

Summary of Findings

1. Studies comparing thromboprophylaxis with no thromboprophylaxis

Table 3 Summary of Findings – Thromboprophylaxis versus no thromboprophylaxis with outcomes thrombotic complications (including right ventricle to pulmonary artery conduit thrombosis, pulmonary embolism), shunt occlusion, ischemic stroke, hemorrhage, mortality, quality of life (QOL), and adverse events (including pain post injection)

Population: Children with an indication for 1) aortopulmonary (AP) or 2) right ventricle-to-pulmonary (RVP) artery/Sano shunt surgery (specified in summary column of table)

Intervention: Thromboprophylaxis (specified in summary column of table)

Comparator: No thromboprophylaxis

Outcome	Study results and measurements	Absolute effect estimates		Certainty of the Evidence (Quality of evidence)	Summary
		No thromboprophylaxis	Thromboprophylaxis		
Shunt occlusion (critical)	<p>A. Clopidogrel</p> <p>Relative risk: 0.36 (95% CI 0.04 to 3.34)</p> <p>Based on data from 110 participants in 1 study Follow-up: median 6 months for overall study population</p>	5 per 100	2 per 100	<p>Very low Due to serious risk of bias, due to very serious imprecision¹</p>	<p>The evidence is very uncertain about the effect of clopidogrel on shunt occlusion when compared to no thromboprophylaxis in infants with an indication for systemic-to-pulmonary-artery shunt surgery</p> <p>(Wessel, 2013)</p>
	<p>Difference: 3 fewer per 100 (95% CI 10 fewer to 3 more)</p>				
	<p>B. Aspirin</p> <p>Relative risk: 0.90 (95% CI 0.27 to 2.94)</p> <p>Based on data from 439 participants in 1 study Follow-up: median 6 months for overall study population</p>	5 per 100	5 per 100	<p>Very low Due to serious risk of bias, due to very serious imprecision²</p>	<p>The evidence is very uncertain about the effect of aspirin on shunt occlusion when compared to no thromboprophylaxis in infants with an indication for systemic-to-pulmonary-artery shunt surgery</p> <p>(Wessel, 2013)</p>
<p>Difference: 1 fewer per 100 (95% CI 7 fewer to 6 more)</p>					
	<p>C. Clopidogrel + aspirin</p>	5 per 100	6 per 100		

Outcome	Study results and measurements	Absolute effect estimates		Certainty of the Evidence (Quality of evidence)	Summary
		No thromboprophylaxis	Thromboprophylaxis		
	<p>Relative risk: 1.15 (95% CI 0.36 to 3.68)</p> <p>Based on data from 471 participants in 1 study Follow-up: median 6 months for overall study population</p>	<p>Difference: 1 more per 100 (95% CI 5 fewer to 7 more)</p>		<p>Very low Due to serious risk of bias, due to very serious imprecision³</p>	<p>The evidence is very uncertain about the effect of clopidogrel + aspirin on shunt occlusion when compared to no thromboprophylaxis in infants with an indication for systemic-to-pulmonary-artery shunt surgery</p> <p>(Wessel, 2013)</p>
Mortality (important)	<p>Children with an indication for mBTT-shunt surgery:</p> <p>Hazard ratio: 0.1 (95% CI 0.06 to 0.17)</p> <p>Based on data from 323 participants in 1 study Follow-up: 1 year</p>	-		<p>Low Due to very serious risk of bias⁴</p>	<p>Thromboprophylaxis (aspirin) may reduce the hazard of mortality when compared with no thromboprophylaxis in children with an indication for modified BT shunt surgery</p> <p>(Li, 2007)</p>
	<p>Children with an indication for Sano shunt surgery:</p> <p>Hazard ratio: 0.68 95% CI (0.09 to 5.33)</p> <p>Based on data from 50 participants in 1 study Follow-up: 1 year</p>			<p>Very low Due to very serious risk of bias, due to very serious imprecision⁵</p>	<p>The evidence is very uncertain about the effect of thromboprophylaxis (aspirin) on mortality when compared with no thromboprophylaxis in children with an indication for Sano shunt surgery</p> <p>(Li, 2007)</p>

Outcome	Study results and measurements	Absolute effect estimates		Certainty of the Evidence (Quality of evidence)	Summary
		No thromboprophylaxis	Thromboprophylaxis		
Thrombotic complications (critical) Ischemic stroke (important) (Gastrointestinal) hemorrhage (important) Quality of life (QOL) (important) Adverse events (important)	-	-	-	No GRADE (No evidence was found)	No evidence was found regarding the effect of thromboprophylaxis on thrombotic complications, ischemic stroke, (gastrointestinal) hemorrhage, quality of life (QOL), and adverse events, when compared with no thromboprophylaxis in children with an indication for AP or RVP/Sano shunt surgery

1. **Risk of Bias: serious (-1 level).** No reporting on allocation concealment, and potential funding bias. **Imprecision: very serious (-2 levels).** Confidence interval crosses both borders of clinical relevance.
2. **Risk of Bias: serious (-1 level).** No reporting on allocation concealment, and potential funding bias. **Imprecision: very serious (-2 levels).** Confidence interval crosses both borders of clinical relevance.
3. **Risk of Bias: serious (-1 level).** No reporting on allocation concealment, and potential funding bias. **Imprecision: very serious (-2 levels).** Confidence interval crosses both borders of clinical relevance.
4. **Risk of Bias: very serious (-2 levels).** No assessment of and adjustment for confounding factors, and no reporting on missing data.
5. **Risk of Bias: very serious (-2 levels).** No assessment of and adjustment for confounding factors, and no reporting on missing data. **Imprecision: very serious (-2 levels).** Confidence interval crosses both borders of clinical relevance

* Not reported in article

2. Studies comparing thromboprophylaxis A with no thromboprophylaxis/thromboprophylaxis B

Table 4 Summary of Findings – Thromboprophylaxis versus no thromboprophylaxis with outcomes thrombotic complications (including right ventricle to pulmonary artery conduit thrombosis, pulmonary embolism), shunt occlusion, ischemic stroke, hemorrhage, mortality, quality of life (QOL), and adverse events (including pain post injection)

Population: Infants with an indication for 1) aortopulmonary (AP) or 2) right ventricle-to-pulmonary (RVP) artery/Sano shunt surgery (specified in summary column of table)

Intervention: Tromboprophylaxis A (specified in summary column of table)

Comparator: No thromboprophylaxis/thromboprophylaxis B (specified in summary column of table)

Outcome	Study results and measurements	Absolute effect estimates		Certainty of the Evidence (Quality of evidence)	
		No thromboprophylaxis/thromboprophylaxis B	Thromboprophylaxis A		
Shunt occlusion (critical)	Relative risk: 1.21 (95% CI 0.69 to 2.11) Based on data from 906 participants in 1 study Follow-up: median 6 months for overall study population	5 per 100	6 per 100	Very low Due to serious risk of bias, due to very serious imprecision ¹	The evidence is very uncertain about the effect of clopidogrel (+ possible concomitant aspirin) on shunt occlusion when compared to placebo (+ possible concomitant aspirin) in infants with an indication for systemic-to-pulmonary-artery shunts (Wessel, 2013)
		Difference: 1 more per 100 (95% CI 2 fewer to 4 more)			
Hemorrhage (important)	Relative risk: 1.88 (95% CI 0.65 to 5.45) Based on data from 906 participants in 1 study Follow-up: median 6 months for overall study population	1 per 100	2 per 100	Very low Due to very serious risk of bias, due to very serious imprecision ²	The evidence is very uncertain about the effect of clopidogrel (+ possible concomitant aspirin) on (gastrointestinal) hemorrhage when compared to placebo (+ possible concomitant aspirin) in infants with an indication for systemic-to-pulmonary-artery shunt surgery (Wessel, 2013)
		Difference: 1 more per 100 (95% CI 1 fewer to 3 more)			

Mortality (important)	Relative risk: 0.86 (95% CI 0.61 to 1.21) Based on data from 906 participants in 1 study Follow-up: median 6 months for overall study population	14 per 100	12 per 100	Low Due to serious risk of bias, due to serious imprecision ³	There may be little to no difference in the risk of mortality when comparing treatment with clopidogrel (+ possible concomitant aspirin) to treatment with placebo (+ possible concomitant aspirin) in infants with an indication for systemic-to-pulmonary-artery shunt surgery (Wessel, 2013)
		Difference: 2 fewer per 100 (95% CI 6 fewer to 2 more)			
Adverse events (important)	Relative risk: 1.07 (95% CI 0.99 to 1.16) Based on data from 906 participants in 1 study Follow-up: median 6 months for overall study population	71 per 100	76 per 100	Moderate Due to serious risk of bias ⁴	There is likely little to no difference in the risk of adverse events when comparing treatment with clopidogrel (+ possible concomitant aspirin) to treatment with placebo (+ possible concomitant aspirin) in infants with an indication for systemic-to-pulmonary-artery shunt surgery (Wessel, 2013)
		Difference: 16 more per 100 (95% CI 20 fewer to 53 more)			
Thrombotic complications (critical)				No GRADE (No evidence was found)	No evidence was found regarding the effect of thromboprophylaxis A on thrombotic complications, ischemic stroke, and quality of life (QOL) when compared with no thromboprophylaxis/thro
Ischemic stroke (important)	-	-			
Quality of life (QOL) (important)					

				mboprophylaxis B in infants with an indication for systemic-to-pulmonary-artery shunt surgery
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3. **Risk of Bias: serious (-1 level).** No reporting on allocation concealment, and potential funding bias. **Imprecision: serious (-1 level).** Confidence interval crosses one border of clinical relevance.
4. **Risk of Bias: serious (-1 level).** No reporting on allocation concealment, and potential funding bias.