F.2 Transcatheter valve implantation

Table 17: Clinical evidence profile: SAPT versus DAPT in transcatheter valve implantation

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	SAPT	DAPT	Relative (95% CI)	Absolute		
All-cause mortality at ≤12 months (follow-up 3-12 months)												
4	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	29/541 (5.4%)	5.6%	OR 0.94 (0.56 to 1.6)[3]	3 fewer per 1000 (from 24 fewer to 31 more)	⊕OOO VERY LOW	CRITICAL
Health-related quality of life at ≤12 months - not measured												
0	-	-	-	-	-	none	-	-	-	-		CRITICAL

Major bleeding at ≤12 months (follow-up 3-12 months)												
4	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	28/541 (5.2%)	10%	OR 0.48 (0.3 to 0.77)[3]	49 fewer per 1000 (from 21 fewer to 68 fewer)	⊕⊕⊕O MODERATE	CRITICAL
Minor bleeding at ≤12 months (follow-up 6-12 months)												
2	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[4]	none	36/371 (9.7%)	13.1%	RR 0.64 (0.43 to 0.94)	47 fewer per 1000 (from 8 fewer to 75 fewer)	⊕⊕OO LOW	CRITICAL
Arterial thromboembolic events at ≤12 months (follow-up 3-6 months)												
3	randomised trials	serious[1]	no serious inconsistency	serious[5]	very serious[2]	none	0/111 (0%)	4%	OR ranged from 0.21 to 2.24[3,6]	-	⊕OOO VERY LOW	CRITICAL
Stroke (arterial thromboembolic events) at 12 months (follow-up mean 12 months)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	17/331 (5.1%)	5.7%	RR 0.9 (0.48 to 1.71)	6 fewer per 1000 (from 30 fewer to 40 more)	⊕OOO VERY LOW	CRITICAL
Myocardial infarction (arterial thromboembolic events) at 12 months (follow-up mean 12 months)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	4/331 (1.2%)	1.8%	RR 0.67 (0.19 to 2.36)	6 fewer per 1000 (from 15 fewer to 24 more)	⊕OOO VERY LOW	CRITICAL
All-cause mortality at >12 months - not measured												
0	-	-	-	-	-	none	-	-	-	-		CRITICAL
Health-related quality of life at >12 months - not measured												
0	-	-	-	-	-	none	-	-	-	-		CRITICAL
Major bleeding at >12 months - not measured												
0	-	-	-	-	-	none	-	-	-	-		CRITICAL
Minor bleeding at >12 months - not measured												

0	-	-	-	-	-	none	-	-	-	-		CRITICAL
Arterial thromboembolic events at >12 months - not measured												
0	-	-	-	-	-	none	-	-	-	-		CRITICAL
Hospital readmission at 12 months - not measured												
0	-	-	-	-	-	none	-	-	-	-		IMPORTANT
Withdrawal due to adverse events at 12 months - not measured												
0	-	-	-	-	-	none	-	-	-	-		IMPORTANT
Symptomatic clinical aortic valve thrombosis (thrombus on imaging) at 12 months (follow-up mean 12 months)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	3/331 (0.91%)	0.3%	OR 2.76 (0.39 to 19.65)	5 more per 1000 (from 2 fewer to 53 more)	⊕OOO VERY LOW	IMPORTANT
Need for reintervention at 6-12 months - not measured												
0	-	-	-	-	-	none	-	-	-	-		IMPORTANT
Need for reintervention at >12 months - not measured												
0	-	-	-	-	-	none	-	-	-	-		IMPORTANT
Mean aortic valve gradient (valve degeneration) at ≤12 months (follow-up mean 6 months; Better indicated by lower values)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision[7]	none	331	334	-	MD 0.20 lower (1.09 lower to 0.69 higher)	⊕⊕⊕O MODERATE	IMPORTANT

[1] Downgraded by 1 increment as the majority of the evidence was at high risk of bias
[2] Downgraded by 2 increments as the confidence interval crossed both MIDs
[3] Odds ratio used because this summary statistic was reported for the two studies included in the IPD MA
[4] Downgraded by 1 increments as the confidence interval crossed one MID
[5] Downgraded by 1 increment as people in the Stabile study who received dual antiplatelet therapy could have received clopidogrel or ticlopidine (no information was provided on proportion of people receiving each drug).
[6] Outcome reported as a range of odds ratios due to heterogeneity between studies with a large difference in point estimates without sufficient study number to form valid subgroups
[7]MIDs used to assess imprecision were ±2.60

Table 18: Clinical evidence profile: DOAC (+ aspirin for 3 months) versus aspirin (+ clopidogrel for 3 months) in transcatheter valve implantation

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	DOAC (+aspirin for 3 months)	aspirin (+clopidogrel for 3 months) post TAVI	Relative (95% CI)	Absolute		
All-cause mortality at ≤12 months - not measured												
0	-	-	-	-	-	none	-	-	-	-		CRITICAL
Health-related quality of life at ≤12 months - not measured												
0	-	-	-	-	-	none	-	-	-	-		CRITICAL
Major bleeding at ≤12 months - not measured												
0	-	-	-	-	-	none	-	-	-	-		CRITICAL
Minor bleeding at ≤12 months - not measured												
0	-	-	-	-	-	none	-	-	-	-		CRITICAL
Arterial thromboembolic events at ≤12 months - not measured												
0	-	-	-	-	-	none	-	-	-	-		CRITICAL
All-cause mortality at >12 months - median treatment duration 428 days (follow-up median 428 days)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	64/826 (7.7%)	4.7%	RR 1.67 (1.13 to 2.46)	31 more per 1000 (from 6 more to 69 more)	⊕⊕OO LOW	CRITICAL
Health-related quality of life at >12 months - not measured												

0	-	-	-	-	-	none	-	-	-	-		CRITICAL
Major bleeding at >12 months - VARC-2 life-threatening, disabling or major bleeding - median treatment 428 days (follow-up median 428 days)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	46/826 (5.6%)	3.8%	RR 1.47 (0.94 to 2.29)	18 more per 1000 (from 2 fewer to 49 more)	⊕⊕OO LOW	CRITICAL
Major bleeding at >12 months - BARC type 2, 3 or 5 bleeding - median treatment 428 days (follow-up mean 428 days)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	148/826 (17.9%)	10.4%	RR 1.72 (1.34 to 2.21)	75 more per 1000 (from 35 more to 126 more)	⊕⊕⊕O MODERATE	CRITICAL
Major bleeding at >12 months - ISTH major bleeding - median treatment 428 days (follow-up median 428 days)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	49/826 (5.9%)	3.7%	RR 1.62 (1.04 to 2.52)	23 more per 1000 (from 1 more to 56 more)	⊕⊕OO LOW	CRITICAL
Minor bleeding at >12 months - TIMI major or minor bleeding - median treatment 428 days (follow-up median 428 days)												
1	randomised trials	serious[1]	no serious inconsistency	serious[3]	serious[2]	none	42/826 (5.1%)	2.9%	RR 1.73 (1.06 to 2.83)	21 more per 1000 (from 2 more to 53 more)	⊕OOO VERY LOW	CRITICAL
Stroke (arterial thromboembolic events) at >12 months - median treatment 428 days (follow-up median 428 days)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[4]	none	30/826 (3.6%)	3.1%	RR 1.19 (0.71 to 2)	6 more per 1000 (from 9 fewer to 31 more)	⊕OOO VERY LOW	CRITICAL
Myocardial infarction (arterial thromboembolic events) at >12 months - median treatment 428 days (follow-up median 428 days)												
1	randomised trials	very serious[5]	no serious inconsistency	no serious indirectness	very serious[4]	none	23/826 (2.8%)	2.1%	RR 1.34 (0.72 to 2.49)	7 more per 1000 (from 6 fewer to 31 more)	⊕OOO VERY LOW	CRITICAL
Pulmonary embolism (arterial thromboembolic events) at >12 months - median treatment 428 days (follow-up median 428 days)												

1	randomised trials	very serious[5]	no serious inconsistency	no serious indirectness	very serious[4]	none	3/826 (0.36%)	0.2%	OR 1.48 (0.26 to 8.55)	1 more per 1000 (from 1 fewer to 15 more)	⊕OOO VERY LOW	CRITICAL
Systemic embolism (arterial thromboembolic events) at >12 months- median treatment 428 days (follow-up median 428 days)												
1	randomised trials	very serious[5]	no serious inconsistency	no serious indirectness	very serious[4]	none	1/826 (0.12%)	0.1%	OR 0.99 (0.06 to 15.85)	0 fewer per 1000 (from 1 fewer to 15 more)	⊕OOO VERY LOW	CRITICAL
Hospital readmission at 12 months - not measured												
0	-	-	-	-	-	none	-	-	-	-		IMPORTANT
Premature study drug discontinuation (withdrawal due to adverse events - thromboembolic, bleeding or other adverse events) at 12 months - median treatment duration 428 days (follow-up median 428 days)												
1	randomised trials	very serious[5]	no serious inconsistency	no serious indirectness	no serious imprecision	none	185/826 (22.4%)	11.1%	RR 2.01 (1.6 to 2.54)	112 more per 1000 (from 67 more to 171 more)	⊕⊕OO LOW	IMPORTANT
Symptomatic valve thrombosis (thrombus on imaging) at <12 months - median treatment duration 428 days (follow-up median 428 days)												
1	randomised trials	very serious[1]	no serious inconsistency	no serious indirectness	very serious[4]	none	3/826 (0.36%)	0.9%	OR 0.44 (0.13 to 1.54)	5 fewer per 1000 (from 8 fewer to 5 more)	⊕OOO VERY LOW	IMPORTANT
Need for reintervention at 6-12 months - not measured												
0	-	-	-	-	-	none	-	-	-	-		IMPORTANT
Need for reintervention at >12 months - not measured												
0	-	-	-	-	-	none	-	-	-	-		IMPORTANT
Valve degeneration (mean transvalvular gradient) at ≥12 months - not measured												
0	-	-	-	-	-	none	-	-	-	-		IMPORTANT

[1] Downgraded by 1 increment as the majority of the evidence was at high risk of bias
[2] Downgraded by 1 increments as the confidence interval crossed one MID
[3] Combines major and minor bleeding rather than reporting minor bleeding events separately
[4] Downgraded by 2 increments as the confidence interval crossed both MIDs
[5] Downgraded by 2 increments as the majority of the evidence was at very high risk of bias

Table 19: Clinical evidence profile: Anticoagulant (VKA or DOAC) + SAPT (clopidogrel) versus anticoagulant (VKA or DOAC) alone in transcatheter valve implantation

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Anticoagulant (VKA or DOAC) + clopidogrel	anticoagulant alone post TAVI	Relative (95% CI)	Absolute		
All-cause mortality at ≤12 months (follow-up mean 12 months)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	24/156 (15.4%)	13.4%	RR 1.15 (0.67 to 1.98)	20 more per 1000 (from 44 fewer to 131 more)	⊕OOO VERY LOW	CRITICAL
Health-related quality of life at ≤12 months - not measured												
0	-	-	-	-	-	none	-	-	-	-		CRITICAL
Major bleeding at ≤12 months - VARC-2 life-threatening, disabling or major bleeding (major bleeding) at 12 months (follow-up mean 12 months)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[4]	none	26/156 (16.7%)	8.9%	RR 1.87 (1.01 to 3.44)	77 more per 1000 (from 1 more to 217 more)	⊕OOO VERY LOW	CRITICAL
Minor bleeding at ≤12 months - VARC-2 minor bleeding (minor bleeding) at 12 months (follow-up mean 12 months)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	serious[4]	none	28/156 (17.9%)	12.7%	RR 1.41 (0.83 to 2.39)	52 more per 1000 (from 22 fewer to 177 more)	⊕OOO VERY LOW	CRITICAL

Stroke (arterial thromboembolic events) at ≤12 months (follow-up mean 12 months)												
1	randomised trials	serious[1]	no serious inconsistency	serious[2]	very serious[3]	none	9/156 (5.8%)	5.7%	RR 1.01 (0.41 to 2.47)	1 more per 1000 (from 34 fewer to 84 more)	⊕OOO VERY LOW	CRITICAL
Myocardial infarction (arterial thromboembolic events) at ≤12 months (follow-up mean 12 months)												
1	randomised trials	very serious[5]	no serious inconsistency	serious[2]	very serious[3]	none	1/156 (0.64%)	0.6%	OR 1.01 (0.06 to 16.16)	0 more per 1000 (from 6 fewer to 83 more)	⊕OOO VERY LOW	CRITICAL
All-cause mortality at >12 months - not measured												
0	-	-	-	-	-	none	-	-	-	-		CRITICAL
Health-related quality of life at >12 months - not measured												
0	-	-	-	-	-	none	-	-	-	-		CRITICAL
Major bleeding at >12 months - not measured												
0	-	-	-	-	-	none	-	-	-	-		CRITICAL
Minor bleeding at >12 months - not measured												
0	-	-	-	-	-	none	-	-	-	-		CRITICAL
Arterial thromboembolic events at >12 months - not measured												
0	-	-	-	-	-	none	-	-	-	-		CRITICAL
Hospital readmission at 12 months - not measured												
0	-	-	-	-	-	none	-	-	-	-		IMPORTANT
Withdrawal due to adverse events at 12 months - not measured												
0	-	-	-	-	-	none	-	-	-	-		IMPORTANT

Thrombus on imaging at <12 months - not measured												
0	-	-	-	-	-	none	-	-	-	-		IMPORTANT
Need for reintervention at 6-12 months - not measured												
0	-	-	-	-	-	none	-	-	-	-		IMPORTANT
Need for reintervention at >12 months - not measured												
0	-	-	-	-	-	none	-	-	-	-		IMPORTANT
Mean aortic valve gradient (valve degeneration - transvalvular gradient) at ≥12 months (follow-up mean 6 months; Better indicated by lower values)												
1	randomised trials	very serious[5]	no serious inconsistency	serious[2]	serious[4,6]	none	129	135	-	MD 1.5 higher (0.29 to 2.71 higher)	⊕OOO VERY LOW	IMPORTANT

[1] Downgraded by 1 increment as the majority of the evidence was at high risk of bias
[2] Anticoagulation includes a mixture of some receiving VKAs and some receiving DOACs, whereas ideally aimed to look at these groups separately
[3] Downgraded by 2 increments as the confidence interval crossed both MIDs
[4] Downgraded by 1 increment as the confidence interval crossed one MID
[5] Downgraded by 2 increments as the majority of the evidence was at very high risk of bias
[6] MIDs used to assess imprecision were ±2.55