Contents

Birth before 28 weeks

Patient or population: Women with signs and symptoms of preterm labour
Settings: Hospital setting
Intervention: Betamimetics, calcium channel blockers, COX inhibitors, magnesium sulphate, nitric oxide donors, oxytocin receptor antagonists, combinations of tocolytics
Comparison: Placebo or no treatment

Outcomes	Direct Evidence		Anticipated absolute effects for direct estimate		
	RR (95% CI)	Certainty	Risk with placebo or no treatment	Risk with tocolytic agent	Risk difference with tocolytic agent
Betamimetics	Not estimable	Not applicable	158 per 1,000	Not estimable	Not estimable
COX inhibitors	Not estimable	Not applicable	158 per 1,000	Not estimable	Not estimable
Calcium channel blockers	Not estimable	Not applicable	158 per 1,000	Not estimable	Not estimable
Magnesium sulphate	1.10 (0.60, 2.05)	⨁⨀⨀⨀ VERY LOW[a]	158 per 1,000	174 per 1,000	16 more per 1,000 (from 63 fewer to 166 more)
Oxytocin receptor antagonists	3.11 (1.02, 9.51)	⨁⨁⨁⨀ MODERATE[b]	158 per 1,000	491 per 1,000	333 more per 1,000 (from 3 more to 1,345 more)
Nitric oxide donors	0.50 (0.23, 1.09)	⨁⨁⨀⨀ LOW[c]	158 per 1,000	79 per 1,000	79 fewer per 1,000 (from 122 fewer to 14 more)
Combinations of tocolytics	Not estimable	Not applicable	158 per 1,000	Not estimable	Not estimable

*The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).CI: Confidence interval; RR: Risk Ratio

GRADE Working Group grades of evidence **High quality:** Further research is very unlikely to change our confidence in the estimate of effect. **Moderate quality:** Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. **Low quality:** Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. **Very low quality:** We are very uncertain about the estimate.
Footnotes [a]Direct evidence downgraded -3 due to multiple limitations in study design and very serious imprecision. [b]Direct evidence downgraded -1 due to serious imprecision. [c]Direct evidence downgraded -2 due to very serious imprecision.

Birth before 32 weeks gestation

Patient or population: Women with signs and symptoms of preterm labour
Settings: Hospital setting
Intervention: Betamimetics, calcium channel blockers, COX inhibitors, magnesium sulphate, nitric oxide donors, oxytocin receptor antagonists, combinations of tocolytics
Comparison: Placebo or no treatment

Outcomes	Direct Evidence		Indirect Evidence		Network Evidence		Anticipated absolute effects for network estimate		
	RR (95% CI)	Certainty	RR (95% CI)	Certainty	RR (95% CI)	Certainty	Risk with placebo or no treatment	Risk with tocolytic agent	Risk difference with tocolytic agent
Betamimetics	0.86 (0.73, 1.01)	⨁⨁◯◯ LOW[a]	Not estimable	Not applicable	0.86 (0.73, 1.01)	⨁⨁◯◯ LOW[b]	476 per 1,000	409 per 1,000	67 fewer per 1,000 (from 129 fewer to 5 more)
COX inhibitors	Not estimable	Not applicable	Not estimable	Not applicable	Not estimable	Not applicable	476 per 1,000	Not estimable	Not estimable
Calcium channel blockers	Not estimable	Not applicable	0.99 (0.71, 1.39)	⨁⨁◯◯ LOW[c]	0.99 (0.71, 1.39)	⨁⨁◯◯ LOW[d]	476 per 1,000	471 per 1,000	5 fewer per 1,000 (from 138 fewer to 186 more)
Magnesium sulphate	1.14 (0.92, 1.43)	⨁⨁◯◯ LOW[a]	1.58 (0.82, 3.04)	⨁◯◯◯ VERY LOW[e]	1.18 (0.96, 1.46)	⨁◯◯◯ VERY LOW[f]	476 per 1,000	562 per 1,000	86 more per 1,000 (from 19 fewer to 219 more)
Oxytocin receptor antagonists	1.33 (0.83, 2.14)	⨁⨁◯◯ LOW[g]	0.96 (0.58, 1.59)	⨁◯◯◯ VERY LOW[e]	1.14 (0.81, 1.62)	⨁⨁◯◯ LOW[b]	476 per 1,000	543 per 1,000	67 more per 1,000 (from 90 fewer to 295 more)

Nitric oxide donors	Not estimable	Not applicable	0.86 (0.46, 1.62)	⨁⊖⊖⊖ VERY LOW[e]	0.86 (0.46, 1.62)	⨁⊖⊖⊖ VERY LOW[i]	476 per 1,000	409 per 1,000	67 fewer per 1,000 (from 257 fewer to 295 more)
Combinations of tocolytics	Not estimable	Not applicable	1.13 (0.07, 17.64)	⨁⊖⊖⊖ VERY LOW[e]	1.13 (0.07, 17.64)	⨁⊖⊖⊖ VERY LOW[i]	476 per 1,000	538 per 1,000	62 more per 1,000 (from 443 fewer to 7,921 more)

*The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).CI: Confidence interval; RR: Risk Ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

Footnotes
[a]Direct evidence downgraded -2 due to multiple limitations in study design and serious imprecision.
[b]Network evidence downgraded -2 due to low certainty direct evidence.
[c]Indirect evidence downgraded -2 due to multiple limitations in study design and serious imprecision.
[d]Network evidence downgraded -2 due to low certainty indirect evidence.
[e]Indirect evidence downgraded -3 due to multiple limitations in study design and very serious imprecision.
[f]Network evidence downgraded -3 due to low certainty indirect evidence further downgraded because of incoherence.
[g]Direct evidence downgraded -2 due to very serious imprecision.
[i]Network evidence downgraded -3 due to very low certainty indirect evidence.

Birth before 34 weeks gestation

Patient or population: Women with signs and symptoms of preterm labour
Settings: Hospital setting
Intervention: Betamimetics, calcium channel blockers, COX inhibitors, magnesium sulphate, nitric oxide donors, oxytocin receptor antagonists, combinations of tocolytics
Comparison: Placebo or no treatment

Outcomes	Direct Evidence		Indirect Evidence		Network Evidence		Anticipated absolute effects for network estimate		
	RR (95% CI)	Certainty	RR (95% CI)	Certainty	RR (95% CI)	Certainty	Risk with placebo or no treatment	Risk with tocolytic agent	Risk difference with tocolytic agent
Betamimetics	0.32 (0.04, 2.85)	⨁⊖⊖⊖ VERY LOW[a]	1.38 (0.80, 2.38)	⨁⊖⊖⊖ VERY LOW[b]	1.07 (0.66, 1.73)	⨁⊖⊖⊖ VERY LOW[c]	313 per 1,000	335 per 1,000	22 more per 1,000 (from 106 fewer to 228 more)
COX inhibitors	Not estimable	Not applicable	0.78 (0.46, 1.34)	⨁⊖⊖⊖ VERY LOW[b]	0.78 (0.46, 1.34)	⨁⊖⊖⊖ VERY LOW[d]	313 per 1,000	244 per 1,000	69 fewer per 1,000 (from 169 fewer to 106 more)
Calcium channel blockers	5.84 (0.74, 46.11)	⨁⊖⊖⊖ VERY LOW[a]	0.76 (0.46, 1.26)	⨁⊖⊖⊖ VERY LOW[b]	0.85 (0.52, 1.40)	⨁⊖⊖⊖ VERY LOW[c]	313 per 1,000	266 per 1,000	47 fewer per 1,000 (from 150 fewer to 125 more)
Magnesium sulphate	Not estimable	Not applicable	0.92 (0.54, 1.56)	⨁⊖⊖⊖ VERY LOW[b]	0.92 (0.54, 1.56)	⨁⊖⊖⊖ VERY LOW[d]	313 per 1,000	288 per 1,000	25 fewer per 1,000 (from 144 fewer to 175 more)

Oxytocin receptor antagonists	Not estimable	Not applicable	1.07 (0.66, 1.73)	⨁⨀⨀⨀ VERY LOW[b]	1.07 (0.66, 1.73)	⨁⨀⨀⨀ VERY LOW[d]	313 per 1,000	335 per 1,000	22 more per 1,000 (from 106 fewer to 228 more)
Nitric oxide donors	0.93 (0.61, 1.41)	⨁⨁⨀⨀ LOW[e]	0.60 (0.23, 1.58)	⨁⨀⨀⨀ VERY LOW[b]	0.86 (0.59, 1.27)	⨁⨁⨀⨀ LOW[f]	313 per 1,000	269 per 1,000	44 fewer per 1,000 (from 128 fewer to 85 more)
Combinations of tocolytics	Not estimable	Not applicable	0.70 (0.32, 1.53)	⨁⨀⨀⨀ VERY LOW[b]	0.70 (0.32, 1.53)	⨁⨀⨀⨀ VERY LOW[d]	313 per 1,000	219 per 1,000	94 fewer per 1,000 (from 213 fewer to 166 more)

*The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).CI: Confidence interval; RR: Risk Ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

Footnotes
[a]Direct evidence downgraded -3 due to multiple limitations in study design and very serious imprecision.
[b]Indirect evidence downgraded -3 due to multiple limitations in study design and very serious imprecision.
[c]Network evidence downgraded -3 due to very low certainty direct and indirect evidence.
[d]Network evidence downgraded -3 due to very low certainty indirect evidence.
[e]Direct evidence downgraded -2 due to very serious imprecision.
[f]Network evidence downgraded -2 due to low certainty direct evidence.

Birth before 37 weeks gestation

Patient or population: Women with signs and symptoms of preterm labour
Settings: Hospital setting
Intervention: Betamimetics, calcium channel blockers, COX inhibitors, magnesium sulphate, nitric oxide donors, oxytocin receptor antagonists, combinations of tocolytics
Comparison: Placebo or no treatment

Outcomes	Direct Evidence		Indirect Evidence		Network Evidence		Anticipated absolute effects for network estimate		
	RR (95% CI)	Certainty	RR (95% CI)	Certainty	RR (95% CI)	Certainty	Risk with placebo or no treatment	Risk with tocolytic agent	Risk difference with tocolytic agent
Betamimetics	0.99 [0.58, 1.72]	⨁⊖⊖⊖ VERY LOW[a]	0.97 (0.79, 1.18)	⨁⊖⊖⊖ VERY LOW[b]	0.97 (0.83, 1.13)	⨁⨁⊖⊖ LOW[c]	571 per 1,000	554 per 1,000	17 fewer per 1,000 (from 97 fewer to 74 more)
COX inhibitors	0.21 (0.07, 0.62)	⨁⊖⊖⊖ VERY LOW[d]	1.13 (0.85, 1.50)	⨁⊖⊖⊖ VERY LOW[e]	1.02 (0.78, 1.34)	⨁⊖⊖⊖ VERY LOW[f]	571 per 1,000	582 per 1,000	11 more per 1,000 (from 126 fewer to 194 more)
Calcium channel blockers	0.98 (0.71, 1.35)	⨁⊖⊖⊖ VERY LOW[a]	0.88 (0.70, 1.11)	⨁⊖⊖⊖ VERY LOW[b]	0.91 (0.78, 1.07)	⨁⨁⊖⊖ LOW[c]	571 per 1,000	520 per 1,000	51 fewer per 1,000 (from 126 fewer to 40 more)
Magnesium sulphate	0.79 (0.15, 4.17)	⨁⊖⊖⊖ VERY LOW[d]	1.05 (0.81, 1.35)	⨁⊖⊖⊖ VERY LOW[b]	1.06 (0.82, 1.36)	⨁⊖⊖⊖ VERY LOW[f]	571 per 1,000	594 per 1,000	23 more per 1,000 (from 97 fewer to 177 more)

Oxytocin receptor antagonists	1.13 (0.98, 1.31)	⨁⨁⨁⨀ MODERATE[g]	1.11 (0.79, 1.56)	⨁⨀⨀⨀ VERY LOW[b]	1.10 (0.89, 1.36)	⨁⨁⨁⨀ MODERATE[h]	571 per 1,000	628 per 1,000	57 more per 1,000 (from 63 fewer to 206 more)
Nitric oxide donors	0.57 (0.17, 1.90)	⨁⨁⨀⨀ LOW[i]	0.78 (0.57, 1.09)	⨁⨀⨀⨀ VERY LOW[b]	0.77 (0.59, 1.00)	⨁⨁⨀⨀ LOW[j]	571 per 1,000	440 per 1,000	131 fewer per 1,000 (from 243 fewer to 0 more)
Combinations of tocolytics	1.32 (0.90, 1.95)	⨁⨀⨀⨀ VERY LOW[d]	0.80 (0.62, 1.03)	⨁⨀⨀⨀ VERY LOW[b]	0.88 (0.69, 1.11)	⨁⨀⨀⨀ VERY LOW[f]	571 per 1,000	497 per 1,000	74 fewer per 1,000 (from 171 fewer to 51 more)

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GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

Footnotes
[a]Direct evidence downgraded -3 due to multiple limitations in study design, severe unexplained statistical heterogeneity, and serious imprecision.
[b]Indirect evidence downgraded -3 due to multiple limitations in study design, severe unexplained statistical heterogeneity, and serious imprecision.
[c]Network evidence downgraded -2 due to very low certainty direct evidence upgraded +1 since the network estimate is precise.
[d]Direct evidence downgraded -3 due to multiple limitations in study design, and very serious imprecision.
[e]Indirect evidence downgraded -3 due to multiple limitations in study design, and very serious imprecision.
[f]Network evidence downgraded -3 due to very low certainty direct and indirect evidence.
[g]Direct evidence downgraded -1 due to serious imprecision.
[h]Network evidence downgraded -1 due to moderate certainty direct evidence.
[i]Direct evidence downgraded -2 due to multiple limitations in study design and very serious imprecision.
[j]Network evidence downgraded -2 due to low certainty direct evidence.

Maternal death

Patient or population: Women with signs and symptoms of preterm labour
Settings: Hospital setting
Intervention: Betamimetics, calcium channel blockers, COX inhibitors, magnesium sulphate, nitric oxide donors, oxytocin receptor antagonists, combinations of tocolytics
Comparison: Placebo or no treatment

Outcomes	Direct Evidence		Indirect Evidence		Network Evidence		Anticipated absolute effects for network estimate		
	RR (95% CI)	Certainty	RR (95% CI)	Certainty	RR (95% CI)	Certainty	Risk with placebo or no treatment	Risk with tocolytic agent	Risk difference with tocolytic agent
Betamimetics	Not estimable	Not applicable	Not estimable	Not applicable	Not estimable	Not applicable	Not estimable	Not estimable	Not estimable
COX inhibitors	Not estimable	Not applicable	Not estimable	Not applicable	Not estimable	Not applicable	Not estimable	Not estimable	Not estimable
Calcium channel blockers	Not estimable	Not applicable	Not estimable	Not applicable	Not estimable	Not applicable	Not estimable	Not estimable	Not estimable
Magnesium sulphate	Not estimable	Not applicable	Not estimable	Not applicable	Not estimable	Not applicable	Not estimable	Not estimable	Not estimable
Oxytocin receptor antagonists	Not estimable	Not applicable	Not estimable	Not applicable	Not estimable	Not applicable	Not estimable	Not estimable	Not estimable
Nitric oxide donors	Not estimable	Not applicable	Not estimable	Not applicable	Not estimable	Not applicable	Not estimable	Not estimable	Not estimable
Combinations of tocolytics	Not estimable	Not applicable	Not estimable	Not applicable	Not estimable	Not applicable	Not estimable	Not estimable	Not estimable

*The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).CI: Confidence interval; RR: Risk Ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

Pulmonary oedema

Patient or population: Women with signs and symptoms of preterm labour
Settings: Hospital setting
Intervention: Betamimetics, calcium channel blockers, COX inhibitors, magnesium sulphate, nitric oxide donors, oxytocin receptor antagonists, combinations of tocolytics
Comparison: Placebo or no treatment

Outcomes	Direct Evidence		Indirect Evidence		Network Evidence		Anticipated absolute effects for network estimate		
	RR (95% CI)	Certainty	RR (95% CI)	Certainty	RR (95% CI)	Certainty	Risk with placebo or no treatment	Risk with tocolytic agent	Risk difference with tocolytic agent
Betamimetics	3.03 (0.12, 74.23)	⨁⊖⊖⊖ VERY LOW[a]	Not estimable	Not applicable	3.03 (0.12, 74.23)	⨁⊖⊖⊖ VERY LOW[b]	Not estimable	Not estimable	Not estimable
COX inhibitors	Not estimable	Not applicable	1.32 (0.01, 180.85)	⨁⊖⊖⊖ VERY LOW[c]	1.32 (0.01, 180.85)	⨁⊖⊖⊖ VERY LOW[d]	Not estimable	Not estimable	Not estimable
Calcium channel blockers	Not estimable	Not estimable	0.82 (0.03, 26.36)	⨁⊖⊖⊖ VERY LOW[c]	0.82 (0.03, 26.36)	⨁⊖⊖⊖ VERY LOW[d]	Not estimable	Not estimable	Not estimable
Magnesium sulphate	Not estimable	Not estimable	4.47 (0.08, 266.15)	⨁⊖⊖⊖ VERY LOW[c]	4.47 (0.08, 266.15)	⨁⊖⊖⊖ VERY LOW[d]	Not estimable	Not estimable	Not estimable
Oxytocin receptor antagonists	Not estimable	Not estimable	1.89 (0.04, 86.07)	⨁⊖⊖⊖ VERY LOW[c]	1.89 (0.04, 86.07)	⨁⊖⊖⊖ VERY LOW[d]	Not estimable	Not estimable	Not estimable
Nitric oxide donors	Not estimable	Not estimable	1.04 (0.01, 95.34)	⨁⊖⊖⊖ VERY LOW[c]	1.04 (0.01, 95.34)	⨁⊖⊖⊖ VERY LOW[d]	Not estimable	Not estimable	Not estimable
Combinations of tocolytics	Not estimable	Not estimable	1.54 (0.03, 80.87)	⨁⊖⊖⊖ VERY LOW[c]	1.54 (0.03, 80.87)	⨁⊖⊖⊖ VERY LOW[d]	Not estimable	Not estimable	Not estimable

*The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).CI: Confidence interval; RR: Risk Ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. **Very low quality:** We are very uncertain about the estimate.
Footnotes [a]Direct evidence downgraded -3 due to multiple limitations in study design and very serious imprecision. [b]Network evidence downgraded -3 due to very low certainty direct evidence. [c]Indirect evidence downgraded -3 due to multiple limitations in study design and very serious imprecision. [d]Network evidence downgraded -3 due to very low certainty indirect evidence.

Dyspnoea

Patient or population: Women with signs and symptoms of preterm labour
Settings: Hospital setting
Intervention: Betamimetics, calcium channel blockers, COX inhibitors, magnesium sulphate, nitric oxide donors, oxytocin receptor antagonists, combinations of tocolytics
Comparison: Placebo or no treatment

Outcomes	Direct Evidence		Indirect Evidence		Network Evidence		Anticipated absolute effects for network estimate		
	RR (95% CI)	Certainty	RR (95% CI)	Certainty	RR (95% CI)	Certainty	Risk with placebo or no treatment	Risk with tocolytic agent	Risk difference with tocolytic agent
Betamimetics	12.09 (4.66, 31.39)	⨁⨁⨁⨀ MODERATE[a]	Not estimable	Not applicable	12.09 (4.66, 31.39)	⨁⨁⨁⨀ MODERATE[b]	11 per 1,000	133 per 1,000	122 more per 1,000 (from 40 more to 334 more)
COX inhibitors	Not estimable	Not applicable	4.31 (0.67, 27.92)	⨁⨁⨀⨀ LOW[c]	4.31 (0.67, 27.92)	⨁⨁⨀⨀ LOW[d]	11 per 1,000	47 per 1,000	36 more per 1,000 (from 4 fewer to 296 more)
Calcium channel blockers	Not estimable	Not applicable	1.42 (0.29, 6.96)	⨁⨀⨀⨀ VERY LOW[e]	1.42 (0.29, 6.96)	⨁⨀⨀⨀ VERY LOW[f]	11 per 1,000	16 per 1,000	5 more per 1,000 (from 8 fewer to 66 more)
Magnesium sulphate	Not estimable	Not applicable	3.34 (0.62, 17.97)	⨁⨀⨀⨀[e] VERY LOW	3.34 (0.62, 17.97)	⨁⨀⨀⨀[f] VERY LOW	11 per 1,000	37 per 1,000	26 more per 1,000 (from 4 fewer to 187 more)
Oxytocin receptor antagonists	Not estimable	Not applicable	1.24 (0.32, 4.78)	⨁⨁⨁⨀ MODERATE[g]	1.24 (0.32, 4.78)	⨁⨁⨁⨀ MODERATE[h]	11 per 1,000	14 per 1,000	3 more per 1,000 (from 7 fewer to 42 more)

Nitric oxide donors	Not estimable	Not applicable	0.82 (0.15, 4.59)	⨁⊖⊖⊖[e] VERY LOW	0.82 (0.15, 4.59)	⨁⊖⊖⊖[f] VERY LOW	11 per 1,000	9 per 1,000	2 fewer per 1,000 (from 9 fewer to 39 more)
Combinations of tocolytics	Not estimable	Not applicable	2.96 (0.39, 22.24)	⨁⊖⊖⊖[e] VERY LOW	2.96 (0.39, 22.24)	⨁⊖⊖⊖[f] VERY LOW	11 per 1,000	33 per 1,000	22 more per 1,000 (from 7 fewer to 234 more)

*The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).CI: Confidence interval; RR: Risk Ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

Footnotes
[a]Direct evidence downgraded -1 due to multiple limitations in study design.
[b]Network evidence downgraded -1 due to moderate certainty direct evidence.
[c]Indirect evidence downgraded -2 due to multiple serious limitations in study design and serious imprecision.
[d]Network evidence downgraded -2 due to low certainty indirect evidence.
[e]Indirect evidence downgraded -3 due to multiple serious limitations in study design and serious imprecision.
[f]Network evidence downgraded -3 due to very low certainty indirect evidence.
[g]Indirect evidence downgraded -1 due to multiple limitations in study design.
[h]Network evidence downgraded -1 due to moderate certainty direct evidence.

Palpitations

Patient or population: Women with signs and symptoms of preterm labour
Settings: Hospital setting
Intervention: Betamimetics, calcium channel blockers, COX inhibitors, magnesium sulphate, nitric oxide donors, oxytocin receptor antagonists, combinations of tocolytics
Comparison: Placebo or no treatment

Outcomes	Direct Evidence		Indirect Evidence		Network Evidence		Anticipated absolute effects for network estimate		
	RR (95% CI)	Certainty	RR (95% CI)	Certainty	RR (95% CI)	Certainty	Risk with placebo or no treatment	Risk with tocolytic agent	Risk difference with tocolytic agent
Betamimetics	8.55 (5.71, 12.79)	⨁⨁⨁⨀ MODERATE[a]	Not estimable	Not applicable	7.39 (3.83, 14.24)	⨁⨁⨁⨀ MODERATE[b]	50 per 1,000	428 per 1,000	378 more per 1,000 (from 236 more to 590 more)
COX inhibitors	Not estimable	Not applicable	0.64 (0.15, 2.68)	⨁⨁⨀⨀ LOW[c]	0.64 (0.15, 2.68)	⨁⨁⨀⨀ LOW[d]	50 per 1,000	32 per 1,000	18 fewer per 1,000 (from 43 fewer to 84 more)
Calcium channel blockers	Not estimable	Not applicable	1.40 (0.62, 3.18)	⨁⨁⨀⨀ LOW[c]	1.40 (0.62, 3.18)	⨁⨁⨀⨀ LOW[d]	50 per 1,000	70 per 1,000	20 more per 1,000 (from 19 fewer to 109 more)
Magnesium sulphate	Not estimable	Not applicable	2.24 (0.25, 20.11)	⨁⨀⨀⨀ VERY LOW[e]	2.24 (0.25, 20.11)	⨁⨀⨀⨀[f] VERY LOW	50 per 1,000	112 per 1,000	62 more per 1,000 (from 38 fewer to 956 more)

Oxytocin receptor antagonists	Not estimable	Not applicable	0.93 (0.32, 2.69)	⨁⨁⊖⊖ LOW[c]	0.93 (0.32, 2.69)	⨁⨁⊖⊖ LOW[d]	50 per 1,000	47 per 1,000	4 fewer per 1,000 (from 34 fewer to 85 more)
Nitric oxide donors	Not estimable	Not applicable	0.67 (0.16, 2.74)	⨁⊖⊖⊖ VERY LOW[e]	0.67 (0.16, 2.74)	⨁⊖⊖⊖[f] VERY LOW	50 per 1,000	34 per 1,000	17 fewer per 1,000 (from 42 fewer to 87 more)
Combinations of tocolytics	Not estimable	Not applicable	4.57 (0.88, 23.61)	⨁⊖⊖⊖ VERY LOW[e]	4.57 (0.88, 23.61)	⨁⊖⊖⊖[f] VERY LOW	50 per 1,000	229 per 1,000	179 more per 1,000 (from 6 fewer to 1,131 more)

*The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).CI: Confidence interval; RR: Risk Ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

Footnotes
[a]Direct evidence downgraded -1 due to multiple limitations in study design.
[b]Network evidence downgraded -1 due to moderate certainty direct evidence.
[c]Indirect evidence downgraded -2 due to multiple limitations in study design and serious imprecision.
[d]Network evidence downgraded -2 due to low certainty indirect evidence.
[e]Indirect evidence downgraded -3 due to multiple limitations in study design, serious imprecision, and suspected publication bias.
[f]Network evidence downgraded -3 due to very low certainty indirect evidence.

Headache

Patient or population: Women with signs and symptoms of preterm labour
Settings: Hospital setting
Intervention: Betamimetics, calcium channel blockers, COX inhibitors, magnesium sulphate, nitric oxide donors, oxytocin receptor antagonists, combinations of tocolytics
Comparison: Placebo or no treatment

Outcomes	Direct Evidence		Indirect Evidence		Network Evidence		Anticipated absolute effects for network estimate		
	RR (95% CI)	Certainty	RR (95% CI)	Certainty	RR (95% CI)	Certainty	Risk with placebo or no treatment	Risk with tocolytic agent	Risk difference with tocolytic agent
Betamimetics	2.94 (1.17, 7.35)	⨁⨁⨁⨀ MODERATE[a]	1.16 (0.56, 2.38)	⨁⨀⨀⨀ VERY LOW[b]	1.91 (1.07, 3.42)	⨁⨁⨀⨀ LOW[c]	131 per 1,000	250 per 1,000	119 more per 1,000 (from 9 more to 317 more)
COX inhibitors	Not estimable	Not applicable	0.48 (0.12, 1.93)	⨁⨁⨀⨀ LOW[d]	0.48 (0.12, 1.93)	⨁⨁⨀⨀ LOW[e]	131 per 1,000	63 per 1,000	68 fewer per 1,000 (from 115 fewer to 122 more)
Calcium channel blockers	2.92 (0.29, 28.90)	⨁⨀⨀⨀ VERY LOW[f]	2.93 (1.42, 6.08)	⨁⨀⨀⨀ VERY LOW[g]	2.59 (1.39, 4.83)	⨁⨁⨀⨀ LOW[h]	131 per 1,000	339 per 1,000	208 more per 1,000 (from 51 more to 502 more)
Magnesium sulphate	3.00 (0.13, 68.26)	⨁⨁⨀⨀ LOW[i]	1.43 (0.56, 3.67	⨁⨀⨀⨀ VERY LOW[g]	1.51 (0.61, 3.74)	⨁⨁⨀⨀ LOW[j]	131 per 1,000	198 per 1,000	67 more per 1,000 (from 51 fewer to 359 more)
Oxytocin receptor antagonists	1.62 (0.13, 19.74)	⨁⨁⨀⨀ LOW[i]	0.86 (0.40, 1.84)	⨁⨁⨁⨀ MODERATE[k]	0.96 (0.47, 1.95)	⨁⨁⨁⨀ MODERATE[l]	131 per 1,000	126 per 1,000	5 fewer per 1,000

									(from 69 fewer to 124 more)
Nitric oxide donors	2.00 (1.35, 2.97)	⨁⨁⨁⨁ HIGH	6.81 (3.04, 15.26)	⨁⨁◯◯ LOW[m]	4.20 (2.13, 8.25)	⨁⨁⨁◯ MODERATE[n]	131 per 1,000	550 per 1,000	419 more per 1,000 (from 148 more to 950 more)
Combinations of tocolytics	Not estimable	Not applicable	1.20 (0.49, 2.92)	⨁◯◯◯ VERY LOW[g]	1.20 (0.49, 2.95)	⨁◯◯◯ VERY LOW[o]	131 per 1,000	157 per 1,000	26 more per 1,000 (from 67 fewer to 252 more)

*The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).CI: Confidence interval; RR: Risk Ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

Footnotes
[a]Direct evidence downgraded -1 due to multiple limitations in study design.
[b]Indirect evidence downgraded -3 due to multiple limitations in study design, serious imprecision, and suspected publication bias.
[c]Network evidence downgraded -2 due to very low certainty indirect evidence.
[d]Indirect evidence downgraded -2 due to multiple limitations in study design and serious imprecision.
[e]Network evidence downgraded -2 due to low certainty indirect evidence.
[f]Direct evidence downgraded -3 due to multiple limitations in study design, severe unexplained statistical heterogeneity, and very serious imprecision.
[g]Indirect evidence downgraded -3 due to multiple limitations in study design and very serious imprecision.
[h]Network evidence downgraded -2 due to very low certainty indirect evidence upgraded +1 since the network estimate is precise.
[i]Direct evidence downgraded -2 due to very serious imprecision.
[j]Network evidence downgraded -2 due to low certainty direct evidence.
[k]Indirect evidence downgraded -1 due to multiple limitations in study design.
[l]Network evidence downgraded -1 due to moderate certainty indirect evidence.
[m]Indirect evidence downgraded -2 due to multiple limitations in study design and severe unexplained statistical heterogeneity.
[n]Network evidence downgraded -1 due to high certainty direct evidence downgraded because of incoherence.
[o]Network evidence downgraded -3 due to very low certainty indirect evidence.

Nausea or vomiting

Patient or population: Women with signs and symptoms of preterm labour
Settings: Hospital setting
Intervention: Betamimetics, calcium channel blockers, COX inhibitors, magnesium sulphate, nitric oxide donors, oxytocin receptor antagonists, combinations of tocolytics
Comparison: Placebo or no treatment

Outcomes	Direct Evidence		Indirect Evidence		Network Evidence		Anticipated absolute effects for network estimate		
	RR (95% CI)	Certainty	RR (95% CI)	Certainty	RR (95% CI)	Certainty	Risk with placebo or no treatment	Risk with tocolytic agent	Risk difference with tocolytic agent
Betamimetics	1.77 (1.29, 2.41)	⨁⨁⨁⨀ MODERATE[a]	2.68 (0.95, 7.61)	⨁⨀⨀⨀ VERY LOW[b]	1.91 (1.25, 2.91)	⨁⨁⨁⨀ MODERATE[c]	113 per 1,000	216 per 1,000	103 more per 1,000 (from 28 more to 216 more)
COX inhibitors	5.00 (0.26, 97.37)	⨁⨀⨀⨀ VERY LOW[d]	2.43 (1.10, 5.37)	⨁⨀⨀⨀ VERY LOW[b]	2.54 (1.18, 5.48)	⨁⨁⨀⨀ LOW[e]	113 per 1,000	287 per 1,000	174 more per 1,000 (from 20 more to 506 more)
Calcium channel blockers	0.78 (0.23, 2.67)	⨁⨀⨀⨀ VERY LOW[d]	0.65 (0.36, 1.19)	⨁⨁⨀⨀ LOW[f]	0.67 (0.39, 1.15)	⨁⨁⨀⨀ LOW[g]	113 per 1,000	76 per 1,000	37 fewer per 1,000 (from 69 fewer to 17 more)
Magnesium sulphate	Not estimable	Not applicable	2.27 (1.08, 4.77)	⨁⨀⨀⨀ VERY LOW[b]	2.27 (1.08, 4.77)	⨁⨀⨀⨀ VERY LOW[h]	113 per 1,000	257 per 1,000	144 more per 1,000 (from 9 more to 426 more)

Oxytocin receptor antagonists	1.60 (0.27, 9.57)	⨁⨁⨀⨀ LOW[i]	0.92 (0.53, 1.60)	⨁⨁⨀⨀ LOW[j]	0.96 (0.56, 1.64)	⨁⨁⨀⨀ LOW[k]	113 per 1,000	108 per 1,000	5 fewer per 1,000 (from 50 fewer to 72 more)
Nitric oxide donors	Not estimable	Not applicable	1.22 (0.61, 2.48)	⨁⨀⨀⨀ VERY LOW[b]	1.22 (0.61, 2.48)	⨁⨀⨀⨀ VERY LOW[h]	113 per 1,000	138 per 1,000	25 more per 1,000 (from 44 fewer to 167 more)
Combinations of tocolytics	Not estimable	Not applicable	1.33 (0.69, 2.54)	⨁⨁⨀⨀ LOW[l]	1.33 (0.69, 2.54)	⨁⨁⨀⨀ LOW[m]	113 per 1,000	150 per 1,000	37 more per 1,000 (from 35 fewer to 174 more)

*The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).CI: Confidence interval; RR: Risk Ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

Footnotes
[a]Direct evidence downgraded -1 due to multiple limitations in study design.
[b]Indirect evidence downgraded -3 due to multiple limitations in study design and very serious imprecision.
[c]Network evidence downgraded -1 due to moderate certainty direct evidence.
[d]Direct evidence downgraded -3 due to multiple limitations in study design and very serious imprecision.
[e]Network evidence downgraded -2 due to very low certainty indirect evidence upgraded since the network estimate is precise.
[f]Indirect evidence downgraded -2 due to multiple limitations in study design and suspected publication bias.
[g]Network evidence downgraded -2 due to low certainty indirect evidence.
[h]Network evidence downgraded -3 due to very low certainty indirect evidence.
[i]Direct evidence downgraded -2 due to very serious imprecision.
[j]Indirect evidence downgraded -2 due to multiple limitations in study design and severe unexplained statistical heterogeneity.
[k]Network evidence downgraded -2 due to low certainty direct and indirect evidence.
[l]Indirect evidence downgraded -2 due to multiple limitations in study design and serious imprecision.
[m]Network evidence downgraded -2 due to low certainty indirect evidence.

Tachycardia

Patient or population: Women with signs and symptoms of preterm labour
Settings: Hospital setting
Intervention: Betamimetics, calcium channel blockers, COX inhibitors, magnesium sulphate, nitric oxide donors, oxytocin receptor antagonists, combinations of tocolytics
Comparison: Placebo or no treatment

Outcomes	Direct Evidence		Indirect Evidence		Network Evidence		Anticipated absolute effects for network estimate		
	RR (95% CI)	Certainty	RR (95% CI)	Certainty	RR (95% CI)	Certainty	Risk with placebo or no treatment	Risk with tocolytic agent	Risk difference with tocolytic agent
Betamimetics	1.72 (0.57, 5.17)	⨁⨁◯◯ LOW[a]	31.94 (4.55, 224.28)	⨁⨁◯◯ LOW[b]	3.01 (1.17, 7.71)	⨁⨁◯◯ LOW[c]	332 per 1,000	999 per 1,000	667 more per 1,000 (from 56 more to 2228 more)
COX inhibitors	Not estimable	Not applicable	0.18 (0.02, 1.60)	⨁⨁◯◯ LOW[d]	0.18 (0.02, 1.60)	⨁⨁◯◯ LOW[e]	332 per 1,000	60 per 1,000	272 fewer per 1,000 (from 325 fewer to 199 more)
Calcium channel blockers	Not estimable	Not applicable	0.93 (0.32, 2.71)	⨁◯◯◯ VERY LOW[f]	0.93 (0.32, 2.71)	⨁◯◯◯ VERY LOW[g]	332 per 1,000	309 per 1,000	23 fewer per 1,000 (from 226 fewer to 568 more)
Magnesium sulphate	Not estimable	Not applicable	0.26 (0.03, 2.26)	⨁◯◯◯ VERY LOW[i]	0.26 (0.03, 2.26)	⨁◯◯◯ VERY LOW[g]	332 per 1,000	86 per 1,000	246 fewer per 1,000 (from 322 fewer to 418 more)

Oxytocin receptor antagonists	1.00 (0.14, 7.07)	⊕⊕⊖⊖ LOW[i]	0.16 (0.05, 0.51)	⊕⊕⊖⊖ LOW[d]	0.23 (0.08, 0.67)	⊕⊕⊖⊖ LOW[j]	332 per 1,000	76 per 1,000	256 fewer per 1,000 (from 305 fewer to 110 fewer)
Nitric oxide donors	4.63 (0.23, 94.99)	⊕⊖⊖⊖ VERY LOW[k]	0.07 (0.02, 0.34)	⊕⊕⊖⊖ LOW[d]	0.16 (0.04, 0.70)	⊕⊕⊖⊖ LOW[l]	332 per 1,000	53 per 1,000	279 fewer per 1,000 (from 319 fewer to 100 fewer)
Combinations of tocolytics	Not estimable	Not applicable	1.62 (0.49, 5.31)	⊕⊕⊖⊖ LOW[d]	1.62 (0.49, 5.31)	⊕⊕⊖⊖ LOW[e]	332 per 1,000	538 per 1,000	206 more per 1,000 (from 169 fewer to 1,431 more)

*The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).CI: Confidence interval; RR: Risk Ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

Footnotes
[a]Direct evidence downgraded -2 due to multiple limitations in study design and serious imprecision.
[b]Indirect evidence downgraded -2 due to very serious imprecision.
[c]Network evidence downgraded -2 due to low certainty direct evidence further downgraded for incoherence and upgraded since the network estimate is precise.
[d]Indirect evidence downgraded -2 due to multiple limitations in study design and serious imprecision.
[e]Network evidence downgraded -2 due to low certainty indirect evidence.
[f]Indirect evidence downgraded -3 due to multiple limitations in study design, severe unexplained statistical heterogeneity, and suspected publication bias.
[g]Network evidence downgraded -3 due to very low certainty indirect evidence.
[h]Indirect evidence downgraded -3 due to multiple limitations in study design and very serious imprecision.
[i]Direct evidence downgraded -2 due to very serious imprecision.
[j]Network evidence downgraded -2 due to low certainty indirect evidence.
[k]Direct evidence downgraded -3 due to multiple limitations in study design and very serious imprecision.
[l]Network evidence downgraded -2 due to low certainty indirect evidence further downgraded as inconsistency present and upgraded since the network estimate is precise.

Maternal cardiac arrhythmias

Patient or population: Women with signs and symptoms of preterm labour
Settings: Hospital setting
Intervention: Betamimetics, calcium channel blockers, COX inhibitors, magnesium sulphate, nitric oxide donors, oxytocin receptor antagonists, combinations of tocolytics
Comparison: Placebo or no treatment

Outcomes	Direct Evidence		Anticipated absolute effects for direct estimate		
	RR (95% CI)	Certainty	Risk with placebo or no treatment	Risk with tocolytic agent	Risk difference with tocolytic agent
Betamimetics	3.43 (0.84, 13.89)	⨁⊖⊖⊖ VERY LOW[a]	6 per 1,000	21 per 1,000	15 more per 1,000 (from 5 fewer to 83 more)
COX inhibitors	Not estimable	Not applicable	6 per 1,000	Not estimable	Not estimable
Calcium channel blockers	Not estimable	Not applicable	6 per 1,000	Not estimable	Not estimable
Magnesium sulphate	Not estimable	Not applicable	6 per 1,000	Not estimable	Not estimable
Oxytocin receptor antagonists	Not estimable	Not applicable	6 per 1,000	Not estimable	Not estimable
Nitric oxide donors	Not estimable	Not applicable	6 per 1,000	Not estimable	Not estimable
Combinations of tocolytics	Not estimable	Not applicable	6 per 1,000	Not estimable	Not estimable

*The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).CI: Confidence interval; RR: Risk Ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

Footnotes
[a]Direct evidence downgraded -3 due to multiple limitations in study design and very serious imprecision.

Hypotension

Patient or population: Women with signs and symptoms of preterm labour
Settings: Hospital setting
Intervention: Betamimetics, calcium channel blockers, COX inhibitors, magnesium sulphate, nitric oxide donors, oxytocin receptor antagonists, combinations of tocolytics
Comparison: Placebo or no treatment

Outcomes	Direct Evidence		Indirect Evidence		Network Evidence		Anticipated absolute effects for network estimate		
	RR (95% CI)	Certainty	RR (95% CI)	Certainty	RR (95% CI)	Certainty	Risk with placebo or no treatment	Risk with tocolytic agent	Risk difference with tocolytic agent
Betamimetics	1.55 (0.12, 19.43)	⨁⨁◯◯ LOW[a]	4.03 (0.53, 30.77)	⨁◯◯◯ VERY LOW[b]	2.51 (0.58, 10.89)	⨁⨁◯◯ LOW[c]	107 per 1,000	269 per 1,000	162 more per 1,000 (from 45 fewer to 1,058 more)
COX inhibitors	Not estimable	Not applicable	0.27 (0.03, 2.87)	⨁◯◯◯ VERY LOW[b]	0.27 (0.03, 2.87)	⨁◯◯◯ VERY LOW[d]	107 per 1,000	29 per 1,000	78 fewer per 1,000 (from 104 fewer to 200 more)
Calcium channel blockers	Not estimable	Not applicable	2.63 (0.61, 11.39)	⨁◯◯◯ VERY LOW[b]	2.63 (0.61, 11.39)	⨁◯◯◯ VERY LOW[d]	107 per 1,000	281 per 1,000	174 more per 1,000 (from 42 fewer to 1,112 more)
Magnesium sulphate	3.16 (0.13, 76.30)	⨁◯◯◯ VERY LOW[e]	0.70 (0.09, 5.50)	⨁◯◯◯ VERY LOW[f]	1.02 (0.17, 6.06)	⨁◯◯◯ VERY LOW[g]	107 per 1,000	109 per 1,000	2 more per 1,000 (from 89 fewer to 541 more)

Oxytocin receptor antagonists	Not estimable	Not applicable	0.95 (0.18, 5.06)	⨁⨁⨀⨀ LOW[h]	0.95 (0.18, 5.06)	⨁⨁⨀⨀ LOW[c]	107 per 1,000	102 per 1,000	5 fewer per 1,000 (from 88 fewer to 434 more)
Nitric oxide donors	2.51 (0.31, 20.64)	⨁⨁⨀⨀ LOW[a]	1.70 (0.16, 18.57)	⨁⨀⨀⨀ VERY LOW[f]	1.95 (0.50, 7.53)	⨁⨁⨀⨀ LOW[c]	107 per 1,000	209 per 1,000	102 more per 1,000 (from 54 fewer to 699 more)
Combinations of tocolytics	Not estimable	Not applicable	1.24 0.23, 6.78)	⨁⨀⨀⨀ VERY LOW[f]	1.24 0.23, 6.78)	⨁⨀⨀⨀ VERY LOW[d]	107 per 1,000	133 per 1,000	26 more per 1,000 (from 82 fewer to 618 more)

*The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).CI: Confidence interval; RR: Risk Ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

Footnotes
[a]Direct evidence downgraded -2 due to very serious imprecision.
[b]Indirect evidence downgraded -3 due to multiple limitations in study design and very serious imprecision.
[c]Network evidence downgraded -2 due to low certainty direct evidence.
[d]Network evidence downgraded -3 due to very low certainty indirect evidence.
[e]Direct evidence downgraded -3 due to multiple limitations in study design and very serious imprecision.
[f]Indirect evidence downgraded -3 due to multiple limitations in study design and very serious imprecision.
[g]Network evidence downgraded -3 due to very low certainty indirect evidence.
[h]Indirect evidence downgraded -2 due to very serious imprecision.

Perinatal death

Patient or population: Women with signs and symptoms of preterm labour
Settings: Hospital setting
Intervention: Betamimetics, calcium channel blockers, COX inhibitors, magnesium sulphate, nitric oxide donors, oxytocin receptor antagonists, combinations of tocolytics
Comparison: Placebo or no treatment

Outcomes	Direct Evidence		Indirect Evidence		Network Evidence		Anticipated absolute effects for network estimate		
	RR (95% CI)	Certainty	RR (95% CI)	Certainty	RR (95% CI)	Certainty	Risk with placebo or no treatment	Risk with tocolytic agent	Risk difference with tocolytic agent
Betamimetics	1.08 (0.75, 1.55)	⨁⨁◯◯ LOW[a]	1.79 (0.82, 3.94)	⨁◯◯◯ VERY LOW[b]	1.17 (0.84, 1.62)	⨁⨁◯◯ LOW[c]	77 per 1,000	90 per 1,000	13 more per 1,000 (from 12 fewer to 48 more)
COX inhibitors	0.63 (0.19, 2.09)	⨁⨁◯◯ LOW[d]	1.87 (0.74, 4.68)	⨁◯◯◯ VERY LOW[b]	1.25 (0.60, 2.59)	⨁⨁◯◯ LOW[c]	77 per 1,000	96 per 1,000	19 more per 1,000 (from 31 fewer to 122 more)
Calcium channel blockers	5.02 (0.60, 41.80)	⨁◯◯◯ VERY LOW[e]	0.97 (0.59, 1.60)	⨁⨁◯◯ LOW[f]	1.06 (0.65, 1.73)	⨁⨁◯◯ LOW[g]	77 per 1,000	82 per 1,000	5 more per 1,000 (from 27 fewer to 56 more)
Magnesium sulphate	1.07 (0.16, 7.15)	⨁◯◯◯ VERY LOW[e]	1.75 (0.67, 4.59)	⨁◯◯◯ VERY LOW[b]	1.33 (0.63, 2.78)	⨁◯◯◯ VERY LOW[h]	77 per 1,000	102 per 1,000	25 more per 1,000 (from 28 fewer to 137 more)

Oxytocin receptor antagonists	2.25 (0.79, 6.38)	⨁⨁⨀⨀ LOW[d]	0.55 (0.28, 1.08)	⨁⨀⨀⨀ VERY LOW[b]	0.83 (0.47, 1.46)	⨁⨀⨀⨀ VERY LOW[i]	77 per 1,000	64 per 1,000	13 fewer per 1,000 (from 41 fewer to 35 more)
Nitric oxide donors	0.41 (0.06, 3.00)	⨁⨁⨀⨀ LOW[d]	0.59 (0.19, 1.84)	⨁⨀⨀⨀ VERY LOW[b]	0.54 (0.20, 1.45)	⨁⨁⨀⨀ LOW[c]	77 per 1,000	42 per 1,000	35 fewer per 1,000 (from 62 fewer to 35 more)
Combinations of tocolytics	Not estimable	Not applicable	0.68 (0.36, 1.31)	⨁⨁⨀⨀ LOW[f]	0.68 (0.36, 1.31)	⨁⨁⨀⨀ LOW[g]	77 per 1,000	52 per 1,000	25 fewer per 1,000 (from 49 fewer to 24 more)

*The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).CI: Confidence interval; RR: Risk Ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

Footnotes
[a]Direct evidence downgraded -2 due to multiple limitations in study design and serious imprecision.
[b]Indirect evidence downgraded -3 due to multiple limitations in study design and very serious imprecision.
[c]Network evidence downgraded -2 due to low certainty direct evidence.
[d]Direct evidence downgraded -2 due very serious imprecision.
[e]Direct evidence downgraded -3 due to multiple limitations in study design and very serious imprecision.
[f]Indirect evidence downgraded -2 due to multiple limitations in study design and serious imprecision.
[g]Network evidence downgraded -2 due to low certainty indirect evidence.
[h]Network evidence downgraded -3 due to very low certainty direct and indirect evidence.
[i]Network evidence downgraded -3 due to low certainty direct evidence further downgraded because of incoherence.

Stillbirth

Patient or population: Women with signs and symptoms of preterm labour
Settings: Hospital setting
Intervention: Betamimetics, calcium channel blockers, COX inhibitors, magnesium sulphate, nitric oxide donors, oxytocin receptor antagonists, combinations of tocolytics
Comparison: Placebo or no treatment

Outcomes	Direct Evidence		Indirect Evidence		Network Evidence		Anticipated absolute effects for network estimate		
	RR (95% CI)	Certainty	RR (95% CI)	Certainty	RR (95% CI)	Certainty	Risk with placebo or no treatment	Risk with tocolytic agent	Risk difference with tocolytic agent
Betamimetics	1.24 (0.66, 2.33)	⨁⨁◯◯ LOW[a]	1.98 (0.24, 16.19)	⨁⨁◯◯ LOW[b]	1.29 (0.70, 2.36)	⨁⨁◯◯ LOW[c]	43 per 1,000	55 per 1,000	12 more per 1,000 (from 13 fewer to 58 more)
COX inhibitors	0.31 (0.01, 7.15)	⨁⨁◯◯ LOW[d]	Not estimable	Not applicable	0.31 (0.01, 7.15)	⨁⨁◯◯ LOW[c]	43 per 1,000	13 per 1,000	30 fewer per 1,000 (from 43 fewer to 264 more)
Calcium channel blockers	Not estimable	Not applicable	0.98 (0.20, 4.78)	⨁⨁◯◯ LOW[b]	0.98 (0.20, 4.78)	⨁⨁◯◯ LOW[e]	43 per 1,000	42 per 1,000	1 fewer per 1,000 (from 34 fewer to 163 more)
Magnesium sulphate	5.70 (0.28, 116.87)	⨁◯◯◯ VERY LOW[f]	0.27 (0.01, 10.03)	⨁◯◯◯ VERY LOW[g]	1.63 (0.16, 16.44)	⨁◯◯◯ VERY LOW[h]	43 per 1,000	70 per 1,000	27 more per 1,000 (from 36 fewer to 664 more)

Oxytocin receptor antagonists	0.41 (0.04, 4.08)	⊕⊕⊖⊖ LOW[d]	0.73 (0.06, 9.05)	⊕⊕⊖⊖ LOW[b]	0.60 (0.18, 2.02)	⊕⊕⊖⊖ LOW[c]	43 per 1,000	26 per 1,000	17 fewer per 1,000 (from 35 fewer to 44 more)
Nitric oxide donors	0.36 (0.01, 8.59)	⊕⊕⊖⊖ LOW[d]	0.44 (0.02, 11.41)	⊕⊖⊖⊖ VERY LOW[g]	0.40 (0.04, 3.85)	⊕⊕⊖⊖ LOW[c]	43 per 1,000	17 per 1,000	26 fewer per 1,000 (from 41 fewer to 123 more)
Combinations of tocolytics	Not estimable	Not applicable	Not estimable	Not applicable	Not estimable	Not applicable	43 per 1,000	Not estimable	Not estimable

*The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).CI: Confidence interval; RR: Risk Ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

Footnotes
[a]Direct evidence downgraded -2 due to multiple limitations in study design and serious imprecision.
[b]Indirect evidence downgraded -2 due to multiple limitations in study design and serious imprecision.
[c]Network evidence downgraded -2 low certainty direct and evidence.
[d]Direct evidence downgraded -2 due to very serious imprecision.
[e]Network evidence downgraded -2 due to low certainty indirect evidence.
[f]Direct evidence downgraded -3 due to multiple limitations in study design and very serious imprecision.
[g]Indirect evidence downgraded -3 due to multiple limitations in study design and very serious imprecision.
[h]Network evidence downgraded -3 due to very low certainty indirect evidence.

Neonatal death before 7 days

Patient or population: Women with signs and symptoms of preterm labour
Settings: Hospital setting
Intervention: Betamimetics, calcium channel blockers, COX inhibitors, magnesium sulphate, nitric oxide donors, oxytocin receptor antagonists, combinations of tocolytics
Comparison: Placebo or no treatment

Outcomes	Direct Evidence		Anticipated absolute effects for direct estimate		
	RR (95% CI)	Certainty	Risk with placebo or no treatment	Risk with tocolytic agent	Risk difference with tocolytic agent
Betamimetics	1.02 (0.50, 2.05)	⨁⨁⨀⨀ LOW[a]	30 per 1,000	31 per 1,000	1 more per 1,000 (from 15 fewer to 32 more)
COX inhibitors	0.94 (0.15, 5.84)	⨁⨁⨀⨀ LOW[b]	30 per 1,000	28 per 1,000	2 fewer per 1,000 (from 26 fewer to 145 more)
Calcium channel blockers	5.18 (0.26, 103.15)	⨁⨁⨀⨀ LOW[b]	30 per 1,000	Not estimable	Not estimable
Magnesium sulphate	2.37 (0.43, 13.01)	⨁⨀⨀⨀ VERY LOW[c]	30 per 1,000	Not estimable	Not estimable
Oxytocin receptor antagonists	6.15 (0.74, 50.73)	⨁⨁⨀⨀ LOW[b]	30 per 1,000	185 per 1,000	155 more per 1,000 (from 8 fewer to 1,492 more)
Nitric oxide donors	Not estimable	Not applicable	30 per 1,000	Not estimable	Not estimable
Combinations of tocolytics	Not estimable	Not applicable	30 per 1,000	Not estimable	Not estimable

*The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).CI: Confidence interval; RR: Risk Ratio

GRADE Working Group grades of evidence **High quality:** Further research is very unlikely to change our confidence in the estimate of effect. **Moderate quality:** Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. **Low quality:** Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. **Very low quality:** We are very uncertain about the estimate.
Footnotes [a]Direct evidence downgraded -2 due to multiple limitations in study design and serious imprecision. [b]Direct evidence downgraded -2 due to very serious imprecision. [c]Direct evidence downgraded -3 due to multiple limitations in study design and very serious imprecision.

Neurodevelopmental morbidity

Patient or population: Women with signs and symptoms of preterm labour
Settings: Hospital setting
Intervention: Betamimetics, calcium channel blockers, COX inhibitors, magnesium sulphate, nitric oxide donors, oxytocin receptor antagonists, combinations of tocolytics
Comparison: Placebo or no treatment

Outcomes	Direct Evidence		Indirect Evidence		Network Evidence		Anticipated absolute effects for network estimate		
	RR (95% CI)	Certainty	RR (95% CI)	Certainty	RR (95% CI)	Certainty	Risk with placebo or no treatment	Risk with tocolytic agent	Risk difference with tocolytic agent
Betamimetics	0.71 (0.45, 1.14)	⨁⨁◯◯ LOW[a]	1.22 (0.64, 2.34)	⨁◯◯◯ VERY LOW[b]	0.86 (0.59, 1.25)	⨁⨁◯◯ LOW[c]	76 per 1,000	65 per 1,000	11 fewer per 1,000 (from 31 fewer to 19 more)
COX inhibitors	Not estimable	Not applicable	0.76 (0.38, 1.50)	⨁◯◯◯ VERY LOW[b]	0.76 (0.38, 1.50)	⨁◯◯◯ VERY LOW[d]	76 per 1,000	58 per 1,000	18 fewer per 1,000 (from 47 fewer to 38 more)
Calcium channel blockers	3.11 (0.13, 73.11)	⨁◯◯◯ VERY LOW[e]	0.48 (0.29, 0.82)	⨁⨁◯◯ LOW[f]	0.51 (0.30, 0.85)	⨁⨁◯◯ LOW[g]	76 per 1,000	39 per 1,000	37 fewer per 1,000 (from 53 fewer to 11 fewer)
Magnesium sulphate	0.63 (0.20, 1.96)	⨁◯◯◯ VERY LOW[e]	0.67 (0.32, 1.41)	⨁◯◯◯ VERY LOW[b]	0.66 (0.36, 1.22)	⨁◯◯◯ VERY LOW[d]	76 per 1,000	50 per 1,000	26 fewer per 1,000 (from 49 fewer to 17 more)

Oxytocin receptor antagonists	0.85 (0.45, 1.62)	⨁⨁⨁⨀ MODERATE[h]	0.65 (0.35, 1.22)	⨁⨁⨀⨀ LOW[i]	0.74 (0.47, 1.16)	⨁⨁⨁⨀ MODERATE[j]	76 per 1,000	56 per 1,000	20 fewer per 1,000 (from 40 fewer to 12 more)
Nitric oxide donors	1.06 (0.16, 7.04)	⨁⨁⨀⨀ LOW[k]	0.20 (0.04, 0.96)	⨁⨀⨀⨀ VERY LOW[b]	0.39 (0.12, 1.32)	⨁⨁⨀⨀ LOW[l]	76 per 1,000	30 per 1,000	46 fewer per 1,000 (from 67 fewer to 24 more)
Combinations of tocolytics	Not estimable	Not applicable	0.61 (0.13, 2.78)	⨁⨀⨀⨀ VERY LOW[b]	0.61 (0.13, 2.80)	⨁⨀⨀⨀ VERY LOW[d]	76 per 1,000	46 per 1,000	30 fewer per 1,000 (from 66 fewer to 135 more)

*The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).CI: Confidence interval; RR: Risk Ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

Footnotes
[a]Direct evidence downgraded -2 due to limitations in study design and serious imprecision.
[b]Indirect evidence downgraded -3 due to multiple limitations in study design and very serious imprecision.
[c]Network evidence downgraded -2 due to low certainty direct evidence.
[d]Network evidence downgraded -3 due to very low certainty indirect evidence.
[e]Direct evidence downgraded -3 due to multiple limitations in study design and very serious imprecision.
[f]Indirect evidence downgraded -2 due to multiple limitations in study design and serious imprecision.
[g]Network evidence downgraded -2 due to low certainty indirect evidence.
[h]Direct evidence downgraded -1 due to limitations in study design.
[i]Indirect evidence downgraded -2 due to multiple limitations in study design and serious imprecision.
[j]Network evidence downgraded -1 due to moderate certainty direct evidence.
[k]Direct evidence downgraded -2 due to very serious imprecision.
[l]Network evidence downgraded -2 due to low certainty direct evidence.

Gastrointestinal morbidity

Patient or population: Women with signs and symptoms of preterm labour
Settings: Hospital setting
Intervention: Betamimetics, calcium channel blockers, COX inhibitors, magnesium sulphate, nitric oxide donors, oxytocin receptor antagonists, combinations of tocolytics
Comparison: Placebo or no treatment

Outcomes	Direct Evidence		Indirect Evidence		Network Evidence		Anticipated absolute effects for network estimate		
	RR (95% CI)	Certainty	RR (95% CI)	Certainty	RR (95% CI)	Certainty	Risk with placebo or no treatment	Risk with tocolytic agent	Risk difference with tocolytic agent
Betamimetics	0.50 (0.12, 2.16)	⊕⊖⊖⊖ VERY LOW[a]	1.44 (0.44, 4.69)	⊕⊖⊖⊖ VERY LOW[b]	0.94 (0.37, 2.36)	⊕⊖⊖⊖ VERY LOW[c]	57 per 1,000	54 per 1,000	3 fewer per 1,000 (from 36 fewer to 78 more)
COX inhibitors	0.91 (0.25, 3.37)	⊕⊕⊖⊖ LOW[d]	1.31 (0.42, 4.09)	⊕⊖⊖⊖ VERY LOW[b]	1.12 (0.47, 2.64)	⊕⊕⊖⊖ LOW[e]	57 per 1,000	64 per 1,000	7 more per 1,000 (from 30 fewer to 93 more)
Calcium channel blockers	5.98 (0.74, 48.42)	⊕⊖⊖⊖ VERY LOW[a]	0.33 (0.12, 0.90)	⊕⊖⊖⊖ VERY LOW[b]	0.57 (0.23, 1.41)	⊕⊖⊖⊖ VERY LOW[f]	57 per 1,000	32 per 1,000	25 fewer per 1,000 (from 44 fewer to 23 more)
Magnesium sulphate	0.90 (0.39, 2.12)	⊕⊖⊖⊖ VERY LOW[a]	0.99 (0.28, 3.57)	⊕⊖⊖⊖ VERY LOW[b]	0.92 (0.45, 1.88)	⊕⊖⊖⊖ VERY LOW[c]	57 per 1,000	52 per 1,000	5 fewer per 1,000 (from 31 fewer to 50 more)

Oxytocin receptor antagonists	0.21 (0.02, 1.76)	⊕⊕⊖⊖ LOW[d]	0.50 (0.13, 1.97)	⊕⊖⊖⊖ VERY LOW[b]	0.38 (0.12, 1.22)	⊕⊕⊖⊖ LOW[e]	57 per 1,000	22 per 1,000	35 fewer per 1,000 (from 50 fewer to 13 more)
Nitric oxide donors	0.75 (0.06, 9.46)	⊕⊕⊖⊖ LOW[d]	0.94 (0.25, 3.48)	⊕⊖⊖⊖ VERY LOW[b]	0.88 (0.29, 2.71)	⊕⊕⊖⊖ LOW[e]	57 per 1,000	50 per 1,000	7 fewer per 1,000 (from 40 fewer to 97 more)
Combinations of tocolytics	Not estimable	Not applicable	1.20 (0.04, 35.33)	⊕⊖⊖⊖ VERY LOW[b]	1.20 (0.04, 35.33)	⊕⊖⊖⊖ VERY LOW[g]	57 per 1,000	68 per 1,000	11 more per 1,000 (from 55 fewer to 1,957 more)

*The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).CI: Confidence interval; RR: Risk Ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

Footnotes
[a]Direct evidence downgraded -3 due to multiple limitations in study design and very serious imprecision.
[b]Indirect evidence downgraded -3 due to multiple limitations in study design and very serious imprecision.
[c]Network evidence downgraded -3 due to very low certainty direct evidence.
[d]Direct evidence downgraded -2 due to very serious imprecision.
[e]Network evidence downgraded -2 due to low certainty direct evidence.
[f]Network evidence downgraded -3 due to very low certainty indirect evidence further downgraded because of inconsistency.
[g]Network evidence downgraded -3 due to very low certainty indirect evidence.

Respiratory morbidity

Patient or population: Women with signs and symptoms of preterm labour
Settings: Hospital setting
Intervention: Betamimetics, calcium channel blockers, COX inhibitors, magnesium sulphate, nitric oxide donors, oxytocin receptor antagonists, combinations of tocolytics
Comparison: Placebo or no treatment

Outcomes	Direct Evidence		Indirect Evidence		Network Evidence		Anticipated absolute effects for network estimate		
	RR (95% CI)	Certainty	RR (95% CI)	Certainty	RR (95% CI)	Certainty	Risk with placebo or no treatment	Risk with tocolytic agent	Risk difference with tocolytic agent
Betamimetics	0.98 (0.72, 1.33)	⨁⨁◯◯ LOW[a]	1.04 (0.77, 1.41)	⨁◯◯◯ VERY LOW[b]	0.95 (0.81, 1.13)	⨁⨁⨁◯ MODERATE[c]	280 per 1,000	266 per 1,000	14 fewer per 1,000 (from 53 fewer to 36 more)
COX inhibitors	0.80 (0.47, 1.36)	⨁⨁◯◯ LOW[d]	1.02 (0.70, 1.49)	⨁◯◯◯ VERY LOW[b]	0.94 (0.70, 1.28)	⨁⨁◯◯ LOW[e]	280 per 1,000	263 per 1,000	17 fewer per 1,000 (from 84 fewer to 78 more)
Calcium channel blockers	0.66 (0.01, 31.39)	⨁◯◯◯ VERY LOW[f]	0.68 (0.53, 0.89)	⨁⨁◯◯ LOW[g]	0.68 (0.53, 0.88)	⨁⨁◯◯ LOW[h]	280 per 1,000	190 per 1,000	90 fewer per 1,000 (from 132 fewer to 34 fewer)
Magnesium sulphate	1.10 (0.68, 1.78)	⨁⨁◯◯ LOW[a]	0.88 (0.64, 1.21)	⨁◯◯◯ VERY LOW[b]	0.94 (0.72, 1.23)	⨁⨁◯◯ LOW[e]	280 per 1,000	263 per 1,000	17 fewer per 1,000 (from 78 fewer to 64 more)

Oxytocin receptor antagonists	1.22 (0.90, 1.66)	⊕⊕⊕⊖ MODERATE[i]	0.95 (0.71, 1.26)	⊕⊕⊖⊖ LOW[g]	1.07 (0.86, 1.33)	⊕⊕⊕⊖ MODERATE[j]	280 per 1,000	300 per 1,000	20 more per 1,000 (from 39 fewer to 92 more)
Nitric oxide donors	0.35 (0.12, 1.00)	⊕⊕⊖⊖ LOW[d]	0.93 (0.38, 2.32)	⊕⊖⊖⊖ VERY LOW[b]	0.61 (0.31, 1.22)	⊕⊖⊖⊖ VERY LOW[k]	280 per 1,000	171 per 1,000	109 fewer per 1,000 (from 193 fewer to 62 more)
Combinations of tocolytics	Not estimable	Not applicable	1.15 (0.64, 2.05)	⊕⊖⊖⊖ VERY LOW[b]	1.15 (0.64, 2.05)	⊕⊖⊖⊖ VERY LOW[l]	280 per 1,000	322 per 1,000	42 more per 1,000 (from 101 fewer to 294 more)

*The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).CI: Confidence interval; RR: Risk Ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

Footnotes
[a]Direct evidence downgraded -2 due to multiple limitations in study design and serious imprecision.
[b]Indirect evidence downgraded -3 due to multiple limitations in study design and very serious imprecision.
[c]Network evidence downgraded -1 due to low certainty direct evidence further upgraded +1 since the network estimate is precise.
[d]Direct evidence downgraded -2 due to very serious imprecision.
[e]Network evidence downgraded -2 due to low certainty direct evidence.
[f]Direct evidence downgraded -3 due to multiple limitations in study design and very serious imprecision.
[g]Indirect evidence downgraded -2 due to multiple limitations in study design and serious imprecision.
[h]Network evidence downgraded -2 due to low certainty indirect evidence.
[i]Direct evidence downgraded -1 due to serious imprecision.
[j]Network evidence downgraded -1 due to moderate certainty direct evidence.
[k]Network evidence downgraded -3 due to low certainty indirect evidence further downgraded because of incoherence.
[l]Network evidence downgraded -3 due to very low certainty indirect evidence.

Mean birthweight

Patient or population: Women with signs and symptoms of preterm labour
Settings: Hospital setting
Intervention: Betamimetics, calcium channel blockers, COX inhibitors, magnesium sulphate, nitric oxide donors, oxytocin receptor antagonists, combinations of tocolytics
Comparison: Placebo or no treatment

Outcomes	Direct Evidence		Indirect Evidence		Network Evidence		Anticipated absolute effects for network estimate		
	RR (95% CI)	Certainty	RR (95% CI)	Certainty	RR (95% CI)	Certainty	Risk with placebo or no treatment	Risk with tocolytic agent	Risk difference with tocolytic agent
Betamimetics	68.28 (-10.92, 147.49)	⊕⊕⊕⊕ HIGH	-43.55 (-152.25, 65.16)	⊕⊖⊖⊖ VERY LOW[a]	-5.52 (-85.23, 74.18)	⊕⊕⊕⊖ MODERATE[b]	2222g	2228g	6g fewer (from 85 fewer to 74 more)
COX inhibitors	713.61 (402.54, 1024.67)	⊕⊕⊖⊖ LOW[c]	-36.76 (-186.75, 113.22)	⊕⊖⊖⊖ VERY LOW[a]	97.60 (-44.70, 239.91)	⊕⊖⊖⊖ VERY LOW[d]	2222g	2320g	98g more (from 45 fewer to 240 more)
Calcium channel blockers	19.56 (-258.79, 297.92)	⊕⊖⊖⊖ VERY LOW[e]	98.77 (2.73, 194.80)	⊕⊕⊕⊖ MODERATE[f]	84.08 (-3.22, 171.38)	⊕⊕⊕⊖ MODERATE[g]	2222g	2306g	84g more (from 3 fewer to 171 more)
Magnesium sulphate	12.65 (-99.04, 124.35)	⊕⊕⊖⊖ LOW[c]	28.13 (-105.20, 161.46)	⊕⊖⊖⊖ VERY LOW[a]	21.07 (-78.12, 120.27)	⊕⊕⊖⊖ LOW[h]	2222g	2243g	21g more (from 78 fewer to 120 more)
Oxytocin receptor antagonists	-68.35 (-228.50, 91.79)	⊕⊕⊕⊖ MODERATE[i]	46.46 (-77.65, 170.57)	⊕⊕⊖⊖ LOW[j]	0.21 (-97.80, 98.22)	⊕⊕⊕⊖ MODERATE[k]	2222g	2222g	0g more (from 98 fewer to 98 more)
Nitric oxide donors	327.00 (-272.13, 926.13)	⊕⊕⊖⊖ LOW[l]	436.69 (223.99, 649.40)	⊕⊕⊖⊖ LOW[j]	425.53 (224.32, 626.74)	⊕⊕⊖⊖ LOW[m]	2222g	2648g	426g more (from 224

									more to 627 more)
Combinations of tocolytics	-287.00 (-562.65, -11.35)	⨁⨁⊖⊖ LOW[c]	140.09 (6.58, 273.59)	⨁⊖⊖⊖ VERY LOW[a]	79.09 (-48.16, 206.34)	⨁⊖⊖⊖ VERY LOW[d]	2222g	2301g	79g more (from 48 fewer to 206 more)

*The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).CI: Confidence interval; RR: Risk Ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

Footnotes
[a]Indirect evidence downgraded -3 due to multiple limitations in study design and very serious imprecision.
[b]Network evidence downgraded -1 due to high certainty direct evidence downgraded because of incoherence.
[c]Direct evidence downgraded -2 due to multiple limitations in study design and serious imprecision.
[d]Network evidence downgraded -3 due to low certainty direct evidence further downgraded because of incoherence.
[e]Direct evidence downgraded -3 due to multiple limitations in study design and very serious imprecision.
[f]Indirect evidence downgraded -1 due to multiple limitations in study design.
[g]Network evidence downgraded -1 due to moderate certainty indirect evidence.
[h]Network evidence downgraded -2 due to low certainty direct evidence.
[i]Direct evidence downgraded -1 due to serious imprecision.
[j]Indirect evidence downgraded -2 due to multiple limitations in study design and serious imprecision.
[k]Network evidence downgraded -1 due to moderate certainty direct evidence.
[k]Indirect evidence downgraded -2 due to multiple limitations in study design and serious imprecision.
[l]Direct evidence downgraded -2 due to very serious imprecision.
[m]Network evidence downgraded -2 due to low certainty direct and indirect evidence.

Birthweight <2000g

Patient or population: Women with signs and symptoms of preterm labour
Settings: Hospital setting
Intervention: Betamimetics, calcium channel blockers, COX inhibitors, magnesium sulphate, nitric oxide donors, oxytocin receptor antagonists, combinations of tocolytics
Comparison: Placebo or no treatment

Outcomes	Direct Evidence		Indirect Evidence		Network Evidence		Anticipated absolute effects for network estimate		
	RR (95% CI)	Certainty	RR (95% CI)	Certainty	RR (95% CI)	Certainty	Risk with placebo or no treatment	Risk with tocolytic agent	Risk difference with tocolytic agent
Betamimetics	0.83 (0.65, 1.07)	⨁⨁◯◯ LOW[a]	1.49 (0.53, 4.18)	⨁◯◯◯ VERY LOW[b]	0.85 (0.67, 1.09)	⨁⨁◯◯ LOW[c]	543 per 1,000	462 per 1,000	81 fewer per 1,000 (from 179 fewer to 49 more)
COX inhibitors	0.50 (0.05, 5.04)	⨁◯◯◯ VERY LOW[d]	Not estimable	Not applicable	0.50 (0.05, 5.04)	⨁◯◯◯ VERY LOW[e]	543 per 1,000	272 per 1,000	272 fewer per 1,000 (from 516 fewer to 2,194 more)
Calcium channel blockers	Not estimable	Not applicable	0.49 (0.28, 0.87)	⨁⨁◯◯ LOW[f]	0.49 (0.28, 0.87)	⨁⨁◯◯ LOW[c]	543 per 1,000	266 per 1,000	277 fewer per 1,000 (from 391 fewer to 71 fewer)
Magnesium sulphate	1.08 (0.82, 1.41)	⨁◯◯◯ VERY LOW[d]	0.84 (0.32, 2.19)	⨁◯◯◯ VERY LOW[b]	1.06 (0.82, 1.38)	⨁◯◯◯ VERY LOW[g]	543 per 1,000	576 per 1,000	33 more per 1,000 (from 98 fewer to 206 more)

Oxytocin receptor antagonists	Not estimable	Not applicable	Not estimable	Not applicable	Not estimable	Not applicable	543 per 1,000	Not estimable	Not estimable
Nitric oxide donors	Not estimable	Not applicable	Not estimable	Not applicable	Not estimable	Not applicable	543 per 1,000	Not estimable	Not estimable
Combinations of tocolytics	Not estimable	Not applicable	0.85 (0.13, 5.79)	⨁⊖⊖⊖ VERY LOW[b]	0.85 (0.13, 5.79)	⨁⊖⊖⊖ VERY LOW[h]	543 per 1,000	462 per 1,000	81 fewer (from 472 fewer to 2,601 more)

*The basis for the assumed risk (e.g. the median control group risk across studies) is provided in footnotes. The corresponding risk (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).CI: Confidence interval; RR: Risk Ratio

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

Footnotes
[a]Direct evidence downgraded -2 due to multiple limitations in study design and serious imprecision.
[b]Indirect evidence downgraded -3 due to multiple limitations in study design and very serious imprecision.
[c]Network evidence downgraded -2 due to low certainty direct evidence.
[d]Direct evidence downgraded -3 due to multiple limitations in study design and very serious imprecision.
[e]Network evidence downgraded -3 due to very low certainty direct evidence.
[f]Indirect evidence downgraded -1 due to multiple limitations in study design and serious imprecision.
[g]Network evidence downgraded -1 due to very low certainty direct and indirect evidence.
[h]Network evidence downgraded -3 due to very low certainty indirect evidence.

Birthweight <2500g

Patient or population: Women with signs and symptoms of preterm labour
Settings: Hospital setting
Intervention: Betamimetics, calcium channel blockers, COX inhibitors, magnesium sulphate, nitric oxide donors, oxytocin receptor antagonists, combinations of tocolytics
Comparison: Placebo or no treatment

Outcomes	Direct Evidence		Indirect Evidence		Network Evidence		Anticipated absolute effects for network estimate		
	RR (95% CI)	Certainty	RR (95% CI)	Certainty	RR (95% CI)	Certainty	Risk with placebo or no treatment	Risk with tocolytic agent	Risk difference with tocolytic agent
Betamimetics	0.92 (0.79, 1.06)	⨁⨁⨁⨀ MODERATE[a]	0.90 (0.66, 1.22)	⨁⨀⨀⨀ VERY LOW[b]	0.92 (0.85, 1.00)	⨁⨁⨁⨀ MODERATE[c]	624 per 1,000	574 per 1,000	50 fewer per 1,000 (from 94 fewer to 0 more)
COX inhibitors	0.21 (0.07, 0.62)	⨁⨁⨀⨀ LOW[d]	Not estimable	Not applicable	0.21 (0.07, 0.62)	⨁⨁⨀⨀ LOW[e]	624 per 1,000	131 per 1,000	493 fewer per 1,000 (from 580 fewer to 237 fewer)
Calcium channel blockers	0.96 (0.60, 1.54)	⨁⨁⨁⨀ MODERATE[f]	0.78 (0.66, 0.92)	⨁⨀⨀⨀ VERY LOW[b]	0.80 (0.69, 0.93)	⨁⨁⨁⨀ MODERATE[c]	624 per 1,000	499 per 1,000	125 fewer per 1,000 (from 193 fewer to 44 fewer)
Magnesium sulphate	0.95 (0.83, 1.09)	⨁⨁⨀⨀ LOW[d]	0.91 (0.72, 1.15)	⨁⨁⨀⨀ LOW[g]	0.94 (0.84, 1.06)	⨁⨁⨀⨀ LOW[h]	624 per 1,000	587 per 1,000	37 fewer per 1,000 (from 100 fewer to 37 more)

Oxytocin receptor antagonists	Not estimable	Not applicable	0.94 (0.79, 1.12)	⨁⨁⊖⊖ LOW[g]	0.94 (0.79, 1.12)	⨁⨁⊖⊖ LOW[i]	624 per 1,000	587 per 1,000	37 fewer per 1,000 (from 131 fewer to 75 more)
Nitric oxide donors	Not estimable	Not applicable	0.40 (0.24, 0.69)	⨁⨁⊖⊖ LOW[g]	0.40 (0.24, 0.69)	⨁⨁⊖⊖ LOW[i]	624 per 1,000	250 per 1,000	374 fewer per 1,000 (from 474 fewer to 193 fewer)
Combinations of tocolytics	Not estimable	Not applicable	0.74 (0.59, 0.93)	⨁⨁⊖⊖ LOW[g]	0.74 (0.59, 0.93)	⨁⨁⊖⊖ LOW[i]	624 per 1,000	462 per 1,000	162 fewer per 1,000 (from 256 fewer to 44 fewer)

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GRADE Working Group grades of evidence
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Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

Footnotes
[a]Direct evidence downgraded -1 due to multiple limitations in study design.
[b]Indirect evidence downgraded -3 due to multiple limitations in study design and very serious imprecision.
[c]Network evidence downgraded -1 due to moderate certainty direct evidence.
[d]Direct evidence downgraded -2 due to multiple limitations in study design and serious imprecision.
[e]Network evidence downgraded -2 due to low certainty direct evidence.
[f]Direct evidence downgraded -1 due to serious imprecision.
[g]Indirect evidence downgraded -2 due to multiple limitations in study design and serious imprecision.
[h]Network evidence downgraded -2 due to low certainty direct and indirect evidence.
[i]Network evidence downgraded -2 due to low certainty indirect evidence.

Gestational age at birth

Patient or population: Women with signs and symptoms of preterm labour
Settings: Hospital setting
Intervention: Betamimetics, calcium channel blockers, COX inhibitors, magnesium sulphate, nitric oxide donors, oxytocin receptor antagonists, combinations of tocolytics
Comparison: Placebo or no treatment

Outcomes	Direct Evidence		Indirect Evidence		Network Evidence		Anticipated absolute effects for network estimate		
	RR (95% CI)	Certainty	RR (95% CI)	Certainty	RR (95% CI)	Certainty	Risk with placebo or no treatment	Risk with tocolytic agent	Risk difference with tocolytic agent
Betamimetics	0.09 (-0.56, 0.75)	⨁⨁⨁⊖ MODERATE[a]	-0.60 (-1.24, 0.04)	⨁⊖⊖⊖ VERY LOW[b]	-0.23 (-0.70, 0.23)	⨁⨁⨁⊖ MODERATE[c]	35.2 weeks	35 weeks	0.2 weeks fewer (from 0.7 fewer to 0.2 more)
COX inhibitors	2.61 (-0.62, 5.84)	⨁⊖⊖⊖ VERY LOW[d]	0.04 (-0.72, 0.79)	⨁⊖⊖⊖ VERY LOW[b]	0.64 (-0.06, 1.33)	⨁⊖⊖⊖ VERY LOW[e]	35.2 weeks	35.8 weeks	0.6 weeks more (0.1 fewer to 1.3 more)
Calcium channel blockers	-0.01 (-1.64, 1.62)	⨁⊖⊖⊖ VERY LOW[f]	0.35 (-0.19, 0.89)	⨁⨁⨁⊖ MODERATE[g]	0.24 (-0.25, 0.73)	⨁⨁⨁⊖ MODERATE[h]	35.2 weeks	35.4 weeks	0.2 weeks more (0.3 fewer to 0.7 more)
Magnesium sulphate	0.62 (-1.35, 0.12)	⨁⨁⊖⊖ LOW[i]	0.29 (-0.43, 1.01)	⨁⊖⊖⊖ VERY LOW[b]	-0.16 (-0.70, 0.38)	⨁⊖⊖⊖ VERY LOW[j]	35.2 weeks	35 weeks	0.2 weeks fewer (from 0.7 fewer to 0.4 more)
Oxytocin receptor antagonists	-0.39 (-1.41, 0.62)	⨁⊖⊖⊖ VERY LOW[f]	0.02 (-0.72, 0.69)	⨁⨁⊖⊖ LOW[k]	-0.08 (-0.70, 0.55)	⨁⨁⊖⊖ LOW[l]	35.2 weeks	35.1 weeks	0.1 weeks fewer (from

									0.7 fewer to 0.6 more)
Nitric oxide donors	1.13 (-0.46, 2.71)	⊕⊕⊖⊖ LOW[m]	1.43 (0.27, 2.59)	⊕⊖⊖⊖ VERY LOW[b]	1.35 (0.37, 2.32)	⊕⊕⊖⊖ LOW[n]	35.2 weeks	36.6 weeks	1.4 weeks more (from 0.4 more to 2.3 more)
Combinations of tocolytics	-0.80 (-1.87, 0.27)	⊕⊕⊖⊖ LOW[m]	0.43 (-0.32, 1.19)	⊕⊕⊖⊖ LOW[k]	0.20 (-0.48, 0.89)	⊕⊖⊖⊖ VERY LOW[o]	35.2 weeks	35.4 weeks	0.2 weeks more (from 0.5 fewer to 0.9 more)

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Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

Footnotes
[a]Direct evidence downgraded -1 due to multiple limitations in study design.
[b]Indirect evidence downgraded -3 due to multiple limitations in study design and very serious imprecision.
[c]Network evidence downgraded -1 due to moderate certainty direct evidence.
[d]Direct evidence downgraded -3 due to severe unexplained statistical heterogeneity, and very serious imprecision.
[e]Network evidence downgraded -3 due to very low certainty direct and indirect evidence.
[f]Direct evidence downgraded -3 due to multiple limitations in study design and very serious imprecision.
[g]Indirect evidence downgraded -1 due to multiple limitations in study design.
[h]Network evidence downgraded -1 due to moderate certainty indirect evidence.
[i]Direct evidence downgraded -2 due to multiple limitations in study design and serious imprecision.
[j]Network evidence downgraded -3 due to low certainty direct evidence further downgraded due to incoherence.
[k]Indirect evidence downgraded -2 due to multiple limitations in study design and serious imprecision.
[l]Network evidence downgraded -2 due to low certainty indirect evidence.
[m]Direct evidence downgraded -2 due to very serious imprecision.
[n]Network evidence downgraded -2 due to low certainty direct evidence.
[o]Network evidence downgraded -3 due to low certainty direct and indirect evidence further downgraded due to incoherence.

Neonatal infection

Patient or population: Women with signs and symptoms of preterm labour
Settings: Hospital setting
Intervention: Betamimetics, calcium channel blockers, COX inhibitors, magnesium sulphate, nitric oxide donors, oxytocin receptor antagonists, combinations of tocolytics
Comparison: Placebo or no treatment

Outcomes	Direct Evidence		Indirect Evidence		Network Evidence		Anticipated absolute effects for network estimate		
	RR (95% CI)	Certainty	RR (95% CI)	Certainty	RR (95% CI)	Certainty	Risk with placebo or no treatment	Risk with tocolytic agent	Risk difference with tocolytic agent
Betamimetics	1.47 (0.71, 3.06)	⨁⨁◯◯ LOW[a]	0.72 (0.36, 1.45)	⨁◯◯◯ VERY LOW[b]	1.10 (0.80, 1.51)	⨁⨁◯◯ LOW[c]	149 per 1,000	164 per 1,000	15 more per 1,000 (from 30 fewer to 76 more)
COX inhibitors	0.51 (0.23, 1.14)	⨁⨁◯◯ LOW[d]	0.94 (0.48, 1.87)	⨁⨁◯◯ LOW[e]	0.73 (0.43, 1.23)	⨁⨁◯◯ LOW[f]	149 per 1,000	109 per 1,000	40 fewer per 1,000 (from 85 fewer to 34 more)
Calcium channel blockers	0.98 (0.39, 2.45)	⨁◯◯◯ VERY LOW[g]	0.75 (0.49, 1.16)	⨁⨁◯◯ LOW[e]	0.79 (0.53, 1.17)	⨁⨁◯◯ LOW[h]	149 per 1,000	118 per 1,000	31 fewer per 1,000 (from 70 fewer to 25 more)
Magnesium sulphate	0.74 (0.26, 2.15)	⨁⨁◯◯ LOW[d]	0.86 (0.43, 1.70)	⨁◯◯◯ VERY LOW[b]	0.70 (0.43, 1.14)	⨁⨁◯◯ LOW[c]	149 per 1,000	104 per 1,000	45 fewer per 1,000 (from 85 fewer to 21 more)

Oxytocin receptor antagonists	Not estimable	Not applicable	0.90 (0.56, 1.43)	⨁⨁⊖⊖ LOW[e]	0.90 (0.56, 1.43)	⨁⨁⊖⊖ LOW[h]	149 per 1,000	134 per 1,000	15 fewer per 1,000 (from 66 fewer to 64 more)
Nitric oxide donors	Not estimable	Not applicable	Not estimable	Not applicable	Not estimable	Not applicable	149 per 1,000	Not estimable	Not estimable
Combinations of tocolytics	Not estimable	Not applicable	1.88 (0.46, 7.63)	⨁⊖⊖⊖ VERY LOW[b]	1.88 (0.46, 7.63)	⨁⊖⊖⊖ VERY LOW[i]	149 per 1,000	280 per 1,000	131 more per 1,000 (from 80 fewer to 948 more)

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Very low quality: We are very uncertain about the estimate.

Footnotes
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[b]Indirect evidence downgraded -3 due to multiple limitations in study design and very serious imprecision.
[c]Network evidence downgraded -3 due to very low certainty indirect evidence.
[d]Direct evidence downgraded -2 due to very serious imprecision.
[e]Indirect evidence downgraded -2 due to multiple limitations in study design and serious imprecision.
[f]Network evidence downgraded -2 due to low certainty direct and indirect evidence.
[g]Direct evidence downgraded -3 due to multiple limitations in study design and very serious imprecision.
[h]Network evidence downgraded -2 due to low certainty indirect evidence.
[i]Network evidence downgraded -3 due to very low certainty indirect evidence.