# Appendix 2: Forest plots and sensitivity analysis

#### 1. Recurrent non-fatal all stroke

	DAP	т	Aspir	in		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year	M-H, Random, 95% Cl
FASTER 2007	13	193	21	192	4.2%	0.62 [0.32, 1.19]	2007	
CHANCE 2013	209	2564	300	2570	64.6%	0.70 [0.59, 0.83]	2013	
POINT 2018	107	2381	150	2401	31.2%	0.72 [0.57, 0.92]	2018	
Total (95% CI)		5138		5163	100.0%	0.70 [0.61, 0.80]		◆
Total events	329		471					
Heterogeneity: Tau <sup>2</sup> =	0.00; Ch	i² = 0.1	9, df = 2 (	P = 0.9	1); l² = 09	6		
Test for overall effect:	Z= 5.16	(P < 0.0	00001)					Favours Clopidogrel and aspirin Favours Aspirin alone

Figure 1: Forest plot showing the risk of recurrent non-fatal all stroke between dual agent antiplatelet therapy and aspirin groups

### 2. Sensitivity Analysis: Recurrent non-fatal all stroke

	DAP	т	Aspir	rin		Risk Ratio			Ri	sk Ratio			
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year		M-H, Ra	ndom, 95	% CI		
FASTER 2007	15	201	21	195	4.4%	0.69 [0.37, 1.30]	2007			—			
CHANCE 2013	214	2584	302	2586	63.8%	0.71 [0.60, 0.84]	2013						
POINT 2018	114	2432	153	2449	31.8%	0.75 [0.59, 0.95]	2018			-			
Total (95% CI)		5217		5230	100.0%	0.72 [0.63, 0.82]			•				
Total events	343		476										
Heterogeneity: Tau <sup>2</sup> =	0.00; Ch	i² = 0.1	6, df = 2 (	P = 0.9	2); I <sup>2</sup> = 09	6				-	1		
Test for overall effect:	Z= 4.82	(P < 0.0	00001)					0.1 0.2 Favours Clopi	0.5 dogrel and aspir	in Favou	z Irs Aspirin a	alone	10

Figure 2: Forest plot showing the risk of recurrent non-fatal all stroke between dual agent antiplatelet therapy and aspirin groups after adjusting for missing data

## 3. Non-fatal ischemic stroke

	DAP	Т	Aspir	rin		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year	M-H, Random, 95% Cl
FASTER 2007	12	193	21	192	4.0%	0.57 [0.29, 1.12]	2007	
CHANCE 2013	203	2564	293	2570	64.1%	0.69 [0.59, 0.82]	2013	
POINT 2018	106	2381	151	2401	31.9%	0.71 [0.56, 0.90]	2018	
Total (95% CI)		5138		5163	100.0%	0.69 [0.60, 0.79]		•
Total events	321		465					
Heterogeneity: Tau² = Test for overall effect				P = 0.8	4); I² = 09	6		0.1 0.2 0.5 1 2 5 10 Favours Clopidogrel and aspirin Favours Aspirin alone

Figure 3: Forest plot showing the risk of non-fatal ischemic stroke between dual agent antiplatelet therapy and aspirin groups

#### 4. Sensitivity Analysis: Non-fatal ischemic stroke

	DAP	т	Aspir	rin		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year	ar M-H, Random, 95% Cl
FASTER 2007	13	201	21	195	4.1%	0.60 [0.31, 1.17]	2007	7
CHANCE 2013	208	2584	295	2586	63.5%	0.71 [0.60, 0.84]	2013	3 🗕
POINT 2018	113	2432	154	2449	32.4%	0.74 [0.58, 0.94]	2018	8
Total (95% CI)		5217		5230	100.0%	0.71 [0.62, 0.81]		◆
Total events	334		470					
Heterogeneity: Tau <sup>2</sup> =	0.00; Ch	i <sup>z</sup> = 0.3i	6, df = 2 (	P = 0.8	4); l <sup>2</sup> = 09	6		
Test for overall effect:	Z=4.96	(P < 0.0	0001)					0.1 0.2 0.5 1 2 5 10 Favours Clopidogrel and aspirin Favours Aspirin alone

Figure 4: Forest plot showing the risk of non-fatal ischemic stroke between dual agent antiplatelet therapy and aspirin groups after adjusting for missing data

# 5. Symptomatic non-fatal intracranial hemorrhage

	DAP	т	Aspir	rin		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year	ar M-H, Random, 95% Cl
FASTER 2007	1	193	0	192	6.7%	2.98 [0.12, 72.81]	2007	• • • • • • • • • • • • • • • • • • • •
CHANCE 2013	6	2564	7	2570	57.6%	0.86 [0.29, 2.55]	2013	3
POINT 2018	6	2381	3	2401	35.7%	2.02 [0.50, 8.05]	2018	8
Total (95% CI)		5138		5163	100.0%	1.27 [0.55, 2.89]		-
Total events	13		10					
Heterogeneity: Tau <sup>2</sup> =	0.00; Ch	i² = 1.2	D, df = 2 (	P = 0.5	5); I <sup>2</sup> = 09	6		
Test for overall effect:	Z = 0.56	(P = 0.5	i8)					Favours Clopidogrel and aspirin Favours Aspirin alone

Figure 5: Forest plot showing the risk of symptomatic non-fatal intracranial hemorrhage between dual agent antiplatelet therapy and aspirin groups

6. All-caus	se mortali	ity			
	DAPT	Aspirin		Risk Ratio	Risk Ratio
Study or Subgroup	Events Total	Events Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
CHANCE 2013	10 2564	10 2570	40.9%	1.00 [0.42, 2.40]	
POINT 2018	18 2276	12 2280	59.1%	1.50 [0.73, 3.11]	_ <b>+∎</b>
Total (95% CI)	4840	4850	100.0%	1.27 [0.73, 2.23]	<b>•</b>
Total events	28	22			
Heterogeneity: Tau <sup>2</sup>	= 0.00; Chi <sup>2</sup> = 0.4	9, df = 1 (P = 0.4	9); I <sup>z</sup> = 09	6	
Test for overall effec	t: Z = 0.85 (P = 0.4	40)			Favours Clopidogrel and aspirin Favours Aspirin alone

Figure 6: Forest plot showing the risk of all-cause mortality between dual agent antiplatelet therapy and aspirin groups

## 7. Moderate or major non-fatal extracranial hemorrhage

	DAP	т	Aspir	rin		Risk Ratio				<b>Risk Ratio</b>		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	Year		N	I-H, Fixed, 95% C	1	
FASTER 2007	3	193	0	192	3.2%	6.96 [0.36, 133.92]	2007				•	
CHANCE 2013	7	2564	8	2570	51.6%	0.88 [0.32, 2.42]	2013					
POINT 2018	16	2276	7	2280	45.2%	2.29 [0.94, 5.56]	2018					
Total (95% CI)		5033		5042	100.0%	1.71 [0.92, 3.20]				•		
Total events	26		15									
Heterogeneity: Chi <sup>2</sup> =	: 2.95, df =	2 (P =	0.23); l² =	= 32%				0.01	0.1		10	100
Test for overall effect	: Z = 1.68	(P = 0.0	)9)							aspirin Favours		100

Figure 7: Forest plot showing the risk of moderate or major non-fatal extracranial hemorrhage between dual agent antiplatelet therapy and aspirin groups after adjusting for missing data

8. Non-fatal functional disability measured using modified Rankin Scale (mRS: 2-5)

	DAP	Т	Aspir	in		Risk Ratio	F	lisk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, R	andom, 95%	CI	
CHANCE 2013	244	2564	289	2570	45.1%	0.85 [0.72, 0.99]	_	-		
POINT 2018	306	2276	323	2280	54.9%	0.95 [0.82, 1.10]				
Total (95% CI)		4840		4850	100.0%	0.90 [0.81, 1.01]		◆		
Total events	550		612							
Heterogeneity: Tau <sup>2</sup> :				P = 0.3	0); I <sup>z</sup> = 79	6	 0.5	1	2	5
Test for overall effect	: Z = 1.82	(P = 0.0	)7)				 pidogrel and asp	irin Eavours	aspirin alon	ie U

Figure 8: Forest plot showing the risk of non-fatal functional disability measure by modified Rankin Scale (mRS: 2-5) between dual agent antiplatelet therapy and aspirin groups

#### 9. Recurrent TIA

	DAP	т	Aspir	in		Risk Ratio		F	Risk Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl		M-H, R	andom, 9	5% CI	
CHANCE 2013	39	2564	47	2570	31.1%	0.83 [0.55, 1.27]					
POINT 2018	89	2381	96	2401	68.9%	0.93 [0.70, 1.24]		-	-		
Total (95% CI)		4945		4971	100.0%	0.90 [0.71, 1.14]		-	•		
Total events	128		143								
Heterogeneity: Tau <sup>2</sup>				P = 0.6	5); I² = 09	6	0.2	0.5	1	2	5
Test for overall effec	t: Z = 0.87	(P = 0.3	(9)				Favours clopid	ogrel and asp	irin Favo	urs aspirin	alone

Figure 7: Forest plot showing the risk of recurrent TIA between dual agent antiplatelet therapy and aspirin groups

#### 10. Mild extracranial bleeding defined by individual studies

	DAP	т	Aspir	rin		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year	M-H, Random, 95% Cl
FASTER 2007	62	193	27	192	48.1%	2.28 [1.52, 3.43]	2007	
CHANCE 2013	30	2564	19	2570	27.9%	1.58 [0.89, 2.80]	2013	+ <b>-</b>
POINT 2018	40	2276	13	2280	24.1%	3.08 [1.65, 5.75]	2018	<b>−•</b> −
Total (95% CI)		5033		5042	100.0%	2.22 [1.60, 3.08]		•
Total events	132		59					
Heterogeneity: Tau <sup>2</sup> = Test for overall effect				(P = 0.3	i0); I² = 18	1%		0.01 0.1 1 10 100 Favours clopidogrel and aspirin Favours aspirin alone

\*Footnote: The POINT 2018 study includes asymptomatic intracranial hemorrhage (5 and 2 in DAPT and aspirin alone group respectively)

Figure 10: Forest plot showing the risk of mild extracranial bleeding defined by individual studies between dual agent antiplatelet therapy and aspirin groups after adjusting for missing data

## 11. Sensitivity Analysis: Mild extracranial bleeding defined by individual studies

	DAP	т	Aspir	in		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year	M-H, Random, 95% Cl
FASTER 2007	65	201	28	195	50.9%	2.25 [1.51, 3.35]	2007	
CHANCE 2013	30	2584	19	2586	24.5%	1.58 [0.89, 2.80]	2013	+
POINT 2018	43	2432	16	2449	24.6%	2.71 [1.53, 4.79]	2018	
Total (95% CI)		5217		5230	100.0%	2.16 [1.63, 2.87]		◆
Total events	138		63					
Heterogeneity: Tau² =	0.00; Ch	i <sup>z</sup> = 1.7	9, df = 2 (	P = 0.4	1); l² = 0%	6		
Test for overall effect:	Z = 5.33	(P < 0.0	00001)					Favours [experimental] Favours [control]

Figure 11: Forest plot showing the risk of mild extracranial bleeding defined by individual studies between dual agent antiplatelet therapy and aspirin groups after adjusting for missing data

#### 12. Myocardial infarction

	DAP	т	Aspir	in		Risk Ratio	Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
CHANCE 2013	3	2564	2	2570	22.5%	1.50 [0.25, 8.99]	
POINT 2018	10	2276	7	2280	77.5%	1.43 [0.55, 3.75]	
Total (95% CI)		4840		4850	100.0%	1.45 [0.62, 3.38]	-
Total events	13		9				
Heterogeneity: Tau <sup>2</sup> =				P = 0.9	6); I <sup>z</sup> = 09	6	
Test for overall effect:	Z = 0.85 (	(P = 0.3	39)				Favours clopidogrel and aspirin Favours aspirin alone

Figure 12: Forest plot showing the risk of myocardial infarction between dual agent antiplatelet therapy and aspirin groups (low quality evidence due to serious imprecision)

#### 13. All recurrent stroke (fatal and non-fatal)

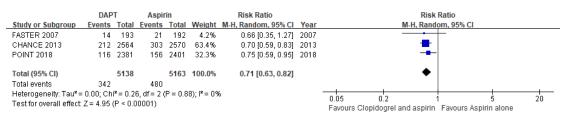


Figure 13: Forest plot showing the risk of all recurrent stroke between dual agent antiplatelet therapy and aspirin groups

#### 14. Sensitivity Analysis: All recurrent stroke (fatal and non-fatal)

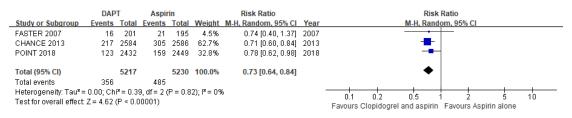


Figure 14: Forest plot showing the risk of all recurrent stroke between dual agent antiplatelet therapy and aspirin groups after adjusting for missing data