Figure e-1. Incidence rates of major bleeding per antiplatelet regimen (pooled estimates)

Aspirin

Time period	Events	Person-years					Inci	idence Rate [95% CI]
0-30 d	17	664		· -				2.77 [1.72 , 4.45]
31-90 d	26	1277		⊢	+			2.08 [1.42 , 3.05]
91-180 d	22	1830	H	-				1.47 [0.86 , 2.52]
181-365 d	59	3526	H	-	—			1.65 [0.80 , 3.41]
>365 d	129	8875		⊢				1.46 [0.97 , 2.19]
			0.00	2.00	4.00	6.00	8.00	
				Pooled IF	R per 100 per	son-years		

Clopidogrel

Time period	Events	Person-years					Inci	idence Rate [95% CI]
0-30 d	32	1315		├				2.50 [1.76 , 3.53]
31-90 d	46	2505		-	4			1.88 [1.17 , 3.02]
91-180 d	53	3557		⊢				1.48 [1.06 , 2.08]
181-365 d	101	6899		⊢				1.39 [1.04 , 1.87]
>365 d	196	15149		H■H				1.30 [1.13 , 1.49]
				1	T	ı		
			0.00	2.00	4.00	6.00	8.00	
				Pooled IF	R per 100 per	son-years		

Aspirin + Dipyridamole

Time period	Events	Person-years					Inci	dence Rate [95% CI]
0-30 d	47	1000		1		•	-	4.94 [2.79 , 8.73]
31-90 d	41	1787	⊢			——		1.69 [0.47 , 6.06]
91-180 d	41	2482		⊢ ■				1.66 [1.22 , 2.25]
181-365 d	66	4745	⊢	-	—			1.43 [0.63 , 3.26]
>365 d	191	13652	-	-				1.20 [0.72 , 2.01]
				T	T	T		
			0.00	2.00	4.00	6.00	8.00	
				Pooled I	R per 100 per	son-years		

Aspirin + Clopidogrel

Time period	Events	Person-years					Inci	dence Rate [95% CI]
0-30 d	27	468			-		-	5.84 [4.01 , 8.52]
31-90 d	26	894		⊢				2.93 [1.91 , 4.50]
91-180 d	39	1266	⊢				—►	2.26 [0.57 , 8.93]
181-365 d	58	2438		⊢-	-			2.39 [1.84 , 3.09]
>365 d	7 5	3400		⊢	\dashv			2.25 [1.49 , 3.41]
				T				
			0.00	2.00	4.00	6.00	8.00	
				Pooled IF	R per 100 per	son-years		

Dipyridamole

Time period	Events	Person-years					Inci	dence Rate [95% CI]
0-30 d	2	124	<u> </u>					1.61 [0.20 , 5.83]
31-90 d	4	217	<u> </u>					1.84 [0.50 , 4.72]
91-180 d	5	293	⊢		——			1.71 [0.55 , 3.98]
181-365 d	5	546	⊢					0.92 [0.30 , 2.14]
>365 d	5	994	⊢■	-				0.50 [0.16 , 1.17]
				ı	T	ı		
			0.00	2.00	4.00	6.00	8.00	
				IR pe	r 100 person-	years		

Time period	Events	Person-years					Inci	dence Rate [95% CI]	
0-30 d	5	123		——			-	4.07 [1.32 , 9.49]	
31-90 d	2	229	⊢		-			0.87 [0.11 , 3.15]	
91-180 d	6	319	—					1.88 [0.69 , 4.09]	
181-365 d	6	603	\vdash	■——				1.00 [0.37 , 2.17]	
>365 d	6	1082	⊢■-	\dashv				0.55 [0.20 , 1.21]	
				ı	ı	T			
			0.00	2.00	4.00	6.00	8.00		
			IR per 100 person-years						

Figure e-2. Incidence rates of major bleeding on aspirin, per trial

Aspirin, CAPRIE

Time period	Events	Person-years					Inc	idence Rate [95% CI]
0-30 d	9	252		ı				3.57 [1.63 , 6.78]
31-90 d	12	483		-				2.48 [1.28 , 4.34]
91-180 d	12	688	ı	-	-			1.74 [0.90 , 3.05]
181-365 d	15	1328	⊢	-				1.13 [0.63 , 1.86]
>365 d	54	2540		⊢∎─				2.13 [1.60 , 2.77]
					T			
			0.00	2.00	4.00	6.00	8.00	
				Incidence R	ate per 100 p	erson years		

Aspirin, ESPS-2

Time period	Events	Person-years					Inci	dence Rate [95% CI]
0-30 d	3	125	⊢				I	2.40 [0.49 , 7.01]
31-90 d	5	235	-			1		2.13 [0.69 , 4.97]
91-180 d	6	331	⊢					1.81 [0.67 , 3.95]
181-365 d	25	620		—				4.03 [2.61 , 5.95]
>365 d	21	1112		⊢				1.89 [1.17 , 2.89]
				T	T			
			0.00	2.00	4.00	6.00	8.00	
				Incidence R	ate per 100 p	erson years		

Aspirin, CHARISMA

Time period	Events	Person-years					Inci	dence Rate [95% CI]
0-30 d	4	174	⊢					2.30 [0.63 , 5.89]
31-90 d	5	337	-		—			1.48 [0.48 , 3.46]
91-180 d	0	485	■					0.00 [0.00 , 0.76]
181-365 d	10	954	-	•—				1.05 [0.50 , 1.93]
>365 d	25	2104	-					1.19 [0.77 , 1.75]
					T	T		
			0.00	2.00	4.00	6.00	8.00	
				Incidence R	ate per 100 p	erson years		

Aspirin, ESPRIT

Time period	Events	Person-years					Inci	idence Rate [95% CI]
0-30 d	1	112	-			ı		0.89 [0.02 , 4.97]
31-90 d	4	222	-					1.80 [0.49 , 4.61]
91-180 d	4	327		-	⊣			1.22 [0.33 , 3.13]
181-365 d	9	624	-					1.44 [0.66 , 2.74]
>365 d	29	3119	H	\vdash				0.93 [0.62 , 1.34]
				T	ı	ı		
			0.00	2.00	4.00	6.00	8.00	
				Incidence R	ate per 100 p	erson years		

Figure e-3. Incidence rates of major bleeding on clopidogrel, per trial

Clopidogrel, CAPRIE

Time period	Events	Person-years					Inci	idence Rate [95% CI]
0-30 d	4	254	_					1.57 [0.43 , 4.03]
31-90 d	14	486		-				2.88 [1.57 , 4.83]
91-180 d	11	689	-					1.60 [0.80 , 2.86]
181-365 d	16	1340	-	■				1.19 [0.68 , 1.94]
>365 d	33	2537	ı	-				1.30 [0.90 , 1.83]
					T			
			0.00	2.00	4.00	6.00	8.00	
				Incidence R	ate per 100 p	erson years		

Clopidogrel, MATCH

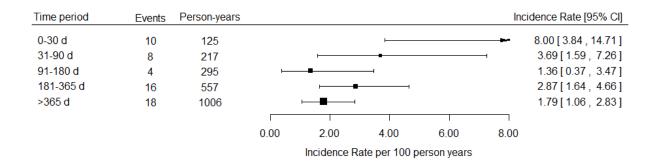
Time period	Events	Person-years					Inci	idence Rate [95% CI]
0-30 d	6	295	-					2.03 [0.75 , 4.43]
31-90 d	6	565	-					1.06 [0.39 , 2.31]
91-180 d	7	805	⊢-					0.87 [0.35 , 1.79]
181-365 d	17	1552	—	■ ──				1.10 [0.64 , 1.75]
>365 d	23	1419		⊢ ■				1.62 [1.03 , 2.43]
				Т	Т	Т		
			0.00	2.00	4.00	6.00	8.00	
				Incidence R	ate per 100 p	erson years		

Clopidogrel, PRoFESS

Time period	Events	Person-years					Inci	dence Rate [95% CI]
0-30 d	22	767						2.87 [1.80 , 4.34]
31-90 d	26	1454		⊢				1.79 [1.17 , 2.62]
91-180 d	35	2064		⊢ ■				1.70 [1.18 , 2.36]
181-365 d	68	4007		⊢ ■				1.70 [1.32 , 2.15]
>365 d	140	11194		₽				1.25 [1.05 , 1.48]
					1			
			0.00	2.00	4.00	6.00	8.00	
				Incidence R	ate per 100 p	erson years		

Figure e-4. Incidence rates of major bleeding on aspirin + dipyridamole, per trial

Aspirin + Dipyridamole, ESPS-2



Aspirin + Dipyridamole, ESPRIT

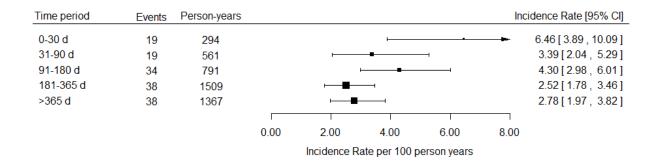
Time period	Events	Person-years					Inci	idence Rate [95% CI]
0-30 d	2	111	-					1.80 [0.22 , 6.51]
31-90 d	0	199	•					0.00 [0.00 , 1.85]
91-180 d	4	274	<u> </u>					1.46 [0.40 , 3.74]
181-365 d	1	504	H II	-				0.20 [0.01 , 1.11]
>365 d	15	2473	⊢	ı				0.61 [0.34 , 1.00]
				T	Т	T		
			0.00	2.00	4.00	6.00	8.00	
				Incidence R	ate per 100 p	erson years		

Aspirin + Dipyridamole, PRoFESS

Time period	Events	Person-years					Inci	dence Rate [95% CI]
0-30 d	35	764			-			4.58 [3.19 , 6.37]
31-90 d	33	1372		-	_			2.41 [1.66 , 3.38]
91-180 d	33	1913		─				1.73 [1.19 , 2.42]
181-365 d	49	3684		⊢ ■				1.33 [0.98 , 1.76]
>365 d	158	10173		H ⊞ ⊣				1.55 [1.32 , 1.82]
				T	T	ı		
			0.00	2.00	4.00	6.00	8.00	
				Incidence R	ate per 100 p	erson years		

Figure e-5. Incidence rates of major bleeding on aspirin + clopidogrel, per trial

Aspirin + Clopidogrel, MATCH



Aspirin + Clopidogrel, CHARISMA

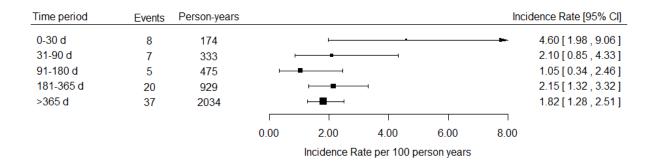
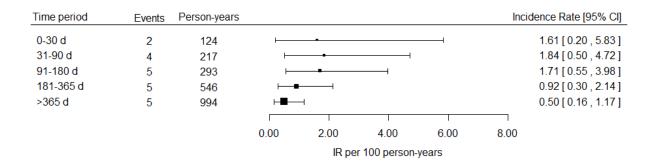


Figure e-6. Incidence rates of major bleeding on dipyridamole and placebo

Dipyridamole



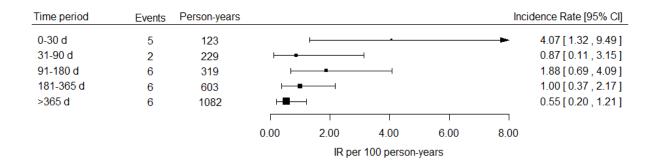


Figure e-7. Incidence rates of gastro-intestinal bleeding per antiplatelet regimen (pooled)

Aspirin

Time period	Events	Person-years					Inci	idence Rate [95% CI]
0-30 d	8	664	⊢					1.30 [0.65 , 2.61]
31-90 d	7	1279						0.70 [0.34 , 1.44]
91-180 d	10	1834		—				0.69 [0.37 , 1.25]
181-365 d	27	3538	⊢					0.80 [0.44 , 1.44]
>365 d	53	8942						0.61 [0.45 , 0.84]
					T	T		
			0.00	2.00	4.00	6.00	8.00	
				Incidence R	ate per 100 p	erson years		

Clopidogrel

Time period	Events	Person-years					Inci	dence Rate [95% CI]
0-30 d	18	1316	-	- ,				1.09 [0.41 , 2.90]
31-90 d	24	2508	-					0.94 [0.47 , 1.89]
91-180 d	22	3565	-	-				0.50 [0.20 , 1.25]
181-365 d	36	6923	■-					0.52 [0.38 , 0.73]
>365 d	93	15263		-				0.60 [0.34 , 1.07]
				Т	T	T		
			0.00	2.00	4.00	6.00	8.00	
				Incidence R	ate per 100 p	erson years		

Aspirin + Dipyridamole

Time period	Events	Person-years					Inci	dence Rate [95% CI]
0-30 d	31	1000		<u> </u>				3.18 [2.24 , 4.53]
31-90 d	22	1790		_				1.33 [0.88 , 2.01]
91-180 d	18	2487	H	→				0.72 [0.46 , 1.15]
181-365 d	22	4763	⊢■—	<u> </u>				0.54 [0.20 , 1.47]
>365 d	85	13757		⊣				0.54 [0.26 , 1.13]
					T	1		
			0.00	2.00	4.00	6.00	8.00	
				Incidence R	ate per 100 p	erson years		

Aspirin + Clopidogrel

Time period	Events	Person-years					Inci	idence Rate [95% CI]
0-30 d	18	468						3.92 [2.47 , 6.23]
31-90 d	17	895		-				1.90 [1.06 , 3.43]
91-180 d	21	1268	—					1.49 [0.61 , 3.64]
181-365 d	28	2446	-	■				1.16 [0.80 , 1.68]
>365 d	45	3421	-					1.34 [0.87 , 2.07]
					Т	1		
			0.00	2.00	4.00	6.00	8.00	
				Incidence R	ate per 100 p	erson vears		

Dipyridamole

Time period	Events	Person-years					Inci	idence Rate [95% CI]
0-30 d	0	124	-		ı			0.00 [0.00 , 2.97]
31-90 d	2	217			—			0.92 [0.11 , 3.33]
91-180 d	1	294		—				0.34 [0.01 , 1.90]
181-365 d	1	549	-	ı				0.18 [0.00 , 1.01]
>365 d	2	1000	-					0.20 [0.02 , 0.72]
						1		
			0.00	2.00	4.00	6.00	8.00	
				Incidence R	ate per 100 p	erson years		

Time period	Events	Person-years					Inci	dence Rate [95% CI]
0-30 d	1	123						0.81 [0.02 , 4.53]
31-90 d	0	229	-					0.00 [0.00 , 1.61]
91-180 d	2	320	-					0.62 [0.08 , 2.26]
181-365 d	2	606	-	-				0.33 [0.04 , 1.19]
>365 d	2	1089						0.18 [0.02 , 0.66]
				T	Т	T		
			0.00	2.00	4.00	6.00	8.00	
				Incidence R	ate per 100 p	erson years		

Figure e-8. Incidence rates of intracranial bleeding per antiplatelet regimen (pooled)

Aspirin

Time period	Events	Person-years		Incidence Rate [95% CI]
0-30 d	4	664		0.84 [0.35 , 2.01]
31-90 d	6	1279	———	0.64 [0.28 , 1.45]
91-180 d	3	1835	⊦≣	0.21 [0.07 , 0.60]
181-365 d	13	3542	H 	0.42 [0.24 , 0.72]
>365 d	39	8954	⊢■	0.40 [0.18 , 0.88]
			0.00 1.00 2.00	
			Incidence Rate per 100 person years	

Clopidogrel

Time period	Events	Person-years		Incidence Rate [95% CI]
0-30 d	2	1316	—	0.23 [0.07 , 0.72]
31-90 d	8	2511	· · · · · · · · · · · · · · · · · · ·	0.41 [0.13 , 1.26]
91-180 d	15	3570		0.46 [0.24 , 0.89]
181-365 d	23	6937	⊢ ■──	0.33 [0.19 , 0.57]
>365 d	49	15303	■-	0.32 [0.25 , 0.43]
			0.00 1.00 2.00	
			Incidence Rate per 100 person years	

Aspirin + Dipyridamole

Time period	Events	Person-years		Incidence Rate [95% CI]
0-30 d	10	1001		1.09 [0.59 , 1.99]
31-90 d	9	1792	□■	0.59 [0.32 , 1.10]
91-180 d	12	2491		0.53 [0.30 , 0.92]
181-365 d	22	4772	⊢■	0.50 [0.33 , 0.75]
>365 d	59	13818	-■	0.35 [0.19 , 0.64]
			0.00 1.00 2.00	
			Incidence Rate per 100 person years	

Aspirin + Clopidogrel

Time period	Events	Person-years		Incidence Rate [95% CI]
0-30 d	2	468	⊢ ■	0.44 [0.11 , 1.77]
31-90 d	4	897	·	0.46 [0.17 , 1.23]
91-180 d	9	1270		0.51 [0.06 , 4.62]
181-365 d	12	2451	⊢■	0.51 [0.29 , 0.90]
>365 d	11	3440	- -	0.33 [0.18 , 0.60]
			0.00 1.00 2.00	
			Incidence Rate per 100 person years	

Dipyridamole

Time period	Events	Person-years		Incidence Rate [95% CI]
0-30 d	0	124		0.00 [0.00 , 2.97]
31-90 d	1	217	└──	0.46 [0.01 , 2.57]
91-180 d	1	293	· · · · · · · · · · · · · · · · · · ·	0.34 [0.01 , 1.90]
181-365 d	2	549	·	0.36 [0.04 , 1.32]
>365 d	0	998		0.00 [0.00 , 0.37]
			0.00 1.00 2.00	
			Incidence Rate per 100 person years	

Time period	Events	Person-years		Incidence Rate [95% CI]
0-30 d	2	123		1.63 [0.20 , 5.87]
31-90 d	0	229	■	0.00 [0.00 , 1.61]
91-180 d	1	321	-	0.31 [0.01 , 1.74]
181-365 d	1	607	⊢ ■	0.16 [0.00 , 0.92]
>365 d	4	1088	· -	0.37 [0.10 , 0.94]
			0.00 1.00 2.00	
			Incidence Rate per 100 person years	

Figure e-9. Time course of major bleeding by age group

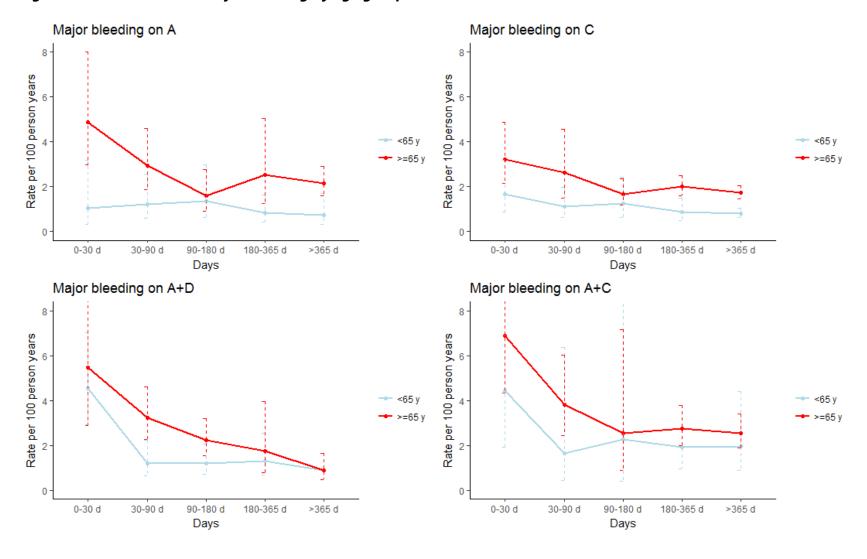
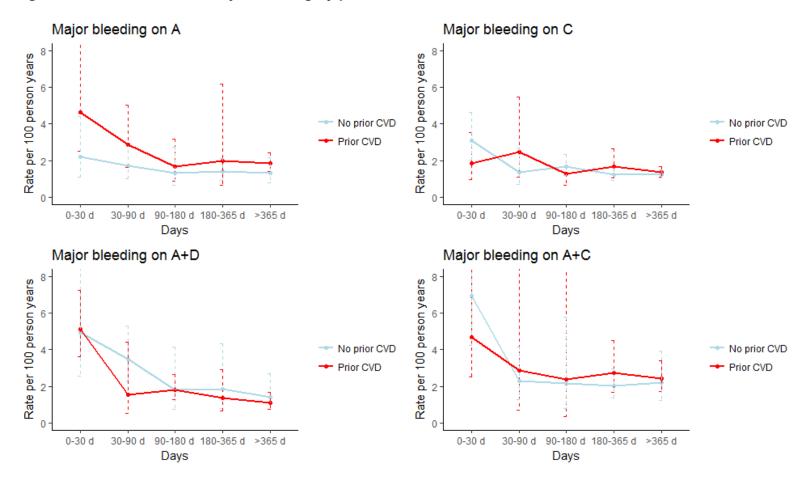


Figure e-10. Time course of major bleeding by prior cardiovascular disease status



CVD: cardiovascular disease