

# Impact of Revised Resource Use on Results Submitted to NICE

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## Summary

Following an in-depth detailed pre-publication review of the economics model for ticagrelor for the treatment of acute coronary syndromes (ACS) minor inconsistencies in some model inputs have been identified.

The model has been revised and the impact on the final incremental cost effectiveness ratio (ICER) assessed. For the base case (40 years) the incremental cost effectiveness ratio for ticagrelor versus clopidogrel for ACS patients the ICER decreases from £3696 per QALY to £3521 per QALY.

Full details of the inconsistencies and the impact on resource figures and final ICERs are provided below.

## Background

The analysis of resource use which was used in the cost-effectiveness model submitted to NICE as part of the single technology appraisal 'Ticagrelor for the treatment of acute coronary syndromes' was based on the work by the independent HECON Substudy Team at Linköping University.

An extract from the PLATO database had been provided to Linköping University and they were responsible for developing the resource use parameters for the With-In Trial Economic Analysis. The prepublication resource use analysis from Linköping University was used by AstraZeneca in the UK to calculate the health state costs which were included in the model and submission document.

During an AstraZeneca final review of a paper on the With-In Trial Economic Analysis inconsistencies in the Resource Use Table were identified. Inconsistencies were observed in the following counts:

1. Stress Test, Echocardiography, and Coronary Angiography
  - The overall number of procedures was underrepresented due to an inadvertent use of the wrong data table. The initial analysis used the Reminder data table rather than the Procedure data table for the count of procedures. The Reminder data table only recorded whether any procedure had been done, where as the Procedure data table counted all procedures performed. The Procedure data table is the correct one and has been used in the revised calculations attached here.
2. CABG
  - In the CRF Page for CABG there were two specific fields to record CABG procedures [with or without valve replacement]. In the main PLATO analysis 6 patients with the word CABG in a free text field for other Cardiac Surgery and other Reoperations were identified. These were not included in the initial analysis. Review of these cases confirmed that they indeed were CABG surgeries and thus were included as CABG in other analysis performed. To stay consistent with other analysis the HECON Substudy Team modified the algorithm for CABG to include these 6 patients as CABG patients.

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As a consequence of these observations all SAS programs and datasets from Linköping University were reviewed internally by SAS Programming and Biostatistics according AstraZeneca Standard Procedures.

All 38 resource use datasets used in the HECON Substudy were reviewed and the only additional findings were:

1. For two patients there was a change in the days spent in various ward types:
  - a. One patient had a change from 13 days in a General Ward to CABG ICU days
  - b. One patient had a change from 2 CCU days to 2 ICU CABG days

### Use of Data in Cost-effectiveness Analysis

The resource use tables provided by Linköping University were multiplied by the UK unit costs to calculate the costs for each Health State in the model. The original health costs used in the submission and the amended health state costs based on the revised resource use tables are shown below.

Health State	Mean Cost Estimates	
	<i>Original</i>	<i>Revised</i>
No Event (ticagrelor)	£8,544	£8,573
Non-fatal MI (ticagrelor)	£16,643	£16,767
Non-fatal stroke (ticagrelor)	£15,394	£15,455
CV death (ticagrelor)	£11,077	£11,261
Non-CV death (ticagrelor)	£17,180	£17,275
All cause mortality (ticagrelor)	£11,753	£11,926
No Event (clopidogrel)	£8,633	£8,676
Non-fatal MI (clopidogrel)	£16,362	£16,563
Non-fatal stroke (clopidogrel)	£17,483	£17,576
CV death (clopidogrel)	£11,501	£11,620
Non-CV death (clopidogrel)	£27,920	£28,332
All cause mortality (clopidogrel)	£13,915	£14,078

It can be seen from the above table that the revisions to the resource use tables make only a minor difference to the health state costs, making each health state slightly more expensive.

### Impact on the Results of the Cost-effective Analysis

In order to assess the impact of these revisions, the model results were re-run using the amended values and the results for the overall patient population, together with the STEMI, NSTEMI and UA subgroups are shown in the following tables. It can be seen from these tables that there is very little impact on the results in any of the patient populations.

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### All patients – original results

Deterministic results with costs and effects discounted				
Time horizon	Ticagrelor	Clopidogrel	Incremental	ICER
<b>40 years</b>				
Costs	£14,135	£13,737	£398	
Life-years	7.736	7.606	0.129	£3,075
<b>QALYs</b>	<b>6.382</b>	<b>6.275</b>	<b>0.108</b>	<b>£3,696</b>
<b>20 years</b>				
Costs	£14,110	£13,713	£397	
Life-years	7.701	7.572	0.129	£3,083
<b>QALYs</b>	<b>6.354</b>	<b>6.247</b>	<b>0.107</b>	<b>£3,705</b>
<b>10 years</b>				
Costs	£13,213	£12,841	£372	
Life-years	6.412	6.306	0.106	£3,499
<b>QALYs</b>	<b>5.302</b>	<b>5.213</b>	<b>0.089</b>	<b>£4,182</b>
<b>5 years</b>				
Costs	£11,722	£11,390	£331	
Life-years	4.068	4.004	0.065	£5,137
<b>QALYs</b>	<b>3.371</b>	<b>3.317</b>	<b>0.055</b>	<b>£6,075</b>
<b>1 year</b>				
Costs	£9,974	£9,690	£284	
Life-years	0.969	0.961	0.008	£33,405
<b>QALYs</b>	<b>0.797</b>	<b>0.789</b>	<b>0.008</b>	<b>£36,177</b>

### All patients – revised results

Deterministic results with costs and effects discounted				
Time horizon	Ticagrelor	Clopidogrel	Incremental	ICER
<b>40 years</b>				
Costs	£14,178	£13,799	£379	
Life-years	7.736	7.606	0.129	£2,929
<b>QALYs</b>	<b>6.382</b>	<b>6.275</b>	<b>0.108</b>	<b>£3,521</b>
<b>20 years</b>				
Costs	£14,154	£13,776	£378	
Life-years	7.701	7.572	0.129	£2,936
<b>QALYs</b>	<b>6.354</b>	<b>6.247</b>	<b>0.107</b>	<b>£3,529</b>
<b>10 years</b>				
Costs	£13,257	£12,903	£354	
Life-years	6.412	6.306	0.106	£3,321
<b>QALYs</b>	<b>5.302</b>	<b>5.213</b>	<b>0.089</b>	<b>£3,970</b>
<b>5 years</b>				
Costs	£11,765	£11,453	£313	
Life-years	4.068	4.004	0.065	£4,844
<b>QALYs</b>	<b>3.371</b>	<b>3.317</b>	<b>0.055</b>	<b>£5,728</b>
<b>1 year</b>				
Costs	£10,017	£9,752	£265	
Life-years	0.969	0.961	0.008	£31,177
<b>QALYs</b>	<b>0.797</b>	<b>0.789</b>	<b>0.008</b>	<b>£33,764</b>

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### STEMI patients – original results

Deterministic results with costs and effects discounted				
<i>Time horizon</i>	<i>Ticagrelor</i>	<i>Clopidogrel</i>	<i>Incremental</i>	<i>ICER</i>
<b>40 years</b>				
Costs	£15,822	£15,483	£339	
Life-years	9.159	9.016	0.143	£2,371
<b>QALYs</b>	<b>7.687</b>	<b>7.567</b>	<b>0.120</b>	<b>£2,825</b>
<b>20 years</b>				
Costs	£15,706	£15,371	£336	
Life-years	9.008	8.867	0.140	£2,391
<b>QALYs</b>	<b>7.562</b>	<b>7.444</b>	<b>0.118</b>	<b>£2,847</b>
<b>10 years</b>				
Costs	£14,198	£13,898	£299	
Life-years	6.915	6.808	0.106	£2,816
<b>QALYs</b>	<b>5.824</b>	<b>5.734</b>	<b>0.090</b>	<b>£3,334</b>
<b>5 years</b>				
Costs	£12,448	£12,190	£257	
Life-years	4.187	4.126	0.061	£4,201
<b>QALYs</b>	<b>3.536</b>	<b>3.484</b>	<b>0.052</b>	<b>£4,946</b>
<b>1 year</b>				
Costs	£10,643	£10,429	£214	
Life-years	0.971	0.964	0.008	£27,331
<b>QALYs</b>	<b>0.816</b>	<b>0.809</b>	<b>0.007</b>	<b>£31,933</b>

### STEMI patients – revised results

Deterministic results with costs and effects discounted				
<i>Time horizon</i>	<i>Ticagrelor</i>	<i>Clopidogrel</i>	<i>Incremental</i>	<i>ICER</i>
<b>40 years</b>				
Costs	£15,882	£15,576	£306	
Life-years	9.159	9.016	0.143	£2,141
<b>QALYs</b>	<b>7.687</b>	<b>7.567</b>	<b>0.120</b>	<b>£2,551</b>
<b>20 years</b>				
Costs	£15,766	£15,463	£303	
Life-years	9.008	8.867	0.140	£2,157
<b>QALYs</b>	<b>7.562</b>	<b>7.444</b>	<b>0.118</b>	<b>£2,568</b>
<b>10 years</b>				
Costs	£14,258	£13,991	£267	
Life-years	6.915	6.808	0.106	£2,506
<b>QALYs</b>	<b>5.824</b>	<b>5.734</b>	<b>0.090</b>	<b>£2,968</b>
<b>5 years</b>				
Costs	£12,508	£12,283	£225	
Life-years	4.187	4.126	0.061	£3,664
<b>QALYs</b>	<b>3.536</b>	<b>3.484</b>	<b>0.052</b>	<b>£4,313</b>
<b>1 year</b>				
Costs	£10,703	£10,522	£181	
Life-years	0.971	0.964	0.008	£23,133
<b>QALYs</b>	<b>0.816</b>	<b>0.809</b>	<b>0.007</b>	<b>£27,029</b>

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### NSTEMI patients – original results

Deterministic results with costs and effects discounted				
<i>Time horizon</i>	<i>Ticagrelor</i>	<i>Clopidogrel</i>	<i>Incremental</i>	<i>ICER</i>
<b>40 years</b>				
Costs	£13,653	£13,140	£512	
Life-years	6.685	6.567	0.118	£4,357
<b>QALYs</b>	<b>5.443</b>	<b>5.345</b>	<b>0.098</b>	<b>£5,230</b>
<b>20 years</b>				
Costs	£13,649	£13,136	£512	
Life-years	6.678	6.560	0.118	£4,359
<b>QALYs</b>	<b>5.437</b>	<b>5.339</b>	<b>0.098</b>	<b>£5,233</b>
<b>10 years</b>				
Costs	£13,145	£12,648	£497	
Life-years	5.905	5.801	0.104	£4,794
<b>QALYs</b>	<b>4.814</b>	<b>4.727</b>	<b>0.087</b>	<b>£5,727</b>
<b>5 years</b>				
Costs	£11,945	£11,484	£461	
Life-years	3.938	3.872	0.066	£6,932
<b>QALYs</b>	<b>3.216</b>	<b>3.159</b>	<b>0.056</b>	<b>£8,162</b>
<b>1 year</b>				
Costs	£10,316	£9,903	£413	
Life-years	0.967	0.958	0.009	£45,567
<b>QALYs</b>	<b>0.782</b>	<b>0.773</b>	<b>0.009</b>	<b>£45,810</b>

### NSTEMI patients – revised results

Deterministic results with costs and effects discounted				
<i>Time horizon</i>	<i>Ticagrelor</i>	<i>Clopidogrel</i>	<i>Incremental</i>	<i>ICER</i>
<b>40 years</b>				
Costs	£13,697	£13,186	£511	
Life-years	6.685	6.567	0.118	£4,345
<b>QALYs</b>	<b>5.443</b>	<b>5.345</b>	<b>0.098</b>	<b>£5,217</b>
<b>20 years</b>				
Costs	£13,693	£13,182	£511	
Life-years	6.678	6.560	0.118	£4,347
<b>QALYs</b>	<b>5.437</b>	<b>5.339</b>	<b>0.098</b>	<b>£5,219</b>
<b>10 years</b>				
Costs	£13,189	£12,694	£496	
Life-years	5.905	5.801	0.104	£4,781
<b>QALYs</b>	<b>4.814</b>	<b>4.727</b>	<b>0.087</b>	<b>£5,711</b>
<b>5 years</b>				
Costs	£11,989	£11,529	£460	
Life-years	3.938	3.872	0.066	£6,912
<b>QALYs</b>	<b>3.216</b>	<b>3.159</b>	<b>0.056</b>	<b>£8,138</b>
<b>1 year</b>				
Costs	£10,360	£9,948	£412	
Life-years	0.967	0.958	0.009	£45,418
<b>QALYs</b>	<b>0.782</b>	<b>0.773</b>	<b>0.009</b>	<b>£45,659</b>

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### UA patients – original results

Deterministic results with costs and effects discounted				
<i>Time horizon</i>	<i>Ticagrelor</i>	<i>Clopidogrel</i>	<i>Incremental</i>	<i>ICER</i>
<b>40 years</b>				
Costs	£12,907	£12,419	£488	
Life-years	8.612	8.502	0.110	£4,423
<b>QALYs</b>	<b>7.170</b>	<b>7.079</b>	<b>0.091</b>	<b>£5,374</b>
<b>20 years</b>				
Costs	£12,844	£12,357	£487	
Life-years	8.529	8.420	0.109	£4,454
<b>QALYs</b>	<b>7.102</b>	<b>7.012</b>	<b>0.090</b>	<b>£5,410</b>
<b>10 years</b>				
Costs	£11,583	£11,123	£460	
Life-years	6.789	6.703	0.086	£5,355
<b>QALYs</b>	<b>5.669</b>	<b>5.598</b>	<b>0.071</b>	<b>£6,484</b>
<b>5 years</b>				
Costs	£9,884	£9,461	£424	
Life-years	4.185	4.135	0.050	£8,398
<b>QALYs</b>	<b>3.505</b>	<b>3.463</b>	<b>0.042</b>	<b>£10,172</b>
<b>1 year</b>				
Costs	£8,043	£7,659	£384	
Life-years	0.976	0.970	0.007	£58,864
<b>QALYs</b>	<b>0.814</b>	<b>0.809</b>	<b>0.005</b>	<b>£78,288</b>

### UA patients – revised version

Deterministic results with costs and effects discounted				
<i>Time horizon</i>	<i>Ticagrelor</i>	<i>Clopidogrel</i>	<i>Incremental</i>	<i>ICER</i>
<b>40 years</b>				
Costs	£12,942	£12,460	£482	
Life-years	8.612	8.502	0.110	£4,370
<b>QALYs</b>	<b>7.170</b>	<b>7.079</b>	<b>0.091</b>	<b>£5,310</b>
<b>20 years</b>				
Costs	£12,879	£12,398	£481	
Life-years	8.529	8.420	0.109	£4,401
<b>QALYs</b>	<b>7.102</b>	<b>7.012</b>	<b>0.090</b>	<b>£5,345</b>
<b>10 years</b>				
Costs	£11,617	£11,163	£454	
Life-years	6.789	6.703	0.086	£5,287
<b>QALYs</b>	<b>5.669</b>	<b>5.598</b>	<b>0.071</b>	<b>£6,402</b>
<b>5 years</b>				
Costs	£9,919	£9,501	£418	
Life-years	4.185	4.135	0.050	£8,282
<b>QALYs</b>	<b>3.505</b>	<b>3.463</b>	<b>0.042</b>	<b>£10,032</b>
<b>1 year</b>				
Costs	£8,078	£7,699	£378	
Life-years	0.976	0.970	0.007	£57,971
<b>QALYs</b>	<b>0.814</b>	<b>0.809</b>	<b>0.005</b>	<b>£77,100</b>