F.2 Transcatheter valve implantation

			Quality as	sessment		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	s (follow-up 3-12 n	nonths)								
4	randomised trials		no serious inconsistency	no serious indirectness	very serious ²	none	29/541 (5.4%)		OR 0.94 (0.56 to 1.6) ³	3 fewer per 1000 (from 24 fewer to 31 more)	⊕OOO VERY LOW	CRITICAL
Health-rel	ated quality o	of life at ≤1	2 months - not me	easured								
0	-	-	-	_	-	none	-	-	-	-		CRITICAL

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Major ble	eding at ≤12 n	nonths (fo	llow-up 3-12 mon	ths)								
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 ble	eding at ≤12 n	nonths (fo	llow-up 6-12 mon	ths)			- -					
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 th	iromboemboli	ic events a	at ≤12 months (fol	low-up 3-6 month	ıs)							
3	randomised trials	serious ¹	no serious inconsistency	serious⁵	very serious ²	none	0/111 (0%)	4%	OR ranged from 0.21 to 2.24 ^{3,6}	-	⊕000 VERY LOW	CRITICAL
Stroke (aı	terial thrombo	oembolic	events) at 12 mon	ths (follow-up me	ean 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)	⊕000 VERY LOW	CRITICAL
Myocardia	al infarction (a	arterial thr	omboembolic eve	ents) at 12 month	s (follow-up mea	an 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 month	s - not measured		•							
0	-	-	-	-	-	none	-	-	-	-		CRITICAL
Health-rel	ated quality o	of life at >1	2 months - not m	easured								
0	-	-	-	-	-	none	-	-	-	-		CRITICAL
Major ble	eding at >12 n	nonths - n	ot measured									
0	-	-	-	-	-	none	_	-	-	-		CRITICAL
Minor ble	eding at >12 n	nonths - n	ot measured									

)	-	-	-	-	-	none	-	-	-	_		CRITICAL
rterial tl	nromboembol	ic events	at >12 months - n	ot measured								
I	-	-	-	-	-	none	-	-	-	-		CRITICAL
lospital	readmission a	at 12 mont	hs - not measured	I								
	-	-	-	-	-	none	-	-	-	-		IMPORTAN
Vithdraw	al due to adv	erse event	ts at 12 months - r	ot measured								
1	-	-	-	-	-	none	-	-	-	-		IMPORTAN
symptom	natic clinical a	ortic valve	e thrombosis (thro	mbus on imagin	g) at 12 months	(follow-up mean 1	2 month	s)				
	randomised trials	serious ¹	no serious inconsistency	no serious indirectness	very serious ²	none	3/331 (0.91%)		OR 2.76 (0.39 to 19.65)	5 more per 1000 (from 2 fewer to 53 more)	⊕OOO VERY LOW	IMPORTAN
leed for	reinterventior	n at 6-12 m	ionths - not meas	ured		•						
				1			1					
	-	-	-	-	-	none	-	-	-	-		IMPORTAN
leed for	-	- n at >12 m	- onths - not measu	- red	-	none	_	-	-	-		IMPORTAN
leed for	- reinterventior	- n at >12 m	- onths - not measu		-	none	-	-	-	- -		IMPORTAN
	_	_	_	_	- - ow-up mean 6 m		- - cated by	- - lower	- - values)	-		

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 ⁷MIDs used to assess imprecision were ±2.60

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

impian												
			Quality as	sessment			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% Cl)	Absolute	Quality	Importance
All-cause	mortality at	: ≤12 mon	ths - not measu	red								
0	-	-	-	-	-	none	-	-	-	-		CRITICAL
Health-re	lated quality	of life at	≤12 months - no	ot measured								
0	-	-	-	-	-	none	-	-	-	-		CRITICAL
Major ble	eding at ≤12	months	- not measured									
0	-	-	-	-	-	none	-	-	-	-		CRITICAL
Minor ble	eding at ≤12	2 months	- not measured							· · ·		
0	-	-	-	-	-	none	-	-	-	-		CRITICAL
Arterial tl	hromboemb	olic event	ts at ≤12 months	- not measured	d					· · ·		
0	-	-	-	-	-	none	-	-	-	-		CRITICAL
All-cause	mortality at	: >12 mon	ths - median tre	atment duration	n 428 days (fol	low-up median 4	28 days)					
	randomised trials			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-re	lated quality	of life at	>12 months - no	ot measured								

	-	-	-	-	-	none	-	-	-	-		CRITICA
or b	leeding at >12	2 months	- VARC-2 life-th	reatening, disa	bling or major	bleeding - media	an treatment 42	8 days (follow-up m	edian 428 da	ays)		
	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	CRITICA
jor b	leeding at >12	2 months	- BARC type 2,	3 or 5 bleeding	- median treat	ment 428 days (i	follow-up mean	428 days)				
	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	CRITICA
ajor b	leeding at >12	2 months	- ISTH major ble	eeding - mediar	n treatment 428	3 days (follow-up	o median 428 da	ays)				
	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	CRITICA
inor b	leeding at >12	2 months	- TIMI major or	minor bleeding	- median treat	ment 428 days (follow-up media	an 428 days)	•		· · · ·	
	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	CRITICA
roke	arterial throm	boembo	lic events) at >1	2 months - mec	lian treatment	428 days (follow	-up median 428	days)	•	•	•	
	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	CRITICA
yocar	dial infarction	(arterial	thromboemboli	c events) at >12	2 months - mee	lian treatment 42	28 days (follow	-up median 428 days	5)			
	randomised trials	very serious⁵	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)	⊕000 VERY LOW	CRITICA

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				r		1		1				
1	randomised trials	very serious⁵	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
Systemi	c embolism (arterial th	nromboembolic	events) at >12 ı	nonths- media	n treatment 428 c	lays (follow-uj	o median 428 days)				
1	randomised trials	very serious⁵	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	readmissior	at 12 mo	onths - not meas	ured	•	•				•		
0	-	-	-	-	-	none	-	-	-	-		IMPORTANT
	re study drug p median 42		inuation (withdr	awal due to adv	verse events -	thromboembolic,	bleeding or o	ther adverse events)	at 12 mont	hs - median treatr	ment duration	n 428 days
1	randomised trials	very serious⁵	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
Symptor	natic valve tl	nrombosi	s (thrombus on	imaging) at <12	2 months - med	lian treatment du	ration 428 day	rs (follow-up median	428 days)			
1	randomised trials	very serious¹	no serious inconsistency	no serious indirectness	very serious ⁴	none	3/826 (0.36%)	0.9%	OR 0.44 (0.13 to	5 fewer per 1000 (from 8 fewer to 5	⊕000 VERY LOW	IMPORTANT
									1.54)	more)		
Need for	· reinterventi	on at 6-12	2 months - not m	easured	1	1	<u> </u>		1.54)	more)		
	reinterventi	on at 6-12	2 months - not m	easured		none		-	-	more)		IMPORTANT
0	-	-	2 months - not m - months - not m	-		none	-	-	-			IMPORTANT
0	-	-	_	-	 	none	-	-				IMPORTANT
0 Need for 0	- reinterventio	- on at >12 -	_	easured	- - ths - not meas	none	-	-	-			

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 asse	ssment			No of pa	tients		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% Cl)	Absolute	Quanty	
All-cause	e mortality at	≤12 mon	ths (follow-up m	ean 12 month	s)							
1	randomised trials		no serious inconsistency		very serious³	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-re	lated quality	of life at	≤12 months - no	t measured								
0	-	-	-	-	-	none	-	-	-	-		CRITICAL
Major ble	eding at ≤12	months -	- VARC-2 life-thro	eatening, disa	abling or maj	or bleeding (majo	or bleeding) at 12 mon	ths (follow-up mea	an 12 month	s)		
1	randomised trials		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 ble	eding at ≤12	months -	- VARC-2 minor I	pleeding (min	or bleeding)	at 12 months (fo	llow-up mean 12 mont	hs)				
1	randomised trials		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 throm	boembol	ic events) at ≤12	months (follo	ow-up mean	12 months)						
1	randomised trials		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)	⊕000 VERY LOW	CRITICAL
Myocar	dial infarction	(arterial	thromboembolic	events) at ≤1	2 months (fe	ollow-up mean 12	months)					
1			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-caus	e mortality at	>12 mon	ths - not measur	ed								
0	-	-	-	-	-	none	-	-	-	-		CRITICAL
Health-r	elated quality	of life at	>12 months - no	t measured	I	I		ſ		Γ		
0	-	-	-	-	-	none	-	-	-	-		CRITICAL
Major b	leeding at >12	months	- not measured									
0	-	-	-	-	-	none	-	-	-	-		CRITICAL
Minor b	leeding at >12	months	- not measured									
0	-	-	-	-	-	none	-	-	-	-		CRITICAL
Arterial	thromboemb	olic event	s at >12 months	- not measur	ed							
0	_	-	-	_	_	none	-	-	-	-		CRITICAL
Hospita	l readmission	at 12 mo	nths - not measu	ired				ł				
0	-	-	-	-	-	none	-	_	-	_		IMPORTANT
Withdra	wal due to ad	verse eve	ents at 12 months	s - not measu	ired							
0	_	_	-	_	_	none	_	-	-	-		IMPORTANT

Thromb	Thrombus on imaging at <12 months - not measured														
0	-	-	-	-	-	none	-	_	-	-		IMPORTANT			
Need for	leed for reintervention at 6-12 months - not measured														
0	-	-	-	-	-	none	-	-	-	-		IMPORTANT			
Need for	leed for reintervention at >12 months - not measured														
0	-	-	-	-	-	none	-	-	-	-		IMPORTANT			
Mean ac	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 serious⁵	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