

LIVERPOOL REVIEWS AND IMPLEMENTATION GROUP (LRiG)

Clopidogrel and modified-release
dipyridamole for the prevention of
occlusive vascular events (review of
Technology Appraisal No. 90)

ADDENDUM 2

This report was commissioned by
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DOES NOT CONTAIN IN CONFIDENCE DATA



UNIVERSITY OF
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REVIEWS AND
IMPLEMENTATION
GROUP

ADDENDUM 2: REVISED DETERMINISTIC RESULTS

Rationale for revision

Following completion of the main multiple technology assessment report submitted by the Assessment Group, further tests designed to explore the robustness of the results obtained using the Assessment Group's model have been carried out.

Of particular interest is the stability of cost-effectiveness findings when the size of the sampled patient population is varied. The results previously reported were based on a sample size of 2,000 patients. Additional exploratory analyses were then conducted with alternative first-order random number sets, and it became evident that there is scope for differing results to be obtained when other random number sets of this size are used to define the sample. Larger sample sizes were found to provide stable results across all populations and scenarios.

It was therefore decided to expand the sample size from 2,000 to 10,000 simulated patients, and re-assess the most cost-effective treatment scenario for each of the four patient groups against the deterministic results previously reported (Table 6-48 in the main Assessment Group report).

Revised optimal strategies

For three of the four patient populations ('MI only', 'PAD only', and MVD) the results of the updated analysis based on a sample size of 10,000 were very similar to those previously reported, and did not show any alterations in the optimal treatment strategy.

For the 'IS only' population, results for two analyses involving use of generic clopidogrel led to a change in the optimal strategy away from use of MRD+ASA as the optimal first-line treatment to first-line use of clopidogrel. Examination of the cost-effectiveness plane plots for these two scenarios (Figures 1 & 2) reveals that all the available 3-step treatment strategies lie very close to the cost-effectiveness frontier, suggesting that the selection of those strategies falling on the frontier rather than those close to it may not be associated with a high level of confidence. In this context, the results of probabilistic sensitivity analysis (PSA) may prove to be useful in arriving at a decision on the preferred optimal strategy.

An updated version of the original Table 6-39 is provided below.

In light of these new findings from deterministic use of the Assessment Group model, the original Table 6-48 has been also updated below.

Table 6-1 (updated) Deterministic results from AG model for treatment of the 'IS only' population

CLOP price	TA90 status	Strategy			Costs	Utility	Step 1	Step 2	Step 3	Step 4	Step 5
		Tx 1	Tx 2	Tx 3	Total	QALYs	ICER	ICER	ICER	ICER	ICER
Generic	MRD +ASA	None	None	None	£35,202	7.056					
		ASA	None	None	£32,955	7.157	-£22,106				
		CloP	None	None	£35,534	7.620	£590	£5,578	Dom		
		M+A	None	None	£35,266	7.591	£120	£5,329	Dom		
		ASA	CloP	None	£34,704	7.687	-£788	£3,300	Dom		
		ASA	M+A	None	£34,710	7.680	-£787	£3,357	Dom		
		CloP	ASA	None	£35,433	7.743	£337	£4,235	£20,716	Dom	
		CloP	M+A	None	£35,722	7.744	£757	£4,720	£28,305	Dom	
		M+A	ASA	None	£35,187	7.730	-£22	£3,898	£21,432	Dom	
		M+A	CloP	None	£35,521	7.734	£471	£4,451	£31,217	Dom	
		ASA	CloP	M+A	£34,727	7.708	-£726	£3,217			
		ASA	M+A	CloP	£34,737	7.696	-£725	£3,312	Dom		
		CloP	ASA	M+A	£35,435	7.769	£327	£4,054	£11,666	£20,675	Dom
		CloP	M+A	ASA	£35,720	7.781	£715	£4,436	£13,717	£22,598	£28,288
		M+A	CloP	ASA	£35,535	7.774	£464	£4,183	£12,269	£20,200	
M+A	ASA	CloP	£35,221	7.759	£28	£3,769	£9,820				
Generic	Not used	None	None	None	£35,267	7.120					
		ASA	None	None	£34,594	7.644	-£1,283				
		CloP	None	None	£35,545	7.680	£496	£26,406	Dom		
		M+A	None	None	£35,434	7.651	£314	£116,441	Dom		
		ASA	CloP	None	£34,791	7.727	-£783	£2,377	Dom		
		ASA	M+A	None	£34,788	7.721	-£797	£2,532	Dom		
		CloP	ASA	None	£35,508	7.804	£352	£5,718	£13,508	Dom	
		CloP	M+A	None	£35,795	7.809	£766	£7,282	£17,424	Dom	
		M+A	ASA	None	£35,355	7.783	£132	£5,494	£18,127	Dom	
		M+A	CloP	None	£35,682	7.789	£620	£7,509	£24,023	Dom	
		ASA	CloP	M+A	£34,823	7.753	-£701	£2,096			
		ASA	M+A	CloP	£34,823	7.740	-£716	£2,377	Dom		
		CloP	ASA	M+A	£35,542	7.832	£387	£5,059	£9,185		
		CloP	M+A	ASA	£35,876	7.856	£827	£6,046	£10,230	£13,558	
		M+A	CloP	ASA	£35,771	7.840	£700	£6,010	£10,934	£27,336	Dom
M+A	ASA	CloP	£35,426	7.812	£230	£4,967	£10,328	Dom			

IC, IQ = incremental cost & QALYs, ICER = incremental cost-effectiveness ratio, M+A = MRD+ASA, Dom = dominated, ICER in **bold** = strategy on cost-effectiveness frontier

Table 6-2 (updated) Summary table of optimal treatment strategy for each patient population obtained from deterministic analysis using the AG model

Clopidogrel price	TA90 guidance	Patient population			
		IS only	MI only	PAD only	MVD
No intolerances					
Branded	Applied	MRD+ASA → ASA → CLOP	ASA → CLOP	CLOP → ASA	CLOP → ASA
Branded	Not applied	MRD+ASA → ASA → CLOP	ASA → CLOP	CLOP → ASA	CLOP → ASA
Generic	Applied	CLOP → MRD+ASA → ASA	ASA → CLOP	CLOP → ASA	CLOP → ASA
Generic	Not applied	CLOP → MRD+ASA → ASA	ASA → CLOP	CLOP → ASA	CLOP → ASA
ASA intolerant					
Branded	Applied	CLOP → MRD	CLOP	CLOP	CLOP
Branded	Not applied	CLOP → MRD	CLOP	CLOP	CLOP
Generic	Applied	CLOP → MRD	CLOP	CLOP	CLOP
Generic	Not applied	CLOP → MRD	CLOP	CLOP	CLOP
MRD intolerant					
Branded	N/A	ASA → CLOP	N/A	N/A	N/A
Generic	N/A	CLOP → ASA	N/A	N/A	N/A
ASA & MRD intolerant					
	N/A	CLOP	N/A	N/A	N/A
	N/A	CLOP	N/A	N/A	N/A

CLOP= clopidogrel; ASA= aspirin; MRD= modified-release dipyridamole; N/A= not applicable; IS= ischaemic stroke; MI= myocardial infarction; PAD= peripheral arterial disease; MVD= multivascular disease

Cost-effectiveness plane displays

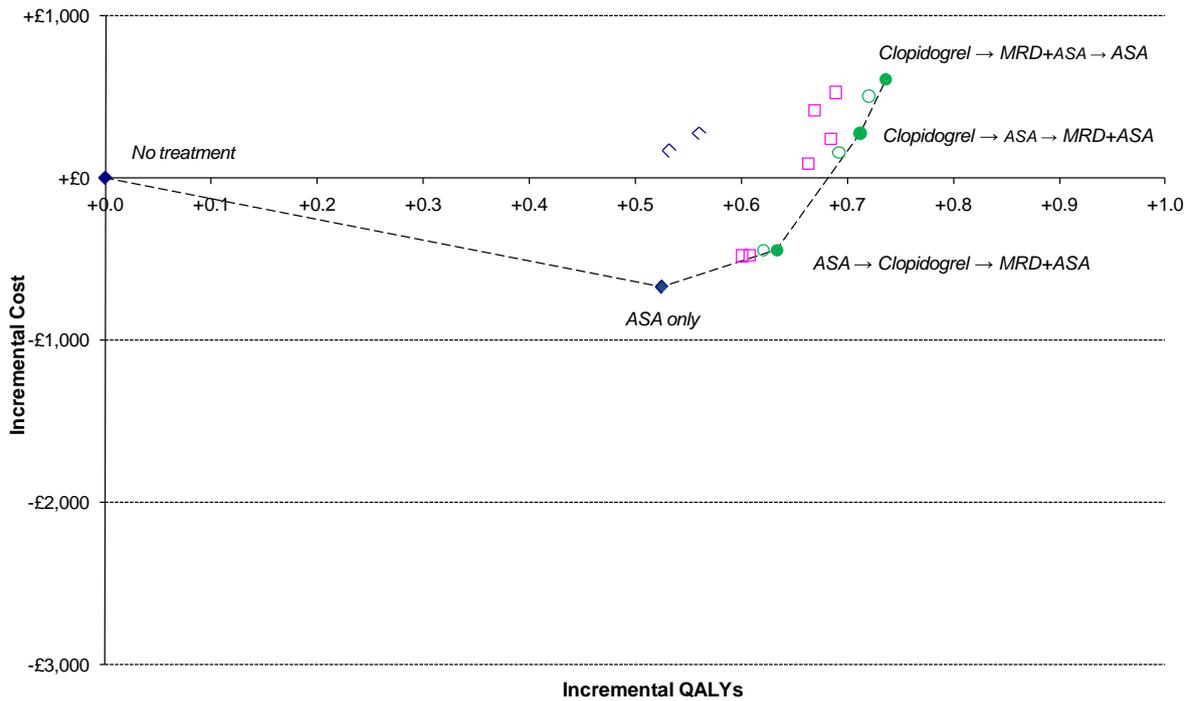


Figure 1 Cost-effectiveness plane for IS only population (generic clopidogrel price, TA90 guidance not applied)

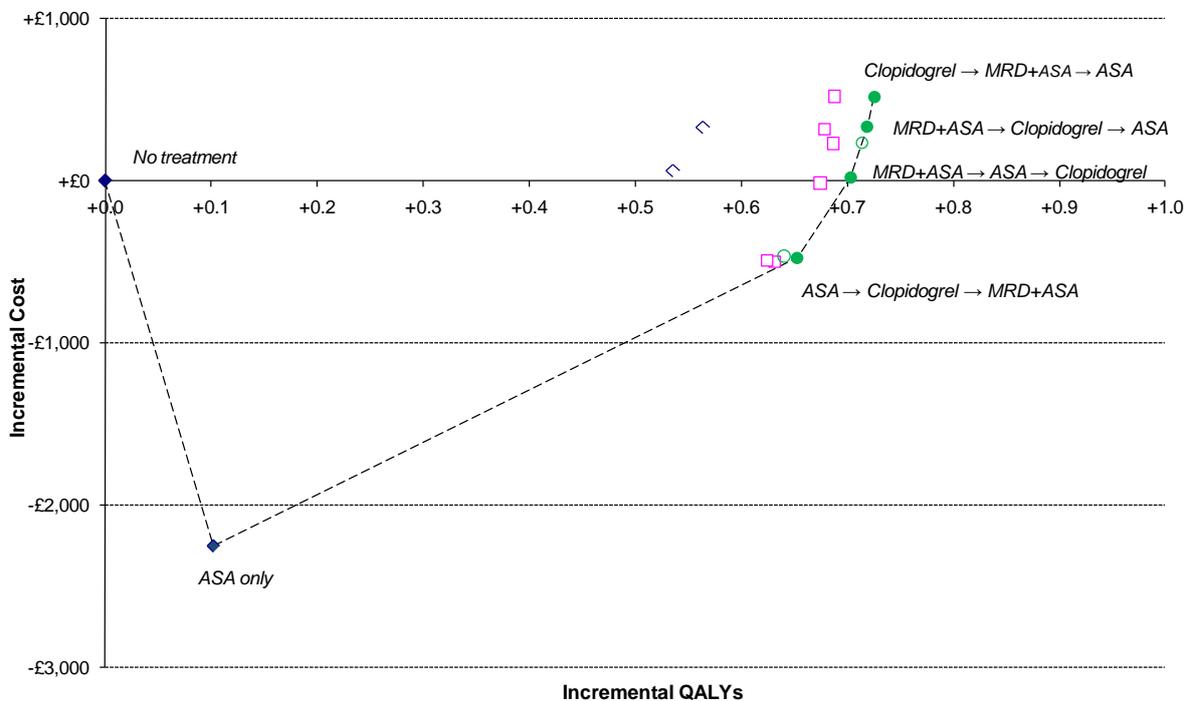


Figure 1 Cost-effectiveness plane for IS only population (generic clopidogrel price, TA90 guidance applied)

Summary of further analysis

Additional analysis using the AG model has indicated that a larger sampled model population is required to arrive at stable cost-effectiveness results for the 'IS only' patient population.

Increasing the sample size from 2,000 to 10,000 resolves this problem.

The new results for two strategies involving use of generic clopidogrel show a change of optimal strategy from first-line use of MRD+ASA to first-line use of generic clopidogrel.

From the deterministic model results it appears that all 3-step treatment strategies lie close to the cost-effectiveness frontier, so that consideration of the reliability of these results in the context of parameter uncertainty (PSA) may be useful in assessing the confidence that can be placed in the findings.