Appendix 2: Forest plots and sensitivity analysis

1.   Recurrent non-fatal all stroke

Study or Subgroup	DAPT Events	Total	Aspirin Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
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: Tau² = 0.00; Chi² = 0.19, df = 2 (P = 0.91); I² = 0%
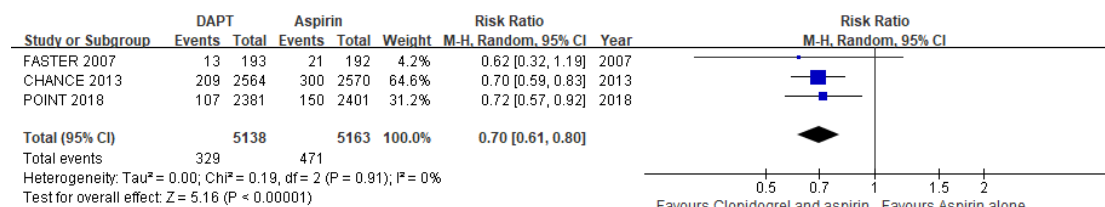Test for overall effect: Z = 5.16 (P < 0.00001)

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

Study or Subgroup	DAPT Events	Total	Aspirin Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
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: Tau² = 0.00; Chi² = 0.16, df = 2 (P = 0.92); I² = 0%
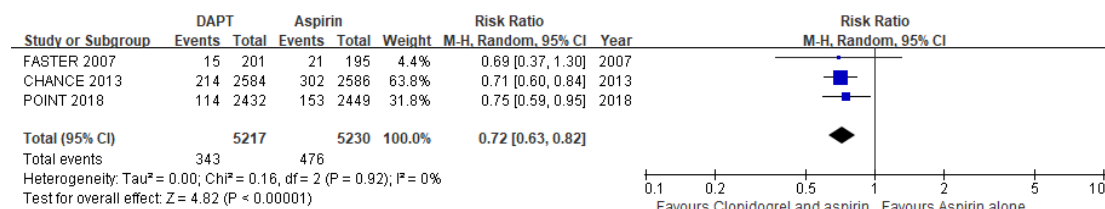Test for overall effect: Z = 4.82 (P < 0.00001)

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

Study or Subgroup	DAPT Events	Total	Aspirin Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
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 = 0.00; Chi² = 0.36, df = 2 (P = 0.84); I² = 0%
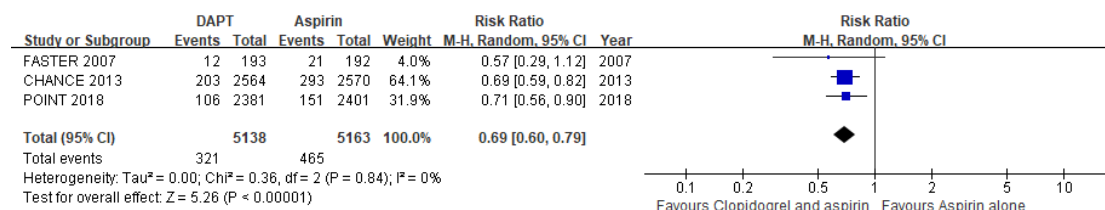Test for overall effect: Z = 5.26 (P < 0.00001)

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

Study or Subgroup	DAPT Events	Total	Aspirin Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
FASTER 2007	13	201	21	195	4.1%	0.60 [0.31, 1.17]	2007
CHANCE 2013	208	2584	295	2586	63.5%	0.71 [0.60, 0.84]	2013
POINT 2018	113	2432	154	2449	32.4%	0.74 [0.58, 0.94]	2018
Total (95% CI)		**5217**		**5230**	**100.0%**	**0.71 [0.62, 0.81]**	
Total events	334		470				

Heterogeneity: Tau² = 0.00; Chi² = 0.36, df = 2 (P = 0.84); I² = 0%
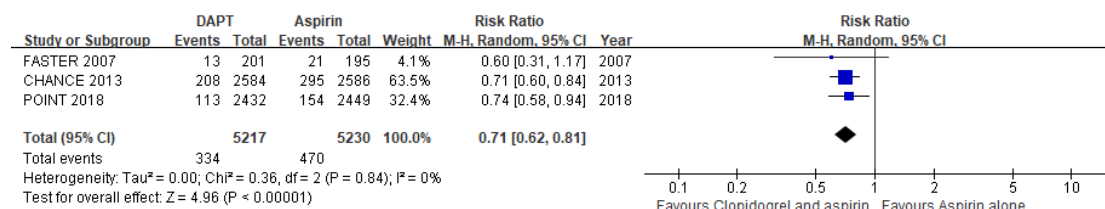Test for overall effect: Z = 4.96 (P < 0.00001)

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

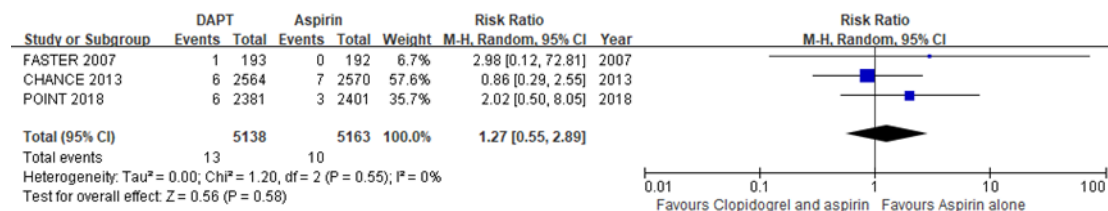Figure 5: Forest plot showing the risk of symptomatic non-fatal intracranial hemorrhage between dual agent antiplatelet therapy and aspirin groups
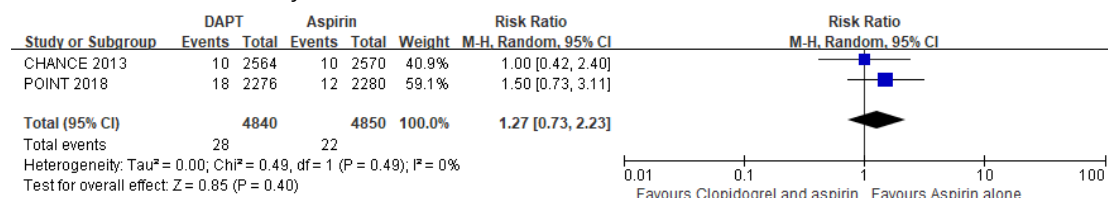
6. All-cause mortality

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

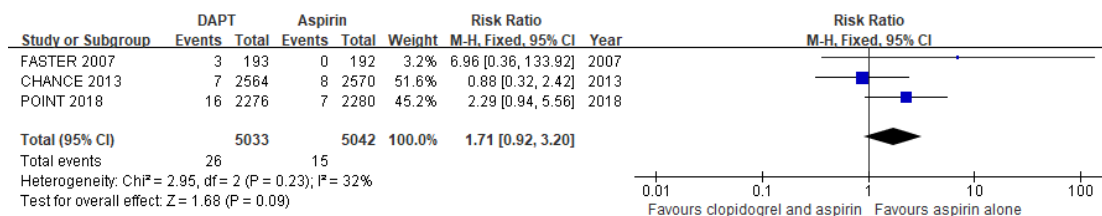## 7. Moderate or major non-fatal extracranial hemorrhage

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)
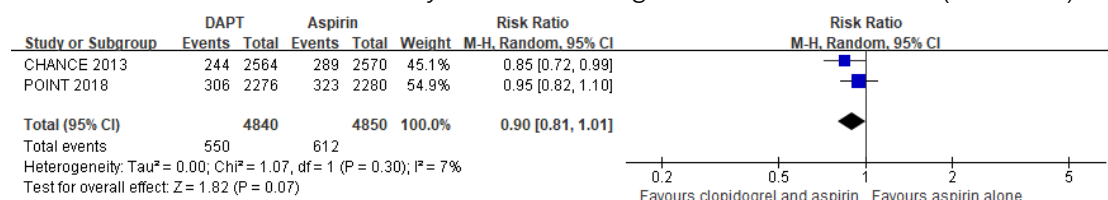

Figure 8: Forest plot showing the risk of non-fatal functional disability measure by modified Rankin Scale (mRS: 2-5) between dual agent antiplatelet therapy and aspirin groups

9. Recurrent TIA

Study or Subgroup	DAPT Events	DAPT Total	Aspirin Events	Aspirin Total	Weight	Risk Ratio M-H, Random, 95% 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: Tau² = 0.00; Chi² = 0.20, df = 1 (P = 0.65); I² = 0%
Test for overall effect: Z = 0.87 (P = 0.39)

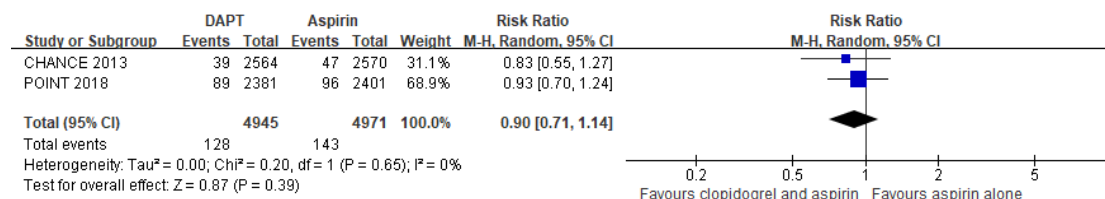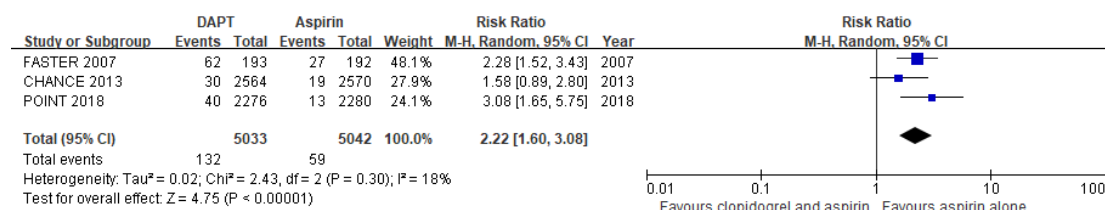Favours clopidogrel and aspirin   Favours aspirin alone

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

Study or Subgroup	DAPT Events	DAPT Total	Aspirin Events	Aspirin Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
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
POINT 2018	40	2276	13	2280	24.1%	3.08 [1.65, 5.75]	2018
Total (95% CI)		**5033**		**5042**	**100.0%**	**2.22 [1.60, 3.08]**	
Total events	132		59				

Heterogeneity: Tau² = 0.02; Chi² = 2.43, df = 2 (P = 0.30); I² = 18%
Test for overall effect: Z = 4.75 (P < 0.00001)

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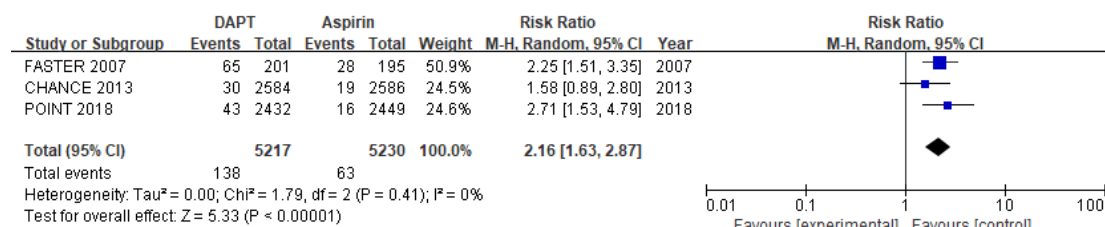
Figure 10: Forest plot showing the risk of mild extracranial bleeding defined by individual studies between dual agent antiplatelet therapy and aspirin groups after adjusting for missing data

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

Study or Subgroup	DAPT Events	DAPT Total	Aspirin Events	Aspirin Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
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; Chi² = 1.79, df = 2 (P = 0.41); I² = 0%
Test for overall effect: Z = 5.33 (P < 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

Study or Subgroup	DAPT Events	DAPT Total	Aspirin Events	Aspirin Total	Weight	Risk Ratio M-H, Random, 95% CI
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: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.96); I² = 0%
Test for overall effect: Z = 0.85 (P = 0.39)

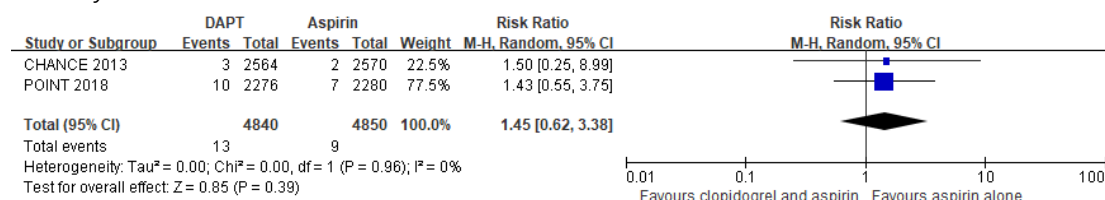Favours clopidogrel and aspirin   Favours aspirin alone

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)

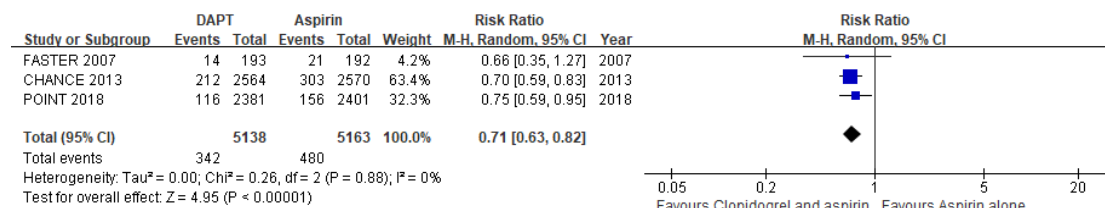## 13. All recurrent stroke (fatal and non-fatal)

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

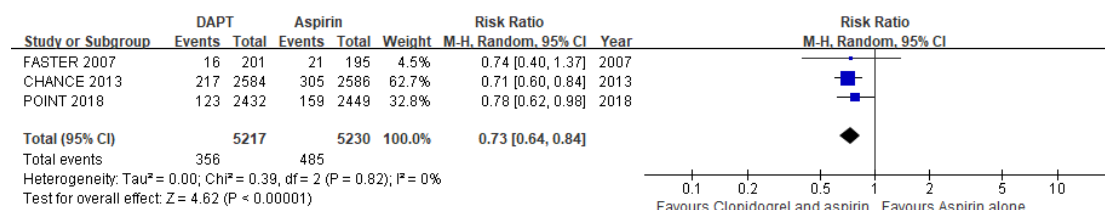## 14. Sensitivity Analysis: All recurrent stroke (fatal and non-fatal)

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