

Mechanical ventilation for newborn infants with respiratory failure due to pulmonary disease (Review)

Henderson-Smart DJ, Wilkinson A, Raynes-Greenow CH



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ABSTRACT

Background

Before the 1960s newborn infants with severe lung disease, usually due to respiratory distress syndrome (RDS), had a very high mortality rate. Standard treatment consisted of supportive measures including supplemental oxygen and correction of metabolic acidosis. Mechanical ventilation (MV) was introduced in the 1960s to correct hypoxaemia and respiratory acidosis in infants who were likely to die. MV is now standard treatment for infants with severe RDS but the degree to which this made a contribution to the outcome of such infants compared with standard neonatal care, is uncertain.

Objectives

To evaluate the effects of the use of MV compared with no MV on mortality and morbidity in newborn infants with severe respiratory failure due to pulmonary disease.

Search strategy

Searches were last updated in March 2005 on the Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library, Issue 1, 2005), MEDLINE from 1966 to March 2005 and EMBASE from 1980 to March 2005. In order to detect trials that may not have been published in full, searches were carried out of the Oxford Database of Perinatal Trials and for abstracts published by the Society for Pediatric Research (1967 to 2004 inclusive) and the European Society for Pediatric Research (1970 to 2004 inclusive). Experts were consulted with emphasis on those who were in active neonatal practice in the 1960s and 1970s when the majority of these trials were likely to have been done.

Selection criteria

Randomised or quasi-randomised controlled trials in newborn infants with respiratory failure due to pulmonary disease evaluating the use of MV versus standard neonatal care without MV.

Data collection and analysis

The standard methods of the Cochrane Collaboration and its Neonatal Review Group were used. Two authors independently assessed eligibility, methodological quality of each trial and extracted the data. Additional information was obtained from all trial authors on methodology or data. The data were analysed using relative risk and risk difference and their 95% confidence intervals. A fixed effect model was used for meta-analyses.

Main results

The five eligible trials reported on a total of 359 infants with RDS. In one study there is a higher neonatal mortality in the mechanical ventilation group [7/10 vs 1/10; RR 7.00 (1.04, 46.95)]. Overall the risk of any reported mortality is less frequent in the mechanical ventilation group with the upper 95% confidence limit on 1.00 [summary RR 0.86 (0.74, 1.00), RD -0.10 (-0.20, -0.01), NNT 10 (5, 100)]. In infants with a birth weight of 1 - 2 kg, no significant difference in mortality is found [summary RR for two trials 0.86 (0.70, 1.07)]. In infants with a birth weight of more than 2 kg, one study reports a significant reduction in mortality in the MV group compared with control [RR 0.67 (0.51, 0.86)]; overall for this birth weight group there is a significant reduction in mortality with MV in the two trials [summary RR 0.67 (0.52, 0.87), RD -0.27 (-0.45, -0.10), NNT 4 (2, 10)].

Any IVH at autopsy is not significantly different between the groups in any study or overall in four studies reporting on 202 infants who had an autopsy. Pneumothorax was reported in two studies of 275 infants and there is a non-significant trend towards an increase in the mechanical ventilation group [summary RR 2.75 (0.72, 10.45)].

Authors' conclusions

When MV was introduced in the 1960s to treat infants with severe respiratory failure due to pulmonary disease, trials showed an overall reduction in mortality which was most marked in infants born with a birthweight of more than 2 kg. This review does not provide information to evaluate the relative benefits or harms of MV in the setting of modern perinatal care. Introduction of mechanical ventilation into new settings, such as those without full intensive care support, should ideally be evaluated in clinical trials.

PLAIN LANGUAGE SUMMARY

Mechanical ventilation of newborn infants with severe lung disease results in reduced mortality.

Mechanical ventilation with intermittent positive or negative pressure was introduced in the 1960s. It was compared with standard treatment in five trials for infants with very severe lung disease and resulted in a reduction in mortality. This effect was observed principally in infants with birth weights over two kilograms. Mechanical ventilation has become standard therapy for severe respiratory failure. There have been no trials in modern neonatal intensive care units so the magnitude of the benefits and harms in current practice are not known.

BACKGROUND

Before the 1960s newborn infants with severe lung disease, usually due to respiratory distress syndrome (RDS), had a very high mortality rate (Sinclair 1966). Standard treatment consisted of supportive measures including supplemental oxygen and correction of metabolic acidosis. Mechanical ventilation (MV) was introduced in the 1960s to correct hypoxemia and respiratory acidosis in infants who were likely to die. MV can be administered as either intermittent positive pressure ventilation (IPPV) or as intermittent negative pressure ventilation (INPV). The former requires intubation of the trachea either by the mouth or the nose for a number of days. This can be associated with upper airway trauma, increased pulmonary secretions or infection. INPV requires the infant to be nursed in a negative pressure chamber with a seal around the neck and this could be associated with trauma to that region. Artificial lung inflation could be associated with physical trauma to the lung leading to acute complications such as pneumothorax or chronic complications such as bronchopulmonary dysplasia. Differences in cardio-respiratory stability with or without MV support could be associated with neurological injury indicated by short term markers such as intraventricular hemorrhage (IVH) or periventricular leukomalacia (PVL) or in adverse long term neurodevelopmental outcome. Both benefits and harms could be different in infants born at lower gestational ages and birth weights.

The introduction of neonatal intensive care, including MV, during the 1960s and its widespread application in the 1970s was associated with increased survival of very low birthweight infants and was shown to be more cost effective in infants of 1 - 1.5 kg birthweight compared with infants of less than 1 kg (Boyle 1983).

Although MV, usually using IPPV, is now a standard treatment (Greenough 1996; Wiswell 2001) it is not clear what the balance of benefits and harms was at the time it was introduced and how these should be interpreted in terms of modern neonatal intensive care. In earlier debates Reynolds 1970 suggested that infants with severe RDS could be managed just as well with excellent standard care, without use of MV. Given the cost of IPPV, the question still arises as to whether it should be introduced as part of neonatal care in resource poor settings, such as in many developing countries (Ho 1996).

The effects of MV have been reviewed previously (Bancalari 1992) but such effects require formal re-examination by repeating the search for randomised controlled trials, including those that may have appeared only in abstract form, to clarify any remaining research questions and to better describe the population of infants who entered these trials.

OBJECTIVES

To evaluate the effects of the use of MV compared with no MV on mortality and morbidity in newborn infants with severe respiratory failure due to pulmonary disease.

Pre-specified sub-group analyses were to be carried out according to:

1. RDS as cause of respiratory failure vs all other causes
2. Early vs late (rescue) treatment with MV
3. Type of MV - either IPPV or INPV
4. Gestation (cut-offs at about 28 and 32 weeks)
5. Birth weight (cut-offs at about 1000 and 1500 grams)

Although no trials comparing MV with head box oxygen are likely to have been conducted since the availability of artificial surfactant or the use of positive end-expiratory pressure, if trials utilizing these latter interventions were found, sub-group analyses were to be done according to the use, or not, of these therapies.

CRITERIA FOR CONSIDERING STUDIES FOR THIS REVIEW

Types of studies

Randomised or quasi-randomised controlled trials

Types of participants

Newborn infants with respiratory failure due to pulmonary disease. Although the original protocol for this review confined the population to preterm infants, the review has been done without that limitation (all newborn infants were eligible) since no upper limit of gestational age was specified in any study.

Types of intervention

MV (IPPV or INPV) versus no MV. Use of rescue MV in controls was allowed.

Not eligible for this review were trials comparing different types of MV (IPPV vs INPV), ventilator techniques (inspiratory times, pressure vs volume cycled or high frequency) or trials in which MV was compared with continuous distending pressure.

Types of outcome measures

Mortality

- first week
- 28 days
- hospital discharge

Morbidity

- pneumothorax
- IVH (all grades and severe grades 3 or 4)
- chronic lung disease (ventilatory support or oxygen at 28 days or at 36 weeks)
- proven systemic infection (positive culture blood, urine, cerebrospinal fluid or other normally sterile body fluid)
- necrotising enterocolitis
- retinopathy of prematurity
- neurodevelopmental abnormalities in childhood (developmental delay, cerebral palsy)

SEARCH METHODS FOR IDENTIFICATION OF STUDIES

See: methods used in reviews.

Searches were last updated in March 2005 on the Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane

Library, Issue 1, 2005), MEDLINE from 1966 to March 2005 and EMBASE from 1980 to March 2005, using MeSH terms mechanical ventilation, infant newborn, respiratory distress syndrome. In order to detect trials that may not have been published in full, searches were carried out of the Oxford Database of Perinatal Trials and for abstracts published by the Society for Pediatric Research (1967 to 2004 inclusive) and the European Society for Pediatric Research (1970 to 2004). Experts were consulted with emphasis on those who were in active neonatal practice in the 1960s and 1970s when the majority of these trials were likely to have been done.

METHODS OF THE REVIEW

The standard methods of the Cochrane Collaboration and its Neonatal Review Group were used. The methodological quality of each trial was reviewed independently by two authors for blinding of randomisation, blinding of outcome measurements, and completeness of follow up. Additional information was obtained from all trial authors on methodology or data.

Two authors independently assessed eligibility of retrieved reports, and extracted data; the results were compared and any differences resolved by discussion and consensus.

The data were synthesised using the standard method of the Neonatal Review Group with use of relative risk and risk difference and their 95% confidence intervals. A fixed effect model was used for meta-analyses.

DESCRIPTION OF STUDIES

Five published trials (Reid 1967, Silverman 1967, Sinclair 1968, Llewellyn 1970, Murdock 1970) were found and included. All trials were carried out in the latter half of the 1960s. No unpublished trials or trials published only in abstract form were found.

Participants

All studies enrolled infants of more than one kilogram birth weight with respiratory distress. In all but one study, the infants all had clinical and radiological RDS. In the other study (Sinclair 1968) 50% had RDS. No gestational age limits were used and only one study (Sinclair 1968) specified an upper limit for birth weight, at 2.5 kg. The severity of respiratory failure based on oxygen requirements varied. From least to most severe, it was oxygen saturation less than 80% in air (Silverman 1967), use of 40-100% oxygen (Reid 1967), PaO₂ 75 mm Hg or less in 50% oxygen (Sinclair 1968), PaO₂ less than 100 mm Hg in more than 95% oxygen (Llewellyn 1970) and PaO₂ less than 50 in 95% or more oxygen (Murdock 1970).

Interventions

Mechanical ventilation was provided in a wide variety of ways. Silverman 1967 and Sinclair 1968 used negative pressure Airshields ventilators, Reid 1967 used IPPV via a naso-tracheal tube and Murdock 1970 gave IPPV via a face-mask. Llewellyn 1970 had one group on INPV, one on IPPV with a pressure cycled ventilator and another on IPPV with a volume cycled ventilator. The authors found no statistical difference in outcomes between these different methods and so combined them in the publication. The original data on outcomes for each type of MV is no longer available for analysis (Swyer personal communication).

Outcomes

Mortality was reported in all studies but the period of follow up (during the study period, neonatal or prior to discharge) was variable. Sinclair 1968 reported deaths during the seven day study and in the neonatal period. Silverman 1967 only reported deaths during the seven day study period. Published reports of three trials did not indicate when the deaths had occurred. Dr Paul Swyer, co-author of two of these trials (Murdock 1970, Llewellyn 1970) was contacted and he recalled that deaths were ascertained by hospital discharge. Dr David Reid (Reid 1967) provided time of death information from his trial indicating that all deaths occurred in the first seven days and that there were no late deaths before discharge. The outcome 'any reported mortality' in this review presents data over the longest period follow-up period in each study. All trials reported IVH, but this was only reported for those with autopsies as ultrasound examination was not available in the 1960s. Overall, autopsies were carried out in 79% of the mechanical ventilation group deaths and 91% of the control group deaths.

METHODOLOGICAL QUALITY

All trials randomly allocated subjects to treatment or control groups and all five concealed the random allocation from clinicians caring for the infants. Neither the treatments nor the outcome assessments were blinded in any trials. Outcomes were ascertained in almost all subjects randomised in each trial.

RESULTS

The five eligible trials reported on a total of 359 infants with RDS.

Mortality

All trials reported mortality. Sinclair 1968 found a higher neonatal mortality in the mechanical ventilation group [7/10 vs 1/10; RR 7.00 (1.04, 46.95)]. Overall in the five trials any reported mortality was less frequent in the mechanical ventilation group with the upper 95% confidence limit of RR on 1.00 [summary RR 0.86 (0.74, 1.00), RD -0.10 (-0.20, -0.01), NNT 10 (5, 100)]. For RR there is a non-significant trend suggesting heterogeneity; for RD there is highly significant heterogeneity.

Two studies reported mortality by birth weight (Reid 1967, Murdock 1970). In infants with a birthweight of 1 - 2 kg no significant difference in mortality was found [summary RR 0.86 (0.70, 1.07)]. In infants with a birth weight of more than 2 kg, one study (Murdock 1970) reported a significant reduction in mortality in the MV group compared with control [RR 0.67 (0.51, 0.86)] and, overall, in the two trials there was a significant reduction in mortality with MV [summary RR 0.67 (0.52, 0.87), RD -0.27 (-0.45, -0.10), NNT 4 (2, 10)].

Intraventricular haemorrhage (IVH)

Any IVH at autopsy was not significantly different between the groups in any study or overall in four studies reporting on 202 infants who had an autopsy [summary RR 1.05 (0.79, 1.39)].

Pneumothorax

Pneumothorax was reported in two studies (Silverman 1967, Llewellyn 1970) of 275 infants and there was a non-significant trend towards an increase in the mechanical ventilation group [summary RR 2.75 (0.72, 10.45)].

Proven systemic infection was only reported in one trial (Murdock 1970) which found five cases of septicaemia in the ventilated group (45 survivors and 96 with postmortem examination) and none in the control group (eight survivors and 45 with postmortem examination).

Other prespecified outcomes could not be assessed.

Subgroup analysis by IPPV and INPV was not done because in the largest study (Llewellyn 1970) outcomes by these modalities were not available. Subgroup analyses by gestation, cause of respiratory distress, and early or late use of intervention could not be carried out.

DISCUSSION

The trials included in this review were carried out in the 1960s when neonatal intensive care was just being introduced and overall care was less sophisticated than current neonatal care. The equipment and methods used to apply mechanical ventilation cannot be compared to those used now (reviewed by Wiswell 2001). Intermittent negative pressure is now rarely used and ventilators for IPPV have been especially developed for use with newborn infants (Wiswell 2001). Mortality rates for infants with moderate or severe RDS, such as those entered in the studies in this review, were much higher (overall 67%) than observed in the 1980s (5%) (Greenough 1985). This is despite the relatively high birth weight of the infants in the included studies compared to current NICU infants. Furthermore, treatments such as antenatal corticosteroids and artificial surfactants were not available. For these reasons there are considerable limitations in applying the results of this review to current NICU practice.

When these trials were done the main question was whether mechanical ventilation could save the lives of infants with severe RDS. Apart from one of the trials, the results suggest that mortality is reduced. Prespecified subgroup analyses could not be carried out to explore the heterogeneity in the overall mortality analysis. Post-hoc examination showed that the trial with a higher mortality in the MV group (Sinclair 1968) had a much lower control group mortality rate (10%) than the other four trials (range 63 - 85%). Caution is also warranted in interpreting the results for 'any mortality' presented here because the outcome was ascertained over different time periods in some studies. As ultrasound and computerised tomographic imaging were not available when these studies were carried out, IVH was ascertained at autopsy and the incidence in survivors is not known.

In some settings, such as some developing countries where resources limit the ability to provide neonatal intensive care, the question of whether MV is worthwhile is still valid (Ho 1996). In such settings it is uncertain what additional benefits MV might provide over oxygen administration alone or other lower cost support such as continuous positive airways pressure (reviewed by Ho 2005a; Ho 2005b).

The results here and those examining the cost effectiveness of neonatal intensive care (Boyle 1983) suggest the infants of greater birthweight might benefit more in settings where MV is being introduced. Furthermore, more MV resources are used in treating the lowest birth weight infants (Doyle 1996).

AUTHORS' CONCLUSIONS

Implications for practice

When MV was introduced in the 1960s to treat infants with severe respiratory failure due to pulmonary disease, trials showed an overall reduction in mortality which was most marked in infants born with a birthweight of more than 2 kg. This review does not

provide information to evaluate the relative benefits or harms of MV in the setting of modern perinatal care.

Implications for research

It is unlikely that further trials comparing MV with headbox oxygen only for neonates with severe pulmonary failure would be carried out in a modern perinatal care setting. Current research questions now focus on comparing different types of MV or comparing MV with other means of support such as CPAP. Introduction of mechanical ventilation into new settings, such as those without full intensive care support, should ideally be evaluated in clinical trials.

POTENTIAL CONFLICT OF INTEREST

None

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External sources of support

- No sources of support supplied

Internal sources of support

- Centre for Perinatal Health Services Research, University of Sydney AUSTRALIA
- Royal Prince Alfred Hospital, Sydney AUSTRALIA
- Neonatal Unit, Department of Paediatrics, Oxford University UK

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* Indicates the major publication for the study

T A B L E S

Characteristics of included studies

Study	Llewellyn 1970
Methods	Concealment of randomisation - yes; blinding of intervention - no; completeness of follow up - yes; blinding of outcome assessment - no
Participants	44 infants of 127 admitted with RDS; PaO ₂ < 100 in > 95%
Interventions	IPPV via face mask using pressure (Bird Mk VIII) or volume (Bourns Pediatric Respirator, model LS 104) cycled ventilator, maximum pressure of 20 cms H ₂ O vs Standard treatment (servocontrolled ventilator, 4 - 6 hrly blood gases, PaO ₂ kept at 50 - 80, metabolic acidosis corrected with NaHCO ₃ , 10% dextrose)
Outcomes	Mortality before discharge, intubation for IPPV, duration of oxygen therapy
Notes	All infants outborn May 1968 - March 1969. Dr Swyer provided additional information that randomisation was concealed, standard errors reported, deaths were before discharge.

Characteristics of included studies (Continued)

Allocation concealment A – Adequate

Study	Murdock 1970
Methods	Concealment of randomisation - yes; blinding of intervention - no; completeness of follow up - yes; blinding of outcome assessment - no
Participants	221 with RDS with PaO ₂ < 50 mmHg in FiO ₂ > 0.95 or cyanosis despite such FiO ₂ and blood gas not available or apnea unresponsive to bag and mask ventilation
Interventions	Mechanical ventilation (IPPV with pressure or volume cycled ventilators and endotracheal tubes, INPV preferably without intubation) vs standard care (FiO ₂ to keep PaO ₂ 60 - 100 mmHg, 10% dextrose, servocontrolled incubator, NaHCO ₃ to keep pH > 7.25)
Outcomes	Mortality before discharge by birthweight, Pneumothorax, IVH at autopsy
Notes	All infants outborn November 1965 - February 1968. Dr Swyer provided additional information that randomisation was concealed, standard errors were reported and deaths were before discharge.
Allocation concealment	A – Adequate

Study	Reid 1967
Methods	Concealment of randomisation - yes (off-site by independant statistician); blinding of intervention - no; completeness of follow up - unclear; blinding of outcome assessment - no
Participants	20 infants with clinical RDS, Silverman Score > 4, in 40 - 100% O ₂ and an initial capillary pH of < 7.20 Infants of < 1000gms birthweight excluded
Interventions	IPPV vs standard treatment (10% dextrose plus NaHCO ₃ , oxygen to prevent cyanosis, heated humidified incubators)
Outcomes	Mortality by birthweight, IVH at autopsy (autopsy rate 100%)
Notes	All infants given Ampicillin and Cloxacillin 1964 - 66. Dr Reid supplied additional information about the method of randomisation and details of the deaths.
Allocation concealment	A – Adequate

Study	Silverman 1967
Methods	Concealment of randomisation - yes, paired by outborn (18) and inborn (36) and in 500gm weight groups; blinding of intervention - no; completeness of follow up - yes; blinding of outcome assessment - no
Participants	474 admissions, 420 did not meet criteria, 54 infants included at mean age of 8 hrs with clinical and radiological (independent assessment) diagnosis of RDS and cyanosis or capillary SaO ₂ < 80% in air or PCO ₂ > 50 mmHg and birthweight > 1kg
Interventions	INPV in Airshields incubator, pressures -15 to -45 cms H ₂ O vs standard care (dextrose and NaCO ₃ IV)
Outcomes	Mortality during the 7 day study period, IVH at autopsy, pneumothorax
Notes	February 1963 - December 1964 Author confirmed that developmental follow up not done
Allocation concealment	A – Adequate

Study	Sinclair 1968
Methods	Concealment of randomisation - yes; blinding of intervention - no; completeness of follow up - yes; blinding of outcome assessment - no

Participants	20 infants (50% with RDS) with birthweight 1000 - 2500gms, < 24 hrs old, pH < 7.25 or PaO ₂ < 76 in FiO ₂ 0.5
Interventions	Randomised to 4 groups according to use of unlimited O ₂ , rapid bicarbonate administration and assisted ventilation with INPV (Airshields) In this review, the 2 groups which received INPV were compared with the 2 groups not receiving INPV.
Outcomes	Mortality (first week and neonatal), IVH at autopsy (any or massive)
Notes	April 1966 - January 1967 Author confirmed that developmental follow up not done
Allocation concealment	A – Adequate

ANALYSES

Comparison 01. Mechanical ventilation vs control

Outcome title	No. of studies	No. of participants	Statistical method	Effect size
01 Any reported mortality	5	359	Relative Risk (Fixed) 95% CI	0.86 [0.74, 1.00]
02 Mortality 1 - 2 kg	2	140	Relative Risk (Fixed) 95% CI	0.86 [0.70, 1.07]
03 Mortality more than 2 kg	2	101	Relative Risk (Fixed) 95% CI	0.67 [0.52, 0.87]
04 Any IVH in infants with an autopsy	5	202	Relative Risk (Fixed) 95% CI	1.05 [0.79, 1.39]
05 Pneumothorax	2	275	Relative Risk (Fixed) 95% CI	2.75 [0.72, 10.45]

INDEX TERMS

Medical Subject Headings (MeSH)

Infant, Newborn; Randomized Controlled Trials; Respiration, Artificial [*methods]; Respiratory Distress Syndrome, Newborn [mortality; *therapy]; Respiratory Insufficiency [mortality; *therapy]

MeSH check words

Humans

COVER SHEET

Title	Mechanical ventilation for newborn infants with respiratory failure due to pulmonary disease
Authors	Henderson-Smart DJ, Wilkinson A, Raynes-Greenow CH
Contribution of author(s)	All authors had input into the protocol for the review. Henderson-Smart and Raynes-Greenow carried out the search, assessed the studies, extracted and entered the data. Henderson-Smart wrote the text and all authors contributed to editing.
Issue protocol first published	2000/4
Review first published	2002/4
Date of most recent amendment	25 May 2005
Date of most recent SUBSTANTIVE amendment	12 August 2002
What's New	This updates the existing review "Mechanical ventilation for newborn infants with respiratory failure due to pulmonary disease" originally published in The Cochrane Library, Issue 4 2002 (Henderson-Smart 2002).

No new trials were found. The reviewers' conclusions regarding the need for further trials has been reworded.

Date new studies sought but none found 01 April 2005

Date new studies found but not yet included/excluded Information not supplied by author

Date new studies found and included/excluded Information not supplied by author

Date authors' conclusions section amended 29 March 2005

Contact address Prof David Henderson-Smart
Director
NSW Centre for Perinatal Health Services Research
Queen Elizabeth II Research Institute
Building DO2
University of Sydney
Sydney
NSW
2006
AUSTRALIA
E-mail: dhs@perinatal.usyd.edu.au
Tel: +61 2 93517318
Fax: +61 2 93517742

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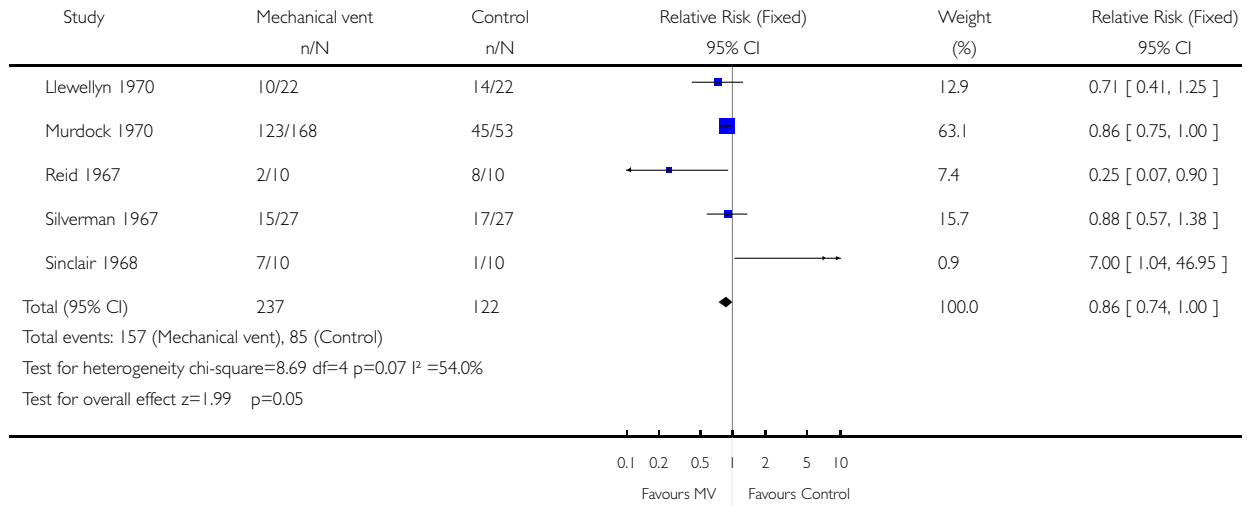
GRAPHS AND OTHER TABLES

Analysis 01.01. Comparison 01 Mechanical ventilation vs control, Outcome 01 Any reported mortality

Review: Mechanical ventilation for newborn infants with respiratory failure due to pulmonary disease

Comparison: 01 Mechanical ventilation vs control

Outcome: 01 Any reported mortality

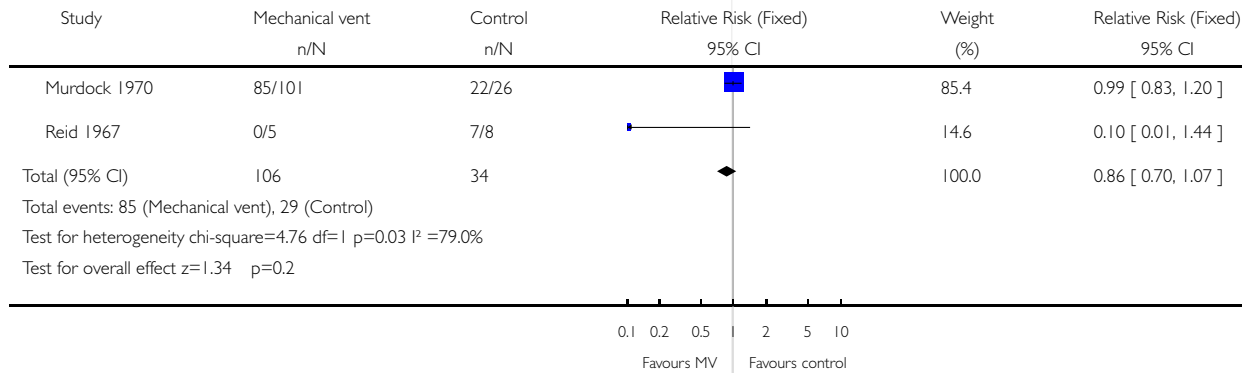


Analysis 01.02. Comparison 01 Mechanical ventilation vs control, Outcome 02 Mortality 1 - 2 kg

Review: Mechanical ventilation for newborn infants with respiratory failure due to pulmonary disease

Comparison: 01 Mechanical ventilation vs control

Outcome: 02 Mortality 1 - 2 kg

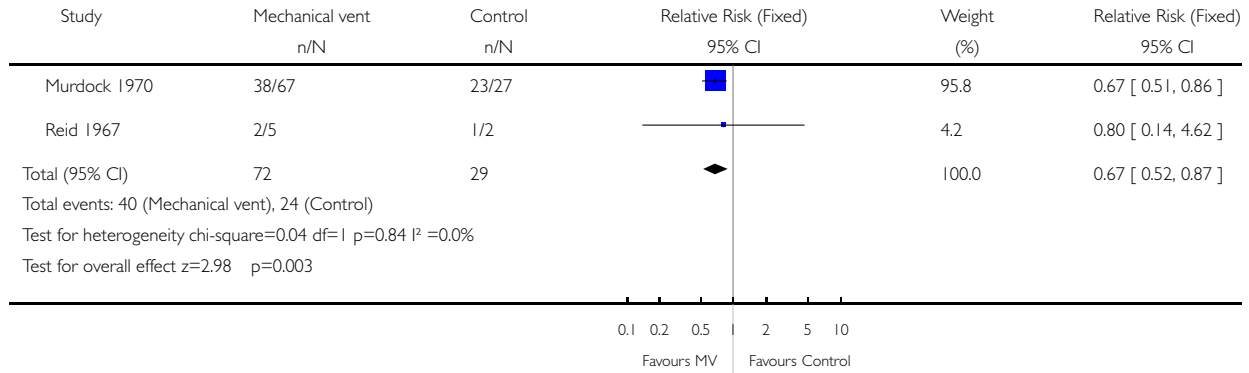


Analysis 01.03. Comparison 01 Mechanical ventilation vs control, Outcome 03 Mortality more than 2 kg

Review: Mechanical ventilation for newborn infants with respiratory failure due to pulmonary disease

Comparison: 01 Mechanical ventilation vs control

Outcome: 03 Mortality more than 2 kg

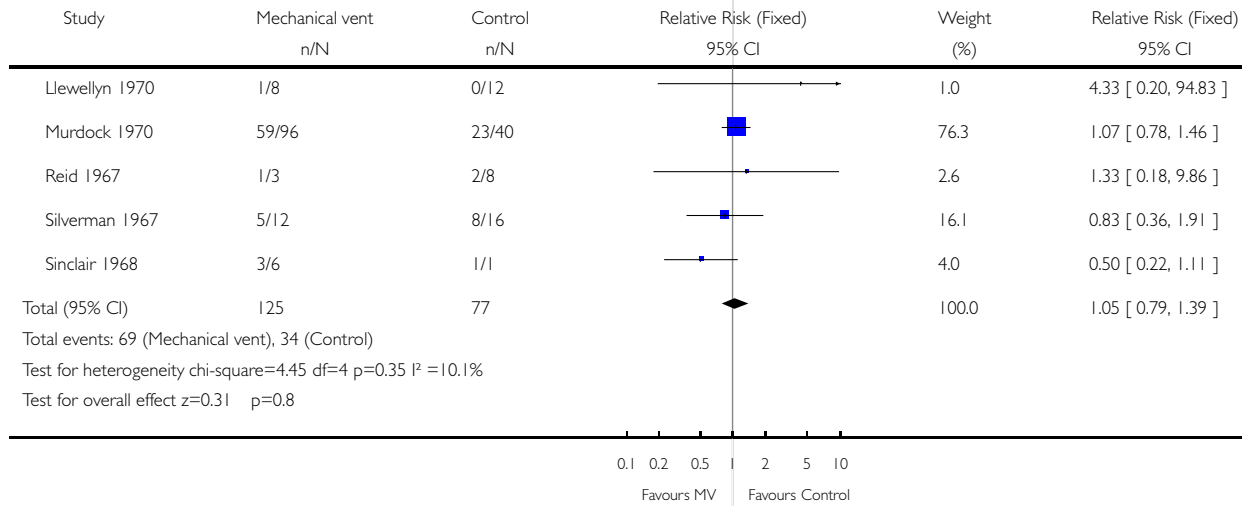


Analysis 01.04. Comparison 01 Mechanical ventilation vs control, Outcome 04 Any IVH in infants with an autopsy

Review: Mechanical ventilation for newborn infants with respiratory failure due to pulmonary disease

Comparison: 01 Mechanical ventilation vs control

Outcome: 04 Any IVH in infants with an autopsy



Analysis 01.05. Comparison 01 Mechanical ventilation vs control, Outcome 05 Pneumothorax

Review: Mechanical ventilation for newborn infants with respiratory failure due to pulmonary disease

Comparison: 01 Mechanical ventilation vs control

Outcome: 05 Pneumothorax

