, stillbirths.

**Figure 3** Forest plot comparing 7-day neonatal mortality between the NRT and the control groups. NRT, neonatal resuscitation training.

**Figure 4** Forest plot comparing 28-day neonatal mortality between the NRT and the control groups. NRT, neonatal resuscitation training.
Effects of interventions

Neonatal and perinatal outcomes were reported in majority of included studies. The overall analysis showed a trend towards reduction in neonatal deaths, early neonatal deaths, perinatal deaths and stillbirths with NRT; most of which are statistically significant.

NRT versus control

The meta-analysis for NRT versus control shows that NRT decreases the risk of all stillbirths by 21% (RR 0.79, 95% CI 0.44 to 1.41; participants=5661; studies=2; $I^2=67\%$) (figure 2), 7-day neonatal deaths by 47% (RR 0.53, 95% CI 0.38 to 0.73; participants=5518; studies=2; $I^2=0\%$) (figure 3), 28-day neonatal deaths by 50% (RR 0.50, 95% CI 0.37 to 0.68; participants=5442; studies=2; $I^2=0\%$) (figure 4), and perinatal deaths by 37% (RR 0.63, 95% CI 0.42 to 0.94; participants=5584; studies=2; $I^2=68\%$) (figure 5). The effect was significant for all 7-day neonatal mortality, 28-day neonatal mortality and perinatal mortality. Significant heterogeneity was observed in analysis of total stillbirths and perinatal mortality.

The grade of quality of evidence for the meta-analysis of the trials was moderate to high (table 4).

Post-NRT versus pre-NRT

The meta-analysis of post-NRT versus pre-NRT shows that post-NRT decreases the risk of all stillbirths by 12% (RR 0.88, 95% CI 0.83 to 0.94; participants=1452; studies=12; $I^2=47\%$, figure 6), fresh stillbirths by 26% (RR 0.74, 95% CI 0.61 to 0.90; participants=296819; studies=8; $I^2=84\%$, figure 7), 1-day neonatal mortality by 42% (RR 0.58, 95% CI 0.42 to 0.82; participants=280080; studies=6; $I^2=89\%$, figure 8), 7-day neonatal mortality by 18% (RR 0.82, 95% CI 0.73 to 0.93; participants=360383; studies=7; $I^2=71\%$, figure 9), 28-day neonatal mortality by 14% (RR 0.86, 95% CI 0.65 to 1.13; $I^2=69\%$, figure 10).

in the analysis for outcomes where data from Msemo et al were not available.

Risk of bias in included studies has been depicted in table 3.

Table 4 Summary of findings for NRT versus control groups

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Anticipated absolute effects (95% CI) – risk with no NRP</th>
<th>Anticipated absolute effects (95% CI) – risk with NRP</th>
<th>Relative effect (95% CI)</th>
<th>No of participants (studies)</th>
<th>Quality of evidence (GRADE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All stillbirth</td>
<td>29 per 1000</td>
<td>23 per 1000</td>
<td>RR 0.79 (0.44 to 1.41)</td>
<td>5661 (2 RCTs)</td>
<td>⬤✗✗✗ Very low†</td>
</tr>
<tr>
<td>Fresh stillbirth</td>
<td>Outcome not reported</td>
<td>Outcome not reported</td>
<td>Outcome not reported</td>
<td>Outcome not reported</td>
<td>Halifax</td>
</tr>
<tr>
<td>1-day neonatal mortality</td>
<td>Outcome not reported</td>
<td>Outcome not reported</td>
<td>Outcome not reported</td>
<td>Outcome not reported</td>
<td>Halifax</td>
</tr>
<tr>
<td>7-day neonatal mortality</td>
<td>39 per 1000</td>
<td>20 per 1000</td>
<td>RR 0.53 (0.38 to 0.73)</td>
<td>5518 (2 RCTs)</td>
<td>➤➤➤ High</td>
</tr>
<tr>
<td>28-day neonatal mortality</td>
<td>49 per 1000</td>
<td>24 per 1000</td>
<td>RR 0.50 (0.37 to 0.68)</td>
<td>5442 (2 RCTs)</td>
<td>➤➤➤ High</td>
</tr>
<tr>
<td>Perinatal mortality</td>
<td>68 per 1000</td>
<td>43 per 1000</td>
<td>RR 0.63 (0.42 to 0.94)</td>
<td>5584 (2 RCTs)</td>
<td>➤➤ High</td>
</tr>
</tbody>
</table>

$I^2$ is 67% and the two trials were inconsistent in the direction of effect. Quality of evidence downgraded by two for inconsistency and imprecision (figure 2).

†The 95% CI of the pooled estimate includes null effect. Quality of evidence downgraded by one for imprecision (figure 2).

‡No evidence to support or refute.

§Though $I^2$ is 68%, the 95% CI of the pooled estimate does not include the null effect. Quality of evidence downgraded by one for inconsistency (figure 5).

NRT, neonatal resuscitation training; RCTs, randomised controlled trial; RR, risk ratio.
This meta-analysis assessed the impact of any NRT programme either by itself or as a part of newborn care package on rates of stillbirths, perinatal mortality, all-cause neonatal mortality on day-1, up till day-7 and till 28th day after birth. We did not evaluate intrapartum-related neonatal deaths or asphyxia/cause-specific neonatal mortality. Mortality in neonates <7 days of life is a proxy measure for intrapartum-related deaths.\textsuperscript{43 78} Meta-analysis of before–after studies showed a significant reduction in all stillbirths by 12% (12 studies) and of FSB by 26% (8 studies). The reduction in fresh stillbirths can be attributed to NRT that helps in resuscitating neonates that appear lifeless at birth.\textsuperscript{17 18} Of 12 studies, seven studies reported a significant and one study reported a non-significant reduction in fresh stillbirths. However, a non-significant increase in risk of stillbirths was reported in three African studies which blunted the impact of NRT on reduction of stillbirths. There was reduction in 1-day mortality of 42% (6 studies) and that of 7-day mortality was 18%. All studies included in the analysis (figures 8 and 9) showed a

### DISCUSSION

This meta-analysis assessed the impact of any NRT programme either by itself or as a part of newborn care package on rates of stillbirths, perinatal mortality, all-cause neonatal mortality on day-1, up till day-7 and till 28th day after birth. We did not evaluate intrapartum-related neonatal deaths or asphyxia/cause-specific neonatal mortality. Mortality in neonates <7 days of life is a proxy measure for intrapartum-related deaths.\textsuperscript{43 78} Meta-analysis of before–after studies showed a significant reduction in all stillbirths by 12% (12 studies) and of FSB by 26% (8 studies). The reduction in fresh stillbirths can be attributed to NRT that helps in resuscitating neonates that appear lifeless at birth.\textsuperscript{17 18} Of 12 studies, seven studies reported a significant and one study reported a non-significant reduction in fresh stillbirths. However, a non-significant increase in risk of stillbirths was reported in three African studies which blunted the impact of NRT on reduction of stillbirths. There was reduction in 1-day mortality of 42% (6 studies) and that of 7-day mortality was 18%. All studies included in the analysis (figures 8 and 9) showed a

### DISCUSSION

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reduction with an exception of one study. Failure to observe reduction in mortality in Bellad et al could be due to two reasons. First, NRT was provided in diverse health systems within a short period of time. Second, mortality was not assessed in facilities where training was imparted but was measured in the population.

The meta-analysis showed a non-significant reduction of 14% in 28-day mortality. Of the seven included studies only two studies reported a significant reduction in mortality. Resuscitation at delivery helps to reduce neonatal mortality in the first hour of birth when the neonate is at the highest risk of intrapartum-related deaths and the impact diminishes subsequently. For reduction of 28-day neonatal mortality, post-resuscitation specialised care for survivors is required and only NRT is unlikely to have the desired impact on 28-day neonatal mortality.

**Figure 8** Forest plot comparing 1-day neonatal mortality between the post-NRT and the pre-NRT groups. NRT, neonatal resuscitation training.

**Figure 9** Forest plot comparing 7-day neonatal mortality between the post-NRT and the pre-NRT groups. NRT, neonatal resuscitation training.

**Figure 10** Forest plot comparing 28-day neonatal mortality between the post-NRT and the pre-NRT groups. NRT, neonatal resuscitation training.
Trials that randomise facilities to NRT versus controls (where NRT is not a standard practice) would be ideal to assess the reduction in neonatal mortality. Trials are also likely to result in higher impact as compared with before–after studies as other changes at health facilities or in communities during the time period of before–after studies can confound the results. Because NRT is a standard practice and randomising individuals or clusters to no resuscitation training is unethical, there were only two trials available for the meta-analysis. They showed a reduction of 7-day neonatal mortality and 28-day mortality by 47% (figure 3) and 50% (figure 4), respectively. The perinatal mortality reduced by 37% (figure 5) with no significant reduction in SB rates.

Previously, an expert panel published a systematic review for community-based studies and conducted a meta-analysis that evaluated whether NRT reduced all-cause neonatal mortality in the first 7 days of life. They reported a 38% reduction in mortality which is larger than the 18% (7 studies) reduction observed in the current meta-analysis. Our meta-analysis included community-based studies that resulted in a smaller effect size. Community-based studies (trials or before–after) report a smaller reduction effect on any day neonatal mortality. The reduction in effect size of neonatal mortality in these studies can arise due to several reasons. All births in the intervention community may not be attended by birth attendants trained in neonatal resuscitation, especially if it is a home delivery. Second, women may decide to deliver at facilities or homes outside communities where NRT has been imparted. Finally, assessing mortality outcomes in the community can be challenging. Another meta-analysis was published in Cochrane which evaluated outcomes such as knowledge, skills, neonatal morbidity, neonatal mortality in first 7 days after birth and from day 8 to 28.

This analysis did not include stillbirths, 1-day neonatal mortality or perinatal mortality that was included in the current meta-analysis. The current meta-analysis consists largely of before–after studies with lack of concurrent control group that limits isolation of effect of resuscitation training alone from other changes at health facilities or in communities during the time period. Other limitation is lack of consistency of settings, duration of training, varying study designs and lack of consistent outcomes which contributed to substantial heterogeneity. Lack of subgroup analysis of type of health facilities may be perceived as a limitation. An improvement in mortality would be maximised in low-resource settings with poor quality of care. However, it is presumed that there is regular training of health workers in basic resuscitation skills in higher levels of care that would translate to higher quality of care. Our recent study that evaluated the knowledge and skills of trainees trained in HBB included 384 tertiary-level facilities in India. Only 3% of physicians and 5% of nurses were able to pass the pre-training bag and mask resuscitation skill assessment. Therefore, in the absence of reporting of pre-training skills of health workers in low-resource or high-resource settings or any indicator of quality of care, it would be erroneous to conduct a subgroup analysis based merely on resource settings and mostly will not change the results or the main message of this meta-analysis. We emphasise that despite the heterogeneity in settings, type

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>NRT–Post Events</th>
<th>NRT–Pre Events</th>
<th>Total Events</th>
<th>Weight</th>
<th>Risk Ratio IV, Random, 95% CI</th>
<th>Risk Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ashjud et al. 2016, Nepal (1)</td>
<td>362</td>
<td>15520</td>
<td>290</td>
<td>9588</td>
<td>0.77 [0.66, 0.90]</td>
<td></td>
</tr>
<tr>
<td>Bellad et al. 2016, Kenya &amp; India (2)</td>
<td>374</td>
<td>15974</td>
<td>380</td>
<td>15205</td>
<td>0.82 [0.80, 1.06]</td>
<td></td>
</tr>
<tr>
<td>Boo et al. 2009, Malaysia</td>
<td>3150</td>
<td>46514</td>
<td>5231</td>
<td>541721</td>
<td>0.70 [0.67, 0.73]</td>
<td></td>
</tr>
<tr>
<td>Carlo et al. 2010, 6 countries (3)</td>
<td>1011</td>
<td>29731</td>
<td>1530</td>
<td>35017</td>
<td>0.88 [0.81, 0.91]</td>
<td></td>
</tr>
<tr>
<td>Carlo et al. 2012, 6 countries (4)</td>
<td>198</td>
<td>21723</td>
<td>283</td>
<td>352</td>
<td>0.91 [0.83, 0.99]</td>
<td></td>
</tr>
<tr>
<td>Jeffery et al. 2004, Macedonia</td>
<td>977</td>
<td>45438</td>
<td>1910</td>
<td>69840</td>
<td>0.79 [0.73, 0.85]</td>
<td></td>
</tr>
</tbody>
</table>

Total (95% CI) 572079 671723 100.0% 0.82 [0.74, 0.91]

Total events 6072 9450

Heterogeneity: Tau^2 = 0.01; Chi^2 = 47.62; df = 5 (P < 0.00001); I^2 = 90%

Test for overall effect: Z = 3.65 (P = 0.0003)

Figure 12  Funnel plot of comparison: Post-NRT versus Pre-NRT for all SB. NRT, neonatal resuscitation training; RR, risk ratio; SB, stillbirths.

Figure 11  Forest plot comparing perinatal mortality between the post-NRT and the pre-NRT groups. NRT, neonatal resuscitation training.
Table 5  Summary of findings for Post-NRT versus Pre-NRT groups

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Anticipated absolute effects (95% CI)</th>
<th>Relative effect (95% CI)</th>
<th>No of participants (studies)</th>
<th>Quality of the evidence (GRADE)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Risk with pre-NRP</td>
<td>Risk with post-NRP</td>
<td>RR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>All stillbirths</td>
<td>8 per 1000</td>
<td>7 per 1000 (7 to 8)</td>
<td>RR 0.88 (0.83 to 0.94)</td>
<td>1 425 540 (12 observational studies)</td>
<td>☰◯◯◯◯ Very low††</td>
</tr>
<tr>
<td>Fresh stillbirths</td>
<td>15 per 1000</td>
<td>11 per 1000 (9 to 13)</td>
<td>RR 0.74 (0.61 to 0.90)</td>
<td>296 819 (8 observational studies)</td>
<td>☰◯◯◯◯ Very low†§</td>
</tr>
<tr>
<td>1-day neonatal mortality</td>
<td>8 per 1000</td>
<td>5 per 1000 (4 to 7)</td>
<td>RR 0.58 (0.42 to 0.82)</td>
<td>280 080 (6 observational studies)</td>
<td>☰◯◯◯◯ Very low†</td>
</tr>
<tr>
<td>7-day neonatal mortality</td>
<td>13 per 1000</td>
<td>11 per 1000 (9 to 12)</td>
<td>RR 0.82 (0.73 to 0.93)</td>
<td>360 383 (7 observational studies)</td>
<td>☰◯◯◯◯ Very low†</td>
</tr>
<tr>
<td>28-day neonatal mortality</td>
<td>8 per 1000</td>
<td>7 per 1000 (5 to 9)</td>
<td>RR 0.86 (0.65 to 1.13)</td>
<td>1 116 463 (7 observational studies)</td>
<td>☰◯◯◯◯ Very low††</td>
</tr>
<tr>
<td>Perinatal mortality</td>
<td>14 per 1000</td>
<td>12 per 1000 (10 to 13)</td>
<td>RR 0.82 (0.74 to 0.91)</td>
<td>1 243 802 (6 observational studies)</td>
<td>☰◯◯◯◯ Very low §§¶¶</td>
</tr>
</tbody>
</table>

*Pre–post studies. Quality of evidence downgraded by one for risk of bias (table 1 and 2).
‡Studies differ in the settings, type of NRP, duration and type trainees. Quality of evidence downgraded by one for indirectness (table 1 and 2).
§Publication bias detected in the funnel plot. Quality of evidence downgraded by one for publication bias (figure 12).
¶Although I² is 84%, the effect estimates of all included studies do not differ in the direction of effect. Quality of effect downgraded by one for inconsistency (figure 7).
¶¶Although I² is 89%, the effect estimates of all the included studies (except Bellard et al.) do not differ in the direction of effect. Quality of effect downgraded by one for inconsistency (figure 8).
**Although I² is 71%, the effect estimates of all the included studies (except Bellard et al.) do not differ in the direction of effect. Quality of effect downgraded by one for inconsistency (figure 9).
††I² is 95% and the effect estimates cross the line of no effect. Quality of evidence downgraded by two for inconsistency and imprecision (figure 10).
‡‡The effect estimate crosses the line of no effect. Quality of evidence downgraded by one for imprecision (figure 10).
§§Although I² is 90%, the effect estimates of all the included studies do not differ in the direction of effect. Quality of effect downgraded by one for inconsistency (figure 11).
¶¶Studies differ in setting, type of NRP and trainees. Quality of evidence downgraded by one for indirectness (table 1 and 2).
NRP, Neonatal Resuscitation Program; NRT, neonatal resuscitation trainings; RR, risk ratio; SB, stillbirths.

This review identified several important limitations of the current evidence from included studies. Due to inadequate information about the methodology followed and variability of resuscitation programmes in included studies, the quality of the evidence was downgraded for risk of bias and indirectness resulting in inability to adequately assess the effects of this intervention.

**CONCLUSIONS**

**Implications for practice**
This review shows that the implementation of NRT improves neonatal and perinatal outcomes.

**Implications for research**
Further good quality, multicentric randomised controlled trials addressing the role of NRT for improving neonatal and perinatal outcomes may be warranted. Impact of NRT...
on improving neonatal and perinatal outcomes as well as the best combination of settings and type of trainee should be established in future trials. More studies need to be done to assess the frequency with which NRT needs to be conducted to sustain the existing effect on perinatal mortality reduction.

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Contributors AP: conception of the work, design of the work, manuscript drafting with final approval of the version to be published. MNK: developed and run the search strategy, screened and selected studies, and did meta-analysis, GRADE assessment and manuscript drafting. KK and SB: involved in preparation of characteristic of studies table, data acquisition and manuscript drafting. AB: screening and selection of studies, data acquisition and manuscript drafting.

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Competing interests The authors AP and AB were investigators in two of the studies (Bellad et al and Patel et al) included in the meta-analysis. There were no other competing interest.

Provenance and peer review Not commissioned; externally peer reviewed.

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