# Appendix I Forest plots

## Chapter 4 Determining gestational age and chorionicity

### Gestational age

#### Review question

What are the optimal ultrasound measurements to determine gestational age in multiple pregnancy?

a) Are the measurements and charts (crown–rump length, biparietal diameter and head circumference) used for dating singletons equally effective for twins or are there systematic errors introduced from using these charts?

There are no Forest plots for this review question because no meta-analyses were conducted for the guideline review

b) Which fetus should be used for estimating gestational age in multiple pregnancies?

There are no Forest plots for this review question because no meta-analyses were conducted for the guideline review

## Chorionicity

### Review question

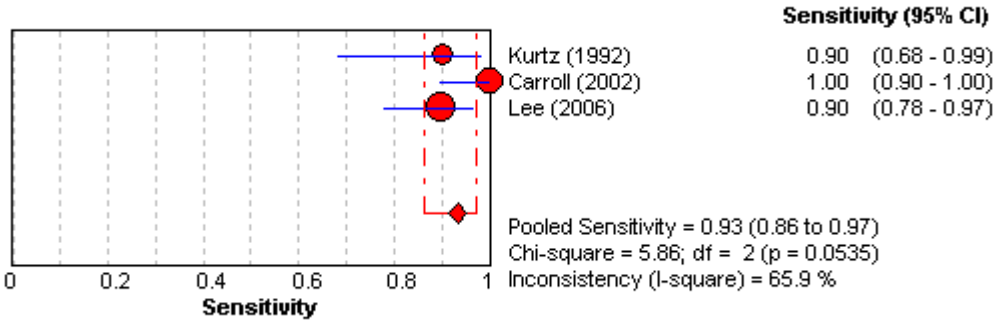
What is the optimal method to determine chorionicity in multiple pregnancies?

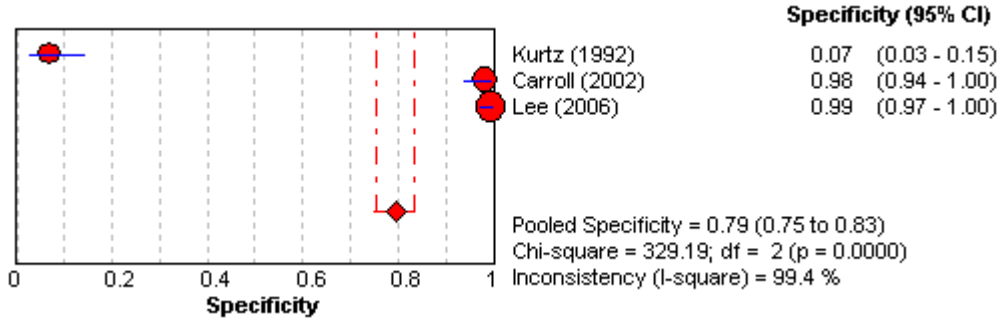
**Figure 4.1** Forest plots for scans performed at 11–14 weeks' gestation (see Table 4.3 in the full guideline main text and in Appendix J)

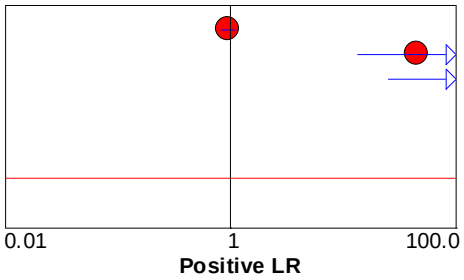
CI confidence interval, df degrees of freedom, LR likelihood ratio

#### *Number of placental masses and Lambda or T-Sign*

Meta-analyses for sensitivity, specificity, positive likelihood ratio and negative likelihood ratio conducted using random effects model



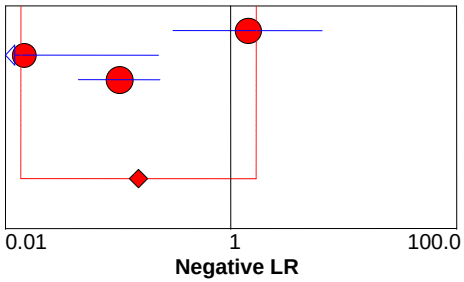






**Positive LR (95% CI)**

| | |
|---|---|
| Kurtz 1992 | 0.97 (0.83 - 1.13) |
| Carroll 2002 | 46.13 (13.53 - 157.34) |
| Lee 2006 | 177.80 (25.11 - 1,258.82 |

Random Effects Model
Pooled Positive LR = 19.68 (0.00 to 137996.27)
Cochran-Q = 426.35; df = 2 (p = 0.0000)
Inconsistency (I-square) = 99.5 %
Tau-squared = 60.7754




**Negative LR (95% CI)**

| | |
|---|---|
| Kurtz 1992 | 1.42 (0.31 - 6.51) |
| Carroll 2002 | 0.01 (0.00 - 0.23) |
| Lee 2006 | 0.10 (0.04 - 0.24) |

Random Effects Model
Pooled Negative LR = 0.15 (0.01 to 1.69)
Cochran-Q = 14.31; df = 2 (p = 0.0008)
Inconsistency (I-square) = 86.0 %
Tau-squared = 3.6981

# Chapter 5 General care

## Information and emotional support

### Review question

Is there benefit in giving women with multiple pregnancy additional information and emotional support during the antenatal period?

There are no Forest plots for this review question because no meta-analyses were conducted for the guideline review

## Nutritional supplements

### Review question

What additional (or different) dietary supplements are effective in improving maternal health and wellbeing (for example, reducing the risk of anaemia) in women with multiple pregnancy?

There are no Forest plots for this review question because no meta-analyses were conducted for the guideline review

## Diet and lifestyle advice

### Review question

Is nutritional advice specific to multiple pregnancies effective in improving maternal and fetal health and wellbeing?

There are no Forest plots for this review question because no meta-analyses were conducted for the guideline review

## Specialist care

### Review question

Do specialist multiple pregnancy clinics improve outcomes in twin and triplet pregnancies?

There are no Forest plots for this review question because no meta-analyses were conducted for the guideline review

# Chapter 6 Fetal complications

## Screening for chromosomal abnormalities

### Review question

When and how should screening be used to identify chromosomal abnormalities in multiple pregnancy?

**Figure 6.1** Forest plot for studies evaluating screening tests for chromosomal abnormalities in twin pregnancies with unreported or mixed chorionicity or in triplet pregnancies (see Table 6.3 in the full guideline main text and in Appendix J)

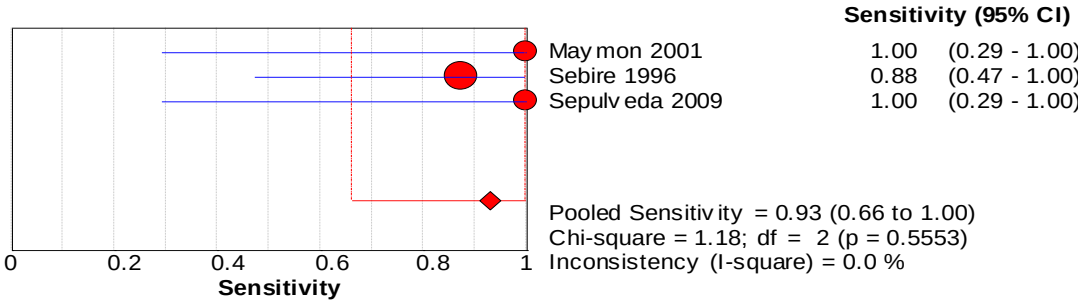
CI confidence interval, df degrees of freedom, FN false negative, FP false positive, LR likelihood ratio, TN true negative, TP true positive

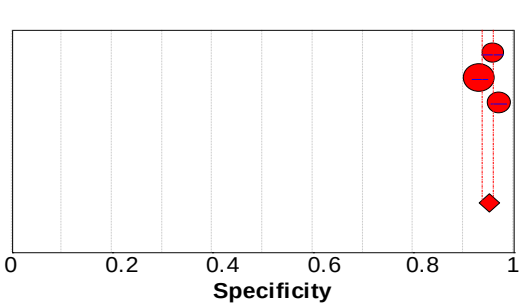
*Nuchal translucency alone*

*More than 95th centile for trisomy 21*

Meta-analysis for sensitivity conducted using fixed effects model

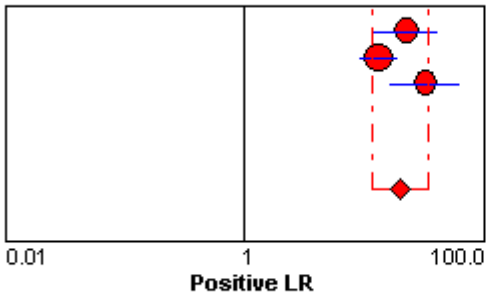
Meta-analyses for specificity, positive likelihood ratio and negative likelihood ratio conducted using random effects model





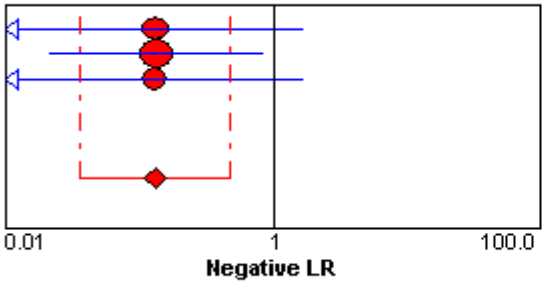

| | Specificity (95% CI) | |
|---|---|---|
| Maymon 2001 | 0.96 | (0.94 - 0.98 |
| Sebire 1996 | 0.93 | (0.92 - 0.95 |
| Sepulveda 2009 | 0.97 | (0.96 - 0.99 |

Pooled Specificity = 0.95 (0.94 to 0.96)
Chi-square = 11.87; df = 2 (p = 0.0026)
Inconsistency (I-square) = 83.2 %




| | Positive LR (95% CI) | |
|---|---|---|
| Maymon 2001 | 22.43 | (11.82 - 42.57) |
| Sebire 1996 | 13.40 | (9.33 - 19.23) |
| Sepulveda 2009 | 33.02 | (16.73 - 65.18) |

Random Effects Model
Pooled Positive LR = 20.24 (11.62 to 35.25)
Cochran-Q = 6.05; df = 2 (p = 0.0484)
Inconsistency (I-square) = 67.0 %
Tau-squared = 0.1598




| | Negative LR (95% CI) | |
|---|---|---|
| Maymon 2001 | 0.13 | (0.01 - 1.74) |
| Sebire 1996 | 0.13 | (0.02 - 0.84) |
| Sepulveda 2009 | 0.13 | (0.01 - 1.72) |

Random Effects Model
Pooled Negative LR = 0.13 (0.04 to 0.48)
Cochran-Q = 0.00; df = 2 (p = 0.9996)
Inconsistency (I-square) = 0.0 %
Tau-squared = 0.0000

## Screening for structural abnormalities

### Review question

When and how should screening be used to identify structural abnormalities in multiple pregnancies?

There are no Forest plots for this review question because no meta-analyses were conducted for the guideline review

## Monitoring forfeto-fetal transfusion syndrome

### Review question

When and how should screening be used to identify feto-fetal transfusion syndrome in multiple pregnancy?

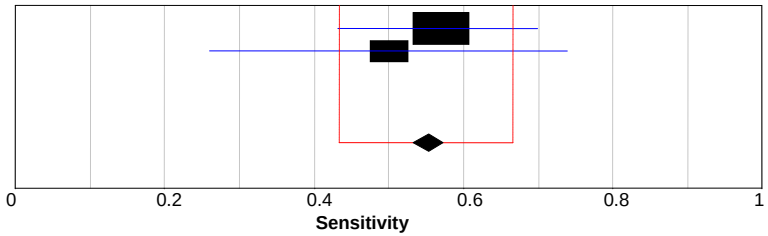
**Figure 6.2** Forest plot for studies reporting diagnostic accuracy measures for screening tests for feto-fetal transfusion syndrome (see Table 6.5 in the full guideline main text and in Appendix J)

CI confidence interval, df degrees of freedom, LR likelihood ratio

*Nuchal translucency – Discordance 20% or more (as a percentage of larger measurement) at 11–14 weeks*

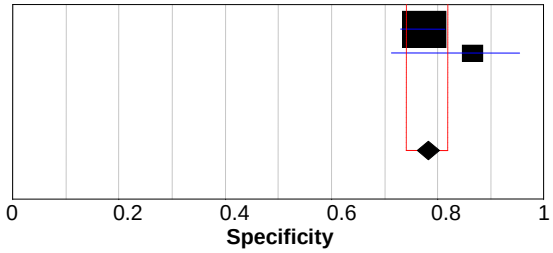
Meta-analyses for sensitivity, positive likelihood ratio and negative likelihood ratio conducted using fixed effects model

Meta-analysis for specificity conducted using random effects model



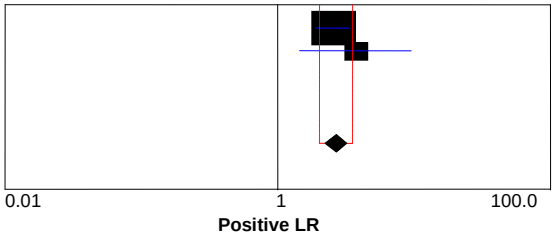

| | Sensitivity (95% CI) |
|---|---|
| Kagan 2007 | 0.57 (0.43 - 0.70) |
| Linsken 2009 | 0.50 (0.26 - 0.74) |

Pooled Sensitivity = 0.55 (0.43 to 0.67)
Chi-square = 0.26; df = 1 (p = 0.6079)
Inconsistency (I-square) = 0.0 %



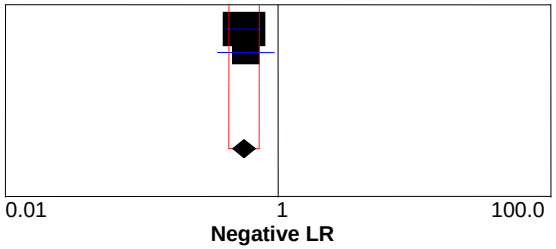

| | Specificity (95% CI) |
|---|---|
| Kagan 2007 | 0.77 (0.73 - 0.81) |
| Linsken 2009 | 0.86 (0.71 - 0.95) |

Pooled Specificity = 0.78 (0.74 to 0.82)
Chi-square = 1.81; df = 1 (p = 0.1789)
Inconsistency (I-square) = 44.7 %




| | Positive LR (95% CI) |
|---|---|
| Kagan 2007 | 2.52 (1.89 - 3.36) |
| Linsken 2009 | 3.70 (1.45 - 9.44) |

Fixed Effects Model
Pooled Positive LR = 2.67 (2.02 to 3.53)
Cochran-Q = 0.62; df = 1 (p = 0.4315)
Inconsistency (I-square) = 0.0 %



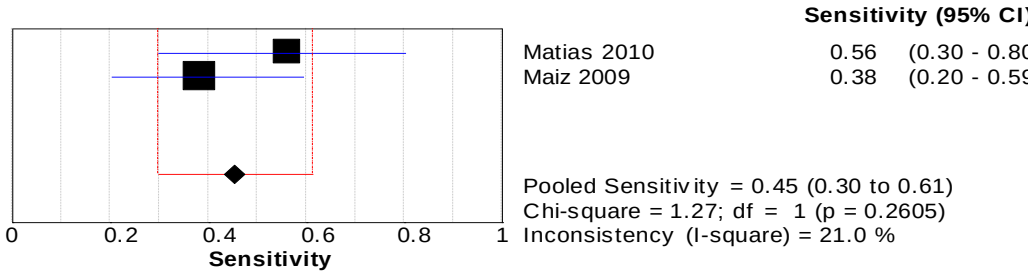

| | Negative LR (95% CI) |
|---|---|
| Kagan 2007 | 0.56 (0.41 - 0.75) |
| Linsken 2009 | 0.58 (0.36 - 0.93) |

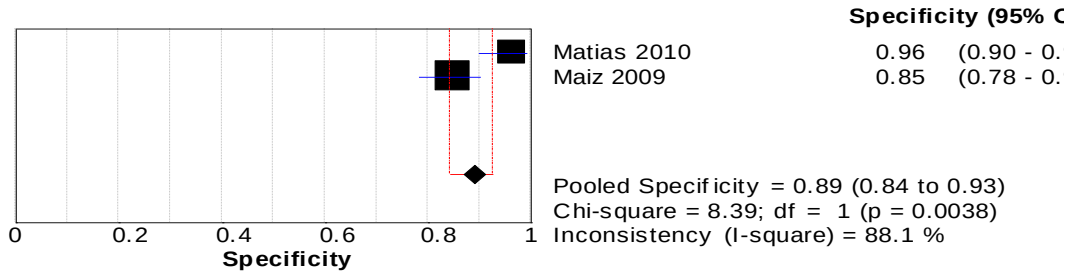
Fixed Effects Model
Pooled Negative LR = 0.56 (0.43 to 0.73)
Cochran-Q = 0.02; df = 1 (p = 0.8947)
Inconsistency (I-square) = 0.0 %

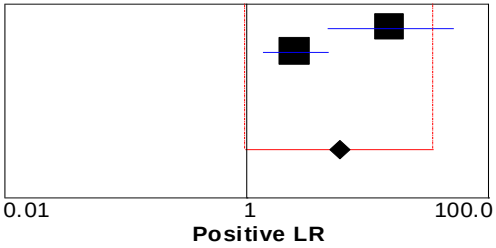
*Ductus venosus blood flow – abnormal wave form in at least one fetus (at 11–14 weeks) (including absent, reversed or reversed a-wave)*

Meta-analysis for sensitivity conducted using fixed effects model

Meta-analyses for specificity, positive likelihood ratio and negative likelihood ratio conducted using random effects model

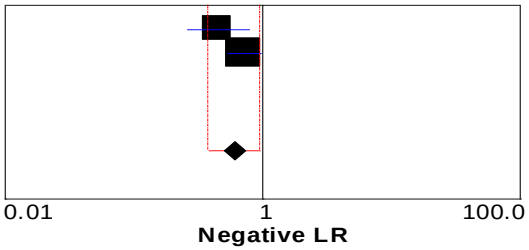





| | Positive LR (95% CI) |
|---|---|
| Matias 2010 | 15.56 (4.72 - 51.2 |
| Maiz 2009 | 2.56 (1.38 - 4.73) |

Random Effects Model
Pooled Positive LR = 5.86 (0.98 to 34.98)
Cochran-Q = 7.14; df = 1 (p = 0.0076)
Inconsistency (I-square) = 86.0 %
Tau-squared = 1.4373




| | Negative LR (95% C |
|---|---|
| Matias 2010 | 0.45 (0.26 - 0.79 |
| Maiz 2009 | 0.72 (0.53 - 0.99 |

Random Effects Model
Pooled Negative LR = 0.61 (0.38 to 0.96)
Cochran-Q = 2.21; df = 1 (p = 0.1372)
Inconsistency (I-square) = 54.7 %
Tau-squared = 0.0641

## Monitoring for intrauterine growth restriction

### Review question

What is the optimal screening programme to detect intrauterine growth restriction in multiple pregnancies?

**Figure 6.3** Forest plots for fetal weight or fetal weight difference estimation using formulae that incorporate two or more fetal biometric measurements (see Table 6.9 in the full guideline main text and in Appendix J)

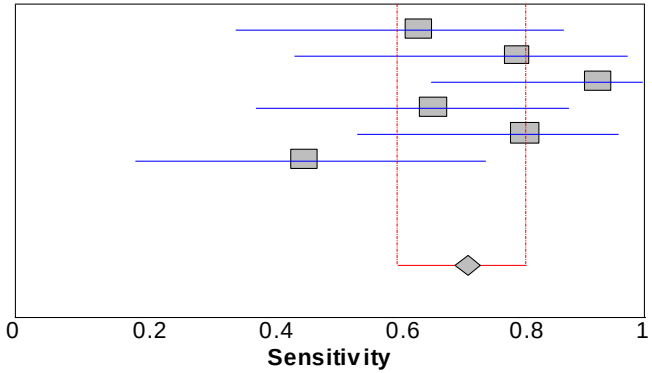
CI confidence interval, df degrees of freedom, LR likelihood ratio

For diagnostic accuracy measures shown to have $I^2$ more than 33%, the reported pooled estimates were obtained using a random effects model

*Estimated fetal weight difference 20% or more for prediction of intertwin birthweight difference 20% or more*

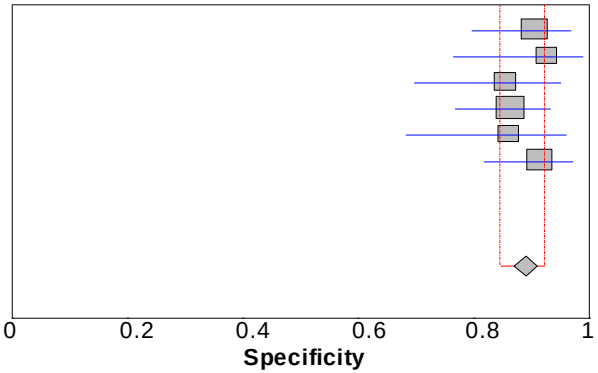
Meta-analyses for specificity and positive likelihood ratio conducted using fixed effects model

Meta-analyses for sensitivity and negative likelihood ratio conducted using random effects model



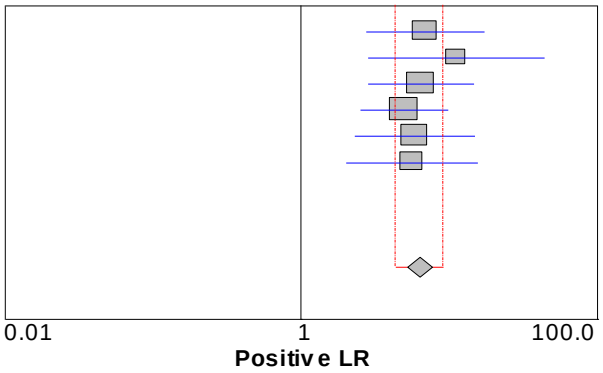

| | Sensitivity (95% CI) | |
|---|---|---|
| Jensen 1995 | 0.64 | (0.35 - 0.87) |
| Storlazzi 1987 | 0.80 | (0.44 - 0.97) |
| Hill 1994 | 0.93 | (0.66 - 1.00) |
| Blickstein 1996 | 0.67 | (0.38 - 0.88) |
| Rodis 1990 | 0.81 | (0.54 - 0.96) |
| Chamberlain 1991 | 0.46 | (0.19 - 0.75) |

Pooled Sensitivity = 0.72 (0.61 to 0.81)
Chi-square = 9.37; df = 5 (p = 0.0950)
Inconsistency (I-square) = 46.7 %



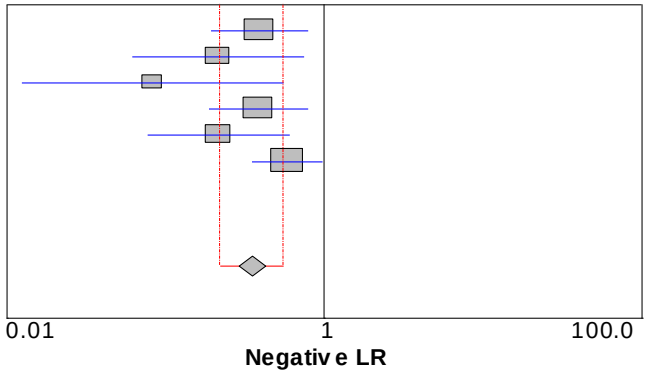

| | Specificity (95% CI) | |
|---|---|---|
| Jensen 1995 | 0.91 | (0.80 - 0.97) |
| Storlazzi 1987 | 0.93 | (0.76 - 0.99) |
| Hill 1994 | 0.86 | (0.70 - 0.95) |
| Blickstein 1996 | 0.87 | (0.77 - 0.93) |
| Rodis 1990 | 0.86 | (0.68 - 0.96) |
| Chamberlain 1991 | 0.92 | (0.82 - 0.97) |

Pooled Specificity = 0.89 (0.85 to 0.92)
Chi-square = 2.15; df = 5 (p = 0.8277)
Inconsistency (I-square) = 0.0 %




| | Positive LR (95% CI) | |
|---|---|---|
| Jensen 1995 | 6.94 | (2.76 - 17.45) |
| Storlazzi 1987 | 11.20 | (2.84 - 44.12) |
| Hill 1994 | 6.50 | (2.85 - 14.82) |
| Blickstein 1996 | 5.00 | (2.54 - 9.86) |
| Rodis 1990 | 5.89 | (2.30 - 15.08) |
| Chamberlain 1991 | 5.63 | (2.02 - 15.69) |

Fixed Effects Model
Pooled Positive LR = 6.33 (4.36 to 9.19)
Cochran-Q = 1.24; df = 5 (p = 0.9406)
Inconsistency (I-square) = 0.0 %

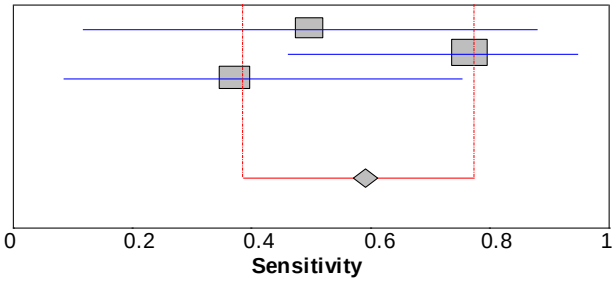



| | Negative LR (95% CI) | |
|---|---|---|
| Jensen 1995 | 0.39 | (0.19 - 0.80) |
| Storlazzi 1987 | 0.22 | (0.06 - 0.75) |
| Hill 1994 | 0.08 | (0.01 - 0.55) |
| Blickstein 1996 | 0.38 | (0.19 - 0.79) |
| Rodis 1990 | 0.22 | (0.08 - 0.61) |
| Chamberlain 1991 | 0.59 | (0.35 - 0.98) |

Random Effects Model
Pooled Negative LR = 0.35 (0.22 to 0.56)
Cochran-Q = 8.54; df = 5 (p = 0.1288)
Inconsistency (I-square) = 41.5 %
Tau-squared = 0.1287

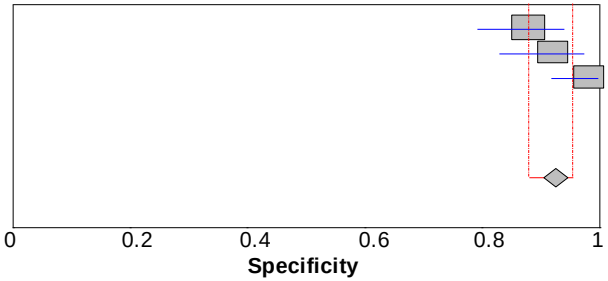
*Estimated fetal weight difference 25% or more for prediction of intertwin birthwight difference 25% or more*

Meta-analyses for sensitivity, specificity, positive likelihood ratio and negative likelihood ratio conducted using random effects model



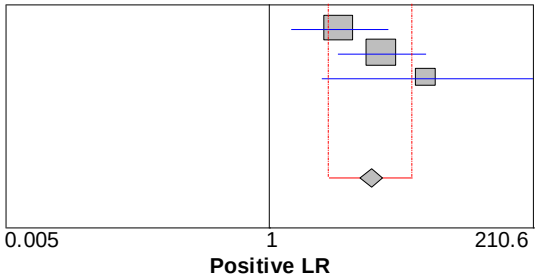

| | Sensitivity (95% CI) | |
|---|---|---|
| Blickstein 1996 | 0.50 | (0.12 - 0.88) |
| Sayegh 1993 | 0.77 | (0.46 - 0.95) |
| Chamberlain 1991 | 0.38 | (0.09 - 0.76) |

Pooled Sensitivity = 0.59 (0.39 to 0.78)
Chi-square = 3.55; df = 2 (p = 0.1694)
Inconsistency (I-square) = 43.7 %



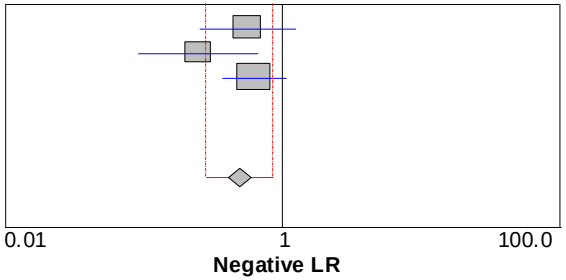

| | Specificity (95% CI) | |
|---|---|---|
| Blickstein 1996 | 0.88 | (0.79 - 0.94) |
| Sayegh 1993 | 0.92 | (0.83 - 0.97) |
| Chamberlain 1991 | 0.98 | (0.92 - 1.00) |

Pooled Specificity = 0.93 (0.88 to 0.96)
Chi-square = 6.97; df = 2 (p = 0.0306)
Inconsistency (I-square) = 71.3 %




| | Positive LR (95% CI) |
|---|---|
| Blickstein 1996 | 4.20 (1.56 - 11.29) |
| Sayegh 1993 | 10.00 (4.09 - 24.43) |
| Chamberlain 1991 | 24.75 (2.91 - 210.56) |

Random Effects Model
Pooled Positive LR = 7.90 (3.41 to 18.30)
Cochran-Q = 3.06; df = 2 (p = 0.2167)
Inconsistency (I-square) = 34.6 %
Tau-squared = 0.1933




| | Negative LR (95% CI) |
|---|---|
| Blickstein 1996 | 0.57 (0.25 - 1.27) |
| Sayegh 1993 | 0.25 (0.09 - 0.68) |
| Chamberlain 1991 | 0.63 (0.37 - 1.09) |

Random Effects Model
Pooled Negative LR = 0.50 (0.28 to 0.87)
Cochran-Q = 3.33; df = 2 (p = 0.1895)
Inconsistency (I-square) = 39.9 %
Tau-squared = 0.0998

# Chapter 7 Maternal complications

## Hypertension

### Review question

What is the optimal screening programme to detect hypertension in multiple pregnancy in the antenatal period?

There are no Forest plots for this review question because no meta-analyses were conducted for the guideline review

# Chapter 8 Preterm birth

## Predicting the risk of preterm birth

### Review question

What is the optimal screening programme to predict the risks of spontaneous preterm delivery?

There are no Forest plots for this review question because no meta-analyses were conducted for the guideline

## Preventing preterm birth

### Review question

What interventions are effective in preventing spontaneous preterm delivery in multiple pregnancy, including bed rest, progesterone and cervical cerclage?

**Figure 8.1** Forest plots for intramuscular or vaginal progesterone versus placebo for the prevention of spontaneous preterm birth in twin pregnancies (see Table 8.14 in the full guideline main text and in Appendix J)

CI confidence interval, df degrees of freedom, M-H Mantel-Haenszel

*Spontaneous preterm birth*

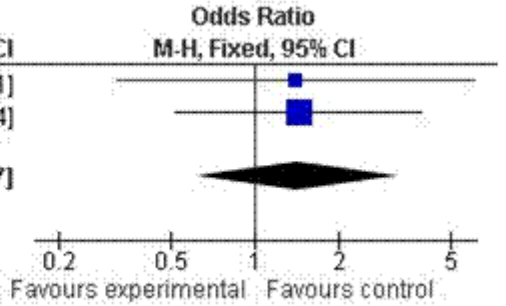
*Less than 37 weeks - intramuscular progesterone*

Meta-analysis conducted using fixed effects model

| | Progesterone group | | Placebo group | | | Odds Ratio |
|---|---|---|---|---|---|---|
| **Study or Subgroup** | **Events** | **Total** | **Events** | **Total** | **Weight** | **M-H, Fixed, 95% CI** |
| Briery, 2009 | 7 | 16 | 5 | 14 | 32.2% | 1.40 [0.32, 6.11] |
| Hartikainen-Sorri, 1980 | 12 | 39 | 9 | 38 | 67.8% | 1.43 [0.52, 3.94] |
| **Total (95% CI)** | | **55** | | **52** | **100.0%** | **1.42 [0.62, 3.27]** |
| Total events | 19 | | 14 | | | |

Heterogeneity: Chi² = 0.00, df = 1 (P = 0.98); I² = 0%

Test for overall effect: Z = 0.83 (P = 0.41)



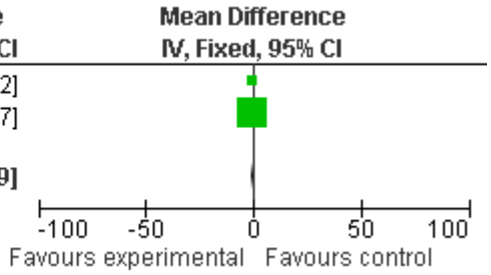

*Gestational age at birth (measured in weeks' gestation; better indicated by higher values)*

Meta-analysis conducted using fixed effects model

| | Progesterone | | | Placebo | | | | Mean Difference |
|---|---|---|---|---|---|---|---|---|
| **Study or Subgroup** | **Mean** | **SD** | **Total** | **Mean** | **SD** | **Total** | **Weight** | **IV, Fixed, 95% CI** |
| Hartikainen-Sorri (1980) | 36.9 | 2.6 | 39 | 37.3 | 2.4 | 38 | 20.8% | -0.40 [-1.52, 0.72] |
| Rouse (2007) | 34.6 | 3.9 | 327 | 34.9 | 3.6 | 334 | 79.2% | -0.30 [-0.87, 0.27] |
| **Total (95% CI)** | | | **366** | | | **372** | **100.0%** | **-0.32 [-0.83, 0.19]** |

Heterogeneity: Chi² = 0.02, df = 1 (P = 0.88); I² = 0%

Test for overall effect: Z = 1.23 (P = 0.22)



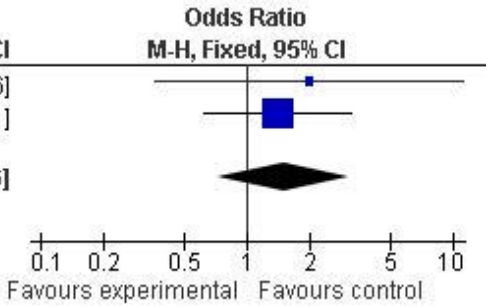
*Perinatal mortality*

Meta-analysis conducted using fixed effects model

| Study or Subgroup | Progesterone group Events | Total | Placebo group Events | Total | Weight | Odds Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Hartikainen-Sorri, 1980 | 4 | 78 | 2 | 76 | 16.5% | 2.00 [0.36, 11.26] |
| Norman 2009 | 14 | 494 | 10 | 494 | 83.5% | 1.41 [0.62, 3.21] |
| **Total (95% CI)** | | **572** | | **570** | **100.0%** | **1.51 [0.72, 3.16]** |
| Total events | 18 | | 12 | | | |

Heterogeneity: Chi² = 0.13, df = 1 (P = 0.72); I² = 0%

Test for overall effect: Z = 1.09 (P = 0.28)



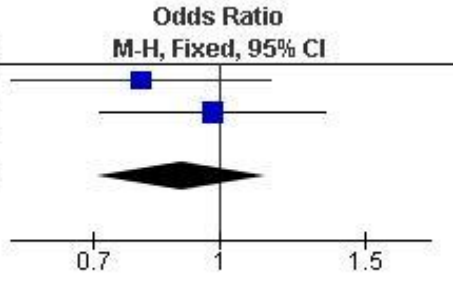

*Caesarean section*

Meta-analysis conducted using fixed effects model

| Study or Subgroup | Progesterone group Events | Total | Placebo group Events | Total | Weight | Odds Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Norman 2009 | 148 | 250 | 161 | 250 | 45.8% | 0.80 [0.56, 1.15] |
| Rouse, 2007 | 200 | 324 | 204 | 328 | 54.2% | 0.98 [0.71, 1.35] |
| **Total (95% CI)** | | **574** | | **578** | **100.0%** | **0.90 [0.71, 1.14]** |
| Total events | 348 | | 365 | | | |

Heterogeneity: Chi² = 0.67, df = 1 (P = 0.41); I² = 0%

Test for overall effect: Z = 0.88 (P = 0.38)



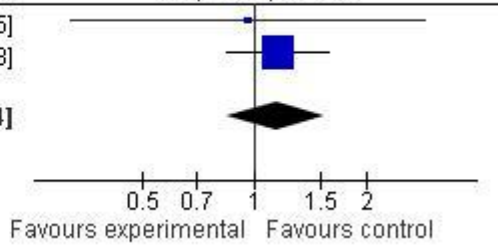
*Respiratory distress syndrome*

Meta-analysis conducted using fixed effects model

| | Progesterone group | | Placebo group | | | Odds Ratio | Odds Ratio |
|---|---|---|---|---|---|---|---|
| **Study or Subgroup** | **Events** | **Total** | **Events** | **Total** | **Weight** | **M-H, Fixed, 95% CI** | **M-H, Fixed, 95% CI** |
| Briery, 2009 | 10 | 32 | 9 | 28 | 8.3% | 0.96 [0.32, 2.85] | |
| Rouse, 2007 | 96 | 632 | 87 | 648 | 91.7% | 1.15 [0.84, 1.58] | |
| **Total (95% CI)** | | **664** | | **676** | **100.0%** | **1.14 [0.84, 1.54]** | |
| Total events | 106 | | 96 | | | | |

Heterogeneity: Chi² = 0.10, df = 1 (P = 0.75); I² = 0%

Test for overall effect: Z = 0.85 (P = 0.40)



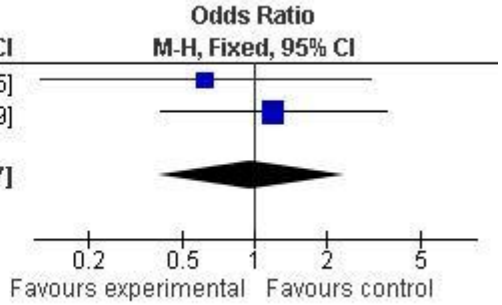

*Intraventricular haemorrhage*

Meta-analysis conducted using fixed effects model

| | Progesterone group | | Placebo group | | | Odds Ratio | Odds Ratio |
|---|---|---|---|---|---|---|---|
| **Study or Subgroup** | **Events** | **Total** | **Events** | **Total** | **Weight** | **M-H, Fixed, 95% CI** | **M-H, Fixed, 95% CI** |
| Briery, 2009 | 3 | 32 | 4 | 28 | 39.8% | 0.62 [0.13, 3.05] | |
| Rouse, 2007 | 7 | 632 | 6 | 648 | 60.2% | 1.20 [0.40, 3.59] | |
| **Total (95% CI)** | | **664** | | **676** | **100.0%** | **0.97 [0.40, 2.37]** | |
| Total events | 10 | | 10 | | | | |

Heterogeneity: Chi² = 0.45, df = 1 (P = 0.50); I² = 0%

Test for overall effect: Z = 0.07 (P = 0.94)



*Necrotising enterocolitis*

Meta-analysis conducted using fixed effects model

| Study or Subgroup | Progesterone group Events | Total | Placebo group Events | Total | Weight | Odds Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Briery, 2009 | 1 | 32 | 0 | 28 | 11.4% | 2.71 [0.11, 69.34] |
| Rouse, 2007 | 3 | 632 | 4 | 648 | 88.6% | 0.77 [0.17, 3.44] |
| **Total (95% CI)** | | **664** | | **676** | **100.0%** | **0.99 [0.26, 3.70]** |
| Total events | 4 | | 4 | | | |

Heterogeneity: Chi² = 0.48, df = 1 (P = 0.49); I² = 0%

Test for overall effect: Z = 0.01 (P = 0.99)

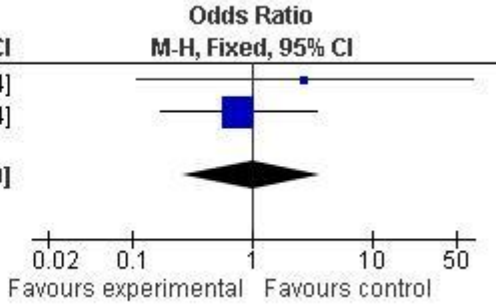


**Figure 8.2** Forest plots for intramuscular progesterone versus placebo for the prevention of spontaneous preterm birth in triplet pregnancies (see Table 8.15 in the full guideline main text and in Appendix J)

CI confidence interval, df degrees of freedom, M-H Mantel-Haenszel

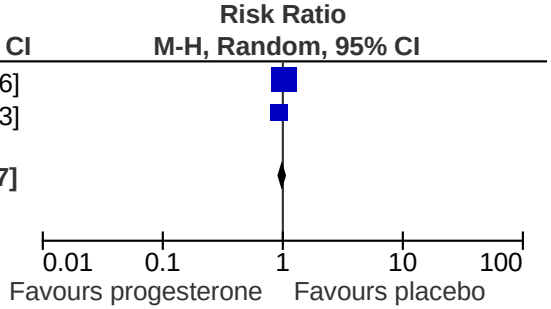
*Caesarean section*

Meta-analysis conducted using random effects model

| Study or Subgroup | Experimental Events | Experimental Total | Control Events | Control Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Caritis 2009 | 71 | 71 | 62 | 63 | 61.9% | 1.02 [0.97, 1.06] |
| Combs 2010 | 52 | 56 | 25 | 25 | 38.1% | 0.94 [0.86, 1.03] |
| **Total (95% CI)** | | **127** | | **88** | **100.0%** | **0.99 [0.91, 1.07]** |
| Total events | 123 | | 87 | | | |

Heterogeneity: Tau² = 0.00; Chi² = 2.76, df = 1 (P = 0.10); I² = 64%

Test for overall effect: Z = 0.32 (P = 0.75)



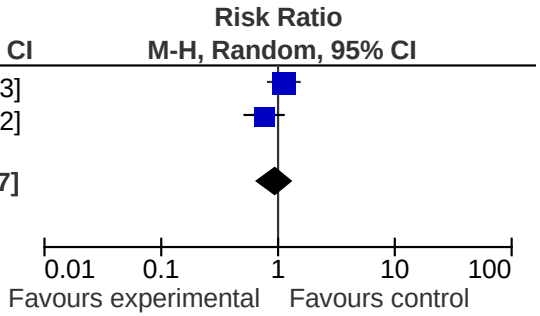

*Respiratory distress syndrome*

Meta-analysis conducted using random effects model

| Study or Subgroup | Progesterone Events | Progesterone Total | Placebo Events | Placebo Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Caritis 2009 | 65 | 212 | 50 | 183 | 54.4% | 1.12 [0.82, 1.53] |
| Combs 2010 | 44 | 155 | 28 | 75 | 45.6% | 0.76 [0.52, 1.12] |
| **Total (95% CI)** | | **367** | | **258** | **100.0%** | **0.94 [0.64, 1.37]** |
| Total events | 109 | | 78 | | | |

Heterogeneity: Tau² = 0.04; Chi² = 2.38, df = 1 (P = 0.12); I² = 58%

Test for overall effect: Z = 0.32 (P = 0.75)



*Intraventricular haemorrhage*

Meta-analysis conducted using fixed effects model

| Study or Subgroup | Progesterone Events | Total | Placebo Events | Total | Weight | Risk Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Caritis 2009 | 2 | 212 | 4 | 183 | 51.8% | 0.43 [0.08, 2.33] |
| Combs 2010 | 4 | 150 | 3 | 75 | 48.2% | 0.67 [0.15, 2.90] |
| **Total (95% CI)** | | **362** | | **258** | **100.0%** | **0.54 [0.18, 1.64]** |
| Total events | 6 | | 7 | | | |

Heterogeneity: Chi² = 0.15, df = 1 (P = 0.70); I² = 0%

Test for overall effect: Z = 1.08 (P = 0.28)

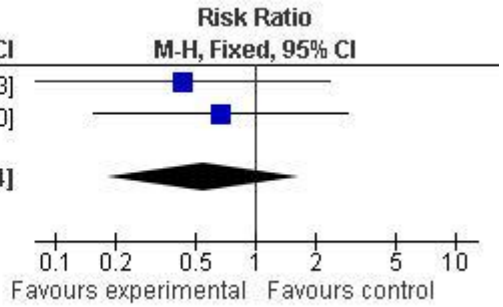


**Figure 8.4** Forest plots for cervical cerclage versus no cerclage for the prevention of spontaneous preterm birth in triplet pregnancies (see Table 8.17 in the full guideline main text and in Appendix J)

CI confidence interval, df degrees of freedom, M-H Mantel-Haenszel

*Spontaneous preterm birth*

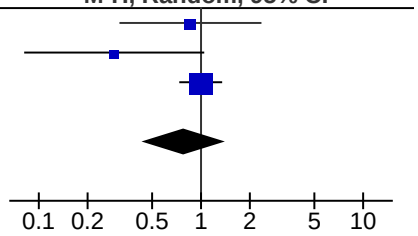
*Less than 32 weeks*

Meta-analysis conducted using random effects model

| Study or Subgroup | cervical cerclage Events | Total | no cerclage Events | Total | Weight | Odds Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Bernasko 2006 | 11 | 55 | 9 | 40 | 23.5% | 0.86 [0.32, 2.33] |
| Elimian 1999 | 4 | 20 | 18 | 39 | 16.6% | 0.29 [0.08, 1.03] |
| Rebarber 2005 | 68 | 248 | 833 | 3030 | 59.9% | 1.00 [0.75, 1.33] |
| **Total (95% CI)** | | **323** | | **3109** | **100.0%** | **0.78 [0.44, 1.42]** |
| Total events | 83 | | 860 | | | |

Heterogeneity: Tau² = 0.13; Chi² = 3.48, df = 2 (P = 0.18); I² = 42%

Test for overall effect: Z = 0.80 (P = 0.42)



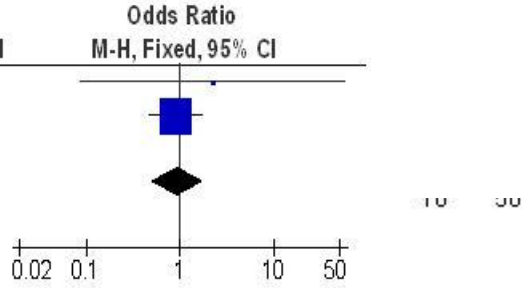

*Less than 28 weeks*

Meta-analysis conducted using fixed effects model

| Study or Subgroup | cervical cerclage Events | Total | no cerclage Events | Total | Weight | Odds Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Bernasko 2006 | 1 | 55 | 0 | 40 | 2.8% | 2.23 [0.09, 56.15] |
| Rebarber 2005 | 10 | 248 | 136 | 3030 | 97.2% | 0.89 [0.46, 1.72] |
| **Total (95% CI)** | | **303** | | **3070** | **100.0%** | **0.93 [0.49, 1.76]** |
| Total events | 11 | | 136 | | | |

Heterogeneity: Chi² = 0.30, df = 1 (P = 0.59); I² = 0%

Test for overall effect: Z = 0.22 (P = 0.83)



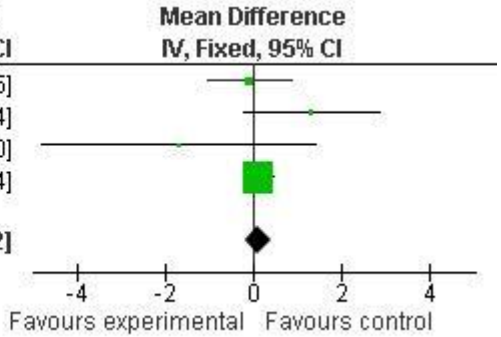
*Gestational age at birth (measured in weeks)*

Meta-analysis conducted using fixed effects model

| Study or Subgroup | cervical cerclage Mean | SD | Total | no cerclage Mean | SD | Total | Weight | Mean Difference IV, Fixed, 95% CI |
|---|---|---|---|---|---|---|---|---|
| Bernasko 2006 | 33.6 | 2.4 | 55 | 33.7 | 2.3 | 40 | 10.5% | -0.10 [-1.05, 0.85] |
| Elimian 1999 | 32.8 | 2.4 | 20 | 31.5 | 3.6 | 39 | 4.0% | 1.30 [-0.24, 2.84] |
| Mordel 1993 | 33 | 5.1 | 12 | 34.7 | 2.8 | 23 | 1.0% | -1.70 [-4.80, 1.40] |
| Rebarber 2005 | 33.1 | 2.6 | 248 | 33 | 2.5 | 3030 | 84.6% | 0.10 [-0.24, 0.44] |
| **Total (95% CI)** | | | **335** | | | **3132** | **100.0%** | **0.11 [-0.20, 0.42]** |

Heterogeneity: Chi² = 3.78, df = 3 (P = 0.29); I² = 21%

Test for overall effect: Z = 0.69 (P = 0.49)



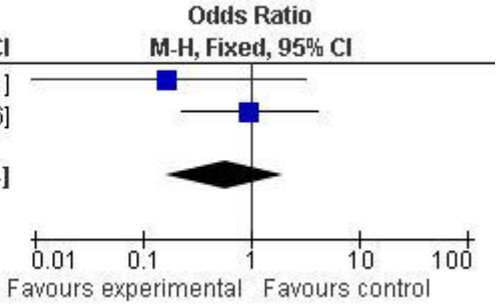

*Perinatal mortality*

Meta-analysis conducted using fixed effects model

| Study or Subgroup | cervical cerclage Events | Total | no cerclage Events | Total | Weight | Odds Ratio M-H, Fixed, 95% CI |
|---|---|---|---|---|---|---|
| Elimian 1999 | 0 | 60 | 5 | 117 | 49.6% | 0.17 [0.01, 3.11] |
| Mordel 1993 | 3 | 36 | 6 | 69 | 50.4% | 0.95 [0.22, 4.06] |
| **Total (95% CI)** | | **96** | | **186** | **100.0%** | **0.56 [0.16, 1.94]** |
| Total events | 3 | | 11 | | | |

Heterogeneity: Chi² = 1.16, df = 1 (P = 0.28); I² = 14%

Test for overall effect: Z = 0.91 (P = 0.36)



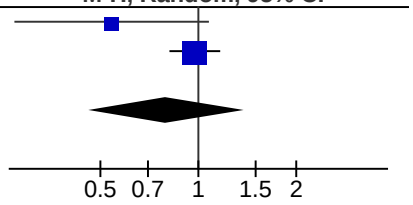
*Very low birthweight (less than 1500 g)*

Meta-analysis conducted using random effects model

| | cervical cerclage | | no cerclage | | | Odds Ratio | Odds Ratio |
|---|---|---|---|---|---|---|---|
| **Study or Subgroup** | **Events** | **Total** | **Events** | **Total** | **Weight** | **M-H, Random, 95% CI** | **M-H, Random, 95% CI** |
| Elimian 1999 | 16 | 60 | 47 | 117 | 33.7% | 0.54 [0.27, 1.07] | |
| Rebarber 2005 | 186 | 744 | 2315 | 9090 | 66.3% | 0.98 [0.82, 1.16] | |
| **Total (95% CI)** | | **804** | | **9207** | **100.0%** | **0.80 [0.46, 1.38]** | |
| Total events | 202 | | 2362 | | | | |

Heterogeneity: Tau² = 0.11; Chi² = 2.69, df = 1 (P = 0.10); I² = 63%

Test for overall effect: Z = 0.80 (P = 0.42)



## Untargeted corticosteroids

### Review question

Is routine/elective antenatal corticosteroid prophylaxis effective in reducing perinatal morbidity, including neonatal respiratory distress syndrome, necrotising colitis and intraventricular haemorrhage, in multiple pregnancy?

There are no Forest plots for this review question because no meta-analyses were conducted for the guideline review

# Chapter 9 Indications for referral to a tertiary level fetal medicine centre

## Review question

What are the clinical indications for referral to subspecialist services?

There are no Forest plots for this review question because no meta-analyses were conducted for the guideline review

# Chapter 10 Timing of birth

## Review question

What is the optimal timing of delivery in women with uncomplicated multiple pregnancies?

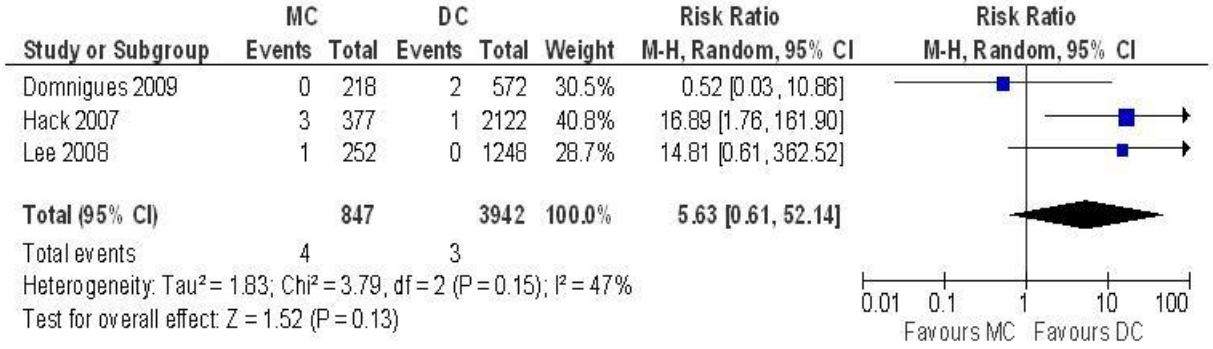
**Figure 10.2** Forest plots for the risk of fetal death by chorionicity at different gestational ages (studies reporting results for monochorionic and dichorionic twin pregnancies; see Table 10.5 in the full guideline main text and in Appendix J)

CI confidence interval, DC dichorionic, df degrees of freedom, MC monochorionic, M-H Mantel-Haenszel

### *Risk of fetal death at given gestational age*

*At 26–27 weeks*

Meta-analyses conducted using random effects model



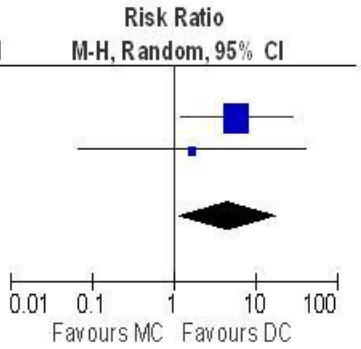
*At 28–29 weeks*

Meta-analyses conducted using random effects model

| Study or Subgroup | MC Events | MC Total | DC Events | DC Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Domnigues 2009 | 0 | 212 | 0 | 558 | | Not estimable |
| Hack 2007 | 3 | 354 | 3 | 2060 | 80.1% | 5.82 [1.18, 28.72] |
| Lee 2008 | 0 | 246 | 1 | 1222 | 19.9% | 1.65 [0.07, 40.40] |
| **Total (95% CI)** | | **812** | | **3840** | **100.0%** | **4.53 [1.08, 18.88]** |
| Total events | 3 | | 4 | | | |

Heterogeneity: Tau² = 0.00; Chi² = 0.48, df = 1 (P = 0.49); I² = 0%

Test for overall effect: Z = 2.07 (P = 0.04)



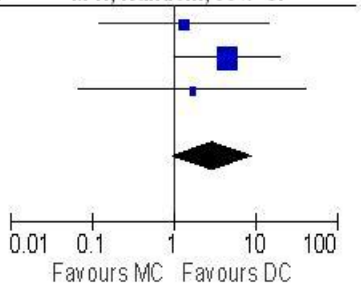

*At 30–31 weeks*

Meta-analyses conducted using random effects model

| Study or Subgroup | MC Events | MC Total | DC Events | DC Total | Weight | Risk Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Domnigues 2009 | 1 | 200 | 2 | 524 | 24.2% | 1.31 [0.12, 14.37] |
| Hack 2007 | 3 | 334 | 4 | 1973 | 62.3% | 4.43 [1.00, 19.71] |
| Lee 2008 | 0 | 234 | 1 | 1182 | 13.6% | 1.68 [0.07, 41.07] |
| **Total (95% CI)** | | **768** | | **3679** | **100.0%** | **2.89 [0.89, 9.39]** |
| Total events | 4 | | 7 | | | |

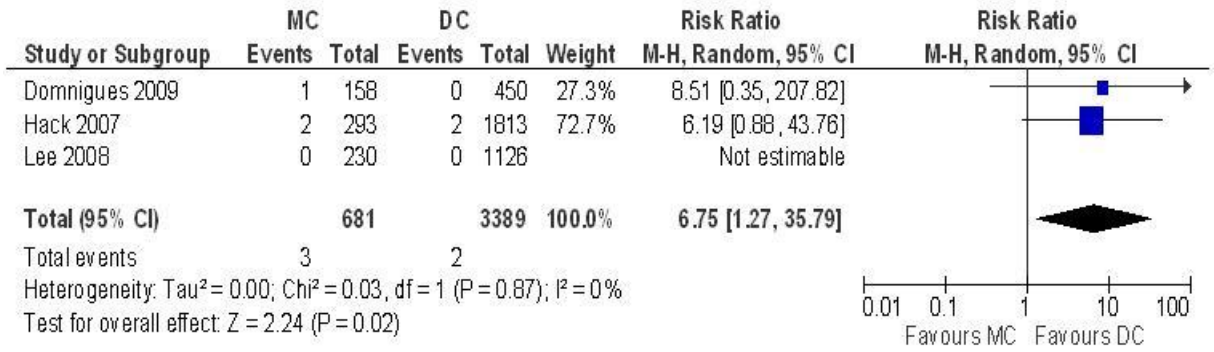
Heterogeneity: Tau² = 0.00; Chi² = 0.86, df = 2 (P = 0.65); I² = 0%

Test for overall effect: Z = 1.77 (P = 0.08)



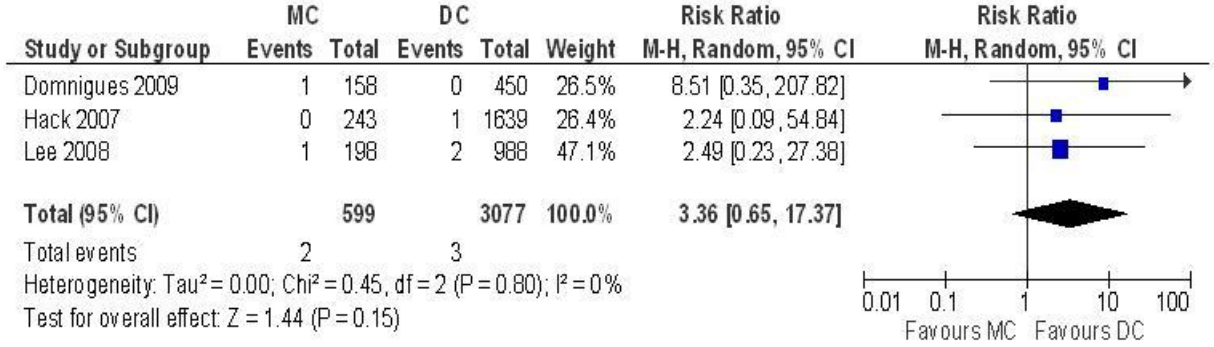
*At 32–33 weeks*

Meta-analyses conducted using random effects model




*At 34–35 weeks*

Meta-analyses conducted using random effects model



*At ≥ 36 weeks*

Meta-analyses conducted using random effects model

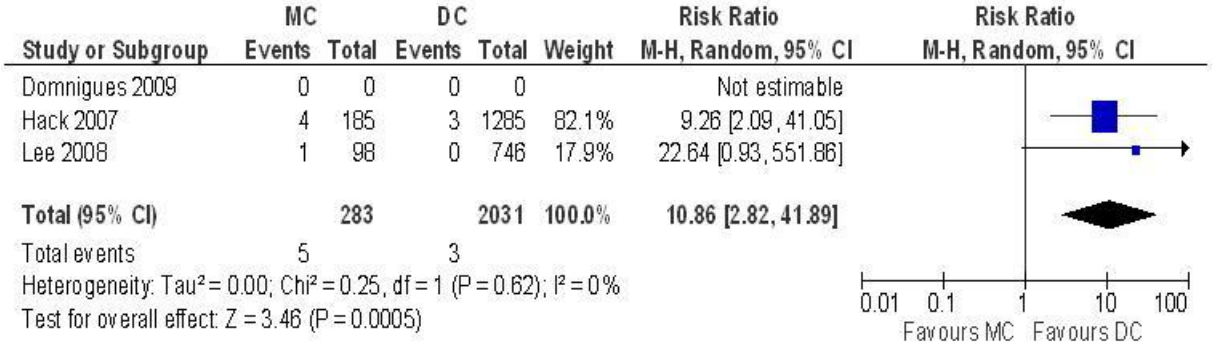


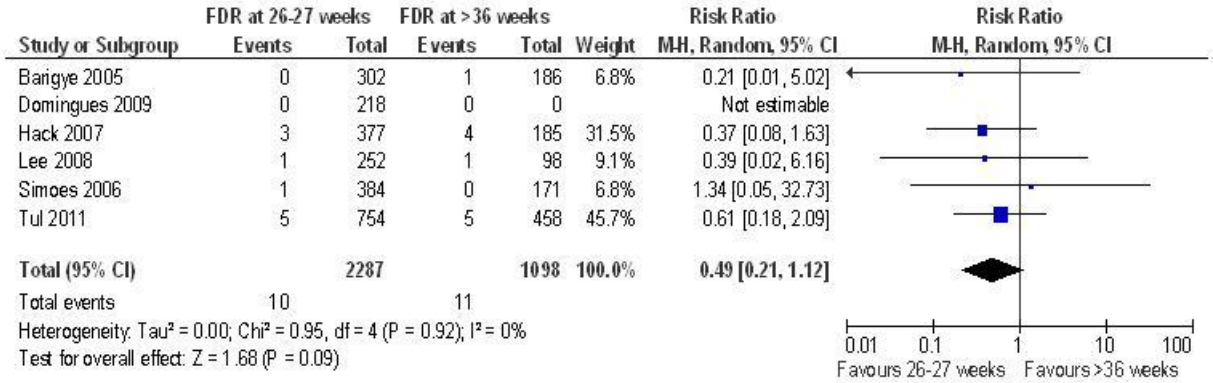
**Figure 10.6** Forest plots for the risk of fetal death at different gestational ages (studies reporting results for monochorionic twin pregnancies; see Table 10.3 in the full guideline main text and in Appendix J)

CI confidence interval, df degrees of freedom, FDR fetal death rate, M-H Mantel-Haenszel

### *Risk of fetal death at given gestational age*

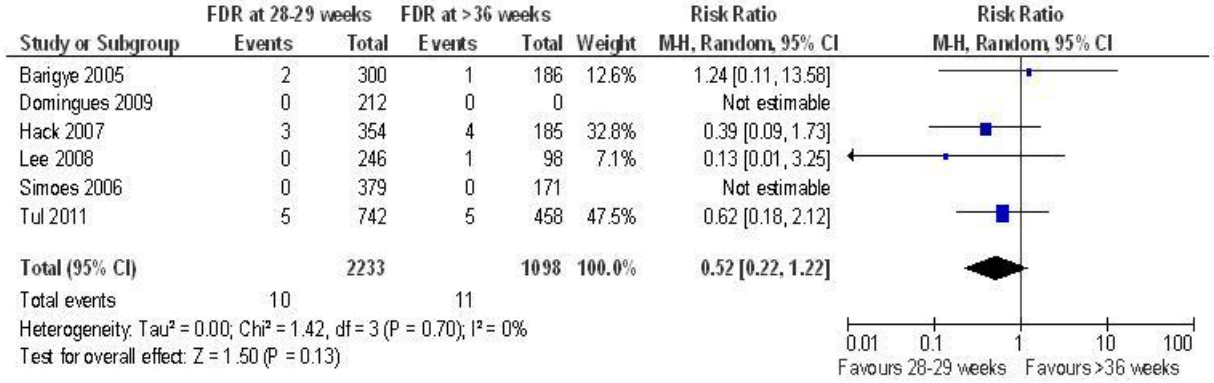
*At 26–27 weeks*

Meta-analyses conducted using random effects model



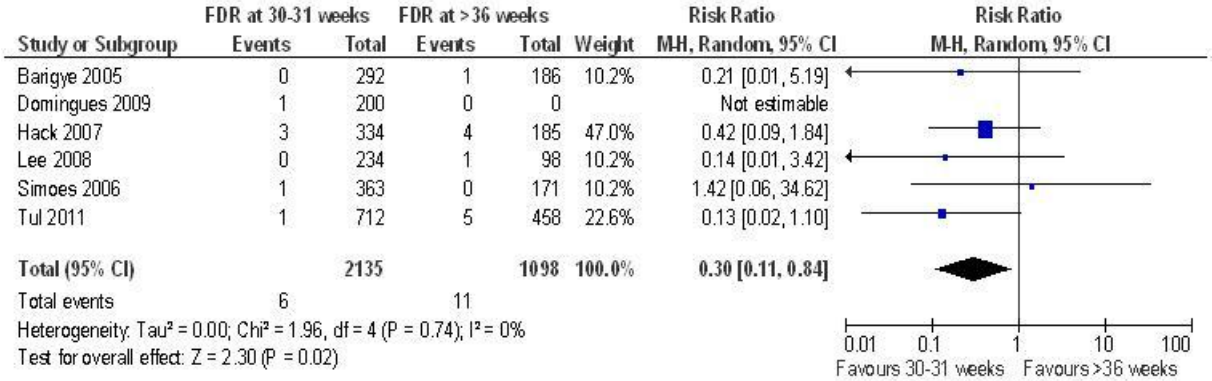

*At 28–29 weeks*

Meta-analyses conducted using random effects model



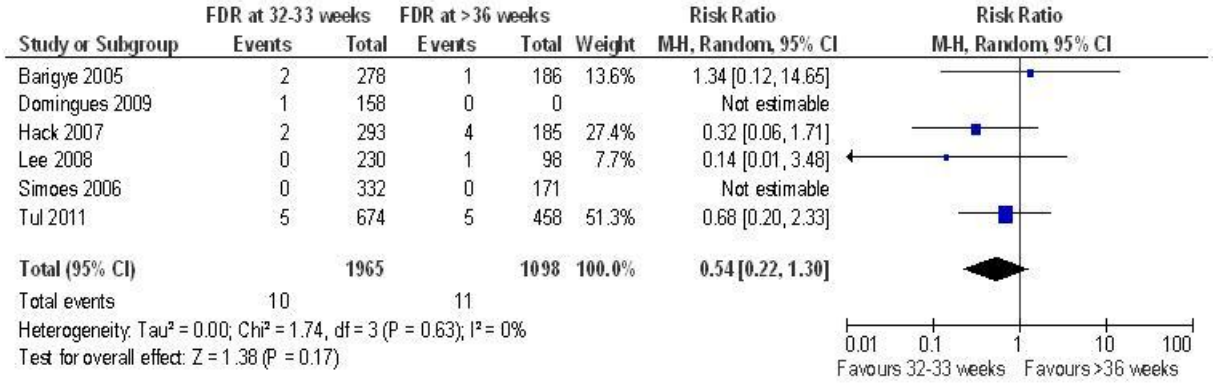
*At 30–31 weeks*

Meta-analyses conducted using random effects model




*At 32–33 weeks*

Meta-analyses conducted using random effects model



*At 34–35 weeks*

Meta-analyses conducted using random effects model

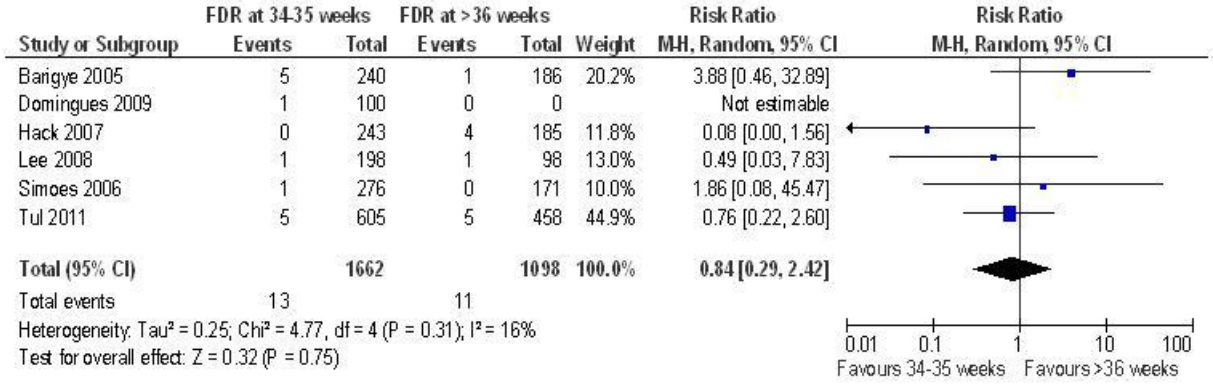


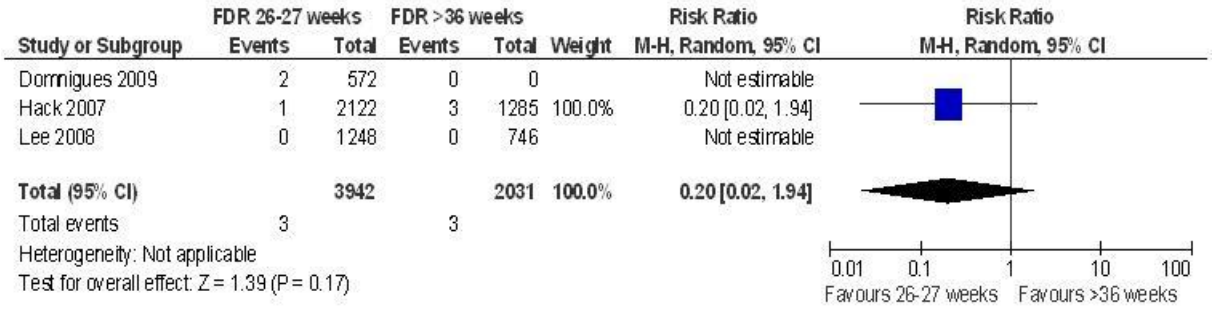
**Figure 10.4** Forest plots for the risk of fetal death at different gestational ages (studies reporting results for dichorionic twin pregnancies; see Table 10.7 in the full guideline main text and in Appendix J)

CI confidence interval, df degrees of freedom, FDR fetal death rate, M-H Mantel-Haenszel

*Risk of fetal death at given gestational age*

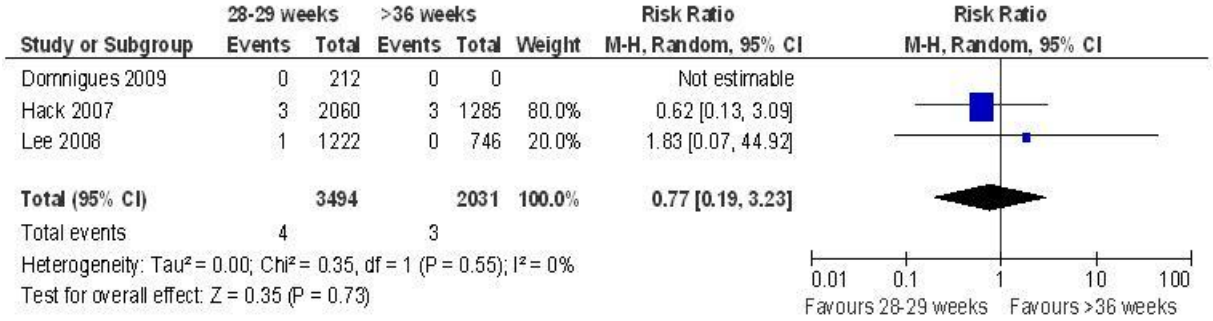
*At 26–27 weeks*

Meta-analyses conducted using random effects model



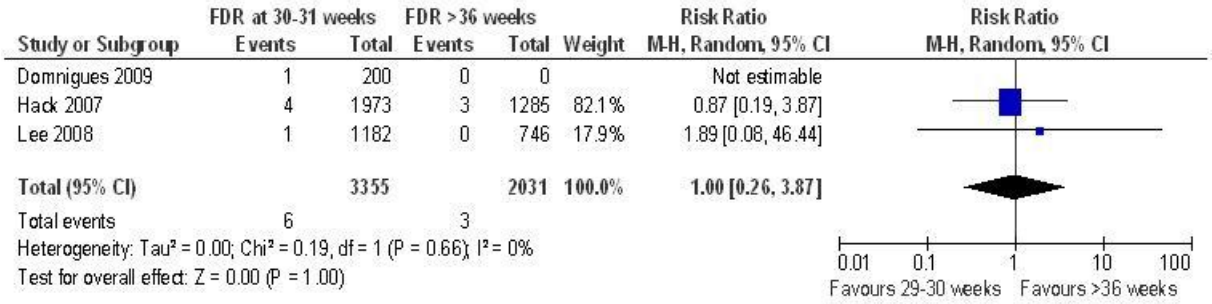

*At 28–29 weeks*

Meta-analyses conducted using random effects model



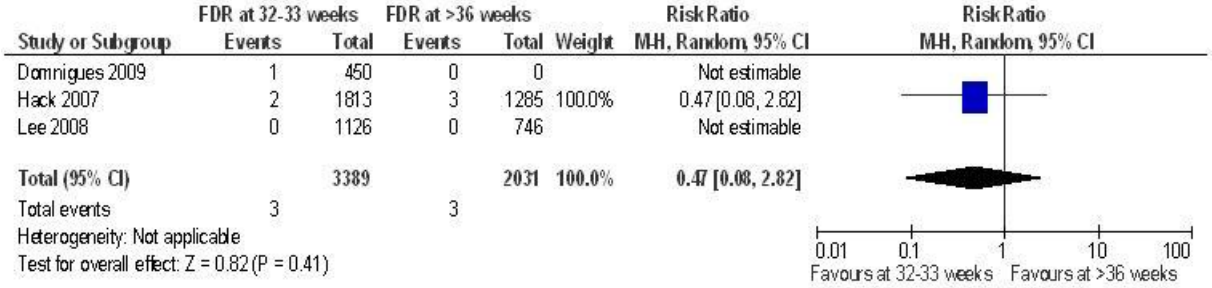
*At 30–31 weeks*

Meta-analyses conducted using random effects model




*At 32–33 weeks*

Meta-analyses conducted using random effects model



*At 34–35 weeks*

Meta-analyses conducted using random effects model

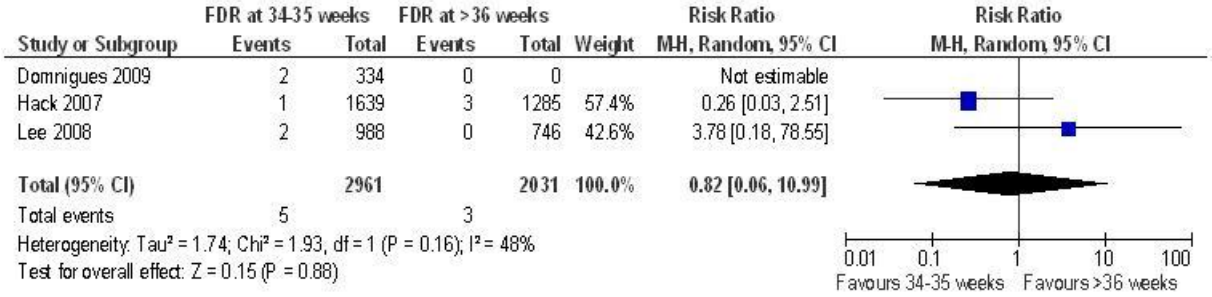


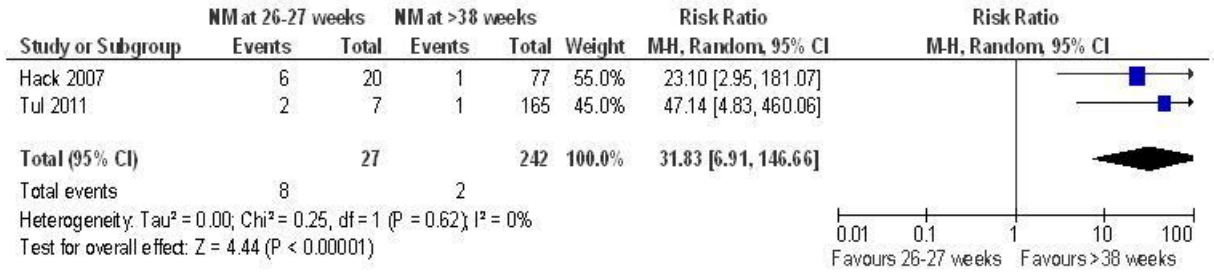
**Figure 10.5** Forest plots for the risk of neonatal death at different gestational ages (studies reporting results for monochorionic twin pregnancies; see Table 10.8 in the full guideline main text and in Appendix J)

CI confidence interval, df degrees of freedom, M-H Mantel-Haenszel, NM neonatal mortality (neonatal death rate)

### *Risk of neonatal death at given gestational age*

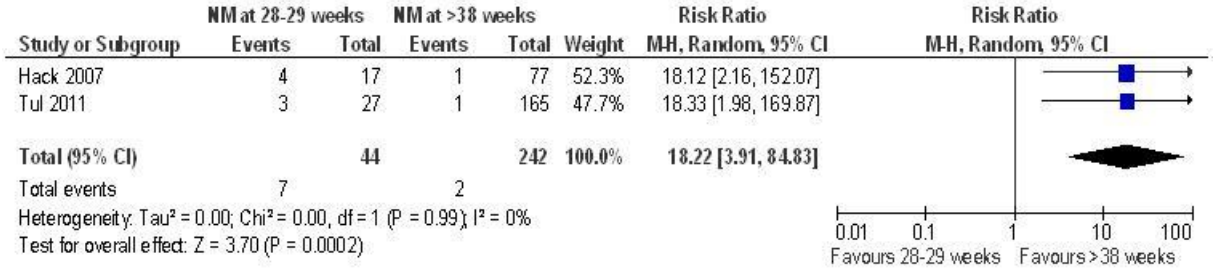
*At 26–27 weeks*

Meta-analyses conducted using random effects model



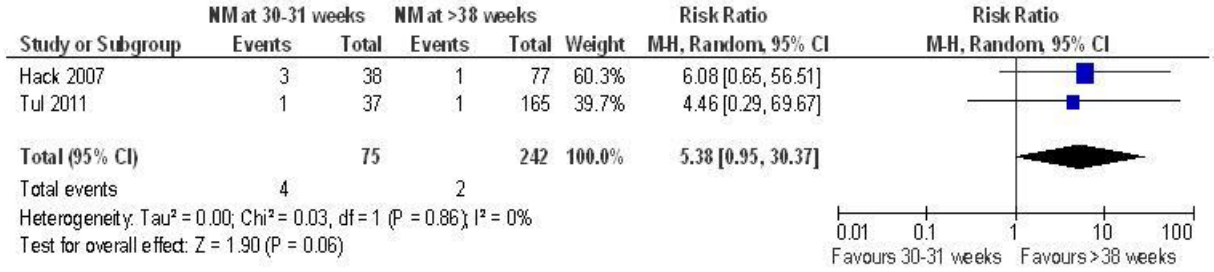

*At 28–29 weeks*

Meta-analyses conducted using random effects model



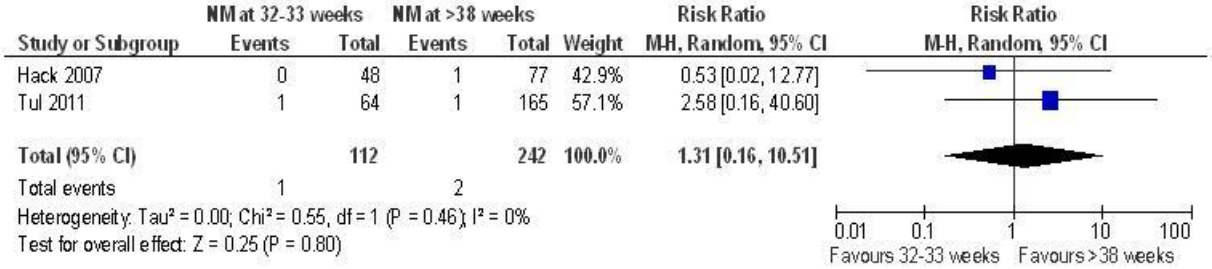
*At 30–31 weeks*

Meta-analyses conducted using random effects model




*At 32–33 weeks*

Meta-analyses conducted using random effects model



*At 34–35 weeks*

Meta-analyses conducted using random effects model


*At 36–37 weeks*

Meta-analyses conducted using random effects model

**Figure 10.6** Forest plots for the risk of neonatal death at different gestational ages (studies reporting results for triplet pregnancies; see Table 10.9 in the full guideline main text and in Appendix J)

CI confidence interval, df degrees of freedom, FDR fetal death rate, M-H Mantel-Haenszel

*Risk of fetal death at given gestational age*

*At 33 weeks*

Meta-analyses conducted using random effects model


*At 34 weeks*

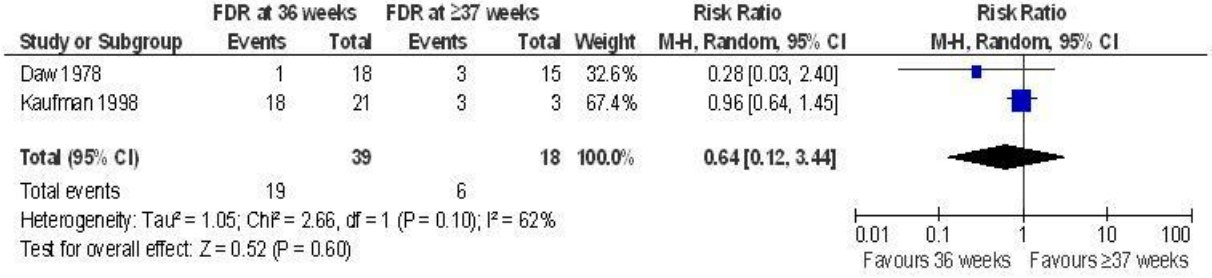
Meta-analyses conducted using random effects model

*At 35 weeks*

Meta-analyses conducted using random effects model


*At 36 weeks*

Meta-analyses conducted using random effects model



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