MTA REPORT ERRATUM 1

LIVERPOOL REVIEWS AND IMPLEMENTATION GROUP (LRiG)

Prasugrel with percutaneous coronary intervention for treating acute coronary syndromes (review of TA182)

Erratum 1

This report was commissioned by the NIHR HTA Programme as project number 12/62/01

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DOES NOT CONTAIN CIC/AIC

UNIVERSITY OF LIVERPOOL

LIVERPOOL REVIEWS AND IMPLEMENTATION GROUP

A MEMBER OF THE RUSSELL GROUP

This document is intended to replace Section 6.4 of the original AG report for prasugrel with percutaneous coronary intervention for treating acute coronary syndromes (review of TA182). The original report contained an error in the calculation of the PSA.

6.4 Independent economic assessment: Results

Results from the AG's model are presented separately for each of the four patient subgroups that were previously considered by the Appraisal Committee when formulating NICE guidance TA182.[21]

For each subgroup, detailed deterministic cost-effectiveness estimates are presented across a range of time periods, namely 1, 5, 10, 20 and 40 years after the index PCI. Univariate sensitivity analysis is presented for the 40 years follow-up scenario. Probabilistic cost-effectiveness results are presented for 5 and 40 years follow-up, with a scatterplot of random replications and a cost-effectiveness acceptability curve (CEAC) for the 40 years follow-up scenario.

6.4.1 STEMI - diabetes subgroup

Deterministic results are detailed in Table 1 (life years), Table 2 (QALYs), Table 3 (costs) and Table 4 (ICERs). The ICER at the end of the first year is high, due to the inclusion of the full additional cost of treatment with prasugrel, whilst only modest health gains have accrued from the reduced incidence of MIs. Over time the estimated ICER decreases steadily, suggesting that incremental benefit continues to accrue over subsequent decades whilst incremental cost increases at a slower rate. The ICER for prasugrel compared with clopidogrel falls below £30,000 per QALY gained after 5 years.

Figure 1 displays the results of univariate sensitivity analysis, indicating that uncertainty from individual model parameters has a modest influence on the magnitude of the ICER in this subgroup: the discount rates for costs and outcomes cause the largest changes, but the ICER remains within the range £1,000 to £2,500 per QALY gained.

Probabilistic analysis at the 40 year follow-up horizon for this subgroup yields a higher estimated ICER (£1,732 per QALY gained) derived from small incremental cost and QALY estimates (+£515 and +0.297 respectively). The scatterplot (Figure 2) and CEAC for this subgroup (Figure 3) indicate the relative cost effectiveness of prasugrel despite the long-term erosion of incremental differences over time.

Table 1 Mean deterministic estimated life years for STEMI patients with diabetes

Follow-up	Mean time in health state				Life years	
Treatment	Event free	MI(s) only	Mild stroke(s) +/- MI(s)	Severe stroke(s) +/- MI(s)	Total	Total discounted
1 year						
Clopidogrel	0.923	0.054	0.003	0.001	0.981	0.981
Prasugrel	0.950	0.031	0.004	0.002	0.986	0.986
Difference	+0.027	-0.024	+0.001	+0.001	+0.005	+0.005
5 years						
Clopidogrel	3.953	0.557	0.066	0.037	4.612	4.320
Prasugrel	4.171	0.397	0.073	0.040	4.681	4.383
Difference	+0.218	-0.160	+0.007	+0.004	+0.069	+0.063
10 years						
Clopidogrel	6.865	1.250	0.234	0.134	8.483	7.375
Prasugrel	7.268	1.010	0.238	0.137	8.653	7.517
Difference	+0.403	-0.241	+0.005	+0.002	+0.170	+0.142
20 years						
Clopidogrel	10.429	2.339	0.640	0.373	13.780	10.664
Prasugrel	11.059	2.067	0.643	0.372	14.141	10.924
Difference	+0.630	-0.272	+0.003	-0.001	+0.361	+0.260
40 years						
Clopidogrel	12.151	2.894	0.925	0.529	16.499	11.823
Prasugrel	12.890	2.637	0.936	0.530	16.994	12.140
Difference	+0.739	-0.257	+0.012	+0.001	+0.495	+0.316

Table 2 Mean deterministic estimated QALYs for STEMI patients with diabetes

Follow-up	Mean QALYs in health state				Event disutility (QALYs)			QALYs	
Treatment	Event free	MI(s) only	Mild stroke +/- MI(s)	Severe stroke +/- MI(s)	MI	Stroke	Death	Total	Total dis-counted
1 year									
Clopidogrel	0.837	0.049	0.002	0.001	-0.005	0.000	-0.003	0.882	0.882
Prasugrel	0.861	0.028	0.004	0.001	-0.003	0.000	-0.002	0.889	0.889
Difference	+0.024	-0.021	+0.001	0.000	+0.002	0.000	+0.001	+0.007	+0.007
5 years									
Clopidogrel	3.554	0.500	0.056	0.019	-0.011	-0.001	-0.011	4.104	3.846
Prasugrel	3.750	0.356	0.062	0.021	-0.009	-0.001	-0.011	4.168	3.904
Difference	+0.196	-0.144	+0.006	+0.002	+0.003	0.000	+0.001	+0.064	+0.059
10 years									
Clopidogrel	6.108	1.108	0.197	0.066	-0.020	-0.003	-0.022	7.434	6.475
Prasugrel	6.467	0.893	0.201	0.067	-0.017	-0.002	-0.022	7.587	6.603
Difference	+0.358	-0.215	+0.004	+0.001	+0.003	0.000	0.000	+0.153	+0.129
20 years									
Clopidogrel	9.126	2.029	0.525	0.175	-0.036	-0.006	-0.043	11.768	9.171
Prasugrel	9.676	1.787	0.528	0.175	-0.033	-0.006	-0.044	12.083	9.400
Difference	+0.550	-0.241	+0.003	+0.000	+0.003	0.000	0.000	+0.314	+0.228
40 years									
Clopidogrel	10.499	2.473	0.742	0.240	-0.046	-0.009	-0.070	13.828	10.054
Prasugrel	11.136	2.243	0.751	0.241	-0.044	-0.008	-0.072	14.247	10.326
Difference	+0.637	-0.229	+0.009	+0.001	+0.003	0.000	-0.002	+0.419	+0.272

QALY=quality adjusted life year

Table 3 Mean deterministic estimated costs for STEMI patients with diabetes

Follow-up	Drug costs	Mean costs in health state				Event costs			Cost	
Treatment		Event free	MI(s) only	Mild stroke +/- MI(s)	Severe stroke +/- MI(s)	MI	Stroke	Death	Total	Total dis-counted
1 year										
Clopidogrel	29	570	33	5	8	683	68	69	1465	1465
Prasugrel	533	587	19	7	12	386	101	51	1695	1695
Difference	+503	+16	-15	+3	+4	-297	+33	-18	+230	+230
5 years										
Clopidogrel	68	2443	344	119	204	1529	838	272	5817	5454
Prasugrel	572	2578	245	131	224	1169	915	257	6090	5723
Difference	+504	+135	-99	+13	+20	-361	+77	-16	+273	+269
10 years										
Clopidogrel	110	4243	773	422	744	2543	2589	528	11951	10277
Prasugrel	615	4492	624	430	756	2149	2646	519	12231	10552
Difference	+505	+249	-149	+9	+12	-394	+56	-9	-280	+275
20 years										
Clopidogrel	166	6446	1445	1154	2063	4040	6523	1041	22878	17013
Prasugrel	673	6835	1277	1160	2060	3651	6580	1050	23287	17363
Difference	+507	+389	-168	+6	-3	-390	+58	+9	+409	+351
40 years										
Clopidogrel	195	7510	1789	1668	2930	4801	9129	1681	29702	19904
Prasugrel	704	7966	1630	1689	2938	4437	9259	1723	30345	20351
Difference	+508	+457	-159	+21	+8	-364	+130	+42	+643	+447

Table 4 Mean deterministic ICER for STEMI patients with diabetes

Follow-up	Total cost		Total QALYs		Incremental		ICER (£ per QALY)
	Clopidogrel	Prasugrel	Clopidogrel	Prasugrel	Cost	QALYs	
1 year	£1,465	£1,695	0.882	0.889	+£230	+0.007	£31,915
5 years	£5,454	£5,723	3.846	3.904	+£269	+0.059	£4,603
10 years	£10,277	£10,552	6.475	6.603	+£275	+0.129	£2,139
20 years	£17,013	£17,363	9.171	9.400	+£350	+0.228	£1,537
40 years	£19,904	£20,351	10.054	10.326	+£447	+0.272	£1,640

ICER=incremental cost-effectiveness ratio; QALY=quality adjusted life year

Figure 1 Univariate sensitivity analysis: 20 most important parameters in determining the ICER for STEMI patients with diabetes

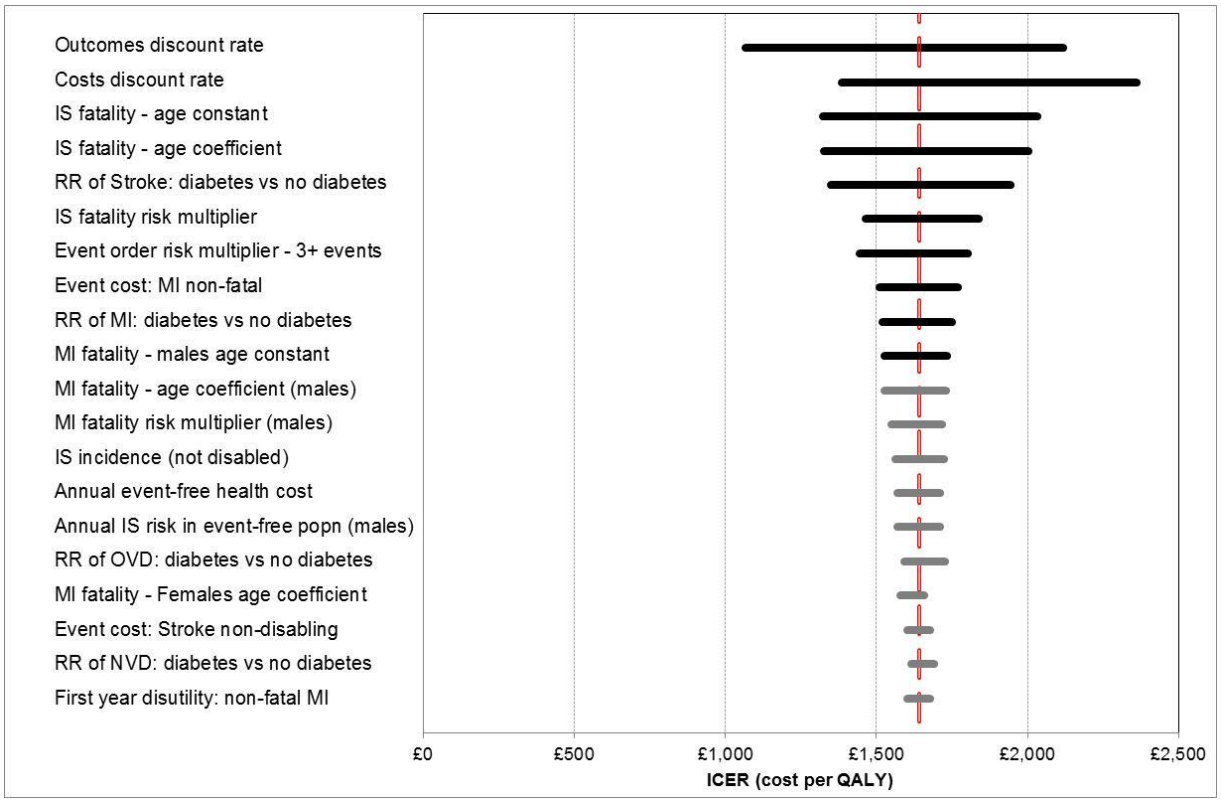


Figure 2 PSA scatterplot of prasugrel vs clopidogrel for STEMI patients with diabetes

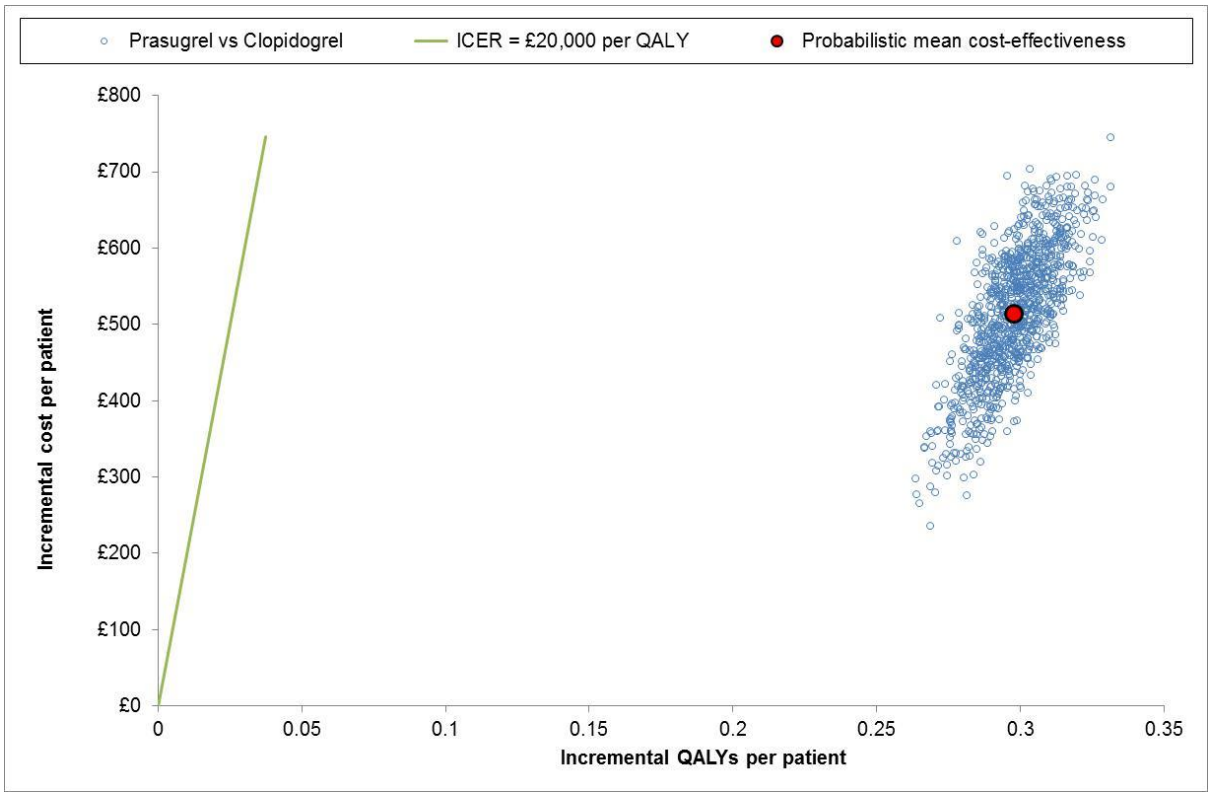
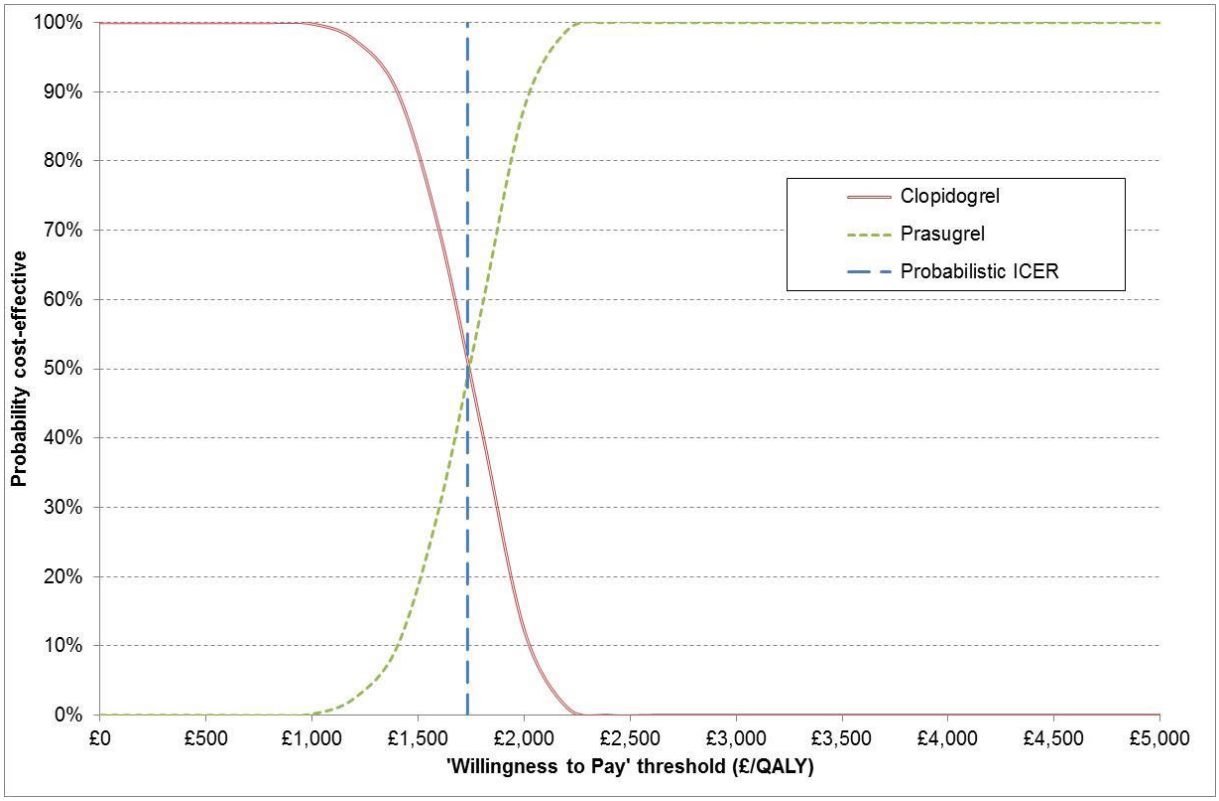


Figure 3 CEAC of prasugrel vs clopidogrel for STEMI patients with diabetes



6.4.2 STEMI - no diabetes subgroup

Deterministic results are detailed in Table 5 (life years),

Table 6 (QALYs), Table 7(costs) and Table 8 (ICERs). The ICER at the end of the first year is high, due to the inclusion of the full additional cost of treatment with prasugrel, whilst only modest health gains have accrued from the reduced incidence of MIs. Over time the estimated ICER decreases steadily, suggesting that incremental benefit continues to accrue over subsequent decades whilst incremental cost increases at a slower rate. The ICER for prasugrel compared with clopidogrel falls below £30,000 per QALY gained at 10 years.

Figure 4 displays the results of univariate sensitivity analyses, which indicate that uncertainty from the discounting rate for outcomes has the largest impact on the estimated ICER (ranging between £4,000 and £9,000 per QALY gained). Other individual model parameters have only a modest influence on the magnitude of the ICER in this subgroup.

Probabilistic analysis at the 40 year follow-up horizon for this subgroup yields a higher estimated ICER (£7,073 per QALY gained) derived from small incremental cost and QALY

estimates (+£609 and +0.086 respectively). The scatterplot (Figure 5) and CEAC for this subgroup (Figure 6) indicate the relative cost effectiveness of prasugrel despite the long-term erosion of incremental differences over time.

Table 5 Mean deterministic estimated life years for STEMI patients without diabetes

Follow-up	Mean time in health state				Life years	
Treatment	Event free	MI(s) only	Mild stroke(s) +/- MI(s)	Severe stroke(s) +/- MI(s)	Total	Total discounted
1 year						
Clopidogrel	0.951	0.037	0.001	0.001	0.990	0.990
Prasugrel	0.960	0.029	0.002	0.001	0.992	0.992
Difference	+0.008	-0.008	+0.001	0.000	+0.001	+0.001
5 years						
Clopidogrel	4.201	0.439	0.050	0.028	4.717	4.417
Prasugrel	4.269	0.382	0.055	0.031	4.736	4.434
Difference	+0.068	-0.057	+0.005	+0.003	+0.019	+0.017
10 years						

Clopidogrel	7.364	1.095	0.200	0.115	8.775	7.617
Prasugrel	7.491	1.008	0.205	0.118	8.823	7.657
Difference	+0.127	-0.087	+0.005	+0.003	+0.048	+0.040
20 years						
Clopidogrel	11.363	2.272	0.612	0.360	14.607	11.230
Prasugrel	11.564	2.171	0.617	0.363	14.714	11.307
Difference	+0.201	-0.101	+0.005	+0.002	+0.107	+0.076
40 years						
Clopidogrel	13.585	3.012	0.971	0.565	18.133	12.711
Prasugrel	13.827	2.916	0.979	0.568	18.291	12.808
Difference	+0.242	-0.096	+0.008	+0.003	+0.158	+0.097

Table 6 Mean deterministic estimated QALYs for STEMI patients without diabetes

Follow-up	Mean QALYs in health state				Event disutility (QALYs)			QALYs	
Treatment	Event free	MI(s) only	Mild stroke +/- MI(s)	Severe stroke +/- MI(s)	MI	Stroke	Death	Total	Total dis-counted
1 year									
Clopidogrel	0.874	0.034	0.001	0.000	-0.003	0.000	-0.002	0.905	0.905
Prasugrel	0.882	0.026	0.002	0.001	-0.002	0.000	-0.001	0.907	0.907
Difference	+0.008	-0.008	+0.001	+0.000	+0.001	0.000	-0.000	+0.002	+0.002
5 years									
Clopidogrel	3.825	0.398	0.044	0.015	-0.009	-0.001	-0.009	4.262	3.992
Prasugrel	3.887	0.347	0.048	0.016	-0.008	-0.001	-0.009	4.279	4.008
Difference	+0.062	-0.052	+0.004	+0.001	+0.001	0.000	0.000	+0.017	+0.016
10 years									
Clopidogrel	6.636	0.982	0.172	0.059	-0.018	-0.002	-0.019	7.809	6.792
Prasugrel	6.751	0.903	0.177	0.060	-0.017	-0.002	-0.019	7.852	6.828
Difference	+0.114	-0.079	+0.005	+0.002	+0.001	0.000	0.000	+0.043	+0.036
20 years									
Clopidogrel	10.067	1.990	0.512	0.175	-0.034	-0.005	-0.040	12.664	9.805
Prasugrel	10.245	1.899	0.516	0.176	-0.033	-0.005	-0.040	12.758	9.872
Difference	+0.178	-0.091	+0.005	+0.001	+0.001	0.000	0.000	+0.094	+0.067
40 years									
Clopidogrel	11.861	2.588	0.791	0.263	-0.047	-0.009	-0.069	15.378	10.950
Prasugrel	12.072	2.502	0.798	0.265	-0.046	-0.009	-0.070	15.512	11.033
Difference	+0.211	-0.087	+0.007	+0.002	+0.001	0.000	-0.001	+0.133	+0.084

QALY=quality adjusted life year

Table 7 Mean deterministic estimated costs for STEMI patients without diabetes

Follow-up	Drug costs	Mean costs in health state				Event costs			Cost	
Treatment		Event free	MI(s) only	Mild stroke +/- MI(s)	Severe stroke +/- MI(s)	MI	Stroke	Death	Total	Total dis-counted
1 year										
Clopidogrel	29	588	23	2	4	463	36	37	1183	1183
Prasugrel	533	593	18	3	6	360	59	33	1605	1605
Difference	+503	+5	-5	+1	+2	-103	+22	-4	+422	+422
5 years										
Clopidogrel	69	2596	271	91	155	1263	725	228	5398	5045
Prasugrel	573	2638	236	99	170	1137	790	224	5867	5510
Difference	+503	+42	-35	+8	+15	-126	+65	-4	+468	+465
10 years										
Clopidogrel	113	4551	677	361	637	2293	2517	469	11617	9931
Prasugrel	616	4630	623	370	654	2153	2595	466	12108	10414
Difference	+504	+78	-54	+9	+17	-139	+78	-2	+490	+482
20 years										
Clopidogrel	175	7022	1404	1104	1994	3951	7095	957	23702	17354
Prasugrel	679	7147	1342	1113	2008	3810	7192	959	24249	17870
Difference	+504	+124	-63	+9	+13	-141	+96	+3	+546	+515
40 years										
Clopidogrel	213	8396	1861	1752	3129	4967	10868	1664	32850	21167
Prasugrel	718	8546	1802	1767	3146	4836	11002	1678	33493	21722
Difference	+505	+150	-59	+15	+17	-132	+134	+13	+643	+555

Table 8 Mean deterministic ICER for STEMI patients without diabetes

Follow-up	Total cost		Total QALYs		Incremental		ICER (£ per QALY)
	Clopidogrel	Prasugrel	Clopidogrel	Prasugrel	Cost	QALYs	
1 year	£1,183	£1,605	0.905	0.907	+£422	+0.002	£224,302
5 years	£5,044	£5,510	3.992	4.008	+£465	+0.016	£29,607
10 years	£9,931	£10,414	6.792	6.828	+£482	+0.036	£13,370
20 years	£17,354	£17,870	9.805	9.872	+£516	+0.067	£7,670
40 years	£21,167	£21,722	10.950	11.033	+£555	+0.084	£6,626

ICER=incremental cost-effectiveness ratio; QALY=quality adjusted life year

Figure 4 Univariate sensitivity analysis: 20 most important parameters in determining the ICER for STEMI patients without diabetes

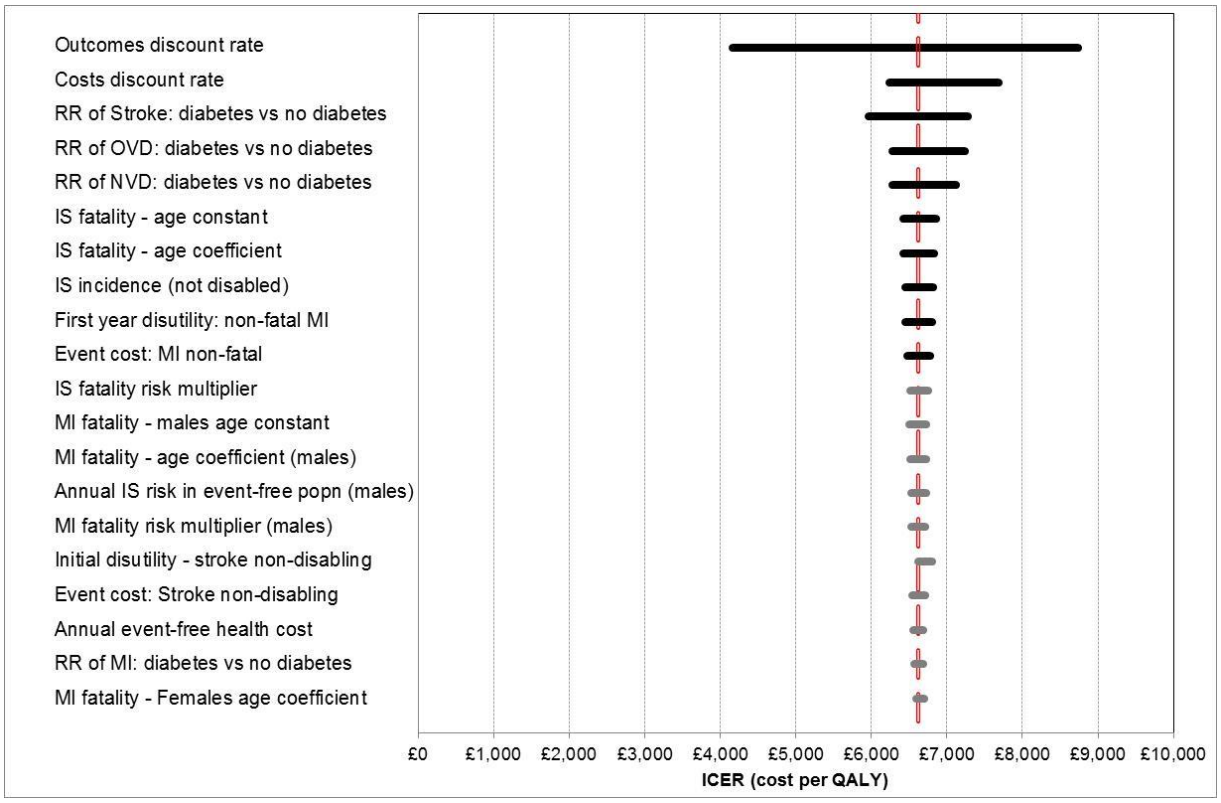


Figure 5 PSA scatterplot of prasugrel vs clopidogrel for STEMI patients without diabetes

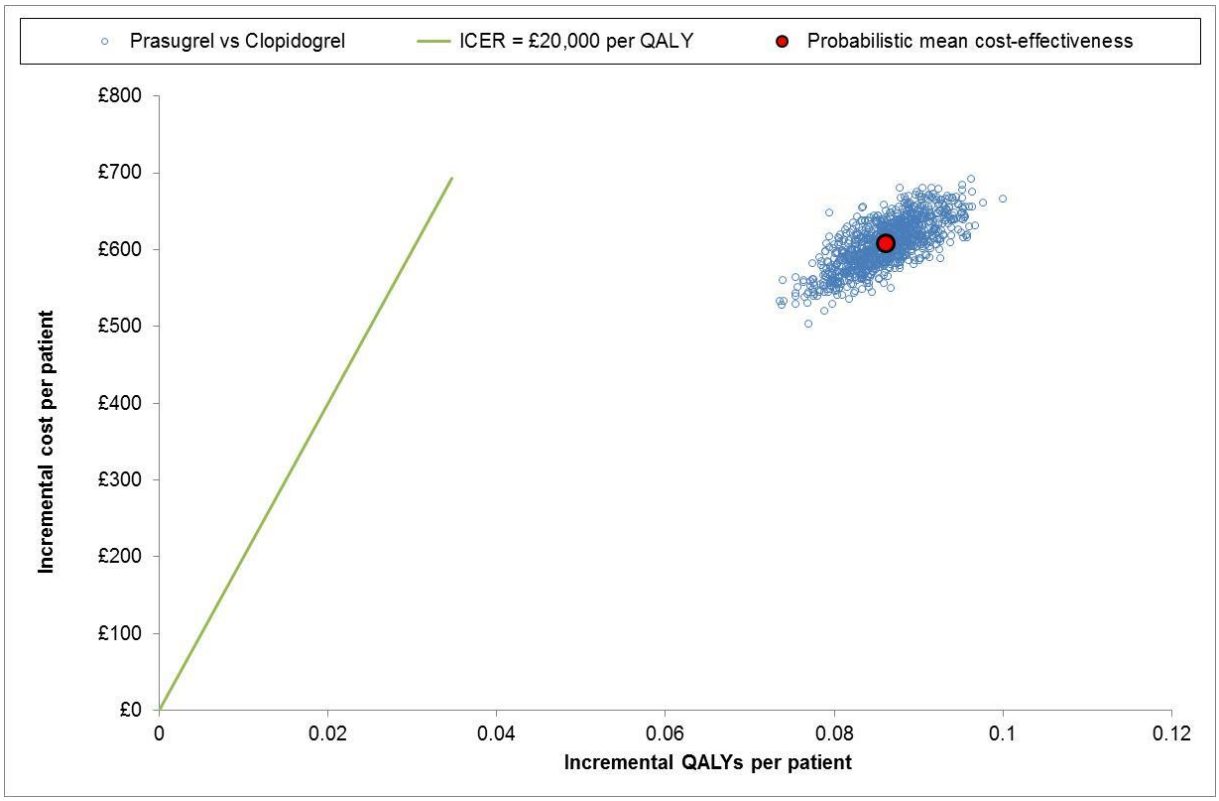
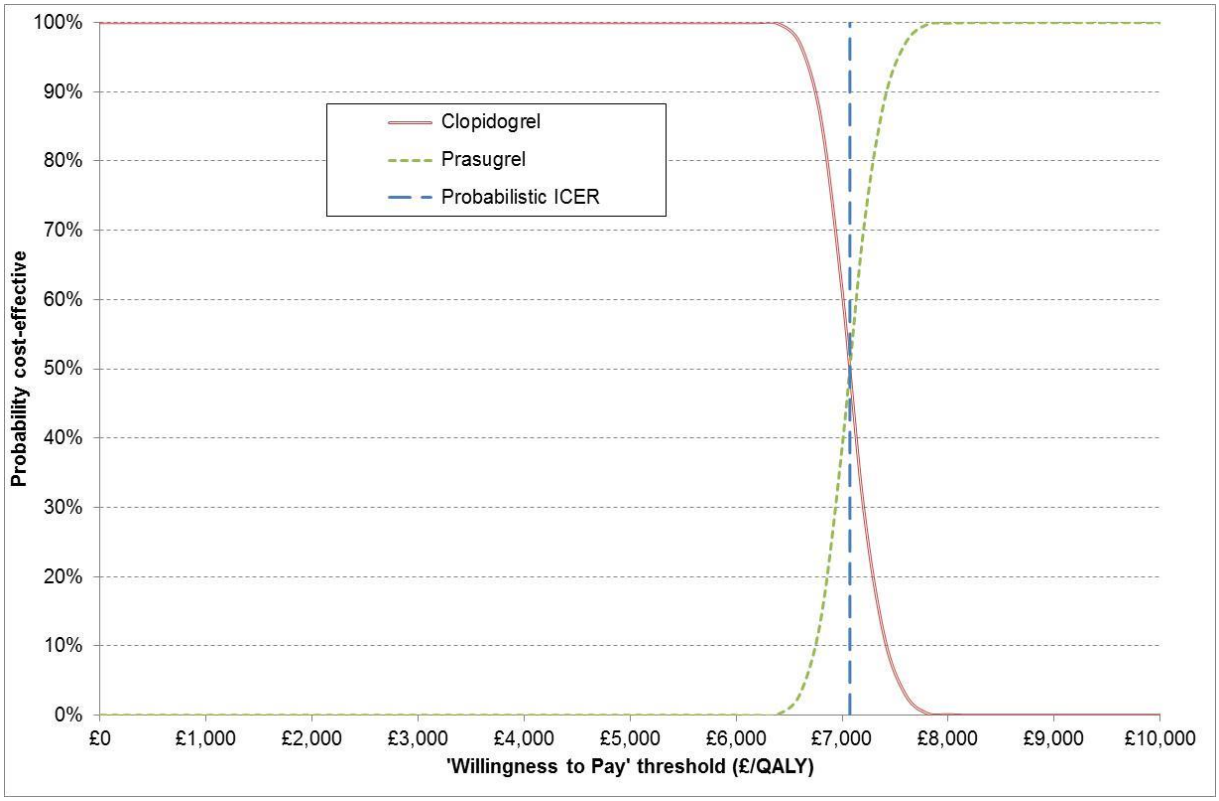


Figure 6 CEAC of prasugrel vs clopidogrel for STEMI patients without diabetes



6.4.3 UA/NSTEMI - diabetes subgroup

Deterministic results are detailed in Table 9 (life years), Table 10 (QALYs),

Table 11 (costs) and Table 12 (ICERs). The ICER at the end of the first year is high, due to the inclusion of the full additional cost of treatment with prasugrel, whilst only modest health gains have accrued from the reduced incidence of MIs. Over time the estimated ICER decreases steadily, suggesting that incremental benefit continues to accrue over subsequent decades whilst incremental cost increases at a slower rate. The ICER for prasugrel compared with clopidogrel falls below £30,000 per QALY gained after 5 years.

Figure 7 displays the results of univariate sensitivity analyses, which indicate that uncertainty from event incidence and fatality rates have the largest effect on the estimated ICER (ranging between -£1,000 and +£400 per QALY gained). Other individual model parameters have only a modest influence on the magnitude of the ICER in this subgroup.

Probabilistic analysis at the 40 year follow-up horizon for this subgroup confirms that prasugrel dominates clopidogrel with a small net cost saving and positive incremental benefit (-£120 and +0.191 respectively). The scatterplot (Figure 8) and CEAC for this subgroup

(Figure 9) indicate the cost effectiveness of prasugrel despite the long-term erosion of incremental differences over time.

Table 9 Mean deterministic estimated life years for UA/NSTEMI patients with diabetes

Follow-up	Mean time in health state				Life years	
Treatment	Event free	MI(s) only	Mild stroke(s) +/- MI(s)	Severe stroke(s) +/- MI(s)	Total	Total discounted
1 year						
Clopidogrel	0.934	0.048	0.003	0.002	0.987	0.987
Prasugrel	0.954	0.031	0.002	0.001	0.989	0.989
Difference	+0.020	-0.017	-0.001	-0.000	+0.002	+0.002
5 years						
Clopidogrel	4.032	0.513	0.071	0.040	4.656	4.361
Prasugrel	4.198	0.400	0.060	0.035	4.692	4.394
Difference	+0.166	-0.113	-0.012	-0.005	+0.036	+0.033
10 years						
Clopidogrel	6.986	1.172	0.242	0.139	8.540	7.426
Prasugrel	7.291	1.004	0.060	0.126	8.639	7.508
Difference	+0.305	-0.168	-0.012	-0.013	+0.099	+0.083
20 years						
Clopidogrel	10.536	2.202	0.645	0.371	13.754	10.667
Prasugrel	11.009	2.015	0.606	0.349	13.980	10.827
Difference	+0.473	-0.186	-0.038	-0.022	+0.226	+0.161
40 years						
Clopidogrel	12.127	2.690	0.907	0.510	16.233	11.733
Prasugrel	12.675	2.515	0.870	0.487	16.547	11.930
Difference	+0.548	-0.176	-0.037	-0.023	+0.313	+0.197

Table 10 Mean deterministic estimated QALYs for UA/NSTEMI patients with diabetes

Follow-up	Mean QALYs in health state				Event disutility (QALYs)			QALYs	
Treatment	Event free	MI(s) only	Mild stroke +/- MI(s)	Severe stroke +/- MI(s)	MI	Stroke	Death	Total	Total dis-counted
1 year									
Clopidogrel	0.842	0.043	0.003	0.001	-0.004	0.000	-0.002	0.883	0.883
Prasugrel	0.860	0.028	0.002	0.001	-0.003	0.000	-0.002	0.887	0.887
Difference	+0.018	-0.015	-0.001	0.000	+0.001	0.000	0.000	+0.003	+0.003
5 years									
Clopidogrel	3.602	0.457	0.061	0.020	-0.011	-0.001	-0.011	4.118	3.858
Prasugrel	3.750	0.356	0.050	0.017	-0.009	-0.001	-0.011	4.154	3.892
Difference	+0.148	-0.101	-0.010	-0.003	+0.002	0.000	0.000	+0.037	+0.034
10 years									
Clopidogrel	6.178	1.032	0.202	0.067	-0.020	-0.002	-0.022	7.434	6.477
Prasugrel	6.447	0.883	0.181	0.061	-0.017	-0.002	-0.022	7.530	6.557
Difference	+0.270	-0.149	-0.021	-0.006	+0.002	0.000	0.000	+0.095	+0.080
20 years									
Clopidogrel	9.164	1.897	0.522	0.171	-0.035	-0.006	-0.045	11.668	9.114
Prasugrel	9.575	1.733	0.490	0.160	-0.033	-0.006	-0.045	11.874	9.261
Difference	+0.411	-0.165	-0.032	-0.011	+0.002	0.000	0.000	+0.205	+0.147
40 years									
Clopidogrel	10.426	2.285	0.719	0.227	-0.044	-0.009	-0.071	13.533	9.919
Prasugrel	10.896	2.129	0.688	0.216	-0.042	-0.008	-0.072	13.806	10.095
Difference	+0.470	-0.156	-0.031	-0.011	+0.002	0.000	-0.002	+0.273	+0.176

QALY=quality adjusted life year

Table 11 Mean deterministic estimated costs for UA/NSTEMI patients with diabetes

Follow-up	Drug costs	Mean costs in health state				Event costs			Cost	
Treatment		Event free	MI(s) only	Mild stroke +/- MI(s)	Severe stroke +/- MI(s)	MI	Stroke	Death	Total	Total dis-counted
1 year										
Clopidogrel	29	577	30	6	10	603	80	47	1383	1383
Prasugrel	533	590	19	4	8	393	52	43	1642	1642
Difference	+503	+13	-10	-2	-3	-210	-27	-4	+259	+259
5 years										
Clopidogrel	69	2492	317	129	222	1436	829	262	5755	5391
Prasugrel	572	2594	247	107	195	1171	691	259	5837	5487
Difference	+504	+103	-70	-21	-27	-265	-138	-3	+82	+96
10 years										
Clopidogrel	110	4318	724	437	770	2421	2430	533	11743	10102
Prasugrel	614	4506	621	392	698	2129	2149	535	11644	10054
Difference	+504	+189	-104	-46	-72	-292	-281	+1	-99	-47
20 years										
Clopidogrel	166	6512	1361	1163	2055	3848	5891	1075	22071	16476
Prasugrel	672	6804	1246	1094	1933	3557	5478	1090	21872	16362
Difference	+506	+292	-115	-69	-122	-292	-413	+15	-199	-114
40 years										
Clopidogrel	192	7495	1663	1636	2822	4519	7987	1706	28019	19015
Prasugrel	699	7834	1554	1569	2697	4243	7575	1743	27915	18939
Difference	+507	+339	-108	-67	-125	-275	-412	+37	-105	-77

Table 12 Mean deterministic ICER for UA/NSTEMI patients with diabetes

Follow-up	Total cost		Total QALYs		Incremental		ICER (£ per QALY)
	Clopidogrel	Prasugrel	Clopidogrel	Prasugrel	Cost	QALYs	
1 year	£1,383	£1,642	0.883	0.887	+£259	+0.003	£76,856
5 years	£5,391	£5,487	3.858	3.892	+£96	+0.034	£2,846
10 years	£10,102	£10,054	6.477	6.557	-£47	+0.080	Dominant
20 years	£16,476	£16,362	9.114	9.261	-£114	+0.147	Dominant
40 years	£19,015	£18,939	9.919	10.095	-£77	+0.176	Dominant

ICER=incremental cost-effectiveness ratio; QALY=quality adjusted life year

Figure 7 Univariate sensitivity analysis: 20 most important parameters in determining the ICER for UA/NSTEMI patients with diabetes

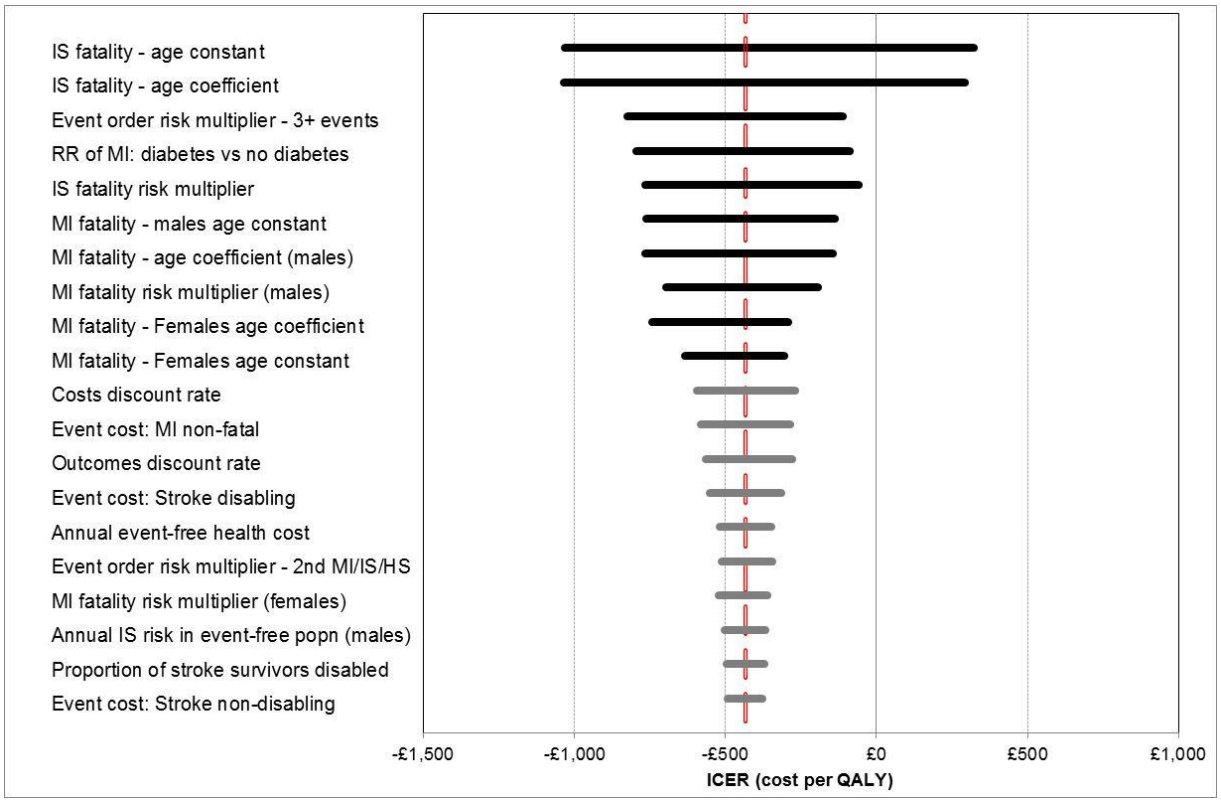


Figure 8 PSA scatterplot of prasugrel vs clopidogrel for UA/NSTEMI patients with diabetes

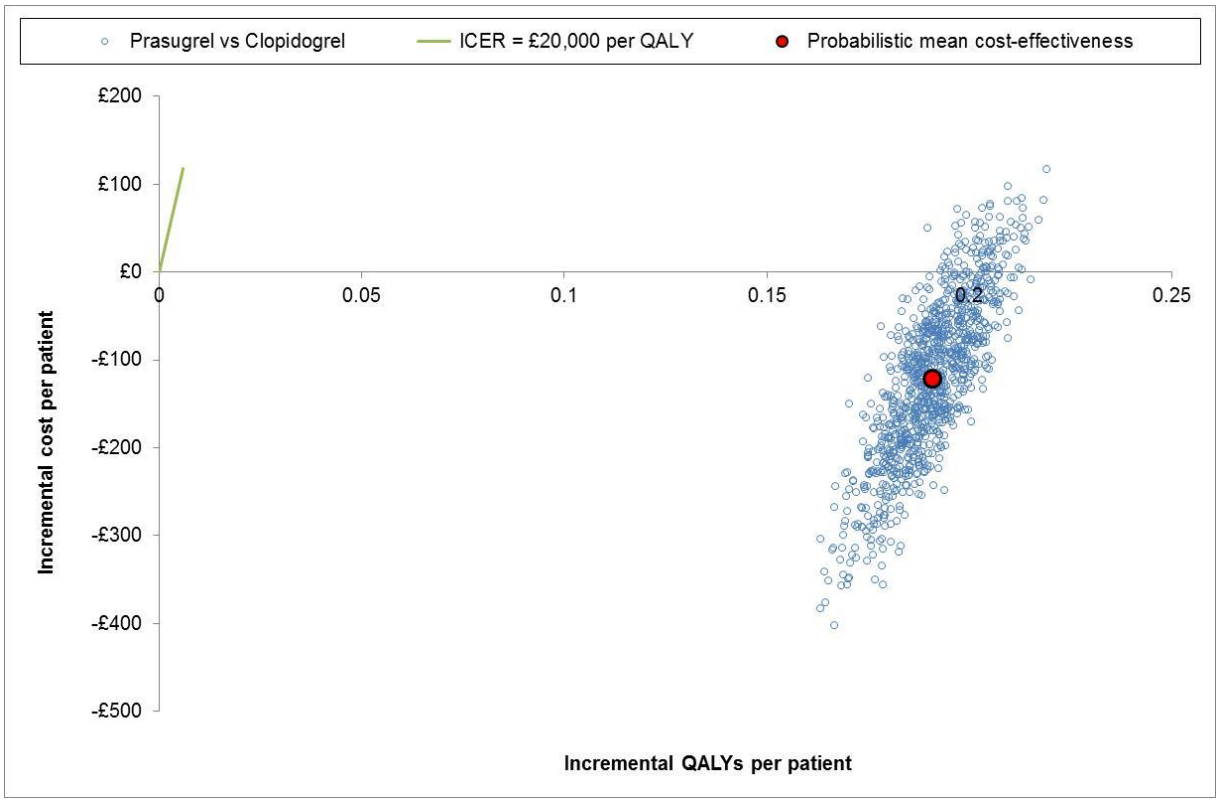
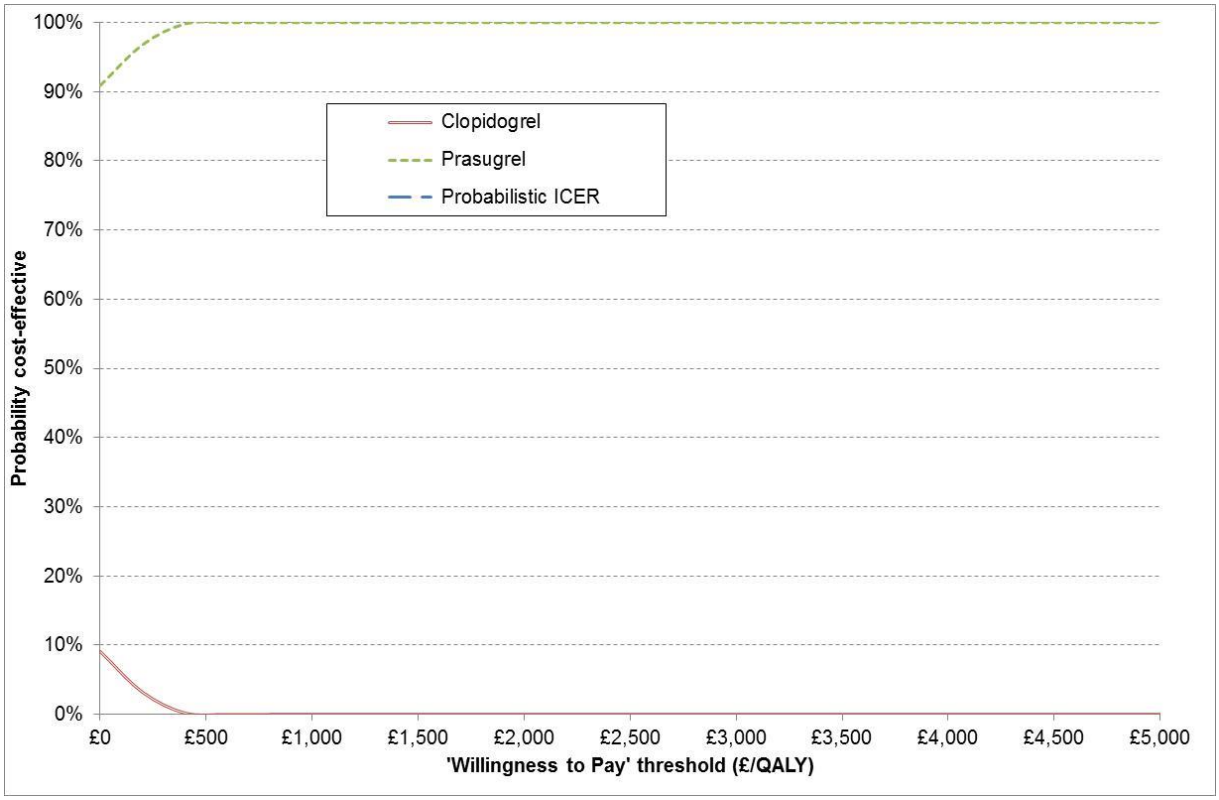


Figure 9 CEAC of prasugrel vs clopidogrel for UA/NSTEMI patients with diabetes



6.4.4 UA/NSTEMI – no diabetes subgroup

Deterministic results are detailed in Table 13 (life years), Table 14 (QALYs), Table 15 (costs) and Table 16 (ICERs). The ICER at the end of the first year is high, due to the inclusion of the full additional cost of treatment with prasugrel, whilst only modest health gains have accrued from the reduced incidence of MIs. Over time the estimated ICER decreases steadily, suggesting that incremental benefit continues to accrue over subsequent decades whilst incremental cost increases at a slower rate. The ICER for prasugrel compared with clopidogrel falls below £30,000 per QALY gained after 10 years.

Figure 10 displays the results of univariate sensitivity analyses, which indicate that uncertainty from discounting rates, and event incidence and fatality rates have the largest effect on the estimated ICER (ranging between £2,500 and +£6,500 per QALY gained). Other individual model parameters have only a modest influence on the magnitude of the ICER in this subgroup.

Probabilistic analysis at the 40 year follow-up horizon for this subgroup yields a lower estimated ICER of £4,154 per QALY gained, derived from small incremental cost and QALY estimates (+£212 and +0.051 respectively). The scatterplot (Figure 11) and CEAC for this subgroup (Figure 12) indicate the relative cost effectiveness of prasugrel despite the long-term erosion of incremental differences over time.

Table 13 Mean deterministic estimated life years for UA/NSTEMI patients without diabetes

Follow-up	Mean time in health state				Life years	
Treatment	Event free	MI(s) only	Mild stroke(s) +/- MI(s)	Severe stroke(s) +/- MI(s)	Total	Total discounted
1 year						
Clopidogrel	0.953	0.038	0.002	0.001	0.993	0.993
Prasugrel	0.960	0.031	0.001	0.001	0.993	0.993
Difference	+0.007	-0.007	-0.000	0.000	0.000	0.000
5 years						
Clopidogrel	4.204	0.443	0.053	0.030	4.730	4.429
Prasugrel	4.262	0.398	0.051	0.028	4.737	4.435
Difference	+0.058	-0.046	-0.004	-0.002	+0.007	+0.006
10 years						
Clopidogrel	7.348	1.092	0.206	0.118	8.764	7.611
Prasugrel	7.454	1.023	0.197	0.113	8.787	7.630
Difference	+0.106	-0.069	-0.009	-0.005	+0.024	+0.019
20 years						
Clopidogrel	11.249	2.219	0.607	0.354	14.429	11.125
Prasugrel	11.417	2.139	0.593	0.345	14.494	11.169
Difference	+0.167	-0.079	-0.015	-0.009	+0.064	+0.044
40 years						
Clopidogrel	13.248	2.863	0.924	0.530	17.565	12.454
Prasugrel	13.446	2.788	0.909	0.520	17.663	12.512
Difference	+0.198	-0.075	-0.015	-0.010	+0.099	+0.058

Table 14 Mean deterministic estimated QALYs for UA/NSTEMI patients without diabetes

Follow-up	Mean QALYs in health state				Event disutility (QALYs)			QALYs	
Treatment	Event free	MI(s) only	Mild stroke +/- MI(s)	Severe stroke +/- MI(s)	MI	Stroke	Death	Total	Total dis-counted
1 year									
Clopidogrel	0.869	0.034	0.001	0.000	-0.003	0.000	-0.001	0.901	0.901
Prasugrel	0.875	0.028	0.001	0.000	-0.002	0.000	-0.001	0.901	0.901
Difference	+0.006	-0.006	0.000	0.000	+0.001	0.000	0.000	0.000	0.000
5 years									
Clopidogrel	3.799	0.399	0.046	0.015	-0.009	-0.001	-0.009	4.241	3.972
Prasugrel	3.851	0.358	0.043	0.014	-0.008	-0.001	-0.010	4.248	3.979
Difference	+0.052	-0.041	-0.003	-0.001	+0.001	0.000	-0.000	+0.007	+0.007
10 years									
Clopidogrel	6.571	0.971	0.175	0.059	-0.018	-0.002	-0.020	7.736	6.732
Prasugrel	6.666	0.909	0.167	0.057	-0.017	-0.002	-0.020	7.760	6.751
Difference	+0.095	-0.062	-0.008	-0.002	+0.001	0.000	0.000	+0.024	+0.020
20 years									
Clopidogrel	9.892	1.929	0.502	0.169	-0.034	-0.005	-0.042	12.411	9.637
Prasugrel	10.039	1.859	0.490	0.164	-0.033	-0.005	-0.042	12.471	9.678
Difference	+0.147	-0.071	-0.013	-0.005	+0.001	0.000	0.000	+0.060	+0.042
40 years									
Clopidogrel	11.494	2.446	0.746	0.243	-0.046	-0.008	-0.070	14.804	10.655
Prasugrel	11.666	2.379	0.733	0.238	-0.045	-0.008	-0.071	14.892	10.708
Difference	+0.172	-0.067	-0.013	-0.005	+0.001	0.000	-0.001	+0.087	+0.053

QALY=quality adjusted life year

Table 15 Mean deterministic estimated costs for UA/NSTEMI patients without diabetes

Follow-up	Drug costs	Mean costs in health state				Event costs			Cost	
Treatment		Event free	MI(s) only	Mild stroke +/- MI(s)	Severe stroke +/- MI(s)	MI	Stroke	Death	Total	Total dis-counted
1 year										
Clopidogrel	29	589	23	3	5	471	45	26	1192	1192
Prasugrel	533	593	19	2	4	388	37	28	1604	1604
Difference	+503	+4	-4	-1	-1	-83	-8	+1	+413	+413
5 years										
Clopidogrel	69	2598	274	96	165	1274	743	228	5447	5091
Prasugrel	573	2634	246	90	156	1168	693	229	5787	5437
Difference	+503	+36	-28	-7	-10	-106	-50	+1	+340	+346
10 years										
Clopidogrel	112	4541	675	371	654	2287	2467	482	11590	9920
Prasugrel	616	4607	632	355	627	2169	2357	485	11848	10200
Difference	+503	+66	-43	-16	-27	-119	-111	+2	+257	+280
20 years										
Clopidogrel	173	6952	1371	1096	1961	3870	6680	1000	23103	17002
Prasugrel	677	7056	1322	1069	1911	3748	6505	1006	23293	17239
Difference	+504	+103	-49	-27	-50	-122	-175	+6	+190	+237
40 years										
Clopidogrel	207	8188	1769	1667	2934	4753	9799	1693	31010	20328
Prasugrel	711	8310	1723	1640	2880	4637	9622	1707	31230	20576
Difference	+504	+123	-46	-27	54	-116	-178	+14	+220	+248

Table 16 Mean deterministic ICER for UA/NSTEMI patients without diabetes

Follow-up	Total cost		Total QALYs		Incremental		ICER (£ per QALY)
	Clopidogrel	Prasugrel	Clopidogrel	Prasugrel	Cost	QALYs	
1 year	£1,192	£1,604	0.90097	0.90134	+£413	+0.00037	£1,101,662
5 years	£5,091	£5,437	3.972	3.979	+£346	+0.007	£52,288
10 years	£9,920	£10,200	6.732	6.751	+£280	+0.020	£14,276
20 years	£17,002	£17,239	9.637	9.678	+£237	+0.042	£5,688
40 years	£20,328	£20,576	10.655	10.708	+£248	+0.053	£4,667

ICER=incremental cost-effectiveness ratio; QALY=quality adjusted life year

Figure 10 Univariate sensitivity analysis: 20 most important parameters in determining the ICER for UA/NSTEMI patients without diabetes

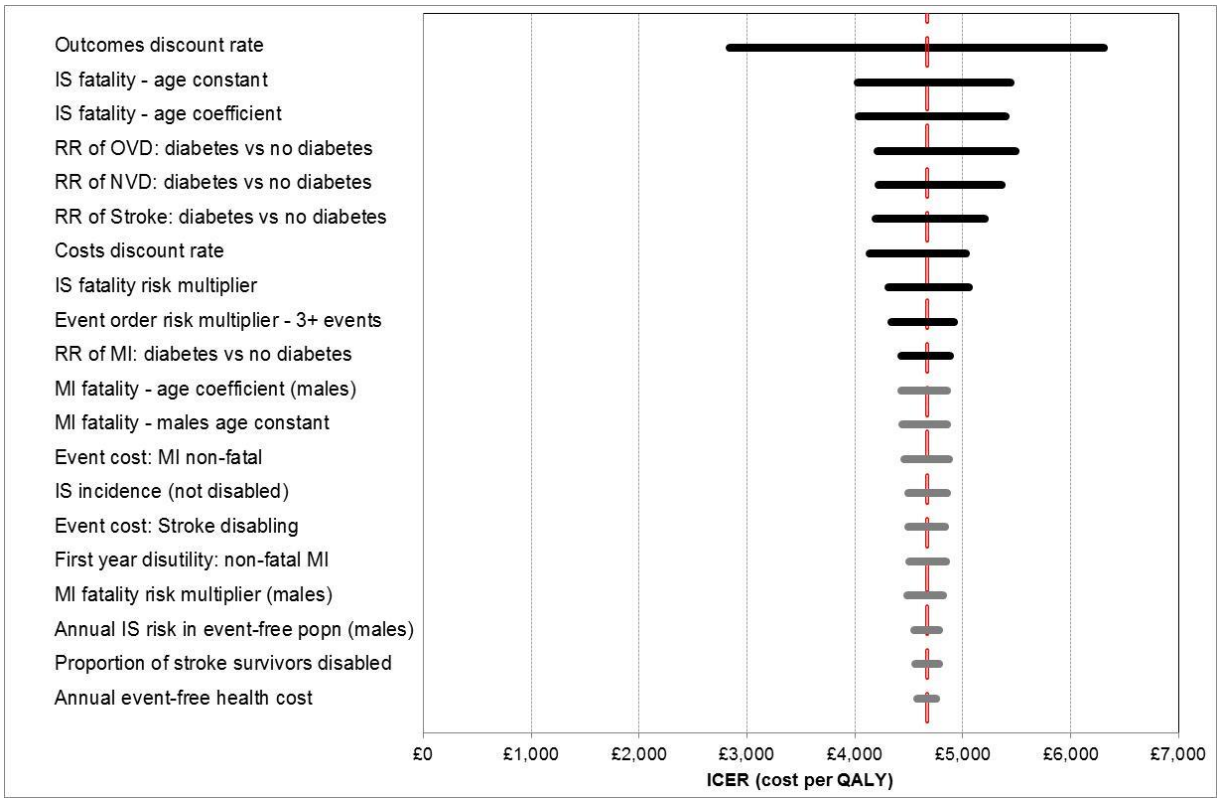


Figure 11 PSA scatterplot of prasugrel vs clopidogrel for UA/NSTEMI patients without diabetes

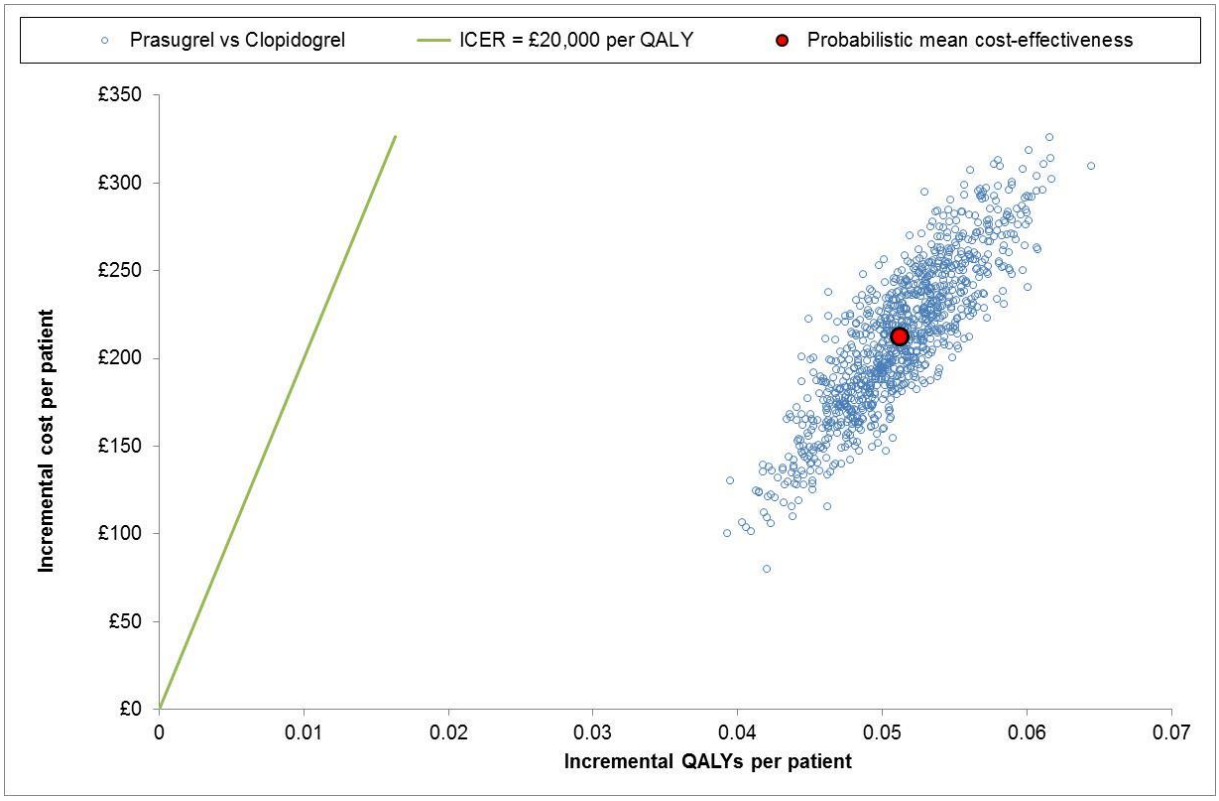
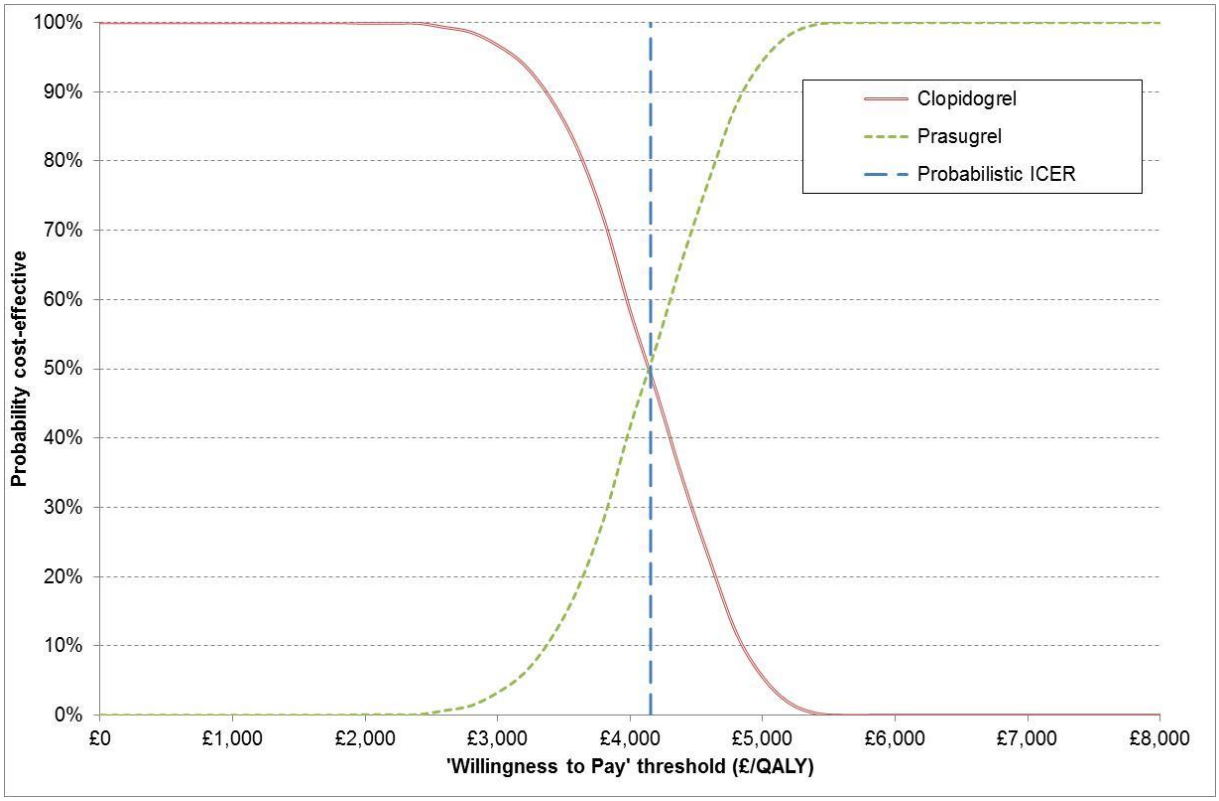


Figure 12 CEAC of prasugrel vs clopidogrel for UA/NSTEMI patients without diabetes



6.5 Independent economic assessment: Discussion of cost-effectiveness evidence

The main concern expressed by the ERG in their critique of the manufacturer's original submission in 2009 was that the very basic nature of projecting patient survival beyond the short follow-up period of the TRITON-TIMI 38[36] trial perpetuated a small effectiveness advantage over a period of 40 years. This projection method failed to allow the possibility of initial health gain being progressively attenuated, and thus worsened the apparent economic comparison of prasugrel compared with clopidogrel. The application of the findings of the CAPRIE91 trial in a similar patient population over a longer follow-up period to populate a long-term model has allowed the issue of clinical and economic benefit to be reassessed in a structured manner. The results from the AG's model suggest that attenuation of the initial benefits is indeed likely to occur, but that it is closely matched by narrowing of the initial cost difference so that estimated ICERs tend to reduce progressively rather than increase.

Simulation of the TRITON-TIMI 3836 trial population within the AG's decision model as four mutually exclusive subgroups has facilitated a reconsideration of the strength of evidence underlying the previous NICE guidance which excluded patients from treatment with prasugrel if they had not suffered from a STEMI event, or been diagnosed with diabetes.