# National Institute for Health and Care Excellence

Final

# Acute Coronary Syndromes

## Cost-effectiveness analysis: Which dual antiplatelet therapy is most cost effective for managing unstable angina or NSTEMI or for managing STEMI in adults undergoing PCI?

*NICE guideline NG185*

*Economic analysis report*

*November 2020*

*Final*

*This guideline was developed by the National Guideline Centre based at the Royal College of Physicians*

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# 1 Introduction

Dual-antiplatelet therapy (DAPT) (aspirin plus: clopidogrel, prasugrel or ticagrelor) is established practice as part of initial management of acute coronary syndrome (ACS) in order to reduce the risk of further cardiovascular events (and is generally continued post-ACS). NICE guideline CG94 updated NICE TA80 on clopidogrel in combination with aspirin for UA/NSTEMI.[40] NICE TA317 recommended prasugrel in combination with aspirin as an option for people with ACS having a percutaneous coronary intervention (PCI).[37] NICE TA236 recommended ticagrelor in combination with aspirin as an option for people with STEMI intended to be treated with primary PCI and people with UA/NSTEMI.[39] This means that all three agents are options in current NHS practice. The TAs were unable to make recommendations regarding prasugrel versus ticagrelor at the time of their development although both did consider this comparison. Audit data from 2017/18 showed that 97.5% of people who have had a myocardial infarction (MI) were discharged on clopidogrel, prasugrel or ticagrelor.[32]

However, there is uncertainty in clinical practice about which option should be used and variations in practice across England.[26] As part of the guideline update the committee therefore considered the question 'Which dual antiplatelet is most clinically and cost effective for managing unstable angina or NSTEMI or for managing STEMI in adults'. The full review of the clinical effectiveness evidence and published cost effectiveness evidence including the committee discussion can be found in 'Evidence report A'.

All agents reduce cardiovascular events but increase bleeding and so there is a trade-off between these effects. Also, mortality could be impacted by both effects. This could result in differences in QALYs and costs downstream. RCTs have suggested benefits of prasugrel and ticagrelor over clopidogrel.

This is an important question for economic modelling as there is variation in current practice. The British Cardiovascular Intervention Society (BCIS)[25,26] audit reported that in 2017 1.0% of people with UA/NSTEMI received prasugrel, 40.2% received ticagrelor and most of the remaining received clopidogrel. For those having PCI with STEMI, 7.2% received prasugrel, 47.5% received ticagrelor and the remaining will have received clopidogrel. Furthermore, there are considerable differences in the costs of these drugs, with ticagrelor being the most expensive option costing approximately £714 per year. Prasugrel costs approximately £100 per year and clopidogrel, costs approximately £22 per year.

There were five health economic studies identified and included in the review for this question, which all found that ticagrelor was cost-effective in comparison to clopidogrel and that prasugrel was cost-effective in comparison to clopidogrel. Some studies compared all three agents together and found ticagrelor to be the most cost effective. However, the committee considered there to still be uncertainty about the cost-effectiveness of these interventions as the treatment effects used in models did not include new clinical data identified in the clinical systematic review undertaken in the guideline, in particular head-to-head studies that compared prasugrel and ticagrelor.

As a result of this uncertainty, which DAPT combination to use in people with ACS undergoing PCI was identified as the highest priority for new economic analysis by the committee. This was because a recommendation for a particular agent would result in a significant change in clinical practice that could have a substantial resource impact for the NHS as drug costs vary substantially between agents and current practice is variable. It was agreed that new cost-effectiveness analysis could reduce the uncertainty by comparing all three agents together and incorporating the most up-to-date clinical effectiveness evidence.

# 2 Methods

## 2.1 Model overview

A cost-utility analysis was undertaken with a lifetime horizon. Quality-adjusted life years (QALYs) and costs from a current UK NHS and personal social services perspective were considered. Both costs and QALYs were discounted at a rate of 3.5% per annum in line with NICE methodological guidance.[34] An incremental analysis was undertaken.

### 2.1.1 Comparators

The comparators selected for the model were:

1. Clopidogrel 75mg once daily + aspirin 75-150mg once daily (300-600mg clopidogrel loading dose) for 12 months
2. Ticagrelor 90mg twice daily + aspirin 75-150mg once daily (180mg ticagrelor loading dose) for 12 months
3. Prasugrel 5-10mg once daily + aspirin 75-150mg once daily (60mg prasugrel loading dose) for 12 months

The analysis did not include aspirin alone as this comparison was not included in the review protocol for this question in the guideline update (see Evidence report A for review protocol) because use of DAPT is well established in ACS. Audit data from 2017/18 showed that 97.5% of people who have had a myocardial infarction (MI) were discharged on clopidogrel, prasugrel or ticagrelor.[32]

The committee discussed discontinuation with DAPT and agreed that in their experience most people will continue DAPT for the full year although noted that average treatment duration varied in trials. It was noted by the committee that some people experiencing a major bleed may have their DAPT treatment stopped but in many cases they might restart taking DAPT. Some people that have a cerebral haemorrhage may stop taking their DAPT indefinitely, however as this would affect a small number of people. Some people may stop for other reasons. Discontinuation was not modelled explicitly except for when people died in the first year; however, drug cost calculations took into account estimated average treatment duration as described in section 2.3.6.1.

People presenting with an acute coronary syndrome and that are going to have a PCI, usually receive dual-antiplatelet therapy before the procedure. For those receiving ticagrelor and clopidogrel, they can start the drug immediately. However, a complication is that prasugrel is only licensed for use during PCI. The vast majority of the STEMI population will receive PCI as their primary management strategy and will receive this early on. However, for UA/NSTEMI it will not be known whether or not a PCI is suitable until angiography has been performed and this may not happen for a few days. In the model, for those with UA/NSTEMI receiving prasugrel it was assumed for costing purposes that they receive no DAPT initially, and then receive prasugrel at the time of PCI. The annual MINAP 2015/16[33] report states that the median time to angiography for NSTEMI is 65 hours, therefore it was assumed for costing purposes that people received aspirin for 3 days and then began taking prasugrel at the time of PCI.

It is acknowledged that ticagrelor can be taken beyond 12 months, however, it is indicated for use irrespective of which initial DAPT was taken, therefore it is assumed that the use of ticagrelor beyond 12 months would be the same between DAPT options and was not incorporated in to the model.

It is also acknowledged that an existing NICE technology appraisal (TA335) recommends low dose rivaroxaban as an option in combination with aspirin plus clopidogrel after acute

management of acute coronary syndrome.[38] It is beyond the scope of the guideline update to make a recommendation about the use of rivaroxaban after ACS however, as rivaroxaban is only indicated for use with clopidogrel, a recommendation for prasugrel or ticagrelor may preclude rivaroxaban's use and so it is potentially relevant to take this into account in the analysis. The committee indicated that current usage is low therefore it was considered via a modification to the clopidogrel arm in a sensitivity analysis which is discussed in section 2.4.

### 2.1.2 Population

Two separate populations were analysed:

- People with STEMI undergoing PCI
- People with UA/NSTEMI undergoing PCI

Although treatment effects were being analysed together for the overall ACS population in the clinical review and meta-analyses, the committee agreed the populations should be modelled separately in the cost effectiveness analysis because they are likely to have different baseline risks. Even if relative treatment effects are considered the same between the populations, if baseline risks vary then absolute differences in numbers of clinical events will also vary and this may affect cost effectiveness.

The vast majority of STEMI patients will receive PCI. People with UA/NSTEMI are risk assessed and those at higher risk or with symptoms undergo angiography with a proportion of these going on to receive PCI where indicated. The economic analysis did not consider people with UA/NSTEMI that are medically managed. This is because prasugrel is not indicated in this population and one published UK economic analysis indicated that ticagrelor is cost-effective compared to clopidogrel in this population and additional economic analyses were not considered necessary by the committee.

For UA/NSTEMI it will not be known whether a PCI is suitable until angiography has been performed and this may not take place for a few days. The committee therefore discussed whether it was appropriate to model the UA/NSTEMI population who receive angiography rather than just the PCI population. It was agreed that this was not necessary because once angiography had been performed and the decision to not undertake PCI had been made people could then receive clopidogrel or ticagrelor. The use of a prasugrel strategy for people undergoing PCI does therefore not limit the treatment options for people not undergoing PCI. The committee also discussed whether use of a prasugrel strategy for people with UA/NSTEMI undergoing PCI would delay DAPT in people not undergoing PCI whilst waiting for angiography and if this would impact outcomes (and so should be captured in the modelling) however it was agreed that they did not think this was a significant issue and did not require incorporation into the model.

## 2.2 Approach to modelling

A two-part model was constructed which included a decision tree to model clinical events in the first year followed by a Markov model for long term extrapolation in order to calculate lifetime costs and QALYs for each comparator.

The initial 1 year decision tree reflects the DAPT treatment period where people receive aspirin plus either clopidogrel, prasugrel or ticagrelor. Estimates of real world UK baseline risks with aspirin plus clopidogrel were used to populate the model and differences in clinical events with prasugrel and ticagrelor were estimated by applying relative treatment effects (odds ratios) from the clinical effectiveness review and evidence syntheses. Costs and clinical events therefore vary by comparator. Details of the decision tree model structure are described in section 2.2.1.

Differential treatment effects were assumed to apply in the first year only. However, in order to fully capture the impact of the differences in clinical events in the first year it is necessary to model the rest of the lifetime of the population, which is standard practice in economic evaluation. For example, if mortality differs between comparators in the first year this will mean that a different number of people will be alive with each treatment at the end of 1 year. Due to this, even assuming no further difference in risk of clinical events between comparators, costs and QALYs will vary for the population beyond one year. A Markov model was used for this extrapolation period and estimated risks for the population in this did not vary by initial DAPT treatment. Details of the Markov model structure are described in section 2.2.2 below.

The model was run for each of the DAPT comparators, with people starting in the decision tree for one year and then entering the Markov model which was run for repeated cycles. The time spent alive in each of the health states was calculated. By attributing costs and quality of life weights (utilities) to the people in each health state total costs and QALYs were calculated for the populations. The Markov model was run for a lifetime (for 40 years, by which time the majority of the cohort had died) in order to calculate lifetime costs and QALYs. Comparing the results for each of the comparators allowed us to identify the most cost effective intervention. See section 2.2.3 for details of how uncertainty was taken into account.

Full details of all model inputs are described in section 2.3.

Summary of key model assumptions:

- Relative treatment effects based on evidence synthesised from any ACS population represent the relative treatment effects for people with STEMI and PCI and UA/NSTEMI and PCI (this is discussed in more detail in section 2.3.3)
- The probabilities of death, reinfarction and stroke after 1 year do not vary by DAPT treatment received in year 1
- People who did not experience an event in the decision tree (year 1) can only experience one event in the Markov model (either reinfarction or stroke); people who experience an event in the decision tree could not experience an event in the Markov model (this is discussed in more detail in section 2.2.2)

### 2.2.1 Model structure: first year treatment period decision tree

The initial 1 year decision tree reflects the DAPT treatment period where people could receive aspirin plus either clopidogrel, prasugrel or ticagrelor. Following the review of clinical evidence and committee discussion, it was agreed that the following outcomes needed to be captured in the 1 year model as they potentially vary between DAPT options:

- All-cause mortality
- Reinfarction
- Stroke
- Major bleed
- Minor bleed

There was some uncertainty in the committee about the inclusion of stroke as the treatment effects estimated in the clinical review had wide confidence intervals and were considered somewhat uncertain. However, previous models in this area have generally included stroke (including the NICE TAs for prasugrel and ticagrelor) and so it was agreed that it should be included.

The committee also discussed the importance of other treatment effects and agreed that a considerable amount of people taking ticagrelor may experience breathing difficulties (dyspnoea) as a side effect. This was demonstrated in the clinical review. It was discussed and the committee agreed that this was not a critical outcome as the numbers seen in real world practice are quite low and so did not need to be considered in the base case analysis.

It was modelled as part of a sensitivity analysis however, which is discussed further in section 2.4.

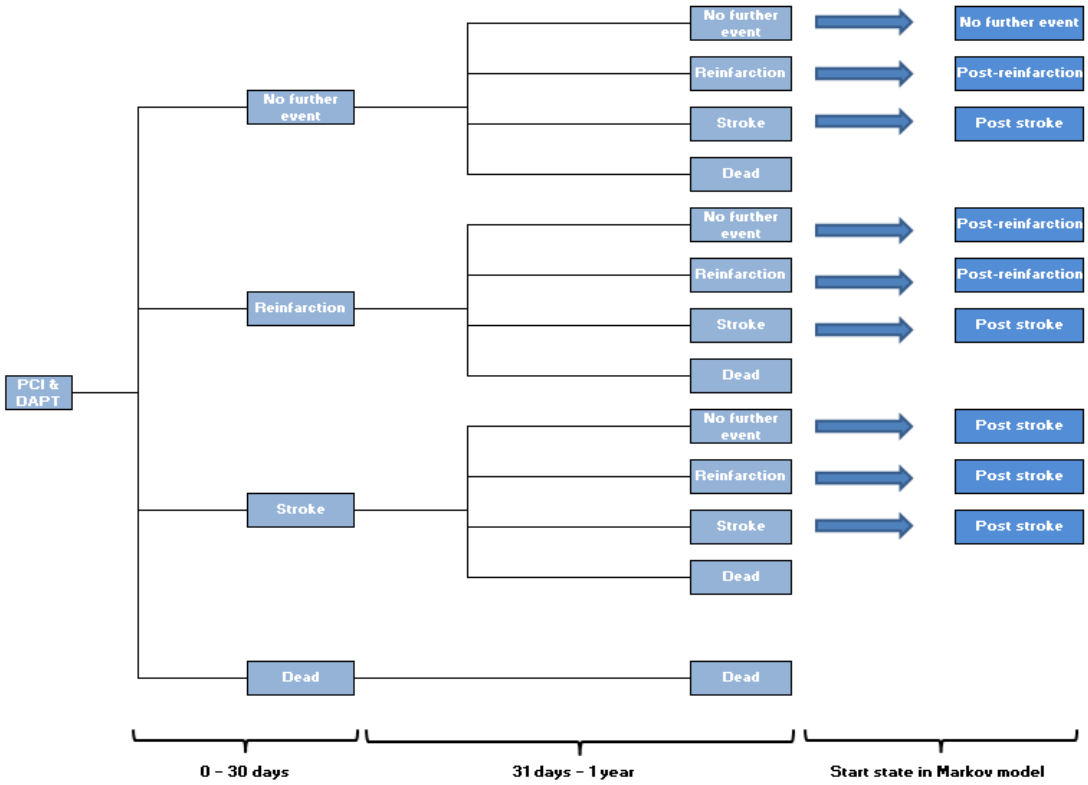
The first year decision tree was broken down into two time periods: 0 to 30 days and 31 days to 1 year as this was considered to make best use of the available clinical data, in particular incorporating new studies that directly compared prasugrel and ticagrelor. The clinical evidence review found outcome data at different time points including at 30 days and 1 year. Until the publication of ISAR-REACT 5 late in guideline development, all of the new studies comparing prasugrel and ticagrelor directly only had 30 day outcomes and the committee agreed that incorporating this new evidence was essential. A network meta-analysis (NMA) was undertaken to combine all 30 day evidence together into a simultaneous set of treatment effects and this was utilised in the model for the 0 to 30 day period. There was inconsistency between the direct and indirect estimates at 1 year and so NMA was considered unreliable and not undertaken. Instead three different treatment effect scenarios were used for the 1 year data in the model that incorporated different clinical data and explored the impact of the inconsistency on conclusions about cost effectiveness. More details about the relative treatment effect data used in the model and the inconsistency in the 1 year outcome data are given in section 2.3.3.

The decision tree included four potential health outcomes at each time point in the decision tree: alive with no further event, alive with reinfarction, alive with stroke and dead. Major and minor bleeding were incorporated as adverse events as the effects were considered to be short-term (except for haemorrhagic stroke which is captured in the stroke outcome). People alive at the end of the 1 year period entered the post-year one Markov model to extrapolate 1 year outcomes to a lifetime perspective. Figure 1 illustrates the structure of the decision tree and which health states people enter the Markov model. The rationale for where people enter the Markov model is discussed in the next section.

It was acknowledged that the major bleeding and stroke outcomes overlap as the stroke outcome included both ischemic and haemorrhagic strokes and a haemorrhagic stroke will also be counted as a major bleed. However, it was felt that capturing strokes explicitly was important as, while they were uncommon, they have a substantial and sustained impact on health and resource use. Major bleeding however is not a separate health state but is a short-term adverse effect and rates of haemorrhagic stroke are low so the committee agreed that the impact on results should not be large and capturing both strokes and major bleeds was the best approach for modelling purposes.

The model structure was the same for STEMI and UA/NSTEMI analyses.

**Figure 1: Model structure: one year treatment period decision tree**




*Note: Probabilities of events are dependent on DAPT being received. People who are alive are also at risk of a short-term major or minor bleeding adverse event.*

### 2.2.2 Model structure: post-one year extrapolation Markov model

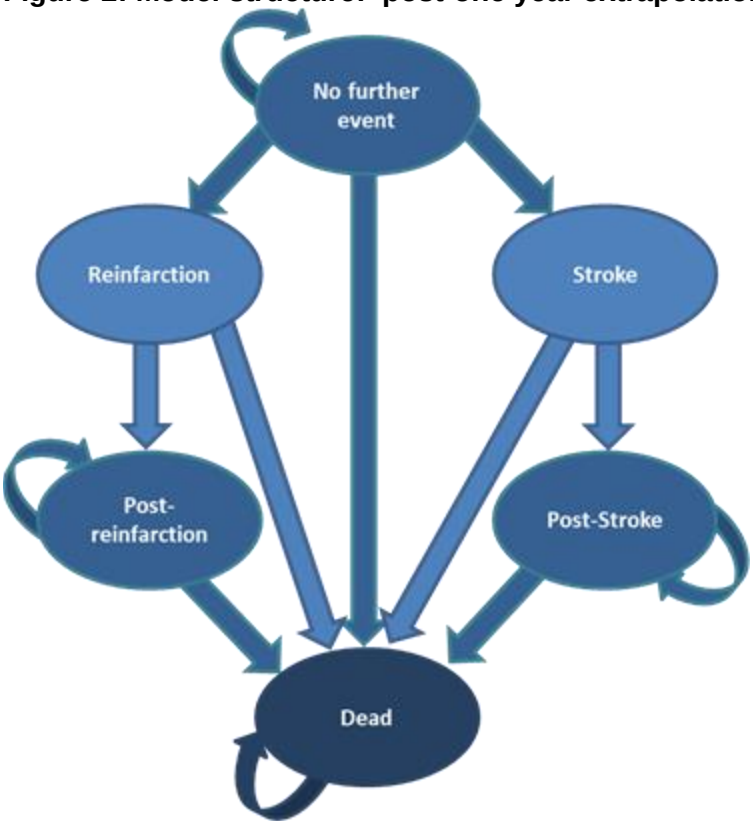
In a Markov model a set of mutually exclusive health states are defined that describe what can happen to the population of interest over time. People in the model can only exist in one of these health states at a time. Possible transitions are defined between each of the health states and the probability of each transition occurring within a defined period of time (a cycle) is assigned to each possible transition.

The Markov model consisted of six health states. These included: no further event, reinfarction, post-reinfarction, stroke, post-stroke and dead. Those that were alive and had experienced no further events at the end of the decision tree entered the 'no further event' health state in the Markov model. Those that had experienced reinfarction (either once or twice) at the end of the decision tree entered the 'post-reinfarction' health state. Those that had experienced a stroke at the end of the decision tree entered the 'post-stroke' health state. For those that experienced both a stroke and reinfarction, it was discussed and agreed with the committee that they should enter the post-stroke health state, as this is the worse health state with substantially higher costs and there may be overlap in treatment received for having reinfarction and having a stroke. Also, those that experienced two strokes or two reinfarctions entered the same health state in the Markov model, which is a simplification for modelling purposes.

Figure 2 illustrates the Markov model structure and the possible transitions between health states. The Markov model used a 1 year cycle length. People in the no further event health state had the possibility of transitioning to reinfarction, stroke or dead. Reinfarction and stroke were tunnel health states, meaning that people only remain in that health state for one cycle, at which point they must transition to dead or the post-reinfarction/post-stroke health

states. The reason for including these tunnel health states is to account for the fact that in the first year after a major event, people will have higher costs, lower quality of life and a higher risk of mortality. Once someone is in the post-reinfarction or post-stroke health state, they cannot experience another event and so either remain in that state or move to the dead state (this includes those that entered the Markov model in the post-event health states). This is a simplification of reality but was considered reasonable for modelling purposes due to the lack of data available to model downstream further events. Also, this is a method employed by other cardiovascular models such as the ticagrelor NICE technology appraisal (TA236), a health technology assessment for clopidogrel and aspirin in NSTEMI[27] and a previous model looking at glycoprotein antagonists in NSTEMI in the UK.[45] This was taken into account when selecting model inputs where possible; for example, cost estimates for a health state that incorporated repeat events were used if available. Dead was an absorbing health state.

**Figure 2: Model structure: post-one year extrapolation Markov model**




*Notes: 1 year cycles; model was run for 40 years at which point most people will be in the dead state; the state people enter model depends on events experienced in year 1 decision tree.*

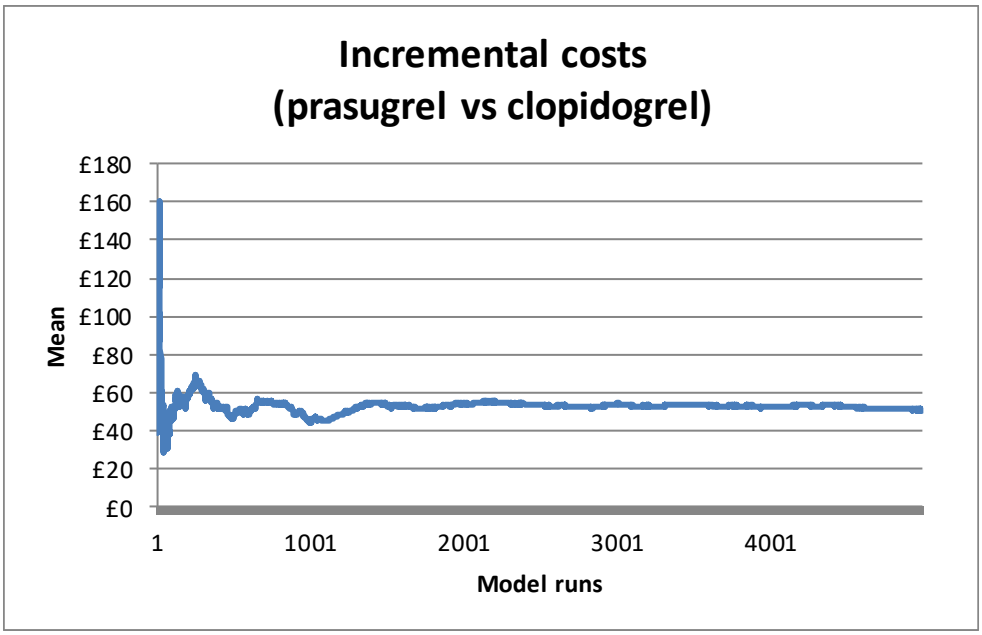
### 2.2.3 Uncertainty

The model was built probabilistically to take account of the uncertainty around input parameter point estimates. A probability distribution was defined for each model input parameter. When the model was run, a value for each input was randomly selected simultaneously from its respective probability distribution; mean costs and mean QALYs were calculated using these values. The model was run repeatedly – 5,000 times for the base case and each sensitivity analysis – and results were summarised in terms of mean costs and QALYs. The percentage of time each comparator was most cost-effective at a threshold of £20,000 per QALY gained was recorded.

When running the probabilistic analysis, multiple runs are required to take into account random variation in sampling. To ensure the number of model runs were sufficient in the probabilistic analysis it was checked for convergence in the incremental costs, incremental QALYs and net monetary benefit at a threshold of £20,000 per QALY gained for each

comparator. This was done by plotting the number of runs against the mean outcome at that point (see example in Figure 3) for the base-case analyses. Convergence was assessed visually and all had stabilised before 5000 runs.

**Figure 3: Checking for convergence: incremental costs (prasugrel vs clopidogrel, STEMI, Scenario 1)**




The way in which distributions are defined reflects the nature of the data, so for example probabilities were given a beta distribution, which is bounded by 0 and 1, reflecting that a probability will not be outside this range. All of the variables that were probabilistic in the model and their distributional parameters are detailed in Table 1. Probability distributions in the analysis were parameterised using error estimates from data sources.

**Table 1: Description of the type and properties of distributions used in the probabilistic sensitivity analysis**

| Parameter | Type of distribution | Properties of distribution |
|---|---|---|
| Baseline risks | Beta | Bounded between 0 and 1. As the sample size and the number of events were specified alpha and beta values were calculated as follows:<br>Alpha = (number of people having event)<br>Beta = (Number of people) − (number of people having event) |
| Odds ratios at 1 year<br>Hazard ratios<br>SMRs | Lognormal | The natural log of the mean was calculated as follows:<br><br>Mean = ln(mean cost) − $SE^2/2$<br><br>Where the natural log of the standard error was calculated by:<br>SE = [ln(upper 95% CI) − ln(lower 95% CI)]/(1.96×2)<br>$\sqrt{\ln \frac{SE^2 + mean^2}{mean^2}}$ |
| Odds ratios (30 days) | Bespoke | The network meta-analysis used simulation methods, which yielded 60,000 individual estimates of each odds ratio. These estimates represent the posterior |

| Parameter | Type of distribution | Properties of distribution |
|---|---|---|
| | | distribution of the odds ratio. A sample of 5,000 preserving correlations was taken from the 60,000 estimates. |
| Utilities | Beta | Bounded between 0 and 1. Derived from mean of a domain or total quality of life score and its standard error, using the method of moments.<br>Alpha and Beta values were calculated as follows:<br>$Alpha = mean^2 \times [(1-mean)/SE^2] - mean$<br>$Beta = Alpha \times [(1-mean)/mean]$ |
| Utility decrements | Gamma | Bounded at 0, positively skewed. Derived from mean and its standard error.<br>Alpha and Beta values were calculated as follows:<br>$Alpha = (mean/SE)^2$<br>$Beta = SE^2/Mean$ |

The following variables were left deterministic (that is, they were not varied in the probabilistic analysis):

- The cost-effectiveness threshold (which was deemed to be fixed by NICE)
- Health state costs (based on analyses that use unit costs from UK national sources)
- Drug costs (based on NHS drug tariff which is fixed)
- Mortality probabilities for general population (based on UK national data)

In addition, various one way and scenario sensitivity analyses were undertaken to test the robustness of model assumptions. In these, one or more inputs were changed and the analysis rerun to evaluate the impact on results and whether conclusions on which intervention should be recommended would change. Details of the sensitivity analyses undertaken can be found in methods section 2.4.

# 2.3 Model inputs

## 2.3.1 Summary table of model inputs

Model inputs were based on clinical evidence identified in the systematic review undertaken for the guideline and supplemented by additional data sources as required. Model inputs were validated with clinical members of the guideline committee. A summary of the model inputs used in the base-case (primary) analysis is provided in Table 2 below. More details about sources, calculations and rationale for selection can be found in the sections that follow.

**Table 2: Summary of base-case model inputs**

| Input | Data | Source |
|---|---|---|
| Comparators | • Clopidogrel & aspirin<br>• Ticagrelor & aspirin<br>• Prasugrel & aspirin | |
| Populations | • Adults with STEMI undergoing PCI<br>• Adults with UA/NSTEMI undergoing PCI | |
| Perspective | UK NHS and PSS | NICE reference case |
| Time horizon | Lifetime | NICE reference case |

| Input | Data | Source |
|---|---|---|
| Discount rate | Costs: 3.5%<br>Outcomes: 3.5% | NICE reference case |
| **Baseline risks with clopidogrel 0 to 30 days** | | |
| *STEMI* | | |
| All-cause mortality | 6.15% | Mortality tracked BCIS PCI audit data, Hulme 2019[17] |
| Reinfarction | 2.91% | Krishnamurthy 2019[21] |
| Stroke | 0.30% | UK audit of PCI data, Myint 2016[31] |
| Major bleed | 0.94% | Calculated based on relationship between bleeds and 30 day and 1 year events from PLATO RCT (see section 2.3.2) |
| Minor bleed | 0.71% | Calculated based on relationship between bleeds and 30 day and 1 year events from PLATO RCT (see section 2.3.2) |
| *UA/NSTEMI* | | |
| All-cause mortality | 1.79% | Mortality tracked BCIS PCI audit data, Hulme 2019[17] |
| Reinfarction | 1.02% | Calculated based on 1 year rate from NICE CG94[40] using PLATO and Swedeheart rates (see section 2.3.2) |
| Stroke | 0.11% | UK audit of PCI data, Myint 2016[31] |
| Major bleed | 0.65% | PLATO RCT, Lindholm 2014[24] |
| Minor bleed | 0.41% | Calculated based on relationship between bleeds and 30 day and 1 year events from PLATO RCT (see section 2.3.2) |
| **Baseline risks with clopidogrel 31 days to 1 year** | | |
| *STEMI* | | |
| All-cause mortality | 3.80% | Mortality tracked BCIS PCI audit data, Hulme 2019[17] |
| Reinfarction | 3.88% | Krishnamurthy 2019[21] and recalculated based on 30 day events (see section 2.3.2) |
| Stroke | 1.01% | Calculated based on 30 day events from Myint 2016[31] using Swedeheart audit data (see section 2.3.2) |
| Major bleed | 2.69% | Steg 2010[54] |
| Minor bleed | 2.03% | Calculated based on relationship between bleeds and 30 day and 1 year events (see section 2.3.2) |
| *UA/NSTEMI* | | |
| All-cause mortality | 3.71% | Mortality tracked BCIS PCI audit data, Hulme 2019[17] |
| Reinfarction | 3.26% | NICE CG94[40] and recalculated based on 30 day events (see section 2.3.2) |
| Stroke | 0.53% | Calculated based on 30 day events from Myint 2016[31] using Swedeheart audit data (see section 2.3.2) |
| Major bleed | 1.77% | Lindholm 2014[24] |
| Minor bleed | 1.12% | Calculated based on relationship between bleeds and 30 day and 1 year events (see section 2.3.2) |

| Input | Data | Source |
|---|---|---|
| **Relative treatment effects versus clopidogrel at 30 days (odds ratios; 95% CI)** | | |
| *Ticagrelor* | | |
| All cause- mortality | 0.85 (0.70 to 1.02) | Systematic review of RCTs undertaken as part of guideline development (network meta-analysis including all evidence comparing any of clopidogrel, prasugrel and ticagrelor) – see Evidence report A and NMA report |
| Reinfarction | 0.68 (0.55 to 0.84) | |
| Stroke | 1.28 (0.86 to 1.83) | |
| Major bleed | 1.00 (0.89 to 1.11) | |
| Minor bleed | 1.28 (0.88 to 1.81) | |
| *Prasugrel* | | |
| All-cause mortality | 0.81 (0.63 to 1.02) | Systematic review of RCTs undertaken as part of guideline development (network meta-analysis including all evidence comparing any of clopidogrel, prasugrel and ticagrelor)) – see Evidence report A and NMA report |
| Reinfarction | 0.80 (0.65 to 0.98) | |
| Stroke | 0.84 (0.46 to 1.39) | |
| Major bleed | 0.99 (0.61 to 1.52) | |
| Minor bleed | 0.74 (0.51 to 1.04) | |
| **Relative treatment effects at 1 year (odds ratios; 95% CI)** | | |
| *Ticagrelor versus clopidogrel (used in scenarios 1 and 3)* | | |
| All-cause mortality | 0.77 (0.68 to 0.88) | Systematic review of RCTs undertaken as part of guideline development (pairwise meta-analysis; 1 year outcomes) – see Evidence report A |
| Reinfarction | 0.82 (0.73 to 0.92) | |
| Stroke | 1.13 (0.89 to 1.44) | |
| Major bleed | 1.04 (0.95 to 1.14) | |
| Minor bleed | 1.37 (1.19 to 1.57) | |
| *Prasugrel versus clopidogrel (used in scenarios 1 and 2)* | | |
| All-cause mortality | 1.00 (0.83 to 1.21) | Systematic review of RCTs undertaken as part of guideline development (pairwise meta-analysis; 1 year outcomes) – see Evidence report A |
| Reinfarction | 0.75 (0.66 to 0.84) | |
| Stroke | 0.93 (0.67 to 1.30) | |
| Major bleeding | 1.43 (1.14 to 1.79) | |
| Minor bleeding | 2.07 (0.88 to 4.87) | |
| *Ticagrelor versus prasugrel (used in scenarios 2 and 3)* | | |
| All-cause mortality | 1.24 (0.90 to 1.70) | Systematic review of RCTs undertaken as part of guideline development (ISAR-REACT 5 analysis; 1 year outcomes) – see Evidence report A |
| Reinfarction | 1.63 (1.17 to 2.26) | |
| Stroke | 1.16 (0.62 to 2.14) | |
| Major bleed | 1.06 (0.78 to 1.44) | |
| Minor bleed | *Note: No data reported in ISAR-REACT 5 for minor bleed* | |
| **Transition probabilities in post year 1 Markov model** | | |
| *Transition probabilities excluding death* | | |
| *STEMI* | | |
| Reinfarction | 4.30% | Calculated from baseline risk data between 31 days and 1 year for STEMI and readjusted to reflect 1 year probability |
| Stroke | 1.12% | |
| *UA/NSTEMI* | | |
| Reinfarction | 3.62% | Calculated from baseline risk data between 31 days and 1 year for UA/NSTEMI and readjusted to reflect 1 year probability |
| Stroke | 0.59% | |
| *Transition probabilities to dead state* | | |

| Input | Data | Source |
|---|---|---|
| General population mortality | Age and sex dependent<br><br>Age entering Markov model:<br>• STEMI:<br>○ Male: 62 years<br>○ Female: 69 years<br>• UA/NSTEMI:<br>○ Male: 64 years<br>○ Female: 69 years<br><br>% male entering Markov model<br>• STEMI: 75%<br>• UA/NSTEMI: 72% | ONS life tables for England 2015-17[44]<br><br>BCIS PCI audit data, Hulme 2019[17] |
| No further event SMR | 2.00 (1.99 to 2.01) | Smolina 2012[53] |
| Reinfarction SMR | 4.50 (4.43 to 4.57) | Smolina 2012[53] |
| Post-reinfarction SMR | 3.00 (2.95 to 3.05) | Smolina 2012[53] |
| Stroke SMR | 4.73 (4.34 to 5.15) | Bronnum-Hansen 2001[6] |
| Post-stroke SMR | 2.32 (2.17 to 2.49) | Bronnum-Hansen 2001[6] |
| **Costs** | | |
| **Treatment costs (cost per year)** | | |
| Aspirin | £24 | Includes loading dose where applicable. Unit costs from NHS Drug Tariff July 2020[41] and dosing from British National Formulary[19], accessed 1st July 2020. |
| Clopidogrel | £22 | |
| Prasugrel | £100 | |
| Ticagrelor | £714 | |
| **Decision tree costs (0 – 30 day event; 31 day to 1 year event)** | | |
| No further event; no further event | £1,640 | See section 2.3.6.2 |
| No further event; reinfarction | £5,564 | See section 2.3.6.2 |
| No further event; stroke | £15,203 | See section 2.3.6.2 |
| No further event; death | £1,168 | See section 2.3.6.2 |
| Reinfarction; no further event | £5,104 | See section 2.3.6.2 |
| Reinfarction; reinfarction | £8,792 | See section 2.3.6.2 |
| Reinfarction; stroke | £18,431 | See section 2.3.6.2 |
| Reinfarction; death | £4,396 | See section 2.3.6.2 |
| Stroke; no further event | £17,323 | See section 2.3.6.2 |
| Stroke; reinfarction | £21,719 | See section 2.3.6.2 |
| Stroke; stroke | £21,014 | See section 2.3.6.2 |
| Stroke; death | £14,035 | See section 2.3.6.2 |
| Death; n/a | £0 | |
| Adverse event costs | | |
| Major bleed | £1,955 | NHS reference costs 2017/18[12], weighted average of gastrointestinal bleeds with interventions |

| Input | Data | Source |
|---|---|---|
| Minor bleed | £176 | NHS reference costs 2017/18[12], weighted average of emergency admission with investigation |
| **Markov model costs** | | |
| No further event | £943 | Danese 2016[9] |
| Reinfarction | £5,104 | Danese 2016[9] |
| Post-reinfarction | £1,415 | Danese 2016[9] |
| Stroke | £18,522 | Xu 2018 SSNAPP project[65] |
| Post-stroke | £6,576 | Xu 2018 SSNAPP project[65] |
| **Quality of life (utilities)** | | |
| **Health states** | | |
| No further event | 0.842 | NICE TA236[39] PLATO health economic subgroup analysis |
| Reinfarction | 0.779 | |
| Post-reinfarction | 0.821 | |
| Non-fatal stroke | 0.703 | |
| Post-stroke | 0.703 | |
| Dead | 0 | By definition |
| Age-adjustment (general population utility by age) | Age and sex dependant | Calculated using formulae from Ara and Brazier 2010.[3] Applied multiplicatively with health state weights. |
| **Adverse event decrements (and duration applied)** | | |
| Major bleed | 0.038 (45.38 days) | Amin 2016[13] |
| Minor bleed | 0.026 (7.60 days) | |

*Abbreviations: NMA = network meta-analysis; ONS = Office for National Statistics; PCI = percutaneous coronary intervention; RCT = randomised controlled trial; SMR = standardised mortality ratio.*

### 2.3.2 Baseline risks in first year treatment period decision tree

The model was populated with baseline risks for those receiving clopidogrel and aspirin (e.g. the probability of death at 30 days etc). When running the model for those receiving ticagrelor and prasugrel a relative treatment effect obtained from the clinical review and evidence synthesis (compared to clopidogrel) was applied to this in order to estimate the difference in number of events with these alternative treatments. The relative treatment effects, and how they are used in the model, are discussed in section 2.3.3.

#### 2.3.2.1 The available data and general issues

The data required for the baseline risks in the first year decision tree was the proportion of people who have died, and who are alive with reinfarction, stroke or no event at 30 days and at 1 year after STEMI and after UA/NSTEMI in people receiving clopidogrel and aspirin. The potential to undertake original analysis of real world patient level data using national audit data linked with mortality and HES data was discussed as this would allow exact calculation of the probabilities required for the model but this was not feasible within guideline development time constraints. Therefore, published analyses of real world risks utilising UK audit data were sought and presented to the committee for discussion of the best available data sources.

No data source was identified that reported data exactly as required however a number of separate UK real-world analyses provided information about mortality, stroke and reinfarction after STEMI and UA/NSTEMI and these were used to estimate the required probabilities for the decision tree. The data used in the model to inform probabilities for each outcome is

described in the subsequent sections in detail. Some general issues and the approach taken are described below first.

One issue was that the model aims to estimate the number of people alive at a particular time point with stroke or reinfarction but the available data analyses mostly looked at all events over the time period (reinfarction for STEMI and stroke for STEMI and UA/NSTEMI was based on all events and reinfarction for UA/NSTEMI was based on non-fatal events). Where this was the case this data has been used but it is acknowledged this may results in an overestimate of the number of people alive having had these events at 1 year and so also underestimate the number alive with no new event (note that the number of people alive will not be affected just whether or not they have an event). Given this, a sensitivity analysis was undertaken using lower probabilities for stroke and reinfarction (as described in section 2.4) to explore whether conclusions were sensitive to this.

Another issue was whether probabilities between 31 days and 1 year should vary depending on what happened between 0 and 30 days. While the committee agreed that in reality it may be the case that prior events will influence these probabilities, the real world UK data identified were for the population as a whole. The committee discussed whether to try and adjust the probabilities to try and account for this but preferred to use the same probability throughout given the available information and agreed that this was a reasonable simplification for modelling purposes given the overall number of people alive in the population will remain correct. Therefore in the model, the same probability of having an event (death, MI or stroke) between 31 days and 1 year was applied irrespective of whether someone experienced MI, stroke or no new event between 0 to 30 days.

Data relating to people with ACS receiving clopidogrel and aspirin were sought however audit data was mostly analysed for the overall cohort, rather than just those that received this dual antiplatelet option. The committee noted that there may be issues with using the most recent audit data for the baseline risks. Firstly, they stated that a high proportion of people will not be taking clopidogrel as the use of ticagrelor and prasugrel has increased in recent years. For those that are on clopidogrel it may be that these people have a higher bleeding risk (e.g. an older population) and therefore were given clopidogrel, which would not be a good representation of the average population.

Therefore, the committee felt that it may be useful to use slightly older audit data to account for this. It was highlighted that there was a balance between choosing a year where clopidogrel use was high but also ensuring that it was still relevant to current practice in terms of other processes, for example, radial access and drug-eluting stent usage. Therefore, BCIS reports were used to obtain the DAPT use for each year in order to help aid committee decisions regarding which data to use. The specific data used in the model and the rationales are described in the sections that follow by outcome.

**Table 3: BCIS audit data[26]**

| | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 |
|---|---|---|---|---|---|---|---|---|
| STEMI | | | | | | | | |
| Prasugrel | 9.3% | 22.2% | 22.6% | 16.1% | 14.1% | 10.5% | 9.9% | 7.2% |
| Ticagrelor | n/a | n/a | 7.04% | 21% | 30.1% | 38.1% | 42.2% | 47.5% |
| Clopidogrel[(a)] | 90.7% | 77.8% | 70.4% | 62.9% | 55.8% | 51.4% | 47.9% | 45.3% |
| DES use | 54.4% | 59.5% | 68.4% | 75.8% | 81.9% | 86.3% | 89.1% | 91.0% |
| Radial access | 50.0% | 57.0% | 65.5% | 71.5% | 75.8% | 80.3% | 82.8% | 85.8% |
| UA/NSTEMI | | | | | | | | |
| Prasugrel | 0.54% | 1.5% | 2.6% | 1.9% | 1.6% | 1.6% | 1.1% | 1.0% |
| Ticagrelor | n/a | n/a | 3.7% | 15.2% | 23.0% | 29.9% | 34.3% | 40.2% |
| Clopidogrel[(a)] | 99.5% | 98.5% | 93.7% | 82.9% | 75.4% | 68.5% | 64.6% | 58.8% |

| | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 |
|---|---|---|---|---|---|---|---|---|
| DES use | 66.6% | 69.8% | 76.8% | 82.5% | 86.9% | 89.7% | 90.9% | 91.5% |
| Radial access | 54% | 62% | 66.7% | 71.9% | 75.6% | 79.8% | 83% | 85.8% |

*(a) Clopidogrel use was not always reported therefore it was assumed that everyone not receiving prasugrel or ticagrelor was receiving clopidogrel.*

**Calculating probabilities for 31 days to 1 year**

To calculate probabilities for 31 days to 1 year, the appropriate numerator (r) and denominator (n) needed to be calculated from the data for this time period. That is the numerator needed to only include events that occurred between 31 days and 1 year and the denominator needed to only include those at risk at 31 days (i.e. those alive).

Probability of event 31 days to 1 year = $\frac{\text{events 31 days to 1 year (r)}}{\text{people at risk at 31 days (n)}}$

Events 31 days to 1 year (r) = events at 1 year – events at 30 days

People at risk at 31 days (n) = total population – people who died 0 to 30 days

As the data analyses identified for each outcome (other than mortality) did not generally report the actual number of people who had died by 30 days this was estimated by multiplying the total population by the 0 to 30 day mortality probability used in the model.

Details of the calculations for each outcome are described in subsequent sections.

**Incorporation of baseline risk into probabilistic analysis**

Each baseline risk probability was incorporated into the probabilistic analysis using an independent beta distribution. These were parameterised using the relevant number of events (r) and number of people at risk (n).

While theoretically the four alternative outcomes at each timepoint would be incorporated using a Dirichlet distribution (used for multinomial data) this was not possible here as not all the probabilities came from the same source. However, checks were built into the model to ensure the overall probabilities generated were appropriate (not exceeding one or negative) and so this is not considered problematic.

In addition, it was noted that there may be covariance between probabilities in the model however data was not available to incorporate this and so independent distributions were used. This is a common approach in cost effectiveness modelling. It is noted that this may result in some additional uncertainty in the analysis results.

#### 2.3.2.2 Mortality

A study by Hulme 2019[17] reported crude and relative survival estimates at 30 days and 1 year for males and females following PCI for England and Wales in the years 2007 to 2014. This analysis was based on mortality tracked BCIS PCI audit data and STEMI and UA/NSTEMI were reported separately. Although the study did not report survival based on clopidogrel use, it was agreed to use a year where BCIS reported higher clopidogrel use (as seen in Table 3), and as a result the year 2011-12 was chosen as clopidogrel use was 77.8% for STEMI and 98.5% for UA/NSTEMI. The data on crude survival was used to obtain the 30 day and 1 year probability of death as demonstrated in Table 4. These were then combined to obtain the overall probabilities for males and females, based on a weighted average.

**Table 4: Hulme 2019 survival and mortality calculations**

| | 30 days crude survival | 30 day mortality[(a)] | 1 year crude survival | 1 year mortality[(a)] |
|---|---|---|---|---|
| STEMI | | | | |
| Female | 0.914 | 1 – 0.914 = 8.6% | 0.865 | 1 – 0.865 = 13.5% |
| Male | 0.947 | 1 – 0.947 = 5.3% | 0.916 | 1 – 0.916 = 8.4% |
| All (male & female) | | 6.15% | | 9.71% |
| UA/NSTEMI | | | | |
| Female | 0.977 | 1 – 0.977 = 2.3% | 0.937 | 1 – 0.937 = 6.3% |
| Male | 0.984 | 1 – 0.984 = 1.6% | 0.949 | 1 – 0.949 = 5.1% |
| All (male & female) | | 1.79% | | 5.43% |

*(a) The probability of mortality at 30 days and 1 year were calculated using the crude survival.*

As described in more detail in Section 2.3.2.1 above, the model structure in the first year was split to model 0 to 30 days and 31 days to 1 year, calculation of the probabilities for 31 days to 1 year needed to account for people who had died at 30 days in the numerator and denominator. Table 5 shows the calculations and resulting model inputs for mortality for STEMI and UA/NSTEMI.

**Table 5: Data inputs for mortality baseline risk in STEMI and UA/NSTEMI**

| N | R | Probability | N | R | Probability |
|---|---|---|---|---|---|
| *STEMI* | | | | | |
| 30 days | | | 1 year | | |
| 40,724 | 2,504 | 6.15% | 40,724 | 3,955 | 9.7% |
| Recalculated for model inputs: | | | | | |
| 0 to 30 days | | | 31 days to 1 year | | |
| 40,724 | 2504 | 6.15% | 40,724 – 2,504 = 38,220 | 3,955 – 2,504 = 1,451 | 1,451/38,220 = 3.80% |
| *UA/NSTEMI* | | | | | |
| 30 days | | | 1 year | | |
| 54,518 | 978 | 1.79% | 54,518 | 2,962 | 5.43% |
| Recalculated for model inputs: | | | | | |
| 0 to 30 days | | | 31 days to 1 year | | |
| 54,518 | 978 | 1.79% | 54,518 - 2,962 = 53,540 | 2,962 – 978 = 1,984 | 1,984/53,540 = 3.71% |

#### 2.3.2.3 Reinfarction

An analysis of reinfarction using national STEMI data was not identified. Krishnamurthy 2019 however reported an analysis of real world data in Leeds comparing the differences in outcomes of people taking clopidogrel, ticagrelor and prasugrel at 30 days and 1 year.[21] This was a study conducted at Leeds General Infirmary and assessed all adults with STEMI that underwent primary PCI between 1 January 2009 and 31 December 2011. The committee agreed this was a reasonable source of baseline risk estimates given national data wasn't available. Table 6 shows the number of people and probability of reinfarction taken from the study. As discussed in more detail above, this probability was for all reinfarctions, and therefore would overestimate the number of people alive with a reinfarction at 1 year. This was addressed in a sensitivity analysis to see if this impacted conclusions.

As described in more detail in Section 2.3.2.1 above, calculation of the probability for 31 days to 1 year for the model needed to account for events that occurred 0 to 30 days in the numerator and people who had died by 30 days in the denominator. Table 7 shows how these were adjusted to obtain the probabilities for 0 to 30 days and 31 days to 1 year.

**Table 6: Reinfarction for STEMI population from Krishnamurthy 2019**

| n | r at 30 days | Probability of reinfarction at 30 days | r at 1 year | Probability of reinfarction at 1 year |
|---|---|---|---|---|
| 1,648 | 48 | 48/1,648 = 2.91% | 108 | 108/1,648 = 6.55% |

*Abbreviations: n = number of people in the study; r = number of events*

**Table 7: Data inputs for reinfarction baseline risk in STEMI**

| N | R | Probability | N | R | Probability |
|---|---|---|---|---|---|
| 30 days | | | 1 year | | |
| 1648 | 48 | 2.91% | 1648 | 108 | 6.55% |
| Recalculated for model inputs: | | | | | |
| 0 to 30 days | | | 31 days to 1 year | | |
| 1648 | 48 | 2.91% | 1648 – (1648*6.15%[a]) = 1547 | 108 – 48 = 60 | 60/1547 = 3.88% |

*(a) This is the probability of death at 30 days, taken from Hulme 2019[17]*

For the UA/NSTEMI population undergoing PCI, the best available source identified was an analysis of MINAP data that was conducted for the previous UA/NSTEMI NICE Guideline CG94.[40] This analysis reported reinfarction at 1 year and reported it separately by type of management, therefore it was available for those who underwent PCI. This analysis was conducted for people with UA/NSTEMI in England from 2005 to 2007. It was discussed that this was quite an old analysis and that treatment may have improved since then, for example, the guideline recommended the use of early angiography and PCI if indicated, meaning that more people with UA/NSTEMI have undergone PCI since then. Only 15% of the people analysed in this dataset underwent PCI. However, one of the positives of using this data was that it was specific to PCI and also the use of ticagrelor and prasugrel had not started, meaning everyone in the analysis would have received clopidogrel. As a result, the committee agreed this was the best available source of data available to estimate baseline risk. Also, the probabilities were for non-fatal events, therefore the correct number of people alive with a reinfarction at one year was available. As a result these were not adjusted in a sensitivity analysis. Table 8 shows the events and probabilities. The committee considered using more recent data from the Swedish national audit Swedeheart as this had published an analysis of UA/NSTEMI outcomes in Sweden including reinfarction[56]. However, UA/NSTEMI overall was analysed and only 47.3% had PCI so the committee agreed the MINAP analysis was preferable.

**Table 8: CG94 probability of reinfarction**

| n | r at 1 year | Probability of reinfarction at 1 year |
|---|---|---|
| 2,392 | 101 | 101/2392 = 4.22% |

*Abbreviations: n = number of people in the study; r = number of events*

As the MINAP analysis did not report reinfarction at 30 days, this was estimated using the 1 year data combined with information about the proportion of 1 year events that happen between 0 and 30 days. The committee agreed the best source of information about this relationship identified was the Swedeheart audit described above.[56] However, as there was some uncertainty due to this analysis not only including people receiving PCI, the committee also wanted to know the relationship between 30 day and 1 year events in the clopidogrel arm of the PLATO RCT[58], as this was the trial which was considered closest to UK practice, as it was the only trial to recruit in the UK. This was only available for the overall ACS

population and was not specific to UA/NSTEMI. Table 9 shows the probability of reinfarction at 30 days and one year from Swedeheart and PLATO, and the resulting proportions of 1 year events that occurred by 30 days.

**Table 9: Relationship between 30 day and 1 year events for reinfarction**

| | n | Probability of reinfarction |
|---|---|---|
| Swedeheart 2011-2012 | | |
| 30 day | 24,962 | 2.0% |
| 1 year | 24,962 | 9.9% |
| Proportion of events that occurred by 30 days | | 2.0%/9.9% = 20.2% |
| PLATO | | |
| 30 day | 9186[(a)] | 1.8% |
| 1 year | 9291 | 6.4% |
| Proportion of events that occurred by 30 days | | 1.8%/6.4% = 28.1% |
| Calculated 30 day probability of reinfarction | | |
| Average proportion of 30 days to 1 year | | (20.2+28.1)/2 = 24.2% |
| Calculated 30 day probability of reinfarction | | 24.2% * 4.22% = 1.02% |

*(a) Note: the authors were contacted for 30 day outcomes and the number of participants was slightly different to those reported in the published paper*

The committee decided to average the percentage obtained from the Swedeheart and PLATO analysis in order to calculate the probability of reinfarction at 30 days as these estimates were similar. Again, adjustments were made in order to obtain the correct number of events between 31 days and 1 year (r) and the total number of people at risk at 31 days (n) in order to calculate the probability of reinfarction 31 days to 1 year. Table 10 shows how the baseline risk was adjusted for reinfarction in UA/NSTEMI.

**Table 10: Data inputs for reinfarction baseline risk in UA/NSTEMI**

| N | R | Probability | N | R | Probability |
|---|---|---|---|---|---|
| 30 days | | | 1 year | | |
| 2,392 | 24 | 1.02% | 2,392 | 101 | 4.22% |
| Recalculated for model inputs: | | | | | |
| 0 to 30 days | | | 31 days to 1 year | | |
| 2,392 | 24 | 1.02% | 2,392 – (2,392*1.79%[a]) = 2,349 | 101 – 24 = 77 | 77/2,349 = 3.26% |

*(a) This is the probability of death at 30 days, taken from Hulme 2019[17]*

#### 2.3.2.4 Stroke

Data on 30 day probability of stroke was taken from Myint 2016[31], which looked at outcomes of stroke following PCI based on BCIS audit data. As described in more detail in Section 2.3.2.1 above, fatal and non-fatal events were included in this data, and therefore will somewhat overestimate the number of people alive with a stroke at 1 year. This was addressed in a sensitivity analysis to see if this impacted conclusions.

**Table 11: Myint 2016[31] stroke outcomes at 30 days**

| n | r (ischaemic stroke) | r (haemorrhagic stroke) | r (all stroke) | Probability of stroke at 30 days |
|---|---|---|---|---|
| STEMI | | | | |
| 102,493 | 256 | 48 | 304 | 304/102,493 = 0.30% |
| UA/NSTEMI | | | | |
| 205,962 | 181 | 41 | 222 | 222/205,962 = 0.11% |

As there was no real world data for 1 year outcomes of stroke, data from Swedeheart and PLATO was used to calculate the relationship between 30 day and 1 year events, as seen in Table 12.

**Table 12: Relationship between 30 day and 1 year events for stroke**

| | n | Probability of stroke |
|---|---|---|
| Swedeheart STEMI 2011-2012 | | |
| 30 day | 117,546 | 0.5% |
| 1 year | 117,546 | 2.1% |
| Percentage increase 1 year relative to 30 days | | 2.1%/0.5% = 420% |
| Swedeheart UA/NSTEMI 2011-2012 | | |
| 30 day | 24,962 | 0.5% |
| 1 year | 24,962 | 2.9% |
| Percentage increase 1 year relative to 30 days | | 2.9%/0.5% = 580% |
| PLATO (overall ACS) | | |
| 30 day | 9186[(a)] | 0.5% |
| 1 year | 9291 | 1.1% |
| Percentage increase 1 year relative to 30 days | | 1.1%/0.5% = 224% |
| Calculated 1 year probability for stroke | | |
| Calculated 1 year probability of stroke for STEMI | | 420% * 0.30% = 1.25% |
| Calculated 1 year probability of stroke for UA/NSTEMI | | 580% * 0.11% = 0.63% |

*(a) Note: the authors were contacted for 30 day outcomes and the number of participants was slightly different to those reported in the published paper*

The estimates obtained from Swedeheart and PLATO were quite different, therefore the committee agreed to use the Swedeheart estimates for both STEMI and UA/NSTEMI in the base case analysis as it is based on large registry data. However due to the differences between the two sources, it was agreed to conduct a sensitivity analysis using the PLATO estimate to assess if this impacted conclusions. The results of this calculation are demonstrated in Table 12. Adjustments were made in order to have the correct number of events between 31 days and 1 year (r) and the total number of people at risk at 31 days (n), in order to calculate the probability of stroke between 31 days and 1 year. Table 13 shows the calculations to obtain these probabilities.

**Table 13: Data inputs for stroke baseline risk in STEMI and UA/NSTEMI**

| N | R | Probability | N | R | Probability |
|---|---|---|---|---|---|
| *STEMI* | | | | | |
| 30 days | | | 1 year | | |
| 102,493 | 304 | 0.30% | 102,493 | 1,277 | 1.25% |

| N | R | Probability | N | R | Probability |
|---|---|---|---|---|---|
| Recalculated for model inputs: | | | | | |
| 0 to 30 days | | | 31 days to 1 year | | |
| 102,493 | 304 | 0.30% | 102,493 – (102493*6.15% [a]) = 96,190 | 1,277 – 304 = 973 | 973/102,493 = 1.01% |
| *UA/NSTEMI* | | | | | |
| 30 days | | | 1 year | | |
| 205,962 | 222 | 0.11% | 205,962 | 1,288 | 0.63% |
| Recalculated for model inputs: | | | | | |
| 0 to 30 days | | | 31 days to 1 year | | |
| 205,962 | 222 | 0.11% | 205,962 – (205,962*1.79% [a]) = 202,266 | 1,288 – 222 = 1,066 | 1,066/202,266 = 0.53% |

*(a) This is the probability of death at 30 days, taken from Hulme 2019[17]*

#### 2.3.2.5 Major and minor bleeding

Suitable real world data about major and minor bleeding for the specific populations in the model were not identified. As a result, the committee agreed that estimates from the PLATO RCT should be used. This was because the committee indicated that this trial was closest to UK practice.

As haemorrhagic stroke would be classified as a major bleed but also be captured in the stroke health state, the major bleeding rate should ideally exclude haemorrhagic stroke to account for double counting. However, the major bleeding rate was not reported without haemorrhagic stroke. As major bleeding was incorporated as a short-term adverse event it was deemed appropriate to assume that there was no overlap for the purposes of the model.

Overall major and minor bleeding rates looked very high in the PLATO RCT, and this was thought to be because their definition of bleeding included CABG related bleeding. They also reported other bleeding outcomes according to different definitions and it was decided by the committee to use the definition which excluded CABG bleeding. However, these were not well reported. Table 14 shows the data that was available on non-CABG major and minor bleeding.

**Table 14: Data available from published sources for non-CABG related bleeding from PLATO**

| | Major bleed | Minor bleed |
|---|---|---|
| STEMI | | |
| 30 day | NR | NR |
| 1 year | 3.46% | 2.61%[(a)] |
| UA/NSTEMI | | |
| 30 day | 0.65% | NR |
| 1 year | 2.38% | NR |

*Abbreviations: NR = not reported*

*(a) This was calculated from published data, using the total number of non-CABG major and minor bleeds and subtracting the number of major bleeds.*

As seen above, there was no data available on minor bleeds for UA/NSTEMI and there was no data on major bleeds at 30 days and minor bleeds for STEMI. As a result, calculations were undertaken to estimate the probabilities.

To estimate the number of major bleeds at 30 days for STEMI, the relationship between 30 day and 1 year events for UA/NSTEMI was applied. For UA/NSTEMI 27% of 1 year events occurred in 30 days. Using this combined with the 1 year STEMI major bleeding rate resulted in an estimated probability of major bleed at 30 days of 0.94% for STEMI. The relationship of 30 day and 1 year events from UA/NSTEMI was used again to obtain the probability of minor bleeds at 30 days, which was 0.71%.

In order to calculate minor bleeds for UA/NSTEMI, the relationship between major and minor bleeds was estimated from a different outcome for bleeding, based on the TIMI criteria. This was deemed appropriate as the probabilities were similar for bleeding events where they reported the same outcome (e.g. major bleeds). Table 15 shows how this was calculated.

**Table 15: Calculations for UA/NSTEMI minor bleed**

| Outcome | Probability |
|---|---|
| Major bleed at 1 year (TIMI) | 2.79% |
| Major and minor bleeds at 1 year (TIMI) | 4.56% |
| Minor bleeds at 1 year (estimated) | 1.77% |
| % minor bleeds related to major bleeds | 63% |
| Minor bleed 30 day (estimated) | Probability of major bleed at 30 days*63% = 0.41% |
| Minor bleed 1 year (estimated) | Probability of major bleed at 1 year*63% = 1.51% |

It was deemed appropriate to use the major bleeding data when estimating rates for minor bleeding because the relationship between minor bleeding at 30 days and 1 year is likely to be similar for major bleeding at 30 days to 1 year. Table 16 shows the probabilities after calculations.

**Table 16: Probabilities of major and minor bleeding**

| | Major bleed | Minor bleed |
|---|---|---|
| STEMI | | |
| 30 day | *0.94%* | *0.71%* |
| 1 year | 3.46% | 2.61% |
| UA/NSTEMI | | |
| 30 day | 0.65% | *0.41%* |
| 1 year | 2.38% | *1.51%* |

*Note: Values in italics indicate that they are calculated estimates.*

As with the previous baseline risks, adjustments were made to obtain the correct number of events between 31 days and 1 year (r) and the total number of people at risk at 31 days (n) in order to calculate the correct probabilities of major or minor bleeding between 31 days and 1 year. These calculations are shown in Table 17 for major bleeding and Table 18 for minor bleeding.

**Table 17: Data inputs for major bleeding baseline risk in STEMI and UA/NSTEMI**

| N | R | Probability | N | R | Probability |
|---|---|---|---|---|---|
| *STEMI* | | | | | |
| 30 days | | | 1 year | | |
| 3,752 | 35 | 0.94% | 3,752 | 130 | 3.46% |
| Recalculated for model inputs: | | | | | |
| 0 to 30 days | | | 31 days to 1 year | | |

| N | R | Probability | N | R | Probability |
|---|---|---|---|---|---|
| 3,752 | 35 | 0.94% | 3,752 – (3,752*6.15%[a]) = 3,521 | 130 – 35 = 95 | 95/3,521 = 2.69% |
| *UA/NSTEMI* | | | | | |
| 30 days | | | 1 year | | |
| 2,617 | 17 | 0.65% | 2,617 | 62 | 2.38% |
| Recalculated for model inputs: | | | | | |
| 0 to 30 days | | | 31 days to 1 year | | |
| 2,617 | 17 | 0.65% | 2,617 – (2,617*1.79%[a]) = 2,570 | 62 – 17 = 45 | 45/2,570 = 1.77% |

*(a) This is the probability of death at 30 days, taken from Hulme 2019[17]*

**Table 18: Data inputs for minor bleeding baseline risk in STEMI and UA/NSTEMI**

| N | R | Probability | N | R | Probability |
|---|---|---|---|---|---|
| *STEMI* | | | | | |
| 30 days | | | 1 year | | |
| 3,752 | 27 | 0.71% | 3,752 | 98 | 2.61% |
| Recalculated for model inputs: | | | | | |
| 0 to 30 days | | | 31 days to 1 year | | |
| 3,752 | 27 | 0.71% | 3,752 – (3,752*6.15%[a]) = 3,521 | 98 – 27 = 71 | 71/3,521 = 2.03% |
| *UA/NSTEMI* | | | | | |
| 30 days | | | 1 year | | |
| 2,617 | 11 | 0.41% | 2,617 | 40 | 1.51% |
| Recalculated for model inputs: | | | | | |
| 0 to 30 days | | | 31 days to 1 year | | |
| 2,617 | 11 | 0.41% | 2,617 – (2,617*1.79%[a]) = 2,570 | 40 – 11 = 29 | 29/2,617 = 1.12% |

*(a) This is the probability of death at 30 days, taken from Hulme 2019[17]*

### 2.3.3 Relative treatment effects in first year treatment period decision tree

Relative treatment effects for ticagrelor and prasugrel compared to clopidogrel were based on the systematic review of clinical evidence for clopidogrel, ticagrelor and prasugrel (in combination with aspirin) which was undertaken as part of guideline development. This is described in full along with the committee discussion of the clinical evidence in Evidence report A.

Note that the committee agreed that the best estimates of treatment effect to use for decision making in the guideline and so also in the model were from evidence syntheses that combined all ACS data together irrespective of ACS subtype (STEMI or UA/NSTEMI) or management approach (revascularisation or not). This was on the basis that the underlying mechanism is the same for all types of ACS and so it is reasonable to assume relative treatment effects may be similar and this maximises the evidence that contributes to the estimates of treatment effect. The committee discussed this issue in detail because there are also rational bases why relative treatment effects may vary between these groups. For example, STEMI is a medical emergency, requiring immediate treatment, so with well-established differential onsets of action of clopidogrel, prasugrel and ticagrelor, it is conceivable that this may impact their relative clinical effectiveness in STEMI patients. To

address this issue and ensure evidence suggesting any potential differential effects was not omitted, the committee reviewed the evidence for all ACS and also stratified by condition (i.e. STEMI or UA/NSTEMI) and management approach (i.e. with or without revascularisation) in pairwise meta-analyses. Following consideration of all the pairwise meta-analyses the committee concluded that it was reasonable to assume that relative treatment effects were consistent and that combined ACS population syntheses provided the best estimate of treatment effects for decision making purposes. Heterogeneity was not identified in the pairwise meta-analyses which suggests that the study populations did not differ in factors that interacted with the relative treatment effects. Following this an NMA was conducted for key 30-day outcomes using the overall ACS population to combine the available data for ticagrelor versus clopidogrel, prasugrel versus clopidogrel and ticagrelor versus prasugrel into a single set of consistent treatment effects using all available data to facilitate interpretation of the evidence and undertaking cost effectiveness analysis. Following publication of the ISAR-REACT 5 trial late in guideline development, NMA was also considered for 1 year outcomes but was not undertaken due to inconsistency in the network. This is discussed in more detail in the sections below.

In the model, relative treatment effects for prasugrel and ticagrelor compared to clopidogrel were applied to the baseline risks obtained for the clopidogrel arm in order to calculate revised risks of different clinical events with prasugrel and ticagrelor. As described in the previous section, baseline risks were specific to the population being evaluated in the model that is split by STEMI and UA/NSTEMI and for people receiving PCI. This means that while the relative treatment effects were not split by subgroup, because the baseline risks differed this resulted in different absolute effects. An example of how this works is demonstrated in Table 19.

**Table 19: Example of absolute effect differences**

| | 30 day probability of reinfarction with clopidogrel[(a)] | Number of people with reinfarction with clopidogrel per 1000 | Odds ratio for ticagrelor | 30 day probability with ticagrelor | Number of people with reinfarction with ticagrelor per 1000 | Difference in number of people with reinfarction per 1000 |
|---|---|---|---|---|---|---|
| STEMI | 2.91% | 29 | 0.81 | 2.03% | 20 | 9 |
| UA/NSTEMI | 1.02% | 10 | | 0.71% | 7 | 3 |

*(a) This is the baseline risk of reinfarction with clopidogrel*

The odds ratios were applied to the baseline probabilities to obtain the probability of events occurring in the prasugrel and ticagrelor arms using the following formula:

$$probability\ in\ comparator\ arm = \frac{\exp(\ln(a) + \ln(b))}{1 + \exp(\ln(a) + \ln(b))}$$

- EXP = exponential
- a = odds of baseline probability
- b = odds ratio

The committee discussed how to use the available relative treatment effects in the model. The committee agreed it was important to incorporate the 30-day outcome data because a considerable amount of the evidence comparing ticagrelor and prasugrel directly (all of it until ISAR-REACT 5 published late in guideline development) only had 30-day outcome data (ticagrelor vs prasugrel 30-day outcomes = 6 studies [PRAGUE18[30], RAPID I[47], RAPID II[46], Alexopoulous 2012[2], Bonello 2015[4] and Laine 2014[22]], total n = 1698; ticagrelor vs prasugrel 1-year outcomes = 1 study [ISAR-REACT 5[52]] total n = 4018). Ideally, 31-day to 1-year relative treatment effects would have been calculated for all comparisons in the model by removing events occurring up to 30 days from 1-year outcome data. However, this was

mostly not possible as 30 day outcomes were not available for the studies and/or populations with 1 year outcomes. Given this, consideration was given to how best to use the available clinical evidence in the model. One option considered was to apply the 30-day relative treatment effects 0-30 days in the model and then apply the 1 year relative treatment effects to the 31 days to 1 year baseline risks in the model, in the absence of 31 day to 1 year relative treatment effects. This approach was initially considered the best way to take account of the full body of evidence that directly compared ticagrelor and prasugrel (agreed before the publication of ISAR-REACT 5) although it did mean that the events generated by the model would not necessarily be consistent with the studies that did have 1 year outcomes. However, it was agreed that a more conservative approach was to ensure the model generated relative event numbers consistent with the 1 year relative treatment effects being used in that scenario. While this puts less weight on the studies with only 30 day outcomes, it reflects the key large studies in this area (when all scenarios of the analysis are considered) including one that directly compared ticagrelor and prasugrel (ISAR-REACT 5). The 30-day relative-treatment data was still incorporated and impacts the timing of events in the first year. How relative treatment effects are applied in the model is described below.

The model calculates 30 day to 1 year probabilities in the following way. Events at 30 days with prasugrel and ticagrelor are calculated by applying the 30 day odds ratio to the 0 to 30 day baseline risk with clopidogrel. Total events over the year are calculated with prasugrel and ticagrelor by applying the 1 year odds ratio to the 0 to 1 year baseline risk with clopidogrel. Events occurring between 30 days and 1 year are calculated by subtracting the 30 day events from the 1 year events. What this means is that the total events over the year in the model is determined by the baseline risk with clopidogrel over the year and the 1 year treatment effect data. However, the timing of events is affected by the 30 day baseline risk with clopidogrel and the 30 day relative treatment effects with prasugrel and ticagrelor. This means a reduction in events at 30 days still will have an impact on QALYs, even if by 1 year there is no treatment difference, due to a delay in the event occurring. In the probabilistic analysis 30 day and 1 year odds ratios were incorporated as independent variables. In reality they may be correlated and so this may increase uncertainty in the analysis. However, it is also noted that the evidence for 30 day and 1 year outcomes does not always come from the same studies and this uncertainty cannot be captured quantitatively. Given this, in some iterations of the probabilistic analysis it may be possible for the combinations of baseline risks and ORs ratios to result in a greater number of event occurring at 30 days than over the year. The model was therefore programmed so that 30 day events were constrained to be no more than the 1 year events to avoid negative probabilities at 30 days to 1 year.

**30 days**

The relative treatment effects applied in the model for the 0 to 30 day period are shown in Table 20. These were from a network meta-analysis that combined RCT evidence for ticagrelor versus clopidogrel (7 RCTs: PLATO[59], DISPERSE-2[7], Dehghani 2017[11], Wang 2016b[60], Wang 2019[61], Han 2019[16] and Jing 2016[18]), prasugrel versus clopidogrel (4 RCTs: TRITON-TIMI 38[29], ETAMI[67], TRILOGY[49] and Dasbiswas 2013[10]) and ticagrelor versus prasugrel (6 RCTs: PRAGUE18[30], RAPID I[47], RAPID II[46], Alexopoulous 2012[2], Bonello 2015[4] and Laine 2014[22]). Full methods for the NMA are described in the separate NMA report. An NMA combines all available evidence into a single set of consistent treatment effects.

**Table 20: Model inputs: relative treatment effects applied 0 to 30 days (from NMA)**

| Outcomes | Intervention | Odds ratio (95% CI) |
|---|---|---|
| All-cause mortality | Ticagrelor versus clopidogrel | 0.85 (0.70 to 1.02) |
| | Prasugrel versus clopidogrel | 0.81 (0.63 to 1.02) |
| | Ticagrelor versus prasugrel | 1.04 (0.79 to 1.39) |
| Reinfarction | Ticagrelor versus clopidogrel | 0.68 (0.55 to 0.84) |

| Outcomes | Intervention | Odds ratio (95% CI) |
|---|---|---|
| | Prasugrel versus clopidogrel | 0.80 (0.65 to 0.98) |
| | Ticagrelor versus prasugrel | 0.84 (0.64 to 1.14) |
| Stroke | Ticagrelor versus clopidogrel | 1.28 (0.86 to 1.83) |
| | Prasugrel versus clopidogrel | 0.84 (0.46 to 1.39) |
| | Ticagrelor versus prasugrel | 1.47 (0.82 to 2.98) |
| Major bleed | Ticagrelor versus clopidogrel | 1.00 (0.89 to 1.11) |
| | Prasugrel versus clopidogrel | 0.99 (0.61 to 1.52) |
| | Ticagrelor versus prasugrel | 1.00 (0.65 to 1.64) |
| Minor bleed | Ticagrelor versus clopidogrel | 1.28 (0.88 to 1.81) |
| | Prasugrel versus clopidogrel | 0.74 (0.51 to 1.04) |
| | Ticagrelor versus prasugrel | 1.69 (1.16 to 2.59) |

*Abbreviations: 95% CI = 95% confidence interval; NMA = network meta-analysis.*

*Source: Systematic review and NMA undertaken as part of guideline development. See Evidence report A and the NMA report for full methods. RCTs incorporated: ticagrelor versus clopidogrel, 7 RCTs (unpublished data obtained from authors for PLATO[59], DISPERSE-2[7], Dehghani 2017[11], Wang 2016b[60], Wang 2019[61], Han 2019[16] and Jing 2016[18]); prasugrel versus clopidogrel, 4 RCTs (STEMI subgroup from TRITON-TIMI 38[29], ETAMI[67], TRILOGY[49] and Dasbiswas 2013[10]); ticagrelor versus prasugrel, 6 RCTs (PRAGUE18[30], RAPID I[47], RAPID II[46], Alexopoulous 2012[2], Bonello 2015[4] and Laine 2014[22]. Note that not all studies report all outcomes of interest.*

The network meta-analysis used simulation methods, which yielded 60,000 individual estimates of each odds ratio. These estimates represent the posterior distribution of the odds ratio. In the probabilistic economic analysis, for each iteration, we sampled at random from these 60,000 estimates. Each time we took both odds ratios (prasugrel vs clopidogrel and ticagrelor vs clopidogrel) from the same NMA iteration, to ensure that the correlation between the different treatment effects was preserved.

### 1 year

The 1 year relative treatment effects applied in the model were obtained from the pairwise meta-analyses described in Evidence report A. The publication of ISAR-REACT 5 resulted in a data loop at 1 year for mortality, reinfarction, stroke and major bleeding (see Figure 4). An NMA for 1 year outcomes was explored, but the results were deemed unreliable due to inconsistency between direct and indirect treatment effects estimates. For example, the ticagrelor vs prasugrel estimate implied by the ticagrelor vs clopidogrel and prasugrel vs clopidogrel studies was statistically different to that obtained from the ticagrelor vs prasugrel study (ISAR-REACT 5). The inconsistency was identified through conducting the Bucher test for inconsistency, which demonstrated that an NMA was not appropriate. Also, the studies and outcome data were all checked for accuracy. See the NMA report for results from the Bucher test. This meant that it was not possible to combine all available evidence into a single set of consistent treatment effects. This was discussed with the committee and it was agreed that in order to take into account all available 1 year evidence, alternative scenarios for the base case model had to be conducted; it wasn't felt to be appropriate to select one set of data as the preferred data a priori. Table 21 shows the relative treatment effects used in each of the alternative base case scenarios. The black text shows the trial data used in each scenario. The grey text indicates the implied odds ratios for the remaining comparison; this was calculated as a standard indirect comparison.

**Figure 4: 1 year evidence network**

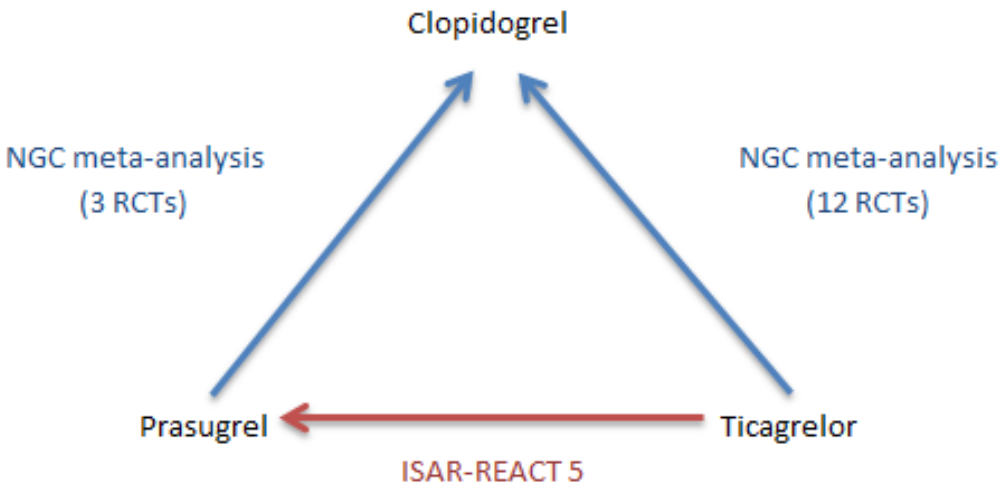



**Table 21: Model inputs: relative treatment effects at 1 year (from pairwise meta-analysis)**

| | Scenario 1 | Scenario 2 | Scenario 3 |
|---|---|---|---|
| Data used | Ticagrelor vs clopidogrel (meta-analysis)<br>Prasugrel vs clopidogrel (meta-analysis)<br>OR (95% CI) | Prasugrel vs clopidogrel (meta-analysis)<br>Ticagrelor versus prasugrel (ISAR REACT 5)<br>OR (95% CI) | Ticagrelor vs clopidogrel (meta-analysis)<br>Ticagrelor versus prasugrel (ISAR REACT 5)<br>OR (95% CI) |
| Ticagrelor vs clopidogrel | | | |
| All-cause mortality | 0.77 (0.68 to 0.88) | 1.24 (0.86 to 1.79) | 0.77 (0.68 to 0.88) |
| Reinfarction | 0.82 (0.73 to 0.92) | 1.22 (0.87 to 1.73) | 0.82 (0.73 to 0.92) |
| Stroke | 1.13 (0.89 to 1.44) | 1.08 (0.54 to 2.17) | 1.13 (0.89 to 1.44) |
| Major bleed | 1.04 (0.95 to 1.14) | 1.52 (1.04 to 2.22) | 1.04 (0.95 to 1.14) |
| Minor bleed | 1.37 (1.19 to 1.57)[a] | 1.37 (1.19 to 1.57)[a] | 1.37 (1.19 to 1.57) |
| Prasugrel vs clopidogrel | | | |
| All-cause mortality | 1.00 (0.83 to 1.21) | 1.00 (0.83 to 1.21) | 0.62 (0.44 to 0.87) |
| Reinfarction | 0.75 (0.66 to 0.84) | 0.75 (0.66 to 0.84) | 0.50 (0.36 to 0.71) |
| Stroke | 0.93 (0.67 to 1.30) | 0.93 (0.67 to 1.30) | 0.97 (0.50 to 1.88) |
| Major bleed | 1.43 (1.14 to 1.79) | 1.43 (1.14 to 1.79) | 0.98 (0.71 to 1.35) |
| Minor bleed | 2.07 (0.88 to 4.87)[a] | 2.07 (0.88 to 4.87)[a] | 2.07 (0.88 to 4.87)[a] |
| Ticagrelor vs prasugrel | | | |
| All-cause mortality | 0.77 (0.61 to 0.97) | 1.24 (0.90 to 1.70) | 1.24 (0.90 to 1.70) |
| Reinfarction | 1.08 (0.92 to 1.27) | 1.63 (1.17 to 2.26) | 1.63 (1.17 to 2.26) |
| Stroke | 1.22 (0.80 to 1.84) | 1.16 (0.62 to 2.14) | 1.16 (0.62 to 2.14) |
| Major bleed | 0.73 (0.57 to 0.93) | 1.06 (0.78 to 1.44) | 1.06 (0.78 to 1.44) |
| Minor bleed | 0.66 (0.28 to 1.57)[b] | 0.66 (0.28 to 1.57)[b] | 0.66 (0.28 to 1.57)[b] |

*Abbreviations: 95% CI = 95% confidence interval; OR = odds ratio.*

*(a) ISAR-REACT 5 did not report minor bleeding therefore treatment effects remained the same as scenario 1.*

*(b) These estimates are the implied treatment effects for minor bleeding using the data for ticagrelor versus clopidogrel and prasugrel versus clopidogrel*

*Note: Black text shows the trial data used in each scenario; grey text is the implied treatment effect calculated from the trial data for other comparisons.*

*Source: Meta analyses of 1 year outcomes undertaken as part of guideline development. See Evidence report A for full methods. RCTs incorporated: ticagrelor versus clopidogrel, 12 RCTs (DISPERSE 2[7], Dehgani 2017[11], Han 2019[16], Li 2018[23], PHILO[14], PLATO[59], Tang 2016[57], Wang 2016[60], Wang 2019[61], Wu 2018[64], Yao 2017[66], Zhang 2016[68]); prasugrel to versus clopidogrel, 3 RCTs (Kitano 2020[20], Savonitto 2018[50], TRITON-TIMI[63]); ticagrelor versus prasugrel, 1 RCT (ISAR-REACT 5[52])*

Odds ratios were incorporated into the probabilistic analysis using a log-normal distribution. This was parameterised using the mean odds ratio stated above and the standard error calculated from the confidence interval.

### 2.3.4 Transition probabilities in post-one year extrapolation Markov model

Differential treatment effects were assumed to apply in the first year only and so probabilities post one year do not vary by initial DAPT treatment.

The transition matrices showing the probabilities of transitions applied in the post-one year extrapolation Markov model for STEMI and UA/NSTEMI are shown in Table 22. Death is age-dependant and changes each cycle, therefore the probabilities of transitioning between the health states is dependent on this and changes every cycle.

**Table 22: Post-one year extrapolation Markov model: transition matrices for STEMI and UA/NSTEMI excluding death**

| **STEMI** | | | | | | |
|---|---|---|---|---|---|---|
| **From** | **To** | | | | | |
| | **No further event** | **Reinfarction** | **Post-reinfarction** | **Stroke** | **Post-stroke** | **Dead** |
| **No further event** | 1 - 4.30% - 1.12% - age-dependant mortality | 4.30% | 0 | 1.12% | 0 | Age-dependant |
| **Reinfarction** | 0 | 0 | 1 – age-dependant mortality | 0 | 0 | Age-dependant |
| **Post-reinfarction** | 0 | 0 | 1 – age-dependant mortality | 0 | 0 | Age-dependant |
| **Stroke** | 0 | 0 | 0 | 0 | 1 – age-dependant mortality | Age-dependant |
| **Post-stroke** | 0 | 0 | 0 | 0 | 1 – age-dependant mortality | Age-dependant |
| **Dead** | 0 | 0 | 0 | 0 | 0 | 1 |
| **UA/NSTEMI** | | | | | | |
| **From** | **To** | | | | | |
| | **No further event** | **Reinfarction** | **Post-reinfarction** | **Stroke** | **Post-stroke** | **Dead** |
| **No further event** | 1 - 3.62% - 0.59% - age-dependant mortality | 3.62% | 0 | 0.59% | 0 | Age-dependant |
| **Reinfarction** | 0 | 0 | 1 – age-dependant mortality | 0 | 0 | Age-dependant |
| **Post-reinfarction** | 0 | 0 | 1 – age-dependant mortality | 0 | 0 | Age-dependant |
| **Stroke** | 0 | 0 | 0 | 0 | 1 – age-dependant mortality | Age-dependant |
| **Post-stroke** | 0 | 0 | 0 | 0 | 1 – age-dependant mortality | Age-dependant |
| **Dead** | 0 | 0 | 0 | 0 | 0 | 1 |

In the post-1 year Markov model, people in the no further event health state had the possibility of transitioning to reinfarction, stroke or dead. The rate of reinfarction or stroke post 1 year was assumed to be the same as the rate for people on aspirin and clopidogrel between 31 days and 1 year. This is a method that has been employed by other models, for example, the previous model in NICE CG94 used the rate between 6 months and 1 year. The committee agreed that this was reasonable given that it excludes events occurring in the first 30 days (where events are more frequent) and as there was no data identified which provided the risk of reinfarction or stroke after 1 year in this population. The baseline risks that were used in the 1 year decision tree between 31 days and 1 year were used in the post year-one Markov model converted to a 1 year probability using standard formulae assuming a constant underlying rate. Also, the conversion accounted for censoring due to mortality.

In the model, reinfarction and stroke were tunnel health states, meaning that people only remain in that health state for one cycle, at which point they must transition to dead or the post-reinfarction/post-stroke health states; the probability of these transitions (excluding death) is therefore 1.

Once someone is in the post-reinfarction or post-stroke health state, they cannot experience another event and so either remain in that state or move to the dead state; the probability of remaining in these states (excluding death) is therefore 1.

**Transition to the dead state**

The transition probability of dying for each of the health states was determined by applying relevant standardised mortality ratios (SMRs) to cycle-specific general population mortality rates. This means that mortality rates increase with age in the model. These were then converted to probabilities using standard methods.

General population mortality was based on data from lifetables for England 2015-17.[44] Cycle-specific general population mortality was calculated taking into account the average age and gender split for the population entering the model and how this changed over time (age will increase by 1 year each cycle and mortality rate will increase with age; as mortality rates differ by gender and the average age by gender also varied in an ACS population, the gender split will change over time). Note that gender population mortality is not available beyond 100 years. Therefore, the model applies the mortality rate for age 100 to those that are older than 100 years. Table 23 shows age and gender split data used in the model. The percentage of people that are male and female that enter the Markov model was obtained from Hulme 2019. It is acknowledged that as the data obtained from Hulme 2019 was used to model mortality in the decision tree, this is the percentage split in the first year, therefore the percentage that are male and female after 1 year could be different. This was explored and showed that after accounting for mortality in the first year the percentage that were male and female remained the same, therefore the same values as reported in Hulme 2019 were used. The average age used in the Markov model to calculate mortality was one year higher than the reported age in the study, to reflect that people enter the Markov model one year after their ACS event.

**Table 23: Model inputs: average age and gender split**

| Population | Model entry age | Male |
|---|---|---|
| STEMI | Male: 63 years<br>Female: 70 years | 75% |
| UA/NSTEMI | Male: 65 years<br>Female: 70 years | 72% |

*Source: Analysis of 2011/2012 PCI audit data for England and Wales by Hulme 2019.[17] Based on 41,974 PCIs for STEMI and 56,152 for UA/NSTEMI. Average start age was calculated from ages reported by gender and gender split reported in paper.*

The model aimed to reflect the real-world population of people with ACS undergoing PCI in England. Data was therefore sought from reports of national audit data. Ideally we were looking for information specifically for people with ACS who have undergone PCI as demographics will be different to the overall ACS population and specific to STEMI and UA/NSTEMI separately as again demographics were considered to potentially vary by type of ACS. An analysis of national audit data in this format was identified in the study reported by Hulme 2019.[17] The data reported for the years 2011/2012 was used and included 40,724 PCIs for STEMI and 54,314 for UA/NSTEMI. More recent audit data is available however these demographics were not reported for these populations separately. It is noted however that for the overall PCI population (ACS and stable) these demographics are very similar in the most recent year and 2013/14.[26]

SMRs were identified from checking other models and published sources, and those used in the Markov model are shown in Table 24.

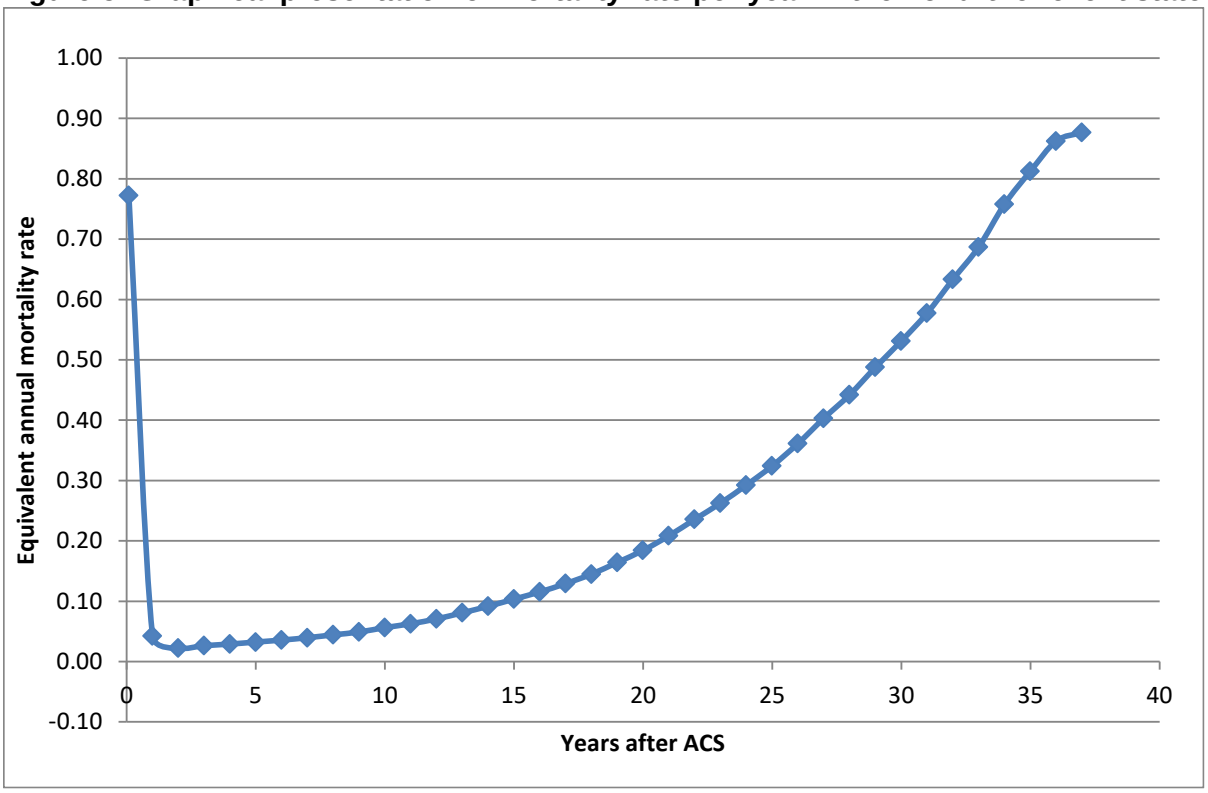
**Table 24: Post-one year extrapolation Markov model: standardised mortality ratios**

| Event | SMR (95% CI) | Source |
|---|---|---|
| No further event | 2.00 (1.99 to 2.01)[(a)] | Smolina 2012.[53] All-cause mortality compared to that expected in the general population after first acute MI. Based on individuals in England admitted to hospital between 2004 and 2010 (n = 371,619). |
| Reinfarction | 4.50 (4.43 to 4.57)[(a)] | Smolina 2012.[53] All-cause mortality compared to that expected in the general population after second acute MI. Based on individuals in England admitted to hospital between 2004 and 2010 (n = 15,833). |
| Post-reinfarction | 3.00 (2.95 to 3.05)[(a)]) | |
| Stroke | 4.73 (4.34 to 5.15) | Bronnum-Hansen 2001.[6] All-cause mortality after first non-fatal stroke compared to that expected in the general population in years 0-1 for males and females. Danish population 1982–1991 (n=8,324). |
| Post-stroke | 2.32 (2.17 to 2.49)[(b)] | Bronnum-Hansen 2001.[6] Average of SMRs for years 1-15 for males and females. All-cause mortality after first non-fatal stroke compared to that expected in general population. Danish population 1982–1991 (n=8,324). |

*(a) CIs were not reported therefore these were calculated by assuming the standard deviation was equal to the mean and using the reported n number – n = 371,619 for first MI and n = 15,833 for second MI.*
*(b) CIs calculated from Monte Carlo simulation.*

Figure 5 illustrates how mortality changes over time in the model for those in the no further event health state. The first two data points are the rates 0 to 30 days and 31 days to 1 year from the UK PCI audit data described in section 2.3.2. Data points after this are based on age and gender dependent general population mortality adjusted using the 'no further event' SMR in Table 24.

**Figure 5: Graphical presentation of mortality rate per year in the no further event state**




The SMR for the no further event and reinfarction/post-reinfarction health states were obtained from Smolina 2012.[53] This study reported long-term survival after a first and second acute MI in England in 387,452 individuals identified between 2004 and 2010. The SMRs were reported graphically and approximate average values for use in the model were obtained by visually assessing the graphs in discussion with clinical committee members. Also, the study reported that the SMR for those with their first MI stabilises at 2.00 by 4 years and for those with a second MI it stabilises at around 3.00 by 4 years. The study did not report confidence intervals (or information from which they could be calculated) and so they were estimated assuming the standard deviation was equal to the mean and the reported n number. The estimated confidence intervals are shown in Table 25.

**Table 25: Estimates of confidence intervals for Smolina 2012[53] SMRs**

| Health state | Sample mean | Estimated standard deviation | Sample size | Estimated confidence intervals |
|---|---|---|---|---|
| No further event | 2.00 | 2.00 | 371,619 | 1.99 to 2.01 |
| Reinfarction | 4.50 | 4.50 | 15,833 | 4.43 to 4.57 |
| Post-reinfarction | 3.00 | 3.00 | 15,833 | 2.95 to 3.05 |

The post-stroke standardised mortality ratios were obtained from Bronnum-Hansen 2001.[6] This study looked at long-term survival following a stroke in people in Denmark. The SMRs were reported separately for different time intervals, initially for years 0 – 1 and also for different intervals between years 2 – 15. To calculate the SMR for the post-stroke health state a straight average was used as the model reflects a lifetime perspective. A confidence interval for the average SMR was obtained using Monte Carlo simulation.

The SMRs were included in the probabilistic analysis using a lognormal distribution which was parameterised using the confidence intervals. General population mortality was not varied probabilistically.

### 2.3.5 Health-related quality of life

#### Health state weights (utilities)

Utilities were sought for the ACS population having dual-antiplatelet therapy who have experienced no additional event, reinfarction and stroke. Table 26 shows the data used in the model. These utilities were applied in both the first year treatment period decision tree and the post-year 1 Markov model.

When an event occurred in the decision tree, it was assumed this happened halfway through the relevant time period, therefore, the utilities were applied as follows:

- For those having an event between 0 and 30 days, it was assumed to occur on average at 15 days (for example, no further event applied for 15 days and stroke applied for 15 days).
- For those having an event between 31 days and 1 year, it was assumed to occur on average after 5.5 months (not including the initial 30 day period) (for example, reinfarction for 5.5 months and dead for 5.5 months).

In the Markov model a half cycle correction was applied, which assumes that events occurred halfway through the cycle (at 6 months).

**Table 26: Model inputs: health state utilities**

| | Mean | SE |
|---|---|---|
| No further event | 0.842 | 0.002 |
| Reinfarction | 0.779 | 0.010 |
| Post-reinfarction | 0.821 | 0.038 |
| Stroke | 0.703 | 0.010 |
| Post-stroke | 0.703 | 0.038 |

*Abbreviations: SE = standard error*

*Source: NICE TA236 2011[39]. EQ-5D-3L completed by patients with ACS as part of PLATO health economic sub-study, UK valuation tariff applied.*

Utilities were sought through checking cost-utility analyses identified in the systematic review of health economic studies in this area undertaken for this guideline update and recent NICE technology appraisals related to ACS. Additional ad-hoc searching was undertaken to establish if there was any more recent published data in the ACS population. The recent rivaroxaban NICE technology appraisal conducted a systematic review and concluded that the best available data was the utilities used in the ticagrelor NICE TA manufacturer model which were obtained from the PLATO health economics sub-study.[39] These were considered appropriate to use by the rivaroxaban TA evidence review group as they distinguished between those that have already had an ACS (no further event health state) and those that have reinfarction. The PLATO health economics sub-study administered the EQ-5D-3L to a subset of people in the RCT and the UK valuation set was used to obtain the utility weights. Although the manufacturer submission for the ticagrelor NICE TA used different utility values for the clopidogrel and ticagrelor arms, the ticagrelor TA evidence review group report indicated that this was not appropriate and that the same utilities should apply to each arm and the only difference in quality of life should be between which health state the person is in. The committee agreed that for this model the event specific utilities from the PLATO health economic sub study should be used as they match the health states in the model and are in line with the NICE reference case. It was agreed that quality of life should be lower in

the first year after having a reinfarction as this was considered clinically appropriate and is in line with other models in ACS.

It was acknowledged that in the decision tree those that have two events (e.g. stroke in 0 to 30 days and a stroke in 31 days to 1 year) may experience a further disutility. Although you may experience further disutility, it was agreed that the disutility associated with the second event would be smaller than the disutility associated with the first event. As a result, using the same utilities was considered a reasonable assumption by the committee.

The health state specific utility values were incorporated into the probabilistic analysis using a beta distribution, which is bounded by 0 and 1 as utilities are generally between these values. It is possible that utility values can be less than 1 (states considered worse than death) however given that the mean estimates for all of the health states are far from zero this was considered reasonable. This was parameterised using the method of moments approach that uses the mean and SE to calculate alpha and beta for the distribution.

### Age adjustment of health state weights

Each year in the model utilities were age-adjusted in order to account for the fact that as people age their quality of life decreases. This is a method that is adopted by many other economic models and was also highlighted in the recent rivaroxaban NICE TA evidence review group report as being something that should be incorporated. If it is not done, QALYs may be overestimated.

Each year in the model age-specific general population EQ-5D-3L utilities were derived using the following formula from Ara 2010[3]:

$$Utility = 0.9508566 + 0.0212126 * Male - 0.0002587 * age - 0.0000332 * age\text{^}2$$

*Note: for variable 'Male', male is equal to 1 and female is equal to 0.*

The average age and gender split of the population was used in calculations as described in Table 23 in Section 2.3.4.

These were then combined with the health-state specific utilities using the multiplicative method.

Age-specific utilities were not varied probabilistically.

### Bleeding adverse events

Minor bleeding and major bleeding (except stroke) were incorporated into the model as short term adverse events. The committee noted that you might expect a short term decrement in quality of life when experiencing a bleeding event and data was sought regarding this. The utility decrements applied for a minor and major bleed in the model along are shown in Table 27 along with the duration they were applied for in order to calculate QALY loss.

**Table 27: Model inputs: minor and major bleeding quality of life decrements**

| Adverse event | Utility decrement[(a)] (95% CI) | Standard error[(b)] | Duration applied for[(c)] |
|---|---|---|---|
| Minor bleed | 0.026 (-0.0470 to -0.0293) | 0.005 | 7.60 days |
| Major bleed | 0.038-(-0.0365 to -0.0148) | 0.006 | 45.38 days |

*(a) Source: Amin 2016[17]. Primary analysis of EQ-5D-3L data (US tariff) from people with ACS on DAPT that experienced a bleed from the TRANSLATE-ACS study, n=9,290. Utility decrement was calculated in analysis by comparing quality of life of those who experienced a bleed to those who did not experience a bleed.*
*(b) Standard errors were calculated using the lower and upper 95% confidence intervals reported in the study*
*(c) Source: Doble 2018[13]*

A systematic review conducted by Doble 2018[13] identified 12 studies that reported quality of life associated with major and minor bleeding for people taking DAPT. The study also conducted a small patient preference elicitation study using EQ-5D-3L and 5L to obtain utilities for major and minor bleeding. The elicitation exercise resulted in data collected from 21 individuals, who were all taking DAPT for ACS or after a coronary intervention. This study was conducted in the UK and used the EQ-5D-3L tariff which is line with NICE current preferred methods. The study reported that most participants completing the elicitation exercise had experienced a minor bleed; however, not everyone had experienced a major bleed. Due to the study being based on a small sample of people and the fact they were not directly affected by the condition, an alternative source that was identified in the systematic review was considered. The TRANSLATE-ACS study was a longitudinal study conducted in the USA looking at DAPT treatment patterns after an ACS event. The study was conducted in over 9,000 people that were treated with PCI and taking DAPT. Bleeding events were reported according to BARC and health related quality of life was recorded. Participant's EQ-5D scores were collected at baseline and 6 months. They reported utility decrements of people who experienced bleeding compared to those in the study that did not experience any bleeding. Although the study used the EQ-5D US tariff, it was felt appropriate to use this data over other studies as the study was conducted on a large number of people who were the population of interest. Although the US tariff was used, it uses the time-trade-off valuation method which is the same as the UK tariff. Also, the Doble 2018 study compared the US and UK valuation tariff in the elicitation exercise and showed that they resulted in small differences, which further supported the use of the values from the TRANSLATE-ACS study.

When applying utility decrements the duration that the event is expected to impact quality of life has to be applied. The TRANSLATE-ACS study did not report the duration that major and minor bleeds impacted quality of life, and the previous prasugrel NICE TA assumed that major bleeds would affect quality of life for 14 days. The Doble 2018 study asked participants in the elicitation exercise how long they would expect a bleed to impact quality of life and the average amount of time was 7.6 days for minor bleeds and 45.38 days for major bleeds. The committee agreed that this was the best source of data as it involved asking people on DAPT that may have experienced a bleed.

The utility decrement associated with major bleeding was incorporated into the probabilistic analysis using a gamma distribution. This is bounded by zero which reflects the assumption that this adverse event will only result in lower QALYs, which was agreed to be clinically appropriate. It was parameterised using the mean utility decrement and standard error calculated from the reported confidence interval.

The utility decrement with minor bleeding was incorporated into the probabilistic analysis using the difference in utility decrement with a minor bleed and a major bleed to ensure that in the probabilistic analysis the utility decrement with a minor bleed is not higher than with a major bleed. A gamma distribution was used for the difference for the same reasons as given above. It was parametrised using the difference in mean utility decrement and standard error calculated from the reported confidence intervals for the decrements for major and minor bleeding.

### 2.3.6 Resource use and costs

#### 2.3.6.1 Intervention costs

In the analysis, DAPT costs varied by comparator in the first year. The unit costs of aspirin, clopidogrel, prasugrel and ticagrelor that are used in the model shown in Table 28. Clopidogrel, prasugrel and ticagrelor all require a loading dose to be used in people presenting with ACS. The loading dose for clopidogrel can either be 300mg or 600mg, but for the purposes of modelling the 600mg dose was used as this is what is often done in current practice. A sensitivity analysis using a 300mg loading dose was conducted as described in section 2.4. The daily dose of prasugrel is 10mg for adults 18 – 74 years and with a body

weight above 60kg, and for anyone under 60kg or 75 years and over the daily dose is 5mg. As the annual cost of the 5mg and 10mg dose is different, an assumption had to be made regarding what proportion of people would be receiving each dose. Recent prescription cost analysis data showed that 90% of prasugrel prescriptions were for the 10mg dose. However, as the current usage of prasugrel is low, this would not reflect the overall PCI population. As a result, a local hospital database was checked and showed that approximately 10 – 20% of people that have undergone PCI for ACS would be eligible for the 5mg dose. Therefore, the model assumed that 15% would receive the 5mg dose and 85% would receive the 10mg dose. All three drugs are taken alongside aspirin therefore the cost of aspirin was included. The doses and resulting costs of these drugs are shown in Table 29.

**Table 28: DAPT unit costs**

| Drug | Tablet size | Tablets per pack | Cost per pack | Cost per tablet |
|---|---|---|---|---|
| Aspirin | 75mg | 28 | £1.84 | £0.07 |
| Clopidogrel | 75mg | 28 | £1.66 | £0.06 |
| Prasugrel | 5mg | 28 | £14.40 | £0.51 |
| | 10mg | 28 | £6.34 | £0.23 |
| Ticagrelor | 90mg | 56 | £54.60 | £0.98 |

*Source: NHS Drug Tariff July 2020[41]*

**Table 29: Model inputs: DAPT costs**

| Drug | Loading dose | Loading dose cost | Daily maintenance dose | Cost per day | Cost per year |
|---|---|---|---|---|---|
| Aspirin | n/a | n/a | 75mg | £0.07 | £24 |
| Clopidogrel | 300mg | £0.24 | 75mg | £0.06 | £22 |
| | 600mg | £0.47 | 75mg | £0.06 | £22 |
| Prasugrel | 60mg | £1.36 | 5mg | £0.51 | £188 |
| | | | 10mg | £0.23 | £83 |
| Ticagrelor | 180mg | £1.95 | 180mg | £1.95 | £712 |

*Source: doses from British National Formulary[19], accessed 1st July 2020; unit costs NHS Drug Tariff July 2020[41]*

Prasugrel can only be given in people undergoing PCI. Standard treatment for STEMI is primary PCI immediately. However, management in people with UA/NSTEMI is different with a proportion of people undergoing angiography to determine if PCI is appropriate. It will not be known if these people will receive PCI until angiography has been undertaken and MINAP audit data showed that on average it takes around 3 days from event angiography (with some taking place sooner and some later). Therefore, intervention costs in the UA/NSTEMI prasugrel group were calculated assuming that they would only receive aspirin for 3 days, and then receive the prasugrel loading dose on day 3 followed by daily prasugrel and aspirin costs. This was to be in line with what was done in the ISAR-REACT 5 trial. A sensitivity analysis was conducted which assumed that these people received clopidogrel until angiography and then were switched to prasugrel as the committee were uncertain about leaving people off DAPT until angiography.

Loading dose costs were applied to everyone in the model. For those that died between 0 to 30 days, the daily treatment costs were applied for 15 days. For those that died between 31 days and 1 year, the first 30 day intervention cost was applied and then the costs were applied for a further 5.5 months to be in line with the assumption that on average events occur halfway through the cycle. For those who were alive at 1 year intervention costs were calculated taking into account an estimate of average treatment duration of 328 days (90% of the year). The same treatment duration was used for all DAPT options. This basis for the treatment duration is discussed further below.

**Treatment duration**

Intervention costs for those alive at one year were calculated taking into account estimated typical treatment duration. The committee discussed that in their experience continuation of DAPT for a year is high however in trials some participants discontinued the study intervention before then and this may result in lower intervention costs.

The committee considered information from 3 key studies: PLATO, TRITON-TIMI and ISAR-REACT-5. This is described below.

The ISAR-REACT 5 trial reported that 15.2%/12.5% of participants on ticagrelor/prasugrel respectively discontinued the trial therapy prematurely and that the median duration in those that discontinued was 84/109 days respectively.[51] Using the discontinuation percentages and median days on treatment (as mean was not reported) for those who discontinued, and assuming those who do did not discontinue prematurely received 365 days of treatment, it was estimated that people received an average of 322/333 days of treatment for ticagrelor/prasugrel respectively. This equates to 328 days across the groups.

The PLATO trial reported 240/245 mean days on treatment for ticagrelor/clopidogrel respectively.[43] This equates to 243 days across the groups.

The assessment report for the NICE technology assessment for prasugrel (TA182) included intervention costs adjusted for treatment duration based on data from TRITON-TIMI 38 as part of a cost effectiveness analysis where maximum DAPT duration was 12 months.[15] Using this and the reported unit costs it was calculated that a treatment duration of around 302 days for both prasugrel and clopidogrel was used.

The committee noted that in their experience continuation with DAPT was high. It was also noted that in PLATO 12 months treatment was not mandated and participants could leave the study at 6, 9 or 12 months if the pre-specified number of endpoints had occurred in the study. It was agreed that the ISAR-REACT-5 estimate of 328 days should be used in the base case analysis as it is the most recent study and a pragmatic trial and so was most likely to represent current real world discontinuation; in the base case analysis, the same treatment duration was applied for all three DAPT options. Different assumptions were explored in sensitivity analyses (see section 2.4).

#### 2.3.6.2 Health states

The sources of cost data for health states were identified by reviewing models in ACS and other cardiovascular models (NICE guidelines, TA models or published economic models) and through non-systematic online searches to identify newer publications. The costs applied in the model are summarised in Table 30 below. More detail about the data sources and calculation are provided in the sections that follow.

Note that in the year 1 decision tree, assuming events occurring between 31 days and 1 year occur around 6 months, costs were attributed assuming the first 6 month costs are determined by what occurs between 0 to 30 days and the second 6 months costs are determined by what event occurs during the 31 day to 1 year period.

**Table 30: Model inputs: year 1 decision tree health state costs**

| 0 to 30 days | 31 day to 1 year | Cost | Source |
|---|---|---|---|
| No further event | No further event | £1,640 | • Danese 2016[9] first MI 1 – 6 months costs with estimated acute cost removed (based on NHS reference cost of PCI[12])<br>• Plus half the Danese 2016[9] annualised post-6 months costs |

| 0 to 30 days | 31 day to 1 year | Cost | Source |
|---|---|---|---|
| No further event | Reinfarction | £5,564 | • Danese 2016[9] first MI 1 – 6 months costs with estimated acute cost removed (based on NHS reference cost of PCI[12])<br>• Plus Danese 2016[9] second MI 1 – 6 months costs |
| No further event | Stroke | £15,203 | • Danese 2016[9] first MI 1 – 6 months costs with estimated acute cost removed (based on NHS reference cost of PCI[12])<br>• Plus the Xu 2018[65] Year 1 stroke costs with recurrence costs removed , 6 month cost post-year 1cost removed, and non-publicly funded social care costs removed |
| No further event | Death | £1,168 | • Danese 2016[9] first MI 1 – 6 months costs with estimated acute cost removed (based on NHS reference cost of PCI[12]) |
| Reinfarction | No new event | £5,104 | • Danese 2016[9] second MI 1 – 6 months costs<br>• Plus half the Danese 2016[9] annualised second MI post-6 months costs |
| Reinfarction | Reinfarction | £8,792 | • Danese 2016[9] second MI 1 – 6 months costs multiplied by 2. |
| Reinfarction | Stroke | £18,431 | • Danese 2016[9] second MI 1 – 6 months costs<br>• Plus the Xu 2018[65] Year 1 stroke costs with recurrence costs removed, 6 month cost post-year 1cost removed, and non-publicly funded social care costs removed |
| Reinfarction | Death | £4,396 | • Danese 2016[9] second MI 1 – 6 months costs |
| Stroke | No new event | £17,323 | • Xu 2018[65] Year 1 stroke costs with recurrence costs removed and non-publicly funded social care costs removed. |
| Stroke | Reinfarction | £21,719 | • Xu 2018[65] Year 1 stroke costs with recurrence costs removed and non-publicly funded social care costs removed.<br>• Plus Danese 2016[9] second MI 1 – 6 months costs |
| Stroke | Stroke | £21,014 | • Xu 2018[65] Year 1 stroke costs with recurrence costs removed and non-publicly funded social care costs removed.<br>• Plus acute stroke costs estimated using method used in Xu 2018[65] and 2017/18 NHS reference costs |
| Stroke | Death | £14,035 | • Xu 2018[65] Year 1 stroke costs with recurrence costs removed, 6 month cost post-year 1cost removed, and non-publicly funded social care costs removed |
| Death | n/a | £0 | Assumption |

### Stroke costs

The cost of stroke was based on Xu 2018[65] which estimated the financial burden of stroke to the NHS and social care services. This was done using a patient simulation based on UK Sentinel Stroke National Audit Programme data. The costs associated with stroke were estimated up to 5 years after the person incurred their first stroke. The costs of stroke were reported for 1 year and 5 years. Costs associated with the NHS and social care services were reported separately. The social care costs in the report included both publicly funded and independently funded costs. Costs from this study are shown in Table 31.

**Table 31: Costs from published sources: stroke**

| Health state | Cost | Source |
|---|---|---|
| Stroke 1 year | £23,052 | Xu 2018 – SSNAP project inflated to 2017/18[65] |
| Stroke 5 year | £47,023 | Xu 2018 – SSNAP project inflated to 2017/18[65] |

*Costs inflated from 2016 to 2017/18 using health services specific indices reported in the PSSRU publication Unit costs for health and social care; 2017/18 was the latest index available[8]*

As this analysis takes an NHS and personal social services perspective, non-publicly funded costs should not be included. A recent report published by the Stroke Association (Patel 2017[48]) used the assumption that approximately 50% of social care costs are publicly funded. Therefore, an assumption was made in the model that 50% of these costs were publicly funded, which was tested in a sensitivity analysis.

In the 1 year decision tree clinical events including stroke are modelled explicitly as you can have a stroke between 0 to 30 days and another between 31 days and 1 year. However, the Xu 2018 costs include repeat stroke events. The costs associated with recurrent strokes was based on unpublished data obtained from the authors and was recorded for the overall 5 year costs; therefore, an adjustment was made to the 1 year costs. When someone experienced a second stroke in the model, the acute costs of stroke were calculated from NHS reference costs, using the same currency codes that were used in the SSNAP 2018 report[65] which involved non-elective stroke, thrombolysis, ambulance and scan costs. These are shown in Table 32. For those that experienced their first stroke in the 31 days to 1 year period, the cost of stroke was adjusted. Instead of halving the 1 year cost of stroke, it was deemed appropriate to assume that the majority of costs in the first year happen in the first 6 months. Therefore, the annual cost of stroke after year 1 was halved and removed from the first year stroke cost to obtain a higher cost. This was done to ensure no costs were lost once people entered the Markov model in the post-stroke health state.

In the Markov model repeat events are not modelled explicitly and so it was deemed appropriate to use the Xu 2018 costs that captured the cost of repeat events.

**Table 32: Cost of acute stroke**

| Currency Code | Currency Description | Activity | National average unit cost |
|---|---|---|---|
| Acute stroke admission | | | |
| *Non-elective long stay* | | | |
| AA35A | Stroke with CC Score 16+ | 12,203 | £8,659 |
| AA35B | Stroke with CC Score 13-15 | 14,461 | £6,419 |
| AA35C | Stroke with CC Score 10-12 | 17,864 | £5,082 |
| AA35D | Stroke with CC Score 7-9 | 20,624 | £4,052 |
| AA35E | Stroke with CC Score 4-6 | 20,118 | £3,420 |
| AA35F | Stroke with CC Score 0-3 | 12,652 | £2,821 |
| *Non-elective short stay* | | | |
| AA35A | Stroke with CC Score 16+ | 2,618 | £951 |
| AA35B | Stroke with CC Score 13-15 | 4,207 | £736 |
| AA35C | Stroke with CC Score 10-12 | 7,568 | £730 |
| AA35D | Stroke with CC Score 7-9 | 12,448 | £712 |
| AA35E | Stroke with CC Score 4-6 | 17,105 | £683 |
| AA35F | Stroke with CC Score 0-3 | 14,922 | £667 |

| Currency Code | Currency Description | Activity | National average unit cost |
|---|---|---|---|
| Cost of admission for stroke (weighted average) | | | £3,310 |
| Thrombolysis[a] | | | |
| YR23A | Percutaneous Transluminal, Embolectomy or Thrombolysis, of Blood Vessel, with CC Score 5+ | 12 | £719 |
| YR23B | Percutaneous Transluminal, Embolectomy or Thrombolysis, of Blood Vessel, with CC Score 0-4 | 64 | £959 |
| Cost of thrombolysis (weighted average) | | | £921 |
| Scan | | | |
| RD01A | Magnetic Resonance Imaging Scan of One Area, without Contrast, 19 years and over | 438,550 | £131 |
| RD20A | Computerised Tomography Scan of One Area, without Contrast, 19 years and over | 167,572 | £79 |
| Cost of scan (weighted average)[b] | | | £80 |
| Ambulance | | | |
| ASS02 | See and treat and convey | 5,325,368 | £252 |
| Cost of ambulance[c] | | | £195 |
| **Total cost of acute stroke:** | | | **£3,692** |

*Source: NHS Reference Costs 2017/18*[12]
*(a) Thrombolysis costs were based on day-case admissions, and assumed that 11.6% received thrombolysis as reported in SSNAP report*
*(b) Cost of scan was based on 98.1% of people having a CT scan and the remaining having an MRI, taken from SSNAP report*
*(c) This was based on 77.3% of people arriving by ambulance, taken from the SSNAP report*

The stroke costs used in the model are summarised in Table 33.

**Table 33: Costs used in the model: stroke**

| | Cost | Source/Assumptions |
|---|---|---|
| Decision tree | | |
| Stroke occurring in 0 – 30 days | £17,323 | Xu 2018[65] 1 year stroke cost removed recurrence costs and 50% of social care costs; based on unpublished data obtained from authors |
| Stroke 31 days to 1 year | £14,035 | Xu 2018[65] 1 year stroke cost removed recurrence costs and 50% of social care costs as well as removed half the annualised cost (£3,288) to account for 6 months of ongoing treatment; based on unpublished data obtained from authors |
| Second stroke | £3,692 | NHS reference costs 2017/18; based on the costs included in Xu 2018[65] |
| Markov model (annual costs) | | |
| Stroke | £18,522 | Xu 2018[65] 1 year costs with 50% of social care costs removed |
| Post-stroke | £6,576 | Xu 2018[65] 5 year costs adjusted to remove 1 year cost and annualised; 50% of social care costs removed. |

### ACS with no further event and ACS with new MI costs

Danese 2016[9] aimed to illustrate the costs to the NHS that are associated with cardiovascular events among adults receiving lipid modifying therapy. This was a retrospective cohort study that used Clinical Practice Research Datalink records from 2006 to 2012. They reported the costs to the NHS associated with having a myocardial infarction. The study recorded first events and repeat events, and the costs were reported separately for these. Costs were reported for the first six months following the acute event, and the cost incurred from 7 to 36 months was presented as an annualised cost. Costs from this study are shown in Table 34.

It was acknowledged that the cost used in the model for people with ACS (MI or unstable angina) but no further event is based on people who have had a myocardial infarction only; however the committee agreed that the downstream resource use and management strategy would be similar for this population especially as this analysis considered people with ACS undergoing PCI.

It was discussed that this study was based on people receiving lipid modifying therapy prior to the cardiovascular event they experienced. However, the committee indicated that whether or not you are taking lipid modifying treatment before an event should not impact the treatment you receive for having a myocardial infarction and therefore these costs could be applied in this model.

**Table 34: Costs from published sources: ACS with and without new MI**

| Health state | Cost | Source |
|---|---|---|
| First MI 1 – 6 months | £4,370 | Danese 2016 inflated to 2017/18[9] |
| First MI post-acute annual cost | £943 | Danese 2016 inflated to 2017/18[9] |
| Second MI 1 – 6 months | £4,396 | Danese 2016 inflated to 2017/18[9] |
| Second MI post-acute annual cost | £1,415 | Danese 2016 inflated to 2017/18[9] |

*Costs inflated from 2014 to 2017/18 using health services specific indices reported in the PSSRU publication Unit costs for health and social care; 2017/18 was the latest index available*[8]

For those that experienced no further event in the model (that is people who have had an ACS but no further event), the cost of having a first MI was applied. For those that had reinfarction in the model, the cost of second MI was applied. In the decision tree it was decided that the cost of the acute event (hospitalisation) should be removed from the initial 6 month cost as everyone in the model experiences an ACS. Danese 2016 did not report a breakdown of the costs in order to remove this acute cost. As a result, the cost of having PCI was obtained from NHS reference costs and this was removed from the overall cost. The NHS reference costs of PCI are shown in Table 35.

**Table 35: NHS reference costs 2017/18 of percutaneous coronary angioplasty**

| Currency Code | Currency Description | Number of FCE's | National average unit cost |
|---|---|---|---|
| Non-elective long stay | | | |
| EY40A | Complex Percutaneous Transluminal Coronary Angioplasty with CC Score 12+ | 752 | £7,572 |
| EY40B | Complex Percutaneous Transluminal Coronary Angioplasty with CC Score 8-11 | 1,335 | £5,447 |
| EY40C | Complex Percutaneous Transluminal Coronary Angioplasty with CC Score 4-7 | 3,165 | £4,485 |

| Currency Code | Currency Description | Number of FCE's | National average unit cost |
|---|---|---|---|
| EY40D | Complex Percutaneous Transluminal Coronary Angioplasty with CC Score 0-3 | 3,061 | £3,969 |
| EY41A | Standard Percutaneous Transluminal Coronary Angioplasty with CC Score 12+ | 1,307 | £6,826 |
| EY41B | Standard Percutaneous Transluminal Coronary Angioplasty with CC Score 8-11 | 2,802 | £4,577 |
| EY41C | Standard Percutaneous Transluminal Coronary Angioplasty with CC Score 4-7 | 9,037 | £3,649 |
| EY41D | Standard Percutaneous Transluminal Coronary Angioplasty with CC Score 0-3 | 10,510 | £3,185 |
| Non-elective short stay | | | |
| EY40A | Complex Percutaneous Transluminal Coronary Angioplasty with CC Score 12+ | 292 | £3,152 |
| EY40B | Complex Percutaneous Transluminal Coronary Angioplasty with CC Score 8-11 | 476 | £2,346 |
| EY40C | Complex Percutaneous Transluminal Coronary Angioplasty with CC Score 4-7 | 1,579 | £2,228 |
| EY40D | Complex Percutaneous Transluminal Coronary Angioplasty with CC Score 0-3 | 2,236 | £2,224 |
| EY41A | Standard Percutaneous Transluminal Coronary Angioplasty with CC Score 12+ | 427 | £2,507 |
| EY41B | Standard Percutaneous Transluminal Coronary Angioplasty with CC Score 8-11 | 1,127 | £1,963 |
| EY41C | Standard Percutaneous Transluminal Coronary Angioplasty with CC Score 4-7 | 5,137 | £1,884 |
| EY41D | Standard Percutaneous Transluminal Coronary Angioplasty with CC Score 0-3 | 8,843 | £1,784 |
| **Weighted average cost (used as acute cost of MI)** | | | **£3,202** |

*Abbreviations: FCE = finished consultant episode*
*Source: NHS Reference Costs, 2017/18[12]; cost of non-elective long stay includes excess bed day cost*

The costs used in the model for people with ACS without any event and with a reinfarction are summarised in Table 36.

**Table 36: Costs used in the model: ACS with and without reinfarction**

| | Cost | Source/Assumptions |
|---|---|---|
| Decision tree | | |
| ACS no further event (0-6 month cost) | £1,263 | Danese 2016 first MI 1 – 6 months with acute cost removed (based on NHS reference cost of PCI) |
| ACS no further event (6 to 12 months cost) | £471 | Danese 2016 first MI annualised post-acute event cost halved |
| Second MI (0 to 6 month cost) | £4,396 | Danese 2016 second MI 1 – 6 months |
| Second MI (6 to 12 months cost) | £708 | Danese 2016 second MI annualised post-acute event cost halved |
| Third infarction | £4,396 | Danese 2016 second MI 1 – 6 months |
| Markov health state costs | | |
| No further event | £943 | Danese 2016 first MI annualised post-acute event cost |

| | Cost | Source/Assumptions |
|---|---|---|
| Reinfarction | £5,104 | Danese 2016 second MI acute cost (1 – 6 months) and annualised post-acute event cost halved |
| Post-reinfarction | £1,415 | Danese 2016 second MI annualised post-acute event cost |

*Source: Danese 2016[9]*

**Deaths occurring between 0 and 30 days costs**

For those that died at 0 to 30 days, no health state costs were included as the cost associated with 15 days would be minimal.

### 2.3.6.3 Adverse events

Major and minor bleeding was incorporated in the model as adverse events. The costs associated with these events were applied as a one off. Previous models in ACS and especially DAPT were explored to see how the cost of bleeding was captured. Various approaches were taken and there was a large difference in the costs used in previous models. It was considered by the committee that these costs can vary from person to person as both minor and major bleeds can vary in severity.

**Minor bleeding**

Although the committee noted that minor bleeds usually don't require interventions, people experiencing a minor bleed may feel worried about the bleed and still seek medical help. As a result, it was considered reasonable to use an A&E visit with investigation. An average of NHS reference costs for all categories of emergency admission (weighted by number of attendances) was used; this is shown in Table 37.

**Table 37: Minor bleeding cost based on emergency medicine admission**

| Currency codes | Currency descriptions | Total attendances | Weighted average cost used in model |
|---|---|---|---|
| VB01Z – VB09Z | Emergency Medicine, Category 1 - 3 Investigation and Emergency Medicine, Any Investigation | 16,250,140 | £176 |

*Source: NHS Reference Costs 2017/18[12]*

The NICE TA for long term ticagrelor use (TA420) used a much higher cost for minor bleeds which was based on an admission for gastrointestinal bleed without intervention. As a result of such differences in costs, this was used in a sensitivity analysis (described in section 2.4).

**Major bleeding**

It was discussed that major bleeding can include intracranial bleeds; however gastrointestinal bleeds are more common in this population taking DAPT. As a result, the average cost of an admission for gastrointestinal bleed was used in the base case analysis. An average of NHS reference costs for all categories of gastrointestinal bleed admission (weighted by number of attendances) was used; this is shown in Table 38 and how it was derived. In a sensitivity analysis the costs of intracranial bleeds were included (described in section 2.4).

**Table 38: Major bleeding costs based on gastrointestinal bleed**

| Currency code | Currency description | Number of FCE's | National average unit cost |
|---|---|---|---|
| Non-elective long stay | | | |

| Currency code | Currency description | Number of FCE's | National average unit cost |
|---|---|---|---|
| FD03A | Gastrointestinal Bleed with Multiple Interventions, with CC Score 5+ | 1,058 | £5,685 |
| FD03B | Gastrointestinal Bleed with Multiple Interventions, with CC Score 0-4 | 955 | £3,637 |
| FD03C | Gastrointestinal Bleed with Single Intervention, with CC Score 8+ | 1,486 | £3,909 |
| FD03D | Gastrointestinal Bleed with Single Intervention, with CC Score 5-7 | 2,244 | £2,828 |
| FD03E | Gastrointestinal Bleed with Single Intervention, with CC Score 0-4 | 5,568 | £2,173 |
| FD03F | Gastrointestinal Bleed without Interventions, with CC Score 9+ | 2,499 | £2,920 |
| FD03G | Gastrointestinal Bleed without Interventions, with CC Score 5-8 | 6,754 | £2,246 |
| Non-elective short stay | | | |
| FD03A | Gastrointestinal Bleed with Multiple Interventions, with CC Score 5+ | 32 | £1,511 |
| FD03B | Gastrointestinal Bleed with Multiple Interventions, with CC Score 0-4 | 25 | £1,130 |
| FD03C | Gastrointestinal Bleed with Single Intervention, with CC Score 8+ | 69 | £1,219 |
| FD03D | Gastrointestinal Bleed with Single Intervention, with CC Score 5-7 | 101 | £1,047 |
| FD03E | Gastrointestinal Bleed with Single Intervention, with CC Score 0-4 | 202 | £1,069 |
| FD03F | Gastrointestinal Bleed without Interventions, with CC Score 9+ | 1,962 | £586 |
| FD03G | Gastrointestinal Bleed without Interventions, with CC Score 5-8 | 9,160 | £538 |
| **Weighted average** | | | **£1,955** |

*Abbreviations: CC = complication and comorbidity; FCE = finished consultant episode*
*Source: NHS Reference Costs 2017/18[12]; non-elective long stay costs including excess bed day costs*

## 2.4 Sensitivity analyses

### 2.4.1 Stroke 1 year baseline risk adjusted (SA1)

In the base case analysis 1 year baseline risk for stroke was estimated using 30 day stroke risk form UK audits and the percentage increase in events at 1 year compared to 30 days from the Swedeheart audits for STEMI and NSTEMI.[55,56] The percentage increase to 1 year relative to 30 days was much lower with the PLATO data.[58] Therefore, an analysis was undertaken where the baseline risk for 1 year was determined by the percentage increase from PLATO. Table 39 shows the values used in the base case analysis and the values used in the sensitivity analysis.

**Table 39: Baseline probability of stroke at 1 year**

| Population | 30 day probability of stroke | % increase used in base case | 1 year probability of stroke used in base case | % increase used in sensitivity analysis | 1 year probability used in sensitivity analysis |
|---|---|---|---|---|---|
| STEMI | 0.30% | 420%[(a)] | 1.25% | 224%[(c)] | 0.72% |
| UA/NSTEMI | 0.11% | 580%[(b)] | 0.63% | 224%[(c)] | 0.26% |

*(a) Source: Szummer 2017; based on Swedeheart registry[55]*
*(b) Source: Szummer 2018; based on Swedeheart registry[56]*
*(c) Source: Wallentin 2009; based on PLATO RCT[58]*

### 2.4.2 Adjusting baseline risks for reinfarction and stroke (SA2)

As discussed in section 2.3.2, some of the probabilities used in the decision tree may overestimate the number of people alive with MI or stroke at 1 year. The data for reinfarction with STEMI included all events (not just people alive with reinfarction at 30 days and 1 year), as well as the stroke data for both STEMI and UA/NSTEMI. It was discussed that this would overestimate the number of people alive with a reinfarction and stroke and therefore a sensitivity analysis was conducted to reduce these probabilities at 1 year. In order to obtain a good estimate of how many of these events would be fatal, data from the ticagrelor TA236[39] was used as it provided a breakdown of events for the clopidogrel arm, which showed that 18% of people that had a reinfarction had died at the end of 1 year, and 20% of people that had a stroke had died at the end of 1 year. Therefore, the 1 year probability for reinfarction in STEMI was reduced by 18% and the 1 year probability for stroke was reduced by 20% for both STEMI and UA/NSTEMI. Reinfarction for UA/NSTEMI remained unchanged as it was the probability for non-fatal events.

### 2.4.3 Reducing SMRs for ACS/Reinfarction (SA3)

The SMRs being used for the no further event, reinfarction and post-reinfarction health states were obtained from Smolina 2012[53] and the SMRs for stroke and post-stroke were obtained from Bronnum-Hansen 2001.[6] As the SMRs were obtained from alternative sources, there is a chance that the SMRs related to ACS and reinfarction may be overestimating death. This is because they will comprise of deaths from any cause, and therefore would include death from having a stroke. In order to account for this, a sensitivity analysis was conducted where the SMRs for no further event, reinfarction and post reinfarction were reduced by 20% to reduce mortality in these health states and to test if this impacts results.

### 2.4.4 Assuming no treatment effect with stroke (SA4 – 6)

There was ambiguity around including the stroke outcome in the model as the committee discussed that it affected small numbers and there was uncertainty in the treatment effect estimates. Stroke has high costs associated with it therefore a small number of people experiencing strokes can have a large impact in results. As a result a sensitivity analysis was conducted where there was no treatment effect applied for prasugrel and ticagrelor (by changing the treatment effect to 1) to see if this impacted results (SA14). Also, a sensitivity analysis was conducted where there was no stroke treatment effect applied for ticagrelor but it was still applied for prasugrel (SA15) and another analysis where the stroke treatment effect for prasugrel was not applied but ticagrelor's treatment effect was still applied (SA16).

### 2.4.5 Rivaroxaban treatment effects included (SA7 – 8)

As discussed in section 2.1.1, there is an existing NICE technology appraisal (TA335) which recommends low dose rivaroxaban as an option in combination with aspirin plus clopidogrel in people who have had an acute coronary syndrome, post-acute management. It is beyond

the scope of the guideline update to make a recommendation about the use of rivaroxaban after ACS however, as rivaroxaban is only indicated for use with clopidogrel, a recommendation for prasugrel or ticagrelor may preclude rivaroxaban's use and so it is potentially relevant to take this into account in this analysis. The committee indicated that current usage is low therefore it was considered via a modification to the clopidogrel arm in a sensitivity analysis. In this exploratory sensitivity analysis treatment effects of low dose rivaroxaban post-ACS were incorporated into the model in those receiving clopidogrel in order to see if this would impact conclusions about which DAPT option was preferred.

Treatment effects were obtained from the ATLAS-TIMI-51 trial.[28] These are shown in Table 40**Error! Reference source not found.**. This study reported hazard ratios at 24 months, which was not in line with the outcomes from our clinical review, which reported outcomes at 30 days and 1 year. In order to undertake the sensitivity analysis an assumption was made to assume that treatment effects remain constant. It was highlighted that the distribution of effects is probably not the same throughout 24 months, for example, bleeding events may be more likely in the first few months, however this was an assumption that was made in the absence of other data. Hazard ratios were used as they were reported by the study. They were applied to the event rates with clopidogrel and aspirin in the model and revised probabilities of events occurring were obtained. These are shown in Table 41.

**Table 40: Relative treatment effects of low dose rivaroxaban plus clopidogrel and aspirin**

| Outcome | Hazard ratio (95% CI) versus clopidogrel and aspirin alone |
|---|---|
| Mortality | 0.68 (0.53 to 0.87) |
| Reinfarction | 0.90 (0.75 to 1.09) |
| Stroke | 1.13 (0.74 to 1.73) |
| Major bleed | 3.46 (2.08 to 5.77) |
| Minor bleed | 1.62 (0.92 to 2.82) |

*Source: ATLAS-TIMI-51 RCT[28]*

**Table 41: Probability of events with clopidogrel and rivaroxaban**

| Outcome | Probability at 30 days | Probability 30 days to 1 year |
|---|---|---|
| STEMI | | |
| All-cause mortality | 4.22% | 2.60% |
| Reinfarction | 2.63% | 3.50% |
| Stroke | 0.34% | 1.14% |
| Major bleed | 3.21% | 9.01% |
| Minor bleed | 1.14% | 3.27% |
| UA/NSTEMI | | |
| All-cause mortality | 1.22% | 2.53% |
| Reinfarction | 0.92% | 2.94% |
| Stroke | 0.12% | 0.60% |
| Major bleed | 2.21% | 5.98% |
| Minor bleed | 0.66% | 1.81% |

The unit costs of the drugs used in this analysis are presented in Table 42. A dose of 2.5mg rivaroxaban twice daily was used.[19] Dosing for aspirin and clopidogrel remained the same as in the base case analysis.

**Table 42: Unit costs of drugs**

| Drug | Tablet size | Tablets per pack | Cost per pack | Cost per tablet |
|---|---|---|---|---|
| Aspirin | 75mg | 28 | £1.84 | £0.07 |
| Clopidogrel | 75mg | 28 | £1.66 | £0.06 |
| Rivaroxaban | 2.5mg | 56 | £50.40 | £0.90 |

*Source: NHS Drug Tariff July 2020*[41]

The committee highlighted that not everyone who receives clopidogrel receives rivaroxaban and that use is currently low. Therefore, in the model the proportion of people taking clopidogrel that receive rivaroxaban was also incorporated. Relevant national audits do not collect information about the use of low dose rivaroxaban after ACS. Usage was therefore estimated using information from the prescription cost analysis 2019, that reported the numbers of prescriptions for 2.5mg rivaroxaban tablets, combined with an estimate of the ACS population that receive clopidogrel based on national audit data. See Table 43 for details. This suggested an estimated 1.8% of people on clopidogrel may also receive rivaroxaban. Usage was not available by indication and 2.5mg rivaroxaban is also used for another indication and so this may be an overestimate. Low dose rivaroxaban can also be used in people only receiving aspirin and so it may also be the case that some of the low dose rivaroxaban usage is in people who aren't receiving clopidogrel which would also mean this value may be an overestimate. However, as the usage estimate was very low this was used as a conservative estimate of current practice (SA7). The model was also run with everyone receiving rivaroxaban (SA8).

**Table 43: Estimated usage of low dose rivaroxaban after ACS (SA7)**

| | Data | Source/assumptions |
|---|---|---|
| **Number of people with ACS starting clopidogrel per year** | | |
| People with ACS | 92,233 | MINAP (confirmed MI) |
| % discharged on clopidogrel, prasugrel or ticagrelor | 97.5% | MINAP |
| Number discharged on clopidogrel, prasugrel or ticagrelor | 89,927 | Calculated |
| % STEMI | 39% | MINAP |
| % STEMI receiving clopidogrel | 45% | BCIS PCI audit; assume that clopidogrel usage in ACS PCI population is generalisable to overall ACS population. |
| % UA/NSTEMI receiving clopidogrel | 58% | |
| Estimated number of people with ACS starting clopidogrel each year | 47,598 | Calculated |
| **Number of people starting low dose rivaroxaban post ACS per year** | | |
| Prescriptions for 2.5mg rivaroxaban 56 tablets | 10,992 | Prescription Cost Analysis 2019 |
| Estimated number of people starting low dose rivaroxaban per year | 843 | Calculation = number of prescriptions × 56 ÷ (2 × 365)<br>Based on 2 tablets a day for 365 days.<br>As the BNF starts that the usual duration is 12 months this is assumed to approximate the number of people starting rivaroxaban in a year as people will start and stop treatment at the same rate. |
| **Estimated % of people on clopidogrel taking rivaroxaban** | 1.8% | Calculated<br>Assumes all 2.5mg usage is for post-ACS indication and only people on clopidogrel have |

| | Data | Source/assumptions |
|---|---|---|
| | | rivaroxaban. BNF also lists low dose rivaroxaban for people with CAD or symptomatic PAD so this may be an overestimate. |

*Source: Myocardial Ischemia National Audit Project (MINAP) 2019 report (2017/18 data)[32]; British Cardiovascular Intervention Society (BCIS) audit returns 2017-18 (PCI data)[25]; Prescription Cost Analysis 2019[42]; dosing from British National Formulary (BNF)[19]*
*Abbreviations: PAD = peripheral arterial disease; PCI = percutaneous coronary intervention.*

### 2.4.6 Dyspnoea included in the analysis (SA9)

As discussed in section 2.2.1, the committee highlighted that a considerable amount of people taking ticagrelor will experience breathing difficulties as a side effect. Although this wasn't considered a critical outcome to include in the base case analysis, it was incorporated as part of a sensitivity analysis to test if this impacted conclusions. Real world estimates of baseline risks for dyspnoea were not available for the clopidogrel arm; therefore, estimates from the clinical review were used in order to obtain the probability of experiencing dyspnoea on clopidogrel. The treatment effects were also obtained from the clinical review (Evidence report A), and both the 1 year baseline risk and treatment effect used in the model are shown in Table 44. The same data was used in the STEMI and UA/NSTEMI analyses. There was no data comparing dyspnoea for prasugrel versus clopidogrel, and only 1 study comparing prasugrel and ticagrelor reported dyspnoea; however, this was based on a small number of participants and at an unspecified time point. Therefore, it was assumed that the rates for prasugrel were the same as clopidogrel, and this was considered an appropriate assumption by the committee.

**Table 44: Dyspnoea baseline risks and treatment effects**

| Time point | Baseline risk with clopidogrel | Treatment effect with ticagrelor (OR, 95% CI) |
|---|---|---|
| 1 year | 7.85% | 1.77 (1.62 to 1.93) |

*Abbreviations: 95% CI = 95% confidence interval; OR = odds ratio*
*Source: Systematic review and meta analyses undertaken as part of guideline (see Evidence report A)*

The committee discussed the impact that experiencing breathing difficulties would have on the adult, and it was agreed that some people might discontinue their antiplatelet. However, it was agreed that discontinuation would not be incorporated for modelling purposes. The committee indicated that a small number of people would stop taking ticagrelor or be swapped to another antiplatelet, and it was discussed that the impact this would have on the treatment effects would be captured. Average treatment duration is also captured in the intervention costs. It was also discussed that people will be informed of this side effect, therefore not everyone will seek medical help. However, a proportion of people may see their GP and the committee discussed that this could lead to a range of different management strategies such as requiring blood tests or an asthma review. Therefore, these resource implications should be captured. For modelling purposes, it was agreed to assume that 80% of people experiencing dyspnoea will see their GP, and 30% will have investigative tests conducted by a nurse. The costs used are presented in Table 45.

**Table 45: Resource use associated with dyspnoea**

| Appointment | Cost | Cost adjusted |
|---|---|---|
| General practitioner | £37 (per 9.22 minutes) | n/a |
| Nurse (GP practice) | £42 (per hour) | £14 (per 20 minutes) |
| **Total cost per person** | | **£34** |

*Source: PSSRU unit costs 2018[8]; assumption that 80% of people would see their GP and 30% will have investigative tests with a nurse.*

### 2.4.7 Clopidogrel loading dose set to 300mg (SA10)

The base case model uses a clopidogrel loading dose of 600mg for costing purposes. However, it is noted that some people may only receive a 300mg loading dose, therefore this was incorporated as a sensitivity analysis to see if this impacted conclusions.

### 2.4.8 UA/NSTEMI prasugrel arm loading dose (SA11)

In the base case analysis it was assumed that the UA/NSTEMI prasugrel arm would not receive any dual antiplatelet therapy until the decision to undergo PCI was made. This resulted in the model only applying the cost of aspirin for the first 3 days and then a loading dose of prasugrel on day 3, followed by prasugrel for the rest of the duration. This was conducted to be in line with the ISAR-REACT 5 trial. It was discussed that there may be situations in real practice where the patient has already started another antiplatelet, therefore a sensitivity analysis was conducted where a 600mg clopidogrel loading dose was given on day 1 and clopidogrel and aspirin was costed for 3 days, and then they switched to prasugrel and the cost of prasugrel was accounted for beyond 3 days.

### 2.4.9 Alternative treatment durations in intervention costing (SA12-15)

As discussed in section 2.3.6.1 in the base case treatment duration for those alive at 1 year was based on an estimate from ISAR-REACT 5 of 328 days with the same duration used for all DAPT options. Alternative assumptions regarding treatment duration in the intervention costing were tested in sensitivity analyses.

This included using average treatment duration estimates from TRITON-TIMI 38 and PLATO instead of ISAR-REACT 5. In the base case analysis, the same treatment duration was used for all DAPT options but the estimates for ISAR-REACT 5 were 11 days lower with ticagrelor and so a sensitivity analysis was run using the ISAR-REACT 5 DAPT-specific treatment durations for ticagrelor and prasugrel; treatment duration with clopidogrel was assumed to the same as prasugrel. A sensitivity analysis was also run were people alive at 1 year were assumed to incur a full year of treatment costs.

**Table 46: Treatment durations used for intervention costing in sensitivity analyses**

| | ISAR REACT 5 (base case) | SA12 (TRITON TIMI) | SA13 (PLATO) | SA14 (ISAR-REACT 5 DAPT specific) | SA15 full year |
|---|---|---|---|---|---|
| Clopidogrel | 328 | 302 | 243 | 333 | 365 |
| Prasugrel | 328 | 302 | 243 | 333 | 365 |
| Ticagrelor | 328 | 302 | 243 | 322 | 365 |

*Source: ISAR-REACT 5 - Schulz 2014[51]; TRITON-TIMI 38 – Assessment Group report for NICE TA182[15]; PLATO – Nikolic 2013[43].*

### 2.4.10 Proportion of stroke social care costs that are publicly funded (SA16 – 17)

As described in section 2.3.6.2 the proportion of stroke social care costs that were publicly funded was assumed to be 50%, which was in line with a previous assumption from a published report. This was tested in a sensitivity analysis, by changing the proportion of social care costs that were publicly funded to 70% (SA11) and 30% (SA12), to see if this impacted conclusions on cost-effectiveness.

### 2.4.11 Bleeding costs (SA18 – 23)

As discussed in section 2.3.6.3, the costs associated with bleeding can vary and previous technology appraisals have used different estimates. Therefore, different estimates were used to explore whether this impacted results. Firstly, the cost of minor bleeding was adjusted to include the cost of a gastrointestinal bleed without interventions, which was the

method adopted by the ticagrelor technology appraisal, and is much higher than the cost used in the base case. Also, the committee noted that a large proportion of bleeds would be gastrointestinal; therefore a sensitivity analysis using this cost was considered appropriate. This cost was obtained from NHS Reference Costs and is shown in Table 47.

**Table 47: Cost of minor bleed for sensitivity analysis (SA18)**

| Currency code | Currency description | Number of FCE's | National average unit cost |
|---|---|---|---|
| Non-elective long stay | | | |
| FD03H | Gastrointestinal Bleed without Interventions, with CC Score 0-4 | 15,230 | £1,699 |
| Non-elective short stay | | | |
| FD03H | Gastrointestinal Bleed without Interventions, with CC Score 0-4 | 40,952 | £448 |
| **Weighted average** | | | **£731** |

*Abbreviations: FCE = finished consultant episode*
*Source: NHS reference costs 2017/18[12]; non-elective long stay cost includes the cost of excess bed days*

The cost of major bleeding was varied, in order to capture the cost of intracranial bleeds. The committee highlighted that gastrointestinal bleeds were more prominent in those taking DAPT, therefore the proportion of major bleeds that were intracranial was tested and set to 10%, 20%, 30% and 40%. These costs were obtained from NHS Reference Costs and are shown in Table 48. The change in the cost of a major bleed applied in the analysis is demonstrated in Table 49.

**Table 48: Cost of intracranial bleeds**

| Currency code | Currency description | Number of FCE's | National average unit cost |
|---|---|---|---|
| Non-elective long stay | | | |
| AA23C | Haemorrhagic Cerebrovascular Disorders with CC Score 14+ | 1,224 | £7,666 |
| AA23D | Haemorrhagic Cerebrovascular Disorders with CC Score 10-13 | 1,541 | £4,899 |
| AA23E | Haemorrhagic Cerebrovascular Disorders with CC Score 6-9 | 2,160 | £3,957 |
| AA23F | Haemorrhagic Cerebrovascular Disorders with CC Score 3-5 | 1,522 | £3,503 |
| AA23G | Haemorrhagic Cerebrovascular Disorders with CC Score 0-2 | 994 | £3,226 |
| Non-elective short stay | | | |
| AA23C | Haemorrhagic Cerebrovascular Disorders with CC Score 14+ | 344 | £1,038 |
| AA23D | Haemorrhagic Cerebrovascular Disorders with CC Score 10-13 | 777 | £778 |
| AA23E | Haemorrhagic Cerebrovascular Disorders with CC Score 6-9 | 1,668 | £777 |
| AA23F | Haemorrhagic Cerebrovascular Disorders with CC Score 3-5 | 1,755 | £809 |
| AA23G | Haemorrhagic Cerebrovascular Disorders with CC Score 0-2 | 1,471 | £776 |
| **Weighted average** | | | **£2,625** |

*Abbreviations: FCE = finished consultant episode*
*Source: NHS reference costs 2017/18[12]; non-elective long stay costs include the cost of excess bed days*

**Table 49: Costs used in major bleeding sensitivity analyses**

| Sensitivity analysis | Proportion of major bleeds that are intracranial | Cost used in model |
|---|---|---|
| SA19 | 10% | £2,048 |
| SA20 | 20% | £2,141 |
| SA21 | 30% | £2,234 |
| SA22 | 40% | £2,327 |

Lastly, a sensitivity analysis was conducted where both the cost of minor bleeds and major bleeds were adjusted (SA23). This involved using the higher cost of gastrointestinal bleeds for minor bleeds and the assumption that 20% of major bleeds would be intracranial, and these were adjusted simultaneously to see if this impacted results.

### 2.4.12 Utilities not age-adjusted (SA24)

In the base case analysis, the utility values were age-adjusted in order to account for the fact that as people age their quality of life decreases. Although this is a method that is deemed appropriate and was recommended by the evidence review group report for the rivaroxaban NICE TA, a sensitivity analysis was conducted where the utility values were not adjusted and the mean values described in Table 26 above were used unadjusted. This was conducted for methodological reasons to test if utilities impacted conclusions.

### 2.4.13 Discount rate (SA25)

In-line with NICE methodological guidance a sensitivity analysis was undertaken where the discount rate was set to 1.5% for costs and outcomes instead of 3.5% to explore whether results were sensitive to the discount rate used.

## 2.5 Computations

The model was constructed in Microsoft Excel 2010 and was evaluated by cohort simulation. Time dependency was built in by cross referencing the cohorts age as a respective risk factor for mortality. Baseline utility was also time dependent and was conditional on the number of years after entry to the model.

People started in the decision tree in the 'no further event' health state. People moved to the other health states (reinfarction, stroke and dead) based on probabilities of events occurring which was calculated from baseline risks and treatment effects. Those alive at the end of the decision tree at year 1 entered the Markov model and started in cycle 0. The health state they entered was determined by which health state they were in at the end of year 1 in the decision tree. Those that experienced no further event at the end of year 1 entered the 'no further event' health state in the Markov model. Those that had a reinfarction (once or twice) entered the 'post-reinfarction' health state in the Markov model. Those that had a stroke entered the 'post-stroke' health state in the Markov model. Once entering the Markov model, transition probabilities from the 'no further event' health state to 'reinfarction' and 'stroke' were based on the baseline risks at 1 year in the decision tree. Mortality transition probabilities varied depending on age, sex and which health state they were in.

Standardised mortality ratios for each health state were applied to mortality rates; which were then converted into transition probabilities for the respective cycle length (1 year) before inputting into the Markov model. These were converted using the following formulae:

| | |
|---|---|
| $Transition\ Probability\ (P) = 1 - e^{-rt}$ | Where<br>*r*=selected rate<br>*t*=cycle length (1 year) |

To calculate QALYs for each cycle, life years were weighted by a utility value (this was not treatment dependent). A half-cycle correction was applied, assuming that people transitioned between states on average halfway through a cycle. QALYs were then discounted at 3.5% to reflect time preference. QALYs during the first cycle (in the decision tree) were not discounted. The total discounted QALYs were the sum of the discounted QALYs per cycle.

Costs per cycle were calculated on the same basis as QALYs and were discounted at 3.5% to reflect time preference. Each of the health states had specific costs applied.

Discounting formula:

$$\text{Discounted total} = \frac{\text{Total}}{(1+r)^n}$$

Where:
*r*=discount rate per annum
*n*=time (years)

In the deterministic and probabilistic analyses, the total cost and QALYs accrued by each cohort (STEMI and UA/NSTEMI) was divided by the number of patients in the population to calculate a cost per patient and cost per QALY.

## 2.6 Model validation

The model was developed in consultation with the committee; model structure, inputs and results were presented to and discussed with the committee for clinical validation and interpretation during development.

The model was systematically checked by the health economist undertaking the analysis; this included inputting null and extreme values and checking that results were plausible given inputs. The model was peer reviewed by a second experienced health economist from the NGC; this included systematic checking of the model calculations. The model was also peer reviewed by a health economist at NICE and an executable version of the model with full technical report was made available to registered stakeholders for review at consultation.

## 2.7 Estimation of cost effectiveness

The widely used cost-effectiveness metric is the incremental cost-effectiveness ratio (ICER). This is calculated by dividing the difference in costs associated with 2 alternatives by the difference in QALYs. The decision rule then applied is that if the ICER falls below a given cost per QALY threshold the result is considered to be cost effective. If both costs are lower and QALYs are higher the option is said to dominate and an ICER is not calculated.

$$ICER = \frac{Costs\,(B) - Costs\,(A)}{QALYs\,(B) - QALYs\,(A)}$$

Where: Costs(A) = total costs for option A; QALYs(A) = total QALYs for option A

Cost effective if:
- ICER < Threshold

When there are more than 2 comparators, as in this analysis, options must be ranked in order of increasing cost then options ruled out by dominance or extended dominance before calculating ICERs excluding these options. An option is said to be dominated, and ruled out, if another intervention is less costly and more effective. An option is said to be extendedly dominated if a combination of 2 other options would prove to be less costly and more effective.

It is also possible, for a particular cost-effectiveness threshold, to re-express cost-effectiveness results in term of net monetary benefit (NMB). This is calculated by multiplying the total QALYs for a comparator by the threshold cost per QALY value (for example, £20,000) and then subtracting the total costs (formula below). The decision rule then applied is that the comparator with the highest NMB is the cost-effective option at the specified

threshold. That is the option that provides the highest number of QALYs at an acceptable cost.

$$Net\ Monetary\ Benefit(X) = \left(QALYs(X) \times \lambda\right) - Costs(X)$$

*Where: λ = threshold (£20,000 per QALY gained)*

Cost effective if:
- Highest net benefit

Both methods of determining cost effectiveness will identify exactly the same optimal strategy.

## 2.8 Interpreting results

NICE sets out the principles that committees should consider when judging whether an intervention offers good value for money.[34-36] In general, an intervention was considered to be cost effective if either of the following criteria applied (given that the estimate was considered plausible):

- the intervention dominated other relevant strategies (that is, it was both less costly in terms of resource use and more clinically effective compared with all the other relevant alternative strategies), or
- the intervention cost less than £20,000 per quality-adjusted life-year (QALY) gained compared with the next best strategy.

# 3 Results

## 3.1 Base case

Base case analysis results are presented in Table 50 and shown graphically in Figure 6. In addition, scatter plots showing the distribution of cost and QALY pairs from the probabilistic analysis are shown in Figure 7 to Figure 9. Breakdowns of clinical events and costs are presented in Table 51 and Table 52.

As described in the methods (see section 2.3.3), base case results are presented for three scenarios that utilise different data to inform the relative treatment effects at 1 year in the model (all scenarios also use the 30-day NMA to inform the relative treatment effects 0 to 30 days in the model):

1. Ticagrelor vs clopidogrel (meta-analysis); prasugrel vs clopidogrel (meta-analysis)
2. Prasugrel vs clopidogrel (meta-analysis); ticagrelor versus prasugrel (ISAR-REACT 5)
3. Ticagrelor vs clopidogrel (meta-analysis); ticagrelor versus prasugrel (ISAR-REACT 5)

In the base case analysis, the DAPT option that was most cost effective varied depending on the clinical data used to inform the 1 year relative treatment effects. Ticagrelor was the most cost effective DAPT option for both STEMI and UA/NSTEMI when 1 year relative treatment effect in the model was based on studies comparing prasugrel to clopidogrel and ticagrelor to clopidogrel (data scenario 1). Within this scenario, there was low uncertainty in this conclusion, with ticagrelor being the most cost effective option 93%/86% of the time for STEMI and UA/NSTEMI respectively. However, prasugrel was the most cost effective option for both STEMI and UA/NSTEMI when 1 year relative treatment effect data from ISAR-REACT 5 was incorporated in the model (data scenarios 2 and 3). There was low uncertainty in this conclusion within scenario 3 with prasugrel being the most cost effective option 96%/98% of the time for STEMI and UA/NSTEMI respectively. There was moderate uncertainty within scenario 2 with prasugrel being the most cost effective option 58%/60% of the time, but clopidogrel being the most cost effective option 37%/38% of the time for STEMI and UA/NSTEMI respectively.

Ticagrelor had the highest costs in all scenarios and ACS subgroups but only had the highest QALYs in scenario 1. In scenarios 2 and 3, prasugrel had lower costs than ticagrelor and also higher QALYs; QALYs are greater with prasugrel in these scenarios as when ISAR-REACT 5 was incorporated ticagrelor had a greater number of all clinical events (except minor bleeding) than prasugrel in the first year. Clopidogrel had the lowest costs in all scenarios and had the lowest QALYs in scenarios 1 and 3 for STEMI and UA/NSTEMI; in scenario 2 ticagrelor had the lowest QALYs. The reason ticagrelor had the lowest QALYs in scenario 2 was because 1 year events with ticagrelor were greater than with clopidogrel in this scenario. This scenario inferred the relative treatment effects of ticagrelor versus clopidogrel from the prasugrel versus clopidogrel meta-analysis and the ticagrelor versus prasugrel data. All details of relative treatment effects can be seen in the methods section but for example, at 1 year ticagrelor had greater mortality than prasugrel in the ISAR-REACT 5 trial and prasugrel had the same mortality as clopidogrel in the meta-analysis, therefore using this data ticagrelor had great mortality than clopidogrel.

In all scenarios the main driver of the higher costs with ticagrelor and lower costs with clopidogrel was the intervention costs, as the intervention costs associated with ticagrelor was around £600 more than clopidogrel for both STEMI and UA/NSTEMI. As prasugrel had the second highest intervention costs, this resulted in prasugrel having the second highest lifetime costs.

**Table 50: Base case analysis results (probabilistic analysis) – cost effectiveness results (mean per person)**

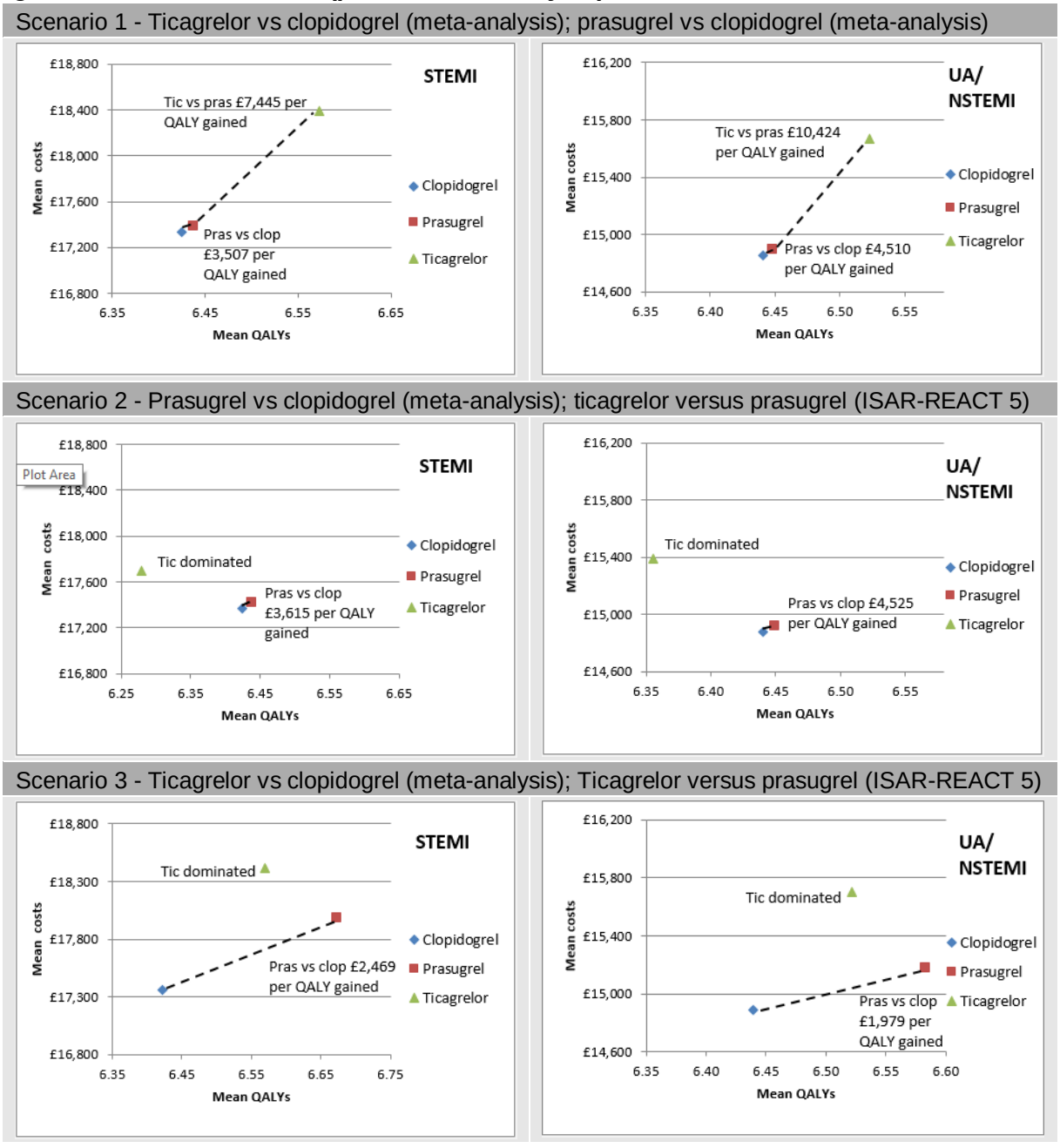
| Intervention | Mean lifetime costs undisc | Mean lifetime costs disc | Mean life years | Mean lifetime QALYs Undisc | Mean lifetime QALYs disc | Incr. cost | Incr. QALYs | ICER | NMB (£20k)* | Rank at £20k* | % CE at £20k* | % Rank 2nd at £20k* | % Rank 3rd at £20k* | % CE at £30k** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Scenario 1 – Ticagrelor vs clopidogrel (meta-analysis); prasugrel vs clopidogrel (meta-analysis)** | | | | | | | | | | | | | | |
| STEMI | | | | | | | | | | | | | | |
| Clopidogrel | £23,068 | £17,336 | 13.05 | 8.29 | 6.42 | | | | £111,149 | 3 | 0% | 40% | 60% | 0% |
| Prasugrel | £23,137 | £17,385 | 13.08 | 8.31 | 6.44 | £49 | 0.01 | £3,507 | £111,381 | 2 | 7% | 54% | 40% | 4% |
| Ticagrelor | £24,299 | £18,387 | 13.36 | 8.48 | 6.57 | £1,002 | 0.13 | £7,455 | £113,067 | 1 | 93% | 7% | 0% | 96% |
| UA/NSTEMI | | | | | | | | | | | | | | |
| Clopidogrel | £19,327 | £14,854 | 12.95 | 8.21 | 6.44 | | | | £113,954 | 3 | 0% | 40% | 60% | 0% |
| Prasugrel | £19,370 | £14,892 | 12.97 | 8.22 | 6.45 | £38 | 0.01 | £4,510 | £114,085 | 2 | 14% | 46% | 39% | 7% |
| Ticagrelor | £20,216 | £15,665 | 13.12 | 8.32 | 6.52 | £774 | 0.07 | £10,424 | £114,795 | 1 | 86% | 14% | 0% | 93% |
| **Scenario 2 – Prasugrel vs clopidogrel (meta-analysis); ticagrelor versus prasugrel (ISAR-REACT 5)** | | | | | | | | | | | | | | |
| STEMI | | | | | | | | | | | | | | |
| Clopidogrel | £23,115 | £17,368 | 13.05 | 8.29 | 6.42 | | | | £111,106 | 2 | 37% | 58% | 5% | 36% |
| Prasugrel | £23,188 | £17,420 | 13.08 | 8.31 | 6.44 | £52 | 0.01 | £3,615 | £111,343 | 1 | 58% | 36% | 6% | 58% |
| Ticagrelor | £23,303 | £17,702 | 12.75 | 8.10 | 6.28 | £282 | -0.16 | Dominated | £107,887 | 3 | 5% | 6% | 90% | 6% |
| UA/NSTEMI | | | | | | | | | | | | | | |
| Clopidogrel | £19,359 | £14,874 | 12.95 | 8.21 | 6.44 | | | | £113,936 | 2 | 38% | 60% | 2% | 37% |
| Prasugrel | £19,403 | £14,914 | 12.97 | 8.22 | 6.45 | £39 | 0.01 | £4,525 | £114,071 | 1 | 60% | 37% | 4% | 59% |
| Ticagrelor | £19,810 | £15,386 | 12.78 | 8.10 | 6.36 | £472 | -0.09 | Dominated | £111,732 | 3 | 2% | 4% | 94% | 4% |
| **Scenario 3 – Ticagrelor vs clopidogrel (meta-analysis); ticagrelor versus prasugrel (ISAR-REACT 5)** | | | | | | | | | | | | | | |
| STEMI | | | | | | | | | | | | | | |
| Clopidogrel | £23,101 | £17,362 | 13.05 | 8.29 | 6.42 | | | | £111,091 | 3 | 0% | 0% | 100% | 0% |
| Prasugrel | £23,996 | £17,983 | 13.57 | 8.62 | 6.67 | £620 | 0.25 | £2,469 | £115,495 | 1 | 96% | 4% | 0% | 95% |
| Ticagrelor | £24,331 | £18,413 | 13.36 | 8.48 | 6.57 | £430 | -0.10 | Dominated | £112,994 | 2 | 4% | 96% | 0% | 5% |

| UA/NSTEMI | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Clopidogrel | £19,374 | £14,890 | 12.96 | 8.21 | 6.44 | | | | £113,893 | 3 | 0% | 1% | 99% | 0% |
| Prasugrel | £19,774 | £15,175 | 13.25 | 8.40 | 6.58 | £286 | 0.14 | £1,979 | £116,493 | 1 | 98% | 2% | 0% | 97% |
| Ticagrelor | £20,262 | £15,701 | 13.12 | 8.32 | 6.52 | £526 | -0.06 | Dominated | £114,727 | 2 | 2% | 98% | 1% | 3% |

*Abbreviations: CE = cost effective; disc. = discounted; Incr. = incremental; NMB = net monetary benefit; QALY = quality-adjusted life years; undisc = undiscounted; £20K = a threshold of £20,000 per QALY gained; £30K = a threshold of £30,000 per QALY gained.*

*Note: Incremental costs and QALYs are versus the comparator with the next lowest costs (the previous line in the table) unless that option has been ruled out by extended dominance in which case they are compared to the option with the lowest costs (the first line in the table).*

**Figure 6: Base case results (probabilistic analysis)**




*Abbreviations: clop = clopidogrel; pras = prasugrel; tic = ticagrelor; QALYs: quality-adjusted life years.*

**Figure 7: Base case results (probabilistic analysis) for scenario 1 – ticagrelor vs clopidogrel (meta-analysis); prasugrel vs clopidogrel (meta-analysis) scatter plots**

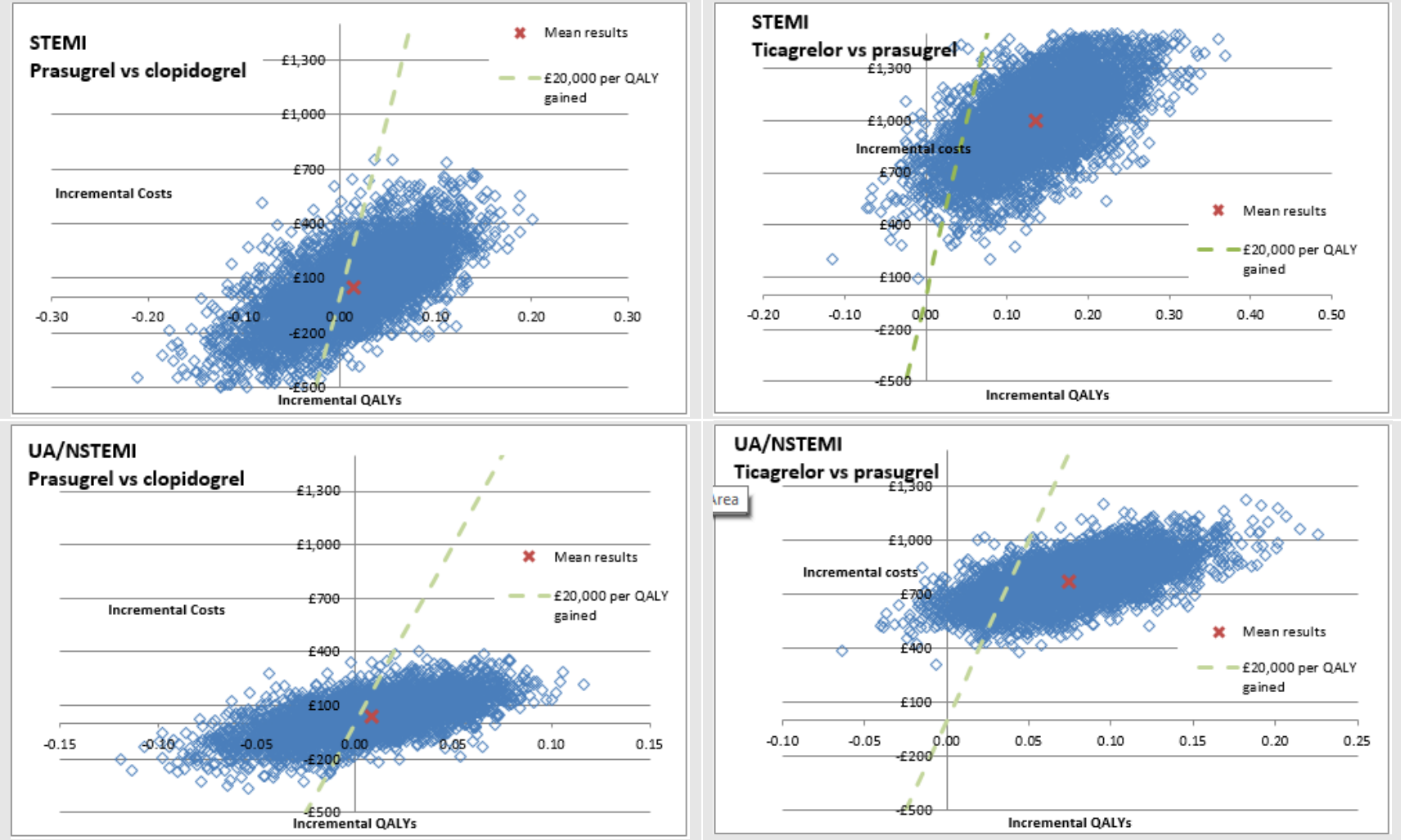


**Figure 8: Base case results (probabilistic analysis) for scenario 2 – prasugrel vs clopidogrel (meta-analysis); ticagrelor versus prasugrel (ISAR-REACT 5) scatter plots**

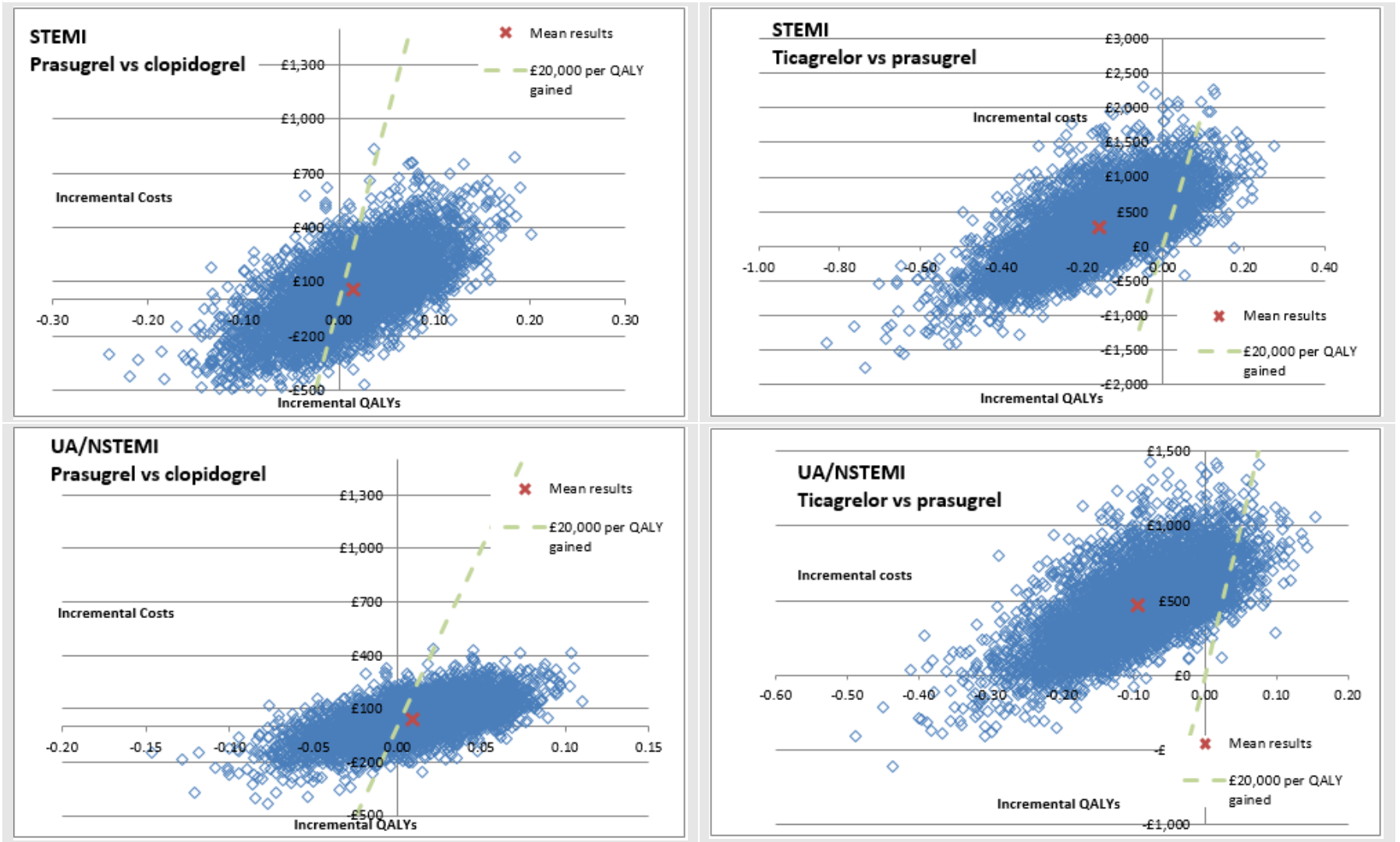


**Figure 9: Base case results (probabilistic analysis) for scenario 3 – ticagrelor vs clopidogrel (meta-analysis); ticagrelor versus prasugrel (ISAR-REACT 5) scatter plots**

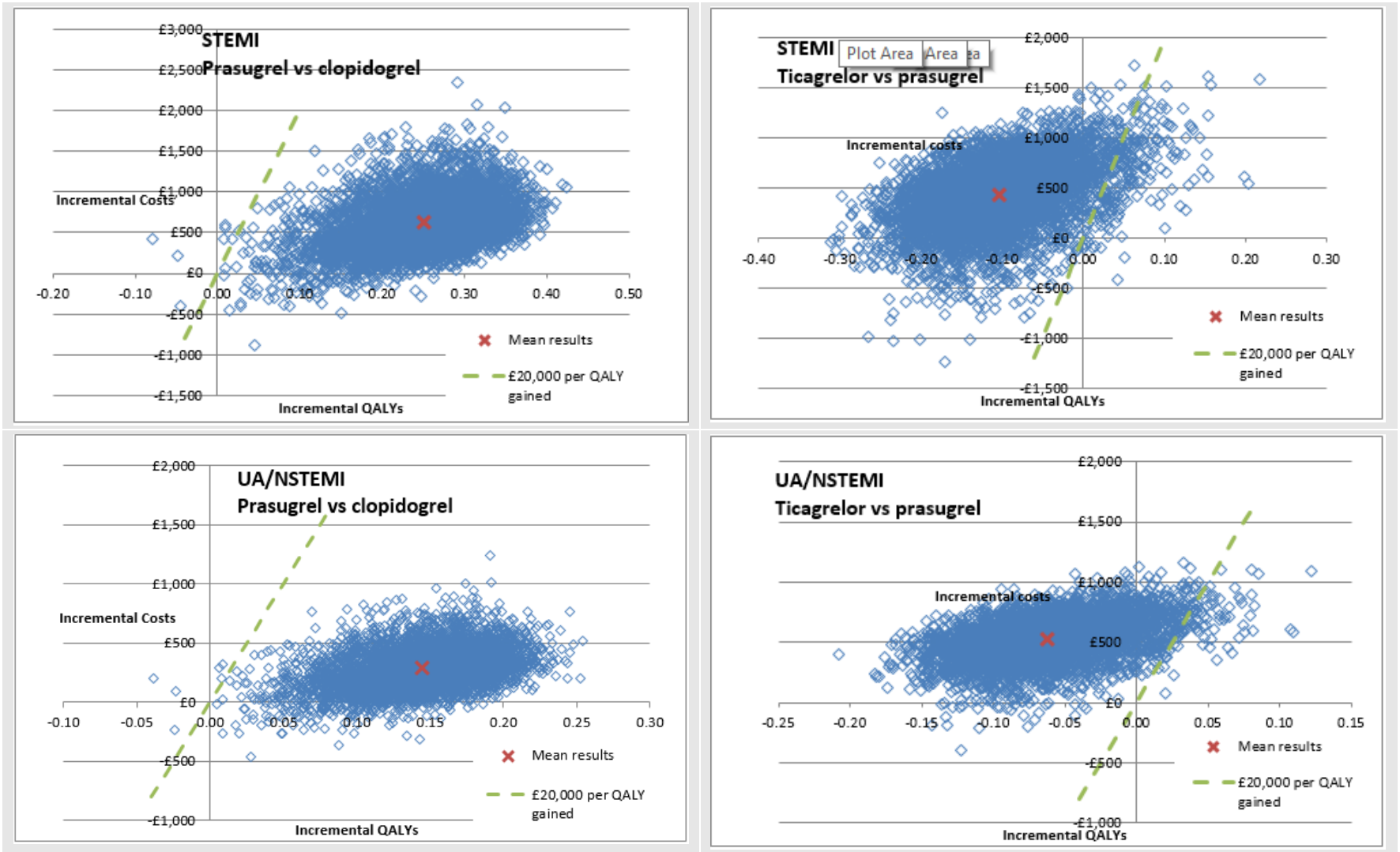


**Table 51: Base case analysis results (probabilistic analysis) – events per 1000**

| Intervention | Reinfarction | | | | Stroke | | | | Major bleed | | | Minor bleed | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 0 – 30 days | 31 days – 1 year | Post 1 year | Total | 0 – 30 days | 31 days – 1 year | Post 1 year | Total | 0 – 30 days | 31 days – 1 year | Total | 0 – 30 days | 31 days – 1 year | Total |
| **Scenario 1 – Ticagrelor vs clopidogrel (meta-analysis); prasugrel vs clopidogrel (meta-analysis)** | | | | | | | | | | | | | | |
| *STEMI* | | | | | | | | | | | | | | |
| Clopidogrel | 29.1 | 36.5 | 342.0 | 407.6 | 3.0 | 9.5 | 89.6 | 102.0 | 9.4 | 25.3 | 34.6 | 7.1 | 19.1 | 26.2 |
| Prasugrel | 23.4 | 26.5 | 348.6 | 398.5 | 2.5 | 9.1 | 91.3 | 102.9 | 9.3 | 39.4 | 48.7 | 5.2 | 46.7 | 51.9 |
| Ticagrelor | 20.1 | 34.3 | 354.1 | 408.5 | 3.8 | 10.2 | 92.8 | 106.8 | 9.4 | 26.6 | 36.0 | 9.0 | 26.4 | 35.5 |
| *UA/NSTEMI* | | | | | | | | | | | | | | |
| Clopidogrel | 10.2 | 32.1 | 326.0 | 368.3 | 1.1 | 5.2 | 52.9 | 59.1 | 6.4 | 17.4 | 23.8 | 4.1 | 11.0 | 15.1 |
| Prasugrel | 8.2 | 23.8 | 329.8 | 361.8 | 0.9 | 4.9 | 53.5 | 59.3 | 6.4 | 27.2 | 33.6 | 3.0 | 27.4 | 30.4 |
| Ticagrelor | 7.0 | 27.9 | 332.6 | 367.5 | 1.4 | 5.7 | 53.5 | 60.5 | 6.4 | 18.3 | 24.7 | 5.2 | 15.3 | 20.5 |
| **Scenario 2 – Prasugrel vs clopidogrel (meta-analysis); ticagrelor versus prasugrel (ISAR-REACT 5)** | | | | | | | | | | | | | | |
| *STEMI* | | | | | | | | | | | | | | |
| Clopidogrel | 29.2 | 36.4 | 341.7 | 407.4 | 3.0 | 9.5 | 89.7 | 102.2 | 9.4 | 25.2 | 34.6 | 7.1 | 19.1 | 26.1 |
| Prasugrel | 23.6 | 26.4 | 348.3 | 398.3 | 2.5 | 9.2 | 91.4 | 103.1 | 9.3 | 39.4 | 48.7 | 5.3 | 46.9 | 52.2 |
| Ticagrelor | 20.2 | 58.9 | 327.6 | 406.7 | 3.8 | 9.6 | 86.0 | 99.4 | 9.4 | 41.9 | 51.3 | 9.0 | 26.4 | 35.4 |
| *UA/NSTEMI* | | | | | | | | | | | | | | |
| Clopidogrel | 10.2 | 32.0 | 325.4 | 367.6 | 1.1 | 5.2 | 52.9 | 59.1 | 6.5 | 17.3 | 23.8 | 4.1 | 11.1 | 15.1 |
| Prasugrel | 8.2 | 23.8 | 329.2 | 361.2 | 0.9 | 4.9 | 53.5 | 59.3 | 6.4 | 27.2 | 33.7 | 3.1 | 27.6 | 30.7 |
| Ticagrelor | 7.0 | 44.1 | 317.5 | 368.7 | 1.4 | 5.3 | 53.5 | 60.2 | 6.5 | 29.0 | 35.5 | 5.3 | 15.4 | 20.6 |
| **Scenario 3 – Ticagrelor vs clopidogrel (meta-analysis); Ticagrelor versus prasugrel (ISAR-REACT 5)** | | | | | | | | | | | | | | |
| *STEMI* | | | | | | | | | | | | | | |
| Clopidogrel | 29.1 | 36.4 | 341.8 | 407.3 | 3.0 | 9.5 | 89.6 | 102.1 | 9.4 | 25.2 | 34.6 | 7.1 | 19.1 | 26.1 |
| Prasugrel | 23.4 | 10.7 | 368.1 | 402.1 | 2.5 | 9.6 | 96.5 | 108.6 | 9.3 | 24.6 | 33.9 | 5.2 | 46.1 | 51.3 |
| Ticagrelor | 20.1 | 34.3 | 353.8 | 408.2 | 3.8 | 10.3 | 92.8 | 106.8 | 9.4 | 26.6 | 36.0 | 9.0 | 26.4 | 35.4 |
| *UA/NSTEMI* | | | | | | | | | | | | | | |

| Intervention | Reinfarction | | | | Stroke | | | | Major bleed | | | Minor bleed | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Clopidogrel | 10.2 | 32.0 | 325.3 | 367.4 | 1.1 | 5.2 | 52.9 | 59.2 | 6.4 | 17.4 | 23.8 | 4.1 | 11.0 | 15.1 |
| Prasugrel | 8.2 | 13.5 | 339.8 | 361.5 | 0.9 | 5.2 | 55.3 | 61.4 | 6.4 | 16.9 | 23.3 | 3.0 | 27.2 | 30.3 |
| Ticagrelor | 7.0 | 27.9 | 331.8 | 366.7 | 1.4 | 5.7 | 55.3 | 62.3 | 6.4 | 18.3 | 24.8 | 5.2 | 15.4 | 20.6 |

**Table 52: Base case analysis results (probabilistic analysis) – cost breakdown (mean per person)**

| | 0 – 1 year | | | | | | Post 1 year | | | Total costs | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Intervention costs | No further event | Reinfarction | Stroke | Major bleed | Minor bleed | No further event | Reinfarction | Stroke | Undiscounted | Discounted |
| **Scenario 1 – Ticagrelor vs clopidogrel (meta-analysis); prasugrel vs clopidogrel (meta-analysis)** | | | | | | | | | | | |
| *STEMI* | | | | | | | | | | | |
| Clopidogrel | £38 | £1,450 | £307 | £184 | £68 | £5 | £7,128 | £6,274 | £7,614 | £23,068 | £17,336 |
| Prasugrel | £104 | £1,478 | £235 | £170 | £95 | £9 | £7,264 | £6,120 | £7,661 | £23,137 | £17,385 |
| Ticagrelor | £624 | £1,484 | £252 | £209 | £70 | £6 | £7,379 | £6,288 | £7,986 | £24,299 | £18,387 |
| *UA/NSTEMI* | | | | | | | | | | | |
| Clopidogrel | £40 | £1,559 | £193 | £91 | £47 | £3 | £8,084 | £5,256 | £4,056 | £19,327 | £14,854 |
| Prasugrel | £107 | £1,570 | £146 | £84 | £66 | £5 | £8,178 | £5,152 | £4,061 | £19,370 | £14,892 |
| Ticagrelor | £646 | £1,574 | £158 | £103 | £48 | £4 | £8,248 | £5,240 | £4,194 | £20,216 | £15,665 |
| **Scenario 2 – Prasugrel vs clopidogrel (meta-analysis); ticagrelor versus prasugrel (ISAR-REACT 5)** | | | | | | | | | | | |
| *STEMI* | | | | | | | | | | | |
| Clopidogrel | £38 | £1,449 | £308 | £184 | £68 | £5 | £7,124 | £6,321 | £7,618 | £23,115 | £17,368 |
| Prasugrel | £104 | £1,477 | £235 | £171 | £95 | £9 | £7,260 | £6,166 | £7,671 | £23,188 | £17,420 |
| Ticagrelor | £613 | £1,453 | £360 | £199 | £100 | £6 | £6,830 | £6,325 | £7,417 | £23,303 | £17,702 |
| *UA/NSTEMI* | | | | | | | | | | | |
| Clopidogrel | £40 | £1,557 | £192 | £91 | £47 | £3 | £8,085 | £5,289 | £4,055 | £19,359 | £14,874 |
| Prasugrel | £107 | £1,569 | £146 | £85 | £66 | £5 | £8,178 | £5,185 | £4,063 | £19,403 | £14,914 |
| Ticagrelor | £640 | £1,554 | £229 | £99 | £69 | £4 | £7,891 | £5,318 | £4,006 | £19,810 | £15,386 |
| **Scenario 3 – Ticagrelor vs clopidogrel (meta-analysis); Ticagrelor versus prasugrel (ISAR-REACT 5)** | | | | | | | | | | | |
| *STEMI* | | | | | | | | | | | |
| Clopidogrel | £38 | £1,452 | £307 | £184 | £68 | £5 | £7,165 | £6,268 | £7,613 | £23,101 | £17,362 |
| Prasugrel | £105 | £1,503 | £166 | £177 | £66 | £9 | £7,714 | £6,168 | £8,087 | £23,996 | £17,983 |

| | 0 – 1 year | | | | | | Post 1 year | | | Total costs | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Ticagrelor | £624 | £1,486 | £252 | £209 | £70 | £6 | £7,416 | £6,281 | £7,985 | £24,331 | £18,413 |
| *UA/NSTEMI* | | | | | | | | | | | |
| Clopidogrel | £40 | £1,561 | £192 | £91 | £47 | £3 | £8,132 | £5,250 | £4,058 | £19,374 | £14,890 |
| Prasugrel | £108 | £1,587 | £101 | £88 | £46 | £5 | £8,494 | £5,142 | £4,204 | £19,774 | £15,175 |
| Ticagrelor | £646 | £1,576 | £158 | £103 | £48 | £4 | £8,296 | £5,233 | £4,197 | £20,262 | £15,701 |

## 3.2 Sensitivity analyses

In addition to probabilistic analysis to assess uncertainty, a range of one-way and scenario sensitivity analyses were undertaken (described in section 2.4) including varying the baseline risk of stroke, inclusion of stroke treatment effects, inclusion of dyspnoea as a side effect, varying bleeding and stroke costs, varying dosing assumptions, incorporation of post-ACS rivaroxaban use, varying event-related mortality in the extrapolation model, varying the baseline risk of stroke and reinfarction to account for overestimation of people alive with an event and varying intervention costing assumptions. Results from the sensitivity analyses are presented for scenario 1 in Table 53 (STEMI) and Table 54 (UA/NSTEMI), for scenario 2 in Table 55 (STEMI) and Table 56 (UA/NSTEMI) and for scenario 3 in Table 57 (STEMI) and Table 58 (UA/NSTEMI).

Conclusions about which DAPT option was the most cost effective were unchanged in most sensitivity analyses in all three scenarios and uncertainty remained similar. In the exploratory sensitivity analyses where adjunctive rivaroxaban use post-ACS was incorporated into the clopidogrel group, in some cases relative costs and QALYs between comparators, and conclusions about cost effectiveness changed, although this depended on the proportion of people assumed to receive rivaroxaban. When it was assumed everyone in the clopidogrel group also received rivaroxaban post-ACS, the clopidogrel group had the highest costs in all scenarios (due to the increase in intervention costs of also having rivaroxaban). QALYs were also increased due to the additional treatment effects of rivaroxaban. In scenarios 1 and 2, QALYs with clopidogrel (incorporating rivaroxaban) were higher than with prasugrel or ticagrelor and clopidogrel became the most cost effective option. In scenario 3, QALYs with clopidogrel were still lower than prasugrel for both STEMI and UA/NSTEMI and so the clopidogrel option was still not cost effective as it was dominated (higher costs and lower QALYs than an alternative). Uncertainty remained low in this analysis with prasugrel being the most cost effective option in 83%/92% of simulations for STEMI and UA/NSTEMI respectively. When rivaroxaban usage was assumed to be 1.8% (as estimated current practice is among people receiving clopidogrel) conclusions about which DAPT option was the most cost effective remained the same as in the base case analysis; uncertainty also remained similar.

**Table 53: Sensitivity analyses results for scenario 1: STEMI population (probabilistic analysis, per person results)**

| Intervention | Mean lifetime costs undisc | Mean lifetime costs disc | Mean life years | Mean lifetime QALYs undisc | Mean lifetime QALYs disc | Incr. cost | Incr. QALYs | ICER | NMB (£20k) | Rank at £20k | % CE at £20k | % Rank 2nd at £20k | % Rank 3rd at £20k | % CE at £30k |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Base case analysis** | | | | | | | | | | | | | | |
| Clopidogrel | £23,068 | £17,336 | 13.05 | 8.29 | 6.42 | | | | £111,149 | 3 | 0% | 40% | 60% | 0% |
| Prasugrel | £23,137 | £17,385 | 13.08 | 8.31 | 6.44 | £49 | 0.01 | £3,507 | £111,381 | 2 | 7% | 54% | 40% | 4% |
| Ticagrelor | £24,299 | £18,387 | 13.36 | 8.48 | 6.57 | £1,002 | 0.13 | £7,455 | £113,067 | 1 | 93% | 7% | 0% | 96% |
| **Baseline risks** | | | | | | | | | | | | | | |
| **SA1: Stroke baseline risks adjusted based on PLATO** | | | | | | | | | | | | | | |
| Clopidogrel | £19,714 | £14,995 | 13.08 | 8.36 | 6.47 | | | | £114,418 | 3 | 0% | 38% | 62% | 0% |
| Prasugrel | £19,763 | £15,034 | 13.11 | 8.38 | 6.49 | £39 | 0.02 | £2,408 | £114,701 | 2 | 6% | 56% | 38% | 4% |
| Ticagrelor | £20,786 | £15,932 | 13.38 | 8.56 | 6.62 | £898 | 0.13 | £6,726 | £116,474 | 1 | 94% | 6% | 0% | 96% |
| **SA2: Include baseline risk adjustment** | | | | | | | | | | | | | | |
| Clopidogrel | £21,845 | £16,419 | 13.17 | 8.38 | 6.48 | | | | £113,196 | 3 | 0% | 37% | 63% | 0% |
| Prasugrel | £21,911 | £16,469 | 13.20 | 8.40 | 6.50 | £50 | 0.02 | £3,031 | £113,477 | 2 | 8% | 55% | 37% | 5% |
| Ticagrelor | £23,014 | £17,426 | 13.48 | 8.58 | 6.63 | £957 | 0.13 | £7,173 | £115,188 | 1 | 92% | 7% | 0% | 95% |
| **SA3: Reduce SMR for ACS/Reinfarction by 20%** | | | | | | | | | | | | | | |
| Clopidogrel | £24,704 | £18,279 | 14.18 | 8.97 | 6.83 | | | | £118,223 | 3 | 0% | 40% | 60% | 0% |
| Prasugrel | £24,775 | £18,329 | 14.20 | 8.99 | 6.84 | £50 | 0.01 | £3,648 | £118,448 | 2 | 7% | 53% | 40% | 4% |
| Ticagrelor | £25,968 | £19,350 | 14.51 | 9.18 | 6.98 | £1,020 | 0.14 | £7,158 | £120,278 | 1 | 93% | 7% | 0% | 96% |
| **Treatment effects** | | | | | | | | | | | | | | |
| **SA4: Stroke treatment effect excluded** | | | | | | | | | | | | | | |
| Clopidogrel | £23,102 | £17,358 | 13.05 | 8.29 | 6.42 | | | | £111,095 | 3 | 0% | 42% | 58% | 0% |
| Prasugrel | £23,239 | £17,462 | 13.08 | 8.31 | 6.44 | £104 | 0.01 | Extendedly dominated | £111,261 | 2 | 4% | 54% | 42% | 3% |
| Ticagrelor | £24,206 | £18,309 | 13.36 | 8.48 | 6.57 | £951 | 0.15 | £6,319 | £113,154 | 1 | 96% | 4% | 0% | 97% |
| **SA5: Ticagrelor's stroke treatment effect not included** | | | | | | | | | | | | | | |
| Clopidogrel | £23,070 | £17,338 | 13.05 | 8.29 | 6.42 | | | | £111,146 | 3 | 0% | 38% | 62% | 0% |
| Prasugrel | £23,141 | £17,388 | 13.08 | 8.31 | 6.44 | £51 | 0.02 | £3,203 | £111,412 | 2 | 5% | 56% | 38% | 4% |
| Ticagrelor | £24,169 | £18,285 | 13.36 | 8.48 | 6.57 | £896 | 0.13 | £6,726 | £113,181 | 1 | 95% | 5% | 0% | 96% |
| **SA6: Prasugrel's stroke treatment effect not included** | | | | | | | | | | | | | | |
| Clopidogrel | £23,122 | £17,375 | 13.05 | 8.29 | 6.42 | | | | £111,100 | 3 | 0% | 42% | 57% | 0% |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Prasugrel | £23,259 | £17,478 | 13.08 | 8.31 | 6.44 | £103 | 0.01 | Extendedly dominated | £111,260 | 2 | 6% | 51% | 42% | 4% |
| Ticagrelor | £24,351 | £18,424 | 13.36 | 8.48 | 6.57 | £1,050 | 0.15 | £7,071 | £113,020 | 1 | 94% | 6% | 0% | 96% |
| **SA7: Rivaroxaban treatment effect included (current practice usage)** | | | | | | | | | | | | | | |
| Clopidogrel | £23,119 | £17,374 | 13.06 | 8.30 | 6.43 | | | | £111,233 | 3 | 0% | 39% | 61% | 0% |
| Prasugrel | £23,163 | £17,402 | 13.08 | 8.31 | 6.44 | £27 | 0.01 | £2,220 | £111,451 | 2 | 7% | 53% | 39% | 5% |
| Ticagrelor | £24,318 | £18,399 | 13.36 | 8.49 | 6.58 | £998 | 0.13 | £7,529 | £113,104 | 1 | 93% | 7% | 0% | 95% |
| **SA8: Rivaroxaban treatment effect included (100% usage)** | | | | | | | | | | | | | | |
| Prasugrel | £23,213 | £17,437 | 13.08 | 8.31 | 6.44 | | | | £111,334 | 3 | 1% | 8% | 90% | 1% |
| Ticagrelor | £24,383 | £18,446 | 13.36 | 8.48 | 6.57 | £1,008 | 0.13 | Extendedly dominated | £112,996 | 2 | 20% | 73% | 7% | 19% |
| Clopidogrel | £24,726 | £18,741 | 13.49 | 8.56 | 6.64 | £1,304 | 0.20 | £6,637 | £113,959 | 1 | 78% | 19% | 3% | 80% |
| **SA9: Dyspnoea included in analysis** | | | | | | | | | | | | | | |
| Clopidogrel | £23,052 | £17,324 | 13.05 | 8.29 | 6.42 | | | | £111,134 | 3 | 0% | 39% | 61% | 0% |
| Prasugrel | £23,126 | £17,377 | 13.08 | 8.31 | 6.44 | £53 | 0.01 | £3,616 | £111,375 | 2 | 7% | 54% | 38% | 4% |
| Ticagrelor | £24,286 | £18,378 | 13.36 | 8.48 | 6.57 | £1,001 | 0.13 | £7,481 | £113,049 | 1 | 93% | 7% | 0% | 96% |
| **Intervention costs** | | | | | | | | | | | | | | |
| **SA10: Clopidogrel 300mg loading dose** | | | | | | | | | | | | | | |
| Clopidogrel | £23,006 | £17,289 | 13.05 | 8.29 | 6.42 | | | | £111,202 | 3 | 0% | 39% | 61% | 0% |
| Prasugrel | £23,075 | £17,338 | 13.08 | 8.31 | 6.44 | £49 | 0.01 | £3,351 | £111,444 | 2 | 8% | 53% | 39% | 5% |
| Ticagrelor | £24,237 | £18,341 | 13.36 | 8.48 | 6.57 | £1,003 | 0.13 | £7,520 | £113,109 | 1 | 92% | 8% | 0% | 95% |
| **SA12: Treatment duration based on TRITON TIMI** | | | | | | | | | | | | | | |
| Clopidogrel | £23,124 | £17,376 | 13.05 | 8.29 | 6.42 | | | | £111,094 | 3 | 0% | 39% | 61% | 0% |
| Prasugrel | £23,190 | £17,421 | 13.08 | 8.31 | 6.44 | £45 | 0.02 | £2,916 | £111,360 | 2 | 6% | 55% | 38% | 4% |
| Ticagrelor | £24,308 | £18,381 | 13.36 | 8.48 | 6.57 | £959 | 0.13 | £7,224 | £113,057 | 1 | 94% | 6% | 0% | 96% |
| **SA13: Treatment duration based on PLATO** | | | | | | | | | | | | | | |
| Clopidogrel | £23,084 | £17,345 | 13.05 | 8.29 | 6.42 | | | | £111,146 | 3 | 0% | 38% | 62% | 0% |
| Prasugrel | £23,145 | £17,384 | 13.08 | 8.31 | 6.44 | £39 | 0.02 | £2,469 | £111,421 | 2 | 5% | 57% | 38% | 4% |
| Ticagrelor | £24,163 | £18,245 | 13.36 | 8.48 | 6.57 | £861 | 0.13 | £6,499 | £113,211 | 1 | 95% | 5% | 0% | 96% |
| **SA14: Treatment duration DAPT specific** | | | | | | | | | | | | | | |
| Clopidogrel | £23,081 | £17,344 | 13.05 | 8.29 | 6.42 | | | | £111,153 | 3 | 0% | 38% | 62% | 0% |
| Prasugrel | £23,157 | £17,399 | 13.09 | 8.31 | 6.44 | £55 | 0.02 | £3,135 | £111,446 | 2 | 8% | 55% | 38% | 5% |
| Ticagrelor | £24,301 | £18,384 | 13.36 | 8.49 | 6.57 | £986 | 0.13 | £7,501 | £113,089 | 1 | 92% | 8% | 0% | 95% |
| **SA15: Treatment duration full year** | | | | | | | | | | | | | | |
| Clopidogrel | £23,158 | £17,402 | 13.05 | 8.29 | 6.42 | | | | £111,097 | 3 | 0% | 40% | 60% | 0% |
| Prasugrel | £23,228 | £17,453 | 13.08 | 8.31 | 6.44 | £51 | 0.01 | £3,614 | £111,326 | 2 | 8% | 52% | 40% | 5% |
| Ticagrelor | £24,452 | £18,517 | 13.36 | 8.48 | 6.57 | £1,064 | 0.13 | £7,930 | £112,945 | 1 | 92% | 8% | 0% | 95% |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Event costs** | | | | | | | | | | | | | | |
| **SA16: Percentage stroke social care costs publicly funded - 30%** | | | | | | | | | | | | | | |
| Clopidogrel | £21,321 | £16,154 | 13.05 | 8.29 | 6.42 | | | | £112,331 | 3 | 0% | 39% | 61% | 0% |
| Prasugrel | £21,389 | £16,206 | 13.08 | 8.31 | 6.44 | £52 | 0.02 | £3,414 | £112,581 | 2 | 6% | 55% | 39% | 4% |
| Ticagrelor | £22,460 | £17,141 | 13.36 | 8.48 | 6.57 | £935 | 0.13 | £7,014 | £114,313 | 1 | 94% | 6% | 0% | 96% |
| **SA17: Percentage stroke social care costs publicly funded - 70%** | | | | | | | | | | | | | | |
| Clopidogrel | £24,833 | £18,527 | 13.05 | 8.29 | 6.42 | | | | £109,954 | 3 | 0% | 40% | 60% | 0% |
| Prasugrel | £24,910 | £18,580 | 13.08 | 8.31 | 6.44 | £53 | 0.01 | £3,633 | £110,192 | 2 | 8% | 52% | 40% | 5% |
| Ticagrelor | £26,154 | £19,642 | 13.36 | 8.48 | 6.57 | £1,062 | 0.13 | £7,939 | £111,805 | 1 | 92% | 8% | 0% | 95% |
| **SA18: Minor bleeding costs set to GI bleed** | | | | | | | | | | | | | | |
| Clopidogrel | £23,156 | £17,401 | 13.05 | 8.29 | 6.43 | | | | £111,103 | 3 | 0% | 39% | 61% | 0% |
| Prasugrel | £23,250 | £17,473 | 13.08 | 8.31 | 6.44 | £72 | 0.02 | £4,312 | £111,364 | 2 | 8% | 54% | 39% | 5% |
| Ticagrelor | £24,391 | £18,457 | 13.36 | 8.48 | 6.57 | £984 | 0.13 | £7,515 | £112,999 | 1 | 92% | 8% | 0% | 95% |
| **SA19: Major bleeding costs including intracranial bleeds (10%)** | | | | | | | | | | | | | | |
| Clopidogrel | £23,085 | £17,348 | 13.05 | 8.29 | 6.42 | | | | £111,141 | 3 | 0% | 39% | 61% | 0% |
| Prasugrel | £23,160 | £17,402 | 13.08 | 8.31 | 6.44 | £54 | 0.02 | £3,542 | £111,393 | 2 | 7% | 54% | 39% | 4% |
| Ticagrelor | £24,317 | £18,400 | 13.36 | 8.48 | 6.57 | £998 | 0.13 | £7,507 | £113,054 | 1 | 93% | 7% | 0% | 96% |
| **SA20: Major bleeding costs including intracranial bleeds (20%)** | | | | | | | | | | | | | | |
| Clopidogrel | £23,131 | £17,382 | 13.05 | 8.29 | 6.42 | | | | £111,107 | 3 | 0% | 40% | 60% | 0% |
| Prasugrel | £23,200 | £17,431 | 13.08 | 8.31 | 6.44 | £49 | 0.01 | £3,467 | £111,342 | 2 | 7% | 53% | 40% | 4% |
| Ticagrelor | £24,361 | £18,433 | 13.36 | 8.48 | 6.57 | £1,002 | 0.13 | £7,463 | £113,025 | 1 | 93% | 7% | 0% | 96% |
| **SA21: Intracranial bleeds set to 30% of major bleeds** | | | | | | | | | | | | | | |
| Clopidogrel | £23,090 | £17,356 | 13.05 | 8.29 | 6.42 | | | | £111,088 | 3 | 0% | 39% | 61% | 0% |
| Prasugrel | £23,164 | £17,410 | 13.08 | 8.31 | 6.44 | £54 | 0.01 | £3,679 | £111,326 | 2 | 7% | 54% | 39% | 4% |
| Ticagrelor | £24,324 | £18,410 | 13.36 | 8.48 | 6.57 | £1,000 | 0.13 | £7,455 | £113,008 | 1 | 93% | 7% | 0% | 96% |
| **SA22: Intracranial bleeds set to 40% of major bleeds** | | | | | | | | | | | | | | |
| Clopidogrel | £23,115 | £17,371 | 13.05 | 8.29 | 6.42 | | | | £111,119 | 3 | 0% | 40% | 60% | 0% |
| Prasugrel | £23,185 | £17,423 | 13.08 | 8.31 | 6.44 | £52 | 0.01 | £3,804 | £111,340 | 2 | 7% | 53% | 40% | 4% |
| Ticagrelor | £24,343 | £18,420 | 13.36 | 8.48 | 6.57 | £998 | 0.13 | £7,429 | £113,028 | 1 | 93% | 7% | 0% | 96% |
| **SA23: Higher minor and major bleeding costs (intracranial 20%)** | | | | | | | | | | | | | | |
| Clopidogrel | £23,060 | £17,335 | 13.05 | 8.29 | 6.42 | | | | £111,143 | 3 | 0% | 39% | 61% | 0% |
| Prasugrel | £23,148 | £17,403 | 13.08 | 8.31 | 6.44 | £68 | 0.02 | £4,498 | £111,376 | 2 | 7% | 54% | 39% | 4% |
| Ticagrelor | £24,296 | £18,391 | 13.36 | 8.48 | 6.57 | £989 | 0.13 | £7,402 | £113,059 | 1 | 93% | 7% | 0% | 96% |
| **Methods** | | | | | | | | | | | | | | |
| **SA24: Utilities not age-adjusted** | | | | | | | | | | | | | | |
| Clopidogrel | £23,060 | £17,327 | 13.05 | 10.76 | 8.27 | | | | £148,121 | 3 | 0% | 38% | 62% | 0% |
| Prasugrel | £23,133 | £17,379 | 13.08 | 10.79 | 8.29 | £52 | 0.02 | £2,590 | £148,470 | 2 | 5% | 56% | 38% | 4% |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Ticagrelor | £24,284 | £18,373 | 13.36 | 11.01 | 8.46 | £994 | 0.17 | £5,826 | £150,889 | 1 | 95% | 5% | 0% | 96% |
| **SA25: Discount rate 1.5%** | | | | | | | | | | | | | | |
| Clopidogrel | £23,071 | £20,266 | 13.05 | 8.29 | 7.38 | | | | £127,424 | 3 | 0% | 38% | 62% | 0% |
| Prasugrel | £23,150 | £20,333 | 13.08 | 8.31 | 7.40 | £67 | 0.02 | £3,274 | £127,765 | 2 | 7% | 55% | 38% | 5% |
| Ticagrelor | £24,299 | £21,406 | 13.36 | 8.48 | 7.56 | £1,073 | 0.15 | £7,088 | £129,720 | 1 | 93% | 7% | 0% | 95% |

*Abbreviations: CE = cost effective; disc. = discounted; Incr. = incremental; NMB = net monetary benefit; QALY = quality-adjusted life years; £20K = a threshold of £20,000 per QALY gained; £30K = a threshold of £30,000 per QALY gained.*
*Note: SA11 is for the UA/NSTEMI population only and so does not appear in this table. Incremental costs and QALYs are versus the comparator with the next lowest costs (the previous line in the table) unless that option has been ruled out by extended dominance in which case they are compared to the option with the lowest costs (the first line in the table).*

**Table 54: Sensitivity analyses results for scenario 1: UA/NSTEMI population (probabilistic analysis, per person results)**

| Intervention | Mean lifetime costs undisc | Mean lifetime costs disc | Mean life years | Mean lifetime QALYs Undisc | Mean lifetime QALYs disc | Incr. cost | Incr. QALYs | ICER | NMB (£20k) | Rank at £20k | % CE at £20k | % Rank 2nd at £20k | % Rank 3rd at £20k | % CE at £30k |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Base case analysis** | | | | | | | | | | | | | | |
| Clopidogrel | £19,327 | £14,854 | 12.95 | 8.21 | 6.44 | | | | £113,954 | 3 | 0% | 40% | 60% | 0% |
| Prasugrel | £19,370 | £14,892 | 12.97 | 8.22 | 6.45 | £38 | 0.01 | £4,510 | £114,085 | 2 | 14% | 46% | 39% | 7% |
| Ticagrelor | £20,216 | £15,665 | 13.12 | 8.32 | 6.52 | £774 | 0.07 | £10,424 | £114,795 | 1 | 86% | 14% | 0% | 93% |
| **Baseline risks** | | | | | | | | | | | | | | |
| **SA1: Stroke baseline risks adjusted based on PLATO** | | | | | | | | | | | | | | |
| Clopidogrel | £16,976 | £13,193 | 12.98 | 8.26 | 6.48 | | | | £116,322 | 3 | 0% | 38% | 61% | 0% |
| Prasugrel | £17,018 | £13,233 | 13.00 | 8.28 | 6.49 | £40 | 0.01 | £4,244 | £116,471 | 2 | 12% | 50% | 38% | 6% |
| Ticagrelor | £17,784 | £13,945 | 13.15 | 8.37 | 6.56 | £712 | 0.07 | £9,640 | £117,236 | 1 | 88% | 12% | 0% | 94% |
| **SA2: Include baseline risk adjustment** | | | | | | | | | | | | | | |
| Clopidogrel | £18,676 | £14,393 | 12.96 | 8.22 | 6.45 | | | | £114,574 | 3 | 0% | 38% | 62% | 0% |
| Prasugrel | £18,722 | £14,433 | 12.98 | 8.24 | 6.46 | £41 | 0.01 | £4,098 | £114,732 | 2 | 15% | 48% | 37% | 8% |
| Ticagrelor | £19,541 | £15,186 | 13.13 | 8.33 | 6.53 | £753 | 0.07 | £10,301 | £115,441 | 1 | 85% | 14% | 1% | 92% |
| **SA3: Reduce SMR for ACS/Reinfarction by 20%** | | | | | | | | | | | | | | |
| Clopidogrel | £20,900 | £15,781 | 14.14 | 8.92 | 6.87 | | | | £121,633 | 3 | 0% | 40% | 60% | 0% |
| Prasugrel | £20,943 | £15,819 | 14.16 | 8.94 | 6.88 | £38 | 0.01 | £4,492 | £121,763 | 2 | 12% | 48% | 40% | 7% |
| Ticagrelor | £21,806 | £16,602 | 14.33 | 9.04 | 6.96 | £784 | 0.08 | £9,904 | £122,562 | 1 | 87% | 12% | 0% | 93% |
| **Treatment effects** | | | | | | | | | | | | | | |
| **SA4: Stroke treatment effect excluded** | | | | | | | | | | | | | | |
| Clopidogrel | £19,357 | £14,872 | 12.95 | 8.21 | 6.44 | | | | £113,910 | 3 | 0% | 41% | 58% | 0% |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Prasugrel | £19,433 | £14,937 | 12.97 | 8.22 | 6.45 | £65 | 0.01 | £8,003 | £114,008 | 2 | 10% | 48% | 41% | 5% |
| Ticagrelor | £20,182 | £15,633 | 13.13 | 8.32 | 6.52 | £696 | 0.08 | £9,199 | £114,825 | 1 | 90% | 10% | 0% | 95% |
| **SA5: Ticagrelor's stroke treatment effect not included** | | | | | | | | | | | | | | |
| Clopidogrel | £19,330 | £14,854 | 12.95 | 8.21 | 6.44 | | | | £113,963 | 3 | 0% | 39% | 61% | 0% |
| Prasugrel | £19,373 | £14,893 | 12.97 | 8.23 | 6.45 | £39 | 0.01 | £4,091 | £114,114 | 2 | 12% | 50% | 39% | 6% |
| Ticagrelor | £20,152 | £15,613 | 13.12 | 8.32 | 6.52 | £720 | 0.07 | £9,793 | £114,864 | 1 | 88% | 12% | 0% | 94% |
| **SA6: Prasugrel's stroke treatment effect not included** | | | | | | | | | | | | | | |
| Clopidogrel | £19,374 | £14,887 | 12.95 | 8.21 | 6.44 | | | | £113,911 | 3 | 0% | 42% | 58% | 0% |
| Prasugrel | £19,450 | £14,952 | 12.97 | 8.22 | 6.45 | £65 | 0.01 | £8,145 | £114,006 | 2 | 13% | 45% | 42% | 7% |
| Ticagrelor | £20,261 | £15,698 | 13.12 | 8.32 | 6.52 | £746 | 0.07 | £9,980 | £114,754 | 1 | 87% | 13% | 0% | 93% |
| **SA7: Rivaroxaban treatment effect included (current practice usage)** | | | | | | | | | | | | | | |
| Clopidogrel | £19,376 | £14,891 | 12.96 | 8.22 | 6.44 | | | | £113,994 | 3 | 0% | 39% | 61% | 0% |
| Prasugrel | £19,401 | £14,912 | 12.97 | 8.23 | 6.45 | £21 | 0.01 | £2,837 | £114,123 | 2 | 15% | 47% | 39% | 8% |
| Ticagrelor | £20,243 | £15,684 | 13.13 | 8.32 | 6.52 | £771 | 0.07 | £10,552 | £114,814 | 1 | 85% | 14% | 1% | 92% |
| **SA8: Rivaroxaban treatment effect included (100% usage)** | | | | | | | | | | | | | | |
| Prasugrel | £19,438 | £14,938 | 12.97 | 8.22 | 6.45 | | | | £114,026 | 3 | 4% | 14% | 82% | 1% |
| Ticagrelor | £20,287 | £15,715 | 13.13 | 8.32 | 6.52 | £777 | 0.07 | Extendedly dominated | £114,726 | 2 | 22% | 65% | 13% | 21% |
| Clopidogrel | £20,466 | £15,874 | 13.19 | 8.36 | 6.55 | £936 | 0.10 | £8,939 | £115,184 | 1 | 74% | 21% | 6% | 77% |
| **SA9: Dyspnoea included in analysis** | | | | | | | | | | | | | | |
| Clopidogrel | £19,310 | £14,841 | 12.95 | 8.21 | 6.44 | | | | £113,944 | 3 | 0% | 39% | 61% | 0% |
| Prasugrel | £19,355 | £14,881 | 12.97 | 8.22 | 6.45 | £40 | 0.01 | £4,566 | £114,080 | 2 | 14% | 48% | 38% | 8% |
| Ticagrelor | £20,200 | £15,654 | 13.13 | 8.32 | 6.52 | £774 | 0.07 | £10,469 | £114,784 | 1 | 86% | 14% | 0% | 92% |
| **Intervention costs** | | | | | | | | | | | | | | |
| **SA10: Clopidogrel 300mg loading dose** | | | | | | | | | | | | | | |
| Clopidogrel | £19,272 | £14,811 | 12.95 | 8.21 | 6.44 | | | | £113,997 | 3 | 0% | 39% | 61% | 0% |
| Prasugrel | £19,315 | £14,849 | 12.97 | 8.22 | 6.45 | £38 | 0.01 | £4,353 | £114,133 | 2 | 14% | 47% | 39% | 8% |
| Ticagrelor | £20,160 | £15,623 | 13.12 | 8.32 | 6.52 | £774 | 0.07 | £10,507 | £114,833 | 1 | 85% | 14% | 0% | 92% |
| **SA11: UA/NSTEMI prasugrel arm receiving clopidogrel loading dose** | | | | | | | | | | | | | | |
| Clopidogrel | £19,357 | £14,875 | 12.96 | 8.21 | 6.44 | | | | £113,922 | 3 | 0% | 39% | 61% | 0% |
| Prasugrel | £19,401 | £14,914 | 12.97 | 8.22 | 6.45 | £39 | 0.01 | £4,262 | £114,065 | 2 | 15% | 46% | 39% | 8% |
| Ticagrelor | £20,246 | £15,687 | 13.13 | 8.32 | 6.52 | £773 | 0.07 | £10,541 | £114,759 | 1 | 85% | 15% | 1% | 92% |
| **SA12: Treatment duration based on TRITON TIMI** | | | | | | | | | | | | | | |
| Clopidogrel | £19,382 | £14,893 | 12.95 | 8.21 | 6.44 | | | | £113,909 | 3 | 0% | 38% | 61% | 0% |
| Prasugrel | £19,420 | £14,926 | 12.97 | 8.22 | 6.45 | £33 | 0.01 | £3,585 | £114,061 | 2 | 14% | 48% | 38% | 7% |
| Ticagrelor | £20,223 | £15,657 | 13.12 | 8.32 | 6.52 | £731 | 0.07 | £9,958 | £114,798 | 1 | 86% | 14% | 0% | 93% |
| **SA13: Treatment duration based on PLATO** | | | | | | | | | | | | | | |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Clopidogrel | £19,338 | £14,858 | 12.95 | 8.21 | 6.44 | | | | £113,948 | 3 | 0% | 37% | 63% | 0% |
| Prasugrel | £19,367 | £14,883 | 12.97 | 8.22 | 6.45 | £24 | 0.01 | £2,569 | £114,112 | 2 | 9% | 53% | 37% | 5% |
| Ticagrelor | £20,071 | £15,515 | 13.12 | 8.32 | 6.52 | £632 | 0.07 | £8,638 | £114,943 | 1 | 91% | 9% | 0% | 95% |
| **SA14: Treatment duration DAPT specific** | | | | | | | | | | | | | | |
| Clopidogrel | £19,342 | £14,863 | 12.95 | 8.21 | 6.44 | | | | £113,954 | 3 | 0% | 38% | 62% | 0% |
| Prasugrel | £19,389 | £14,904 | 12.98 | 8.23 | 6.45 | £41 | 0.01 | £3,971 | £114,119 | 2 | 15% | 47% | 38% | 8% |
| Ticagrelor | £20,218 | £15,662 | 13.13 | 8.32 | 6.52 | £758 | 0.07 | £10,456 | £114,812 | 1 | 85% | 14% | 0% | 92% |
| **SA15: Treatment duration full year** | | | | | | | | | | | | | | |
| Clopidogrel | £19,414 | £14,918 | 12.95 | 8.21 | 6.44 | | | | £113,904 | 3 | 1% | 41% | 59% | 0% |
| Prasugrel | £19,460 | £14,960 | 12.97 | 8.22 | 6.45 | £42 | 0.01 | £5,028 | £114,030 | 2 | 16% | 43% | 40% | 9% |
| Ticagrelor | £20,368 | £15,795 | 13.12 | 8.32 | 6.52 | £835 | 0.07 | £11,271 | £114,677 | 1 | 83% | 16% | 1% | 91% |
| **Event costs** | | | | | | | | | | | | | | |
| **SA16: Percentage stroke social care costs publicly funded - 30%** | | | | | | | | | | | | | | |
| Clopidogrel | £18,423 | £14,233 | 12.95 | 8.21 | 6.44 | | | | £114,579 | 3 | 0% | 39% | 61% | 0% |
| Prasugrel | £18,469 | £14,275 | 12.97 | 8.23 | 6.45 | £42 | 0.01 | £4,633 | £114,718 | 2 | 13% | 48% | 39% | 7% |
| Ticagrelor | £19,276 | £15,019 | 13.12 | 8.32 | 6.52 | £744 | 0.07 | £10,109 | £115,447 | 1 | 87% | 13% | 0% | 93% |
| **SA17: Percentage stroke social care costs publicly funded - 70%** | | | | | | | | | | | | | | |
| Clopidogrel | £20,242 | £15,478 | 12.95 | 8.21 | 6.44 | | | | £113,329 | 3 | 0% | 40% | 59% | 0% |
| Prasugrel | £20,285 | £15,515 | 12.97 | 8.22 | 6.45 | £37 | 0.01 | £4,272 | £113,467 | 2 | 15% | 45% | 40% | 8% |
| Ticagrelor | £21,165 | £16,314 | 13.12 | 8.32 | 6.52 | £799 | 0.07 | £10,807 | £114,146 | 1 | 85% | 15% | 1% | 92% |
| **SA18: Minor bleeding costs set to GI bleed** | | | | | | | | | | | | | | |
| Clopidogrel | £19,399 | £14,908 | 12.95 | 8.21 | 6.44 | | | | £113,896 | 3 | 0% | 39% | 61% | 0% |
| Prasugrel | £19,455 | £14,958 | 12.97 | 8.23 | 6.45 | £50 | 0.01 | £5,089 | £114,044 | 2 | 15% | 46% | 39% | 8% |
| Ticagrelor | £20,290 | £15,722 | 13.12 | 8.32 | 6.52 | £764 | 0.07 | £10,560 | £114,726 | 1 | 84% | 15% | 1% | 92% |
| **SA19: Major bleeding costs including intracranial bleeds (10%)** | | | | | | | | | | | | | | |
| Clopidogrel | £19,342 | £14,864 | 12.96 | 8.21 | 6.44 | | | | £113,947 | 3 | 0% | 39% | 61% | 0% |
| Prasugrel | £19,388 | £14,905 | 12.97 | 8.23 | 6.45 | £41 | 0.01 | £4,481 | £114,088 | 2 | 14% | 47% | 39% | 7% |
| Ticagrelor | £20,230 | £15,676 | 13.13 | 8.32 | 6.52 | £771 | 0.07 | £10,501 | £114,785 | 1 | 86% | 14% | 0% | 93% |
| **SA20: Major bleeding costs including intracranial bleeds (20%)** | | | | | | | | | | | | | | |
| Clopidogrel | £19,384 | £14,895 | 12.95 | 8.21 | 6.44 | | | | £113,910 | 3 | 0% | 40% | 60% | 0% |
| Prasugrel | £19,427 | £14,934 | 12.97 | 8.22 | 6.45 | £38 | 0.01 | £4,516 | £114,042 | 2 | 14% | 46% | 40% | 7% |
| Ticagrelor | £20,272 | £15,706 | 13.12 | 8.32 | 6.52 | £773 | 0.07 | £10,417 | £114,753 | 1 | 86% | 14% | 0% | 92% |
| **SA21: Intracranial bleeds set to 30% of major bleeds** | | | | | | | | | | | | | | |
| Clopidogrel | £19,350 | £14,873 | 12.96 | 8.21 | 6.44 | | | | £113,922 | 3 | 0% | 39% | 61% | 0% |
| Prasugrel | £19,396 | £14,914 | 12.97 | 8.22 | 6.45 | £41 | 0.01 | £4,698 | £114,056 | 2 | 13% | 48% | 39% | 7% |
| Ticagrelor | £20,239 | £15,685 | 13.13 | 8.32 | 6.52 | £771 | 0.07 | £10,422 | £114,765 | 1 | 87% | 13% | 0% | 93% |
| **SA22: Intracranial bleeds set to 40% of major bleeds** | | | | | | | | | | | | | | |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Clopidogrel | £19,364 | £14,881 | 12.96 | 8.21 | 6.44 | | | | £113,930 | 3 | 0% | 40% | 60% | 0% |
| Prasugrel | £19,409 | £14,921 | 12.97 | 8.22 | 6.45 | £40 | 0.01 | £4,912 | £114,054 | 2 | 14% | 47% | 40% | 7% |
| Ticagrelor | £20,251 | £15,692 | 13.13 | 8.32 | 6.52 | £770 | 0.07 | £10,385 | £114,767 | 1 | 86% | 14% | 0% | 93% |
| **SA23: Higher minor and major bleeding costs (intracranial 20%)** | | | | | | | | | | | | | | |
| Clopidogrel | £19,311 | £14,843 | 12.96 | 8.21 | 6.44 | | | | £113,965 | 3 | 0% | 39% | 60% | 0% |
| Prasugrel | £19,366 | £14,893 | 12.97 | 8.22 | 6.45 | £50 | 0.01 | £5,526 | £114,095 | 2 | 13% | 47% | 39% | 7% |
| Ticagrelor | £20,203 | £15,657 | 13.13 | 8.32 | 6.52 | £765 | 0.07 | £10,357 | £114,807 | 1 | 86% | 13% | 0% | 93% |
| **Methods** | | | | | | | | | | | | | | |
| **SA24: Utilities not age-adjusted** | | | | | | | | | | | | | | |
| Clopidogrel | £19,306 | £14,835 | 12.95 | 10.76 | 8.37 | | | | £152,643 | 3 | 0% | 38% | 62% | 0% |
| Prasugrel | £19,351 | £14,875 | 12.97 | 10.78 | 8.39 | £39 | 0.01 | £3,197 | £152,848 | 2 | 9% | 53% | 38% | 5% |
| Ticagrelor | £20,191 | £15,644 | 13.12 | 10.90 | 8.48 | £769 | 0.10 | £8,080 | £153,984 | 1 | 91% | 9% | 0% | 95% |
| **SA25: Discount rate 1.5%** | | | | | | | | | | | | | | |
| Clopidogrel | £19,305 | £17,132 | 12.95 | 8.21 | 7.36 | | | | £130,018 | 3 | 0% | 37% | 62% | 0% |
| Prasugrel | £19,351 | £17,176 | 12.97 | 8.23 | 7.37 | £44 | 0.01 | £3,531 | £130,222 | 2 | 13% | 49% | 37% | 7% |
| Ticagrelor | £20,191 | £17,981 | 13.12 | 8.32 | 7.45 | £805 | 0.08 | £9,698 | £131,077 | 1 | 86% | 13% | 0% | 93% |

*Abbreviations: CE = cost effective; disc. = discounted; ext dom = extendedly dominated; Incr. = incremental; NMB = net monetary benefit; QALY = quality-adjusted life years; £20K = a threshold of £20,000 per QALY gained; £30K = a threshold of £30,000 per QALY gained.*
*Note: Incremental costs and QALYs are versus the comparator with the next lowest costs (the previous line in the table) unless that option has been ruled out by extended dominance in which case they are compared to the option with the lowest costs (the first line in the table).*

**Table 55: Sensitivity analyses results for scenario 2: STEMI population (probabilistic analysis, per person results)**

| Intervention | Mean lifetime costs undisc | Mean lifetime costs disc | Mean life years | Mean lifetime QALYs Undisc | Mean lifetime QALYs disc | Incr. cost | Incr. QALYs | ICER | NMB (£20k) | Rank at £20k | % CE at £20k | % Rank 2nd at £20k | % Rank 3rd at £20k | % CE at £30k |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Base case analysis** | | | | | | | | | | | | | | |
| Clopidogrel | £23,115 | £17,368 | 13.05 | 8.29 | 6.42 | | | | £111,106 | 2 | 37% | 58% | 5% | 36% |
| Prasugrel | £23,188 | £17,420 | 13.08 | 8.31 | 6.44 | £52 | 0.01 | £3,615 | £111,343 | 1 | 58% | 36% | 6% | 58% |
| Ticagrelor | £23,303 | £17,702 | 12.75 | 8.10 | 6.28 | £282 | -0.16 | Dominated | £107,887 | 3 | 5% | 6% | 90% | 6% |
| **Baseline risks** | | | | | | | | | | | | | | |
| **SA1: Stroke baseline risks adjusted based on PLATO** | | | | | | | | | | | | | | |
| Clopidogrel | £19,681 | £14,968 | 13.08 | 8.36 | 6.47 | | | | £114,450 | 2 | 35% | 61% | 4% | 35% |
| Prasugrel | £19,724 | £15,002 | 13.11 | 8.38 | 6.49 | £34 | 0.02 | £2,266 | £114,717 | 1 | 60% | 34% | 6% | 59% |
| Ticagrelor | £19,979 | £15,375 | 12.79 | 8.17 | 6.33 | £373 | -0.16 | Dominated | £111,204 | 3 | 5% | 5% | 90% | 6% |
| **SA2: Include baseline risk adjustment** | | | | | | | | | | | | | | |
| Clopidogrel | £21,903 | £16,461 | 13.17 | 8.38 | 6.48 | | | | £113,109 | 2 | 36% | 60% | 4% | 35% |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Prasugrel | £21,956 | £16,500 | 13.19 | 8.40 | 6.49 | £40 | 0.01 | £2,800 | £113,352 | 1 | 59% | 35% | 6% | 59% |
| Ticagrelor | £22,132 | £16,822 | 12.86 | 8.18 | 6.33 | £322 | -0.16 | Dominated | £109,834 | 3 | 5% | 5% | 90% | 6% |
| **SA3: Reduce SMR for ACS/Reinfarction by 20%** | | | | | | | | | | | | | | |
| Clopidogrel | £24,806 | £18,351 | 14.18 | 8.97 | 6.83 | | | | £118,162 | 2 | 37% | 58% | 5% | 35% |
| Prasugrel | £24,882 | £18,405 | 14.21 | 8.99 | 6.84 | £54 | 0.02 | £3,471 | £118,420 | 1 | 58% | 36% | 6% | 58% |
| Ticagrelor | £24,956 | £18,663 | 13.86 | 8.76 | 6.68 | £258 | -0.17 | Dominated | £114,843 | 3 | 5% | 6% | 89% | 6% |
| **Treatment effects** | | | | | | | | | | | | | | |
| **SA4: Stroke treatment effect excluded** | | | | | | | | | | | | | | |
| Clopidogrel | £23,037 | £17,313 | 13.05 | 8.29 | 6.43 | | | | £111,215 | 2 | 38% | 57% | 4% | 37% |
| Prasugrel | £23,181 | £17,422 | 13.08 | 8.31 | 6.44 | £109 | 0.01 | £7,568 | £111,394 | 1 | 57% | 36% | 7% | 57% |
| Ticagrelor | £23,163 | £17,598 | 12.76 | 8.11 | 6.29 | £176 | -0.16 | Dominated | £108,116 | 3 | 5% | 6% | 89% | 6% |
| **SA5: Ticagrelor's stroke treatment effect not included** | | | | | | | | | | | | | | |
| Clopidogrel | £23,147 | £17,392 | 13.05 | 8.29 | 6.42 | | | | £111,102 | 2 | 36% | 60% | 5% | 35% |
| Prasugrel | £23,217 | £17,441 | 13.08 | 8.31 | 6.44 | £49 | 0.02 | £3,132 | £111,368 | 1 | 60% | 34% | 6% | 59% |
| Ticagrelor | £23,276 | £17,678 | 12.76 | 8.10 | 6.28 | £237 | -0.16 | Dominated | £108,005 | 3 | 5% | 6% | 89% | 6% |
| **SA6: Prasugrel's stroke treatment effect not included** | | | | | | | | | | | | | | |
| Clopidogrel | £23,115 | £17,369 | 13.05 | 8.29 | 6.42 | | | | £111,109 | 2 | 40% | 56% | 5% | 38% |
| Prasugrel | £23,256 | £17,474 | 13.08 | 8.31 | 6.44 | £106 | 0.01 | £7,372 | £111,290 | 1 | 56% | 39% | 6% | 56% |
| Ticagrelor | £23,321 | £17,716 | 12.76 | 8.10 | 6.28 | £242 | -0.16 | Dominated | £107,922 | 3 | 5% | 6% | 90% | 6% |
| **SA7: Rivaroxaban treatment effect included (current practice usage)** | | | | | | | | | | | | | | |
| Clopidogrel | £23,101 | £17,363 | 13.06 | 8.29 | 6.43 | | | | £111,182 | 2 | 39% | 57% | 4% | 38% |
| Prasugrel | £23,140 | £17,387 | 13.08 | 8.31 | 6.44 | £24 | 0.01 | £2,213 | £111,371 | 1 | 57% | 37% | 6% | 56% |
| Ticagrelor | £23,261 | £17,673 | 12.75 | 8.10 | 6.28 | £287 | -0.16 | Dominated | £107,896 | 3 | 4% | 6% | 90% | 6% |
| **SA8: Rivaroxaban treatment effect included (100% usage)** | | | | | | | | | | | | | | |
| Prasugrel | £23,102 | £17,361 | 13.08 | 8.31 | 6.44 | | | | £111,369 | 2 | 4% | 88% | 8% | 2% |
| Ticagrelor | £23,239 | £17,659 | 12.76 | 8.10 | 6.28 | £298 | -0.16 | Dominated | £107,952 | 3 | 0% | 8% | 92% | 0% |
| Clopidogrel | £24,613 | £18,664 | 13.49 | 8.56 | 6.63 | £1,005 | 0.35 | £6,617 | £114,004 | 1 | 96% | 4% | 0% | 97% |
| **SA9: Dyspnoea included in analysis** | | | | | | | | | | | | | | |
| Clopidogrel | £23,074 | £17,337 | 13.05 | 8.29 | 6.43 | | | | £111,168 | 2 | 36% | 60% | 4% | 35% |
| Prasugrel | £23,138 | £17,382 | 13.08 | 8.31 | 6.44 | £45 | 0.01 | £3,090 | £111,417 | 1 | 59% | 34% | 6% | 59% |
| Ticagrelor | £23,275 | £17,681 | 12.75 | 8.10 | 6.28 | £299 | -0.16 | Dominated | £107,961 | 3 | 5% | 6% | 90% | 6% |
| **Intervention costs** | | | | | | | | | | | | | | |
| **SA10: Clopidogrel 300mg loading dose** | | | | | | | | | | | | | | |
| Clopidogrel | £23,062 | £17,330 | 13.05 | 8.29 | 6.42 | | | | £111,149 | 2 | 37% | 59% | 5% | 35% |
| Prasugrel | £23,132 | £17,380 | 13.08 | 8.31 | 6.44 | £50 | 0.01 | £3,419 | £111,391 | 1 | 58% | 36% | 6% | 58% |
| Ticagrelor | £23,259 | £17,670 | 12.75 | 8.10 | 6.28 | £291 | -0.16 | Dominated | £107,928 | 3 | 5% | 6% | 90% | 6% |
| **SA12: Treatment duration based on TRITON TIMI** | | | | | | | | | | | | | | |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Clopidogrel | £23,080 | £17,343 | 13.05 | 8.29 | 6.42 | | | | £111,154 | 2 | 35% | 60% | 5% | 34% |
| Prasugrel | £23,150 | £17,391 | 13.08 | 8.31 | 6.44 | £48 | 0.02 | £3,050 | £111,421 | 1 | 60% | 34% | 6% | 60% |
| Ticagrelor | £23,231 | £17,638 | 12.75 | 8.10 | 6.28 | £247 | -0.16 | Dominated | £107,988 | 3 | 5% | 6% | 89% | 6% |
| **SA13: Treatment duration based on PLATO** | | | | | | | | | | | | | | |
| Clopidogrel | £23,063 | £17,329 | 13.05 | 8.29 | 6.42 | | | | £111,144 | 2 | 34% | 61% | 5% | 33% |
| Prasugrel | £23,123 | £17,367 | 13.08 | 8.31 | 6.44 | £38 | 0.02 | £2,350 | £111,428 | 1 | 61% | 33% | 6% | 60% |
| Ticagrelor | £23,109 | £17,521 | 12.75 | 8.10 | 6.28 | £154 | -0.16 | Dominated | £108,059 | 3 | 5% | 6% | 89% | 6% |
| **SA14: Treatment duration DAPT specific** | | | | | | | | | | | | | | |
| Clopidogrel | £23,118 | £17,366 | 13.05 | 8.29 | 6.42 | | | | £111,102 | 2 | 36% | 60% | 4% | 35% |
| Prasugrel | £23,193 | £17,420 | 13.08 | 8.31 | 6.44 | £54 | 0.01 | £3,604 | £111,347 | 1 | 59% | 35% | 6% | 59% |
| Ticagrelor | £23,296 | £17,689 | 12.75 | 8.10 | 6.28 | £270 | -0.16 | Dominated | £107,894 | 3 | 5% | 5% | 90% | 6% |
| **SA15: Treatment duration full year** | | | | | | | | | | | | | | |
| Clopidogrel | £23,070 | £17,339 | 13.05 | 8.29 | 6.42 | | | | £111,131 | 2 | 37% | 59% | 4% | 36% |
| Prasugrel | £23,152 | £17,400 | 13.08 | 8.31 | 6.44 | £61 | 0.02 | £3,884 | £111,383 | 1 | 59% | 36% | 6% | 58% |
| Ticagrelor | £23,314 | £17,730 | 12.75 | 8.09 | 6.28 | £330 | -0.16 | Dominated | £107,803 | 3 | 4% | 5% | 91% | 6% |
| **Event costs** | | | | | | | | | | | | | | |
| **SA16: Percentage stroke social care costs publicly funded - 30%** | | | | | | | | | | | | | | |
| Clopidogrel | £21,361 | £16,185 | 13.05 | 8.29 | 6.42 | | | | £112,284 | 2 | 34% | 61% | 4% | 33% |
| Prasugrel | £21,431 | £16,238 | 13.08 | 8.31 | 6.44 | £53 | 0.02 | £3,189 | £112,563 | 1 | 60% | 33% | 6% | 60% |
| Ticagrelor | £21,595 | £16,548 | 12.76 | 8.10 | 6.28 | £309 | -0.16 | Dominated | £109,089 | 3 | 5% | 5% | 89% | 7% |
| **SA17: Percentage stroke social care costs publicly funded - 70%** | | | | | | | | | | | | | | |
| Clopidogrel | £24,941 | £18,605 | 13.05 | 8.29 | 6.42 | | | | £109,887 | 2 | 35% | 60% | 5% | 35% |
| Prasugrel | £25,022 | £18,661 | 13.08 | 8.31 | 6.44 | £56 | 0.02 | £3,436 | £110,155 | 1 | 60% | 35% | 5% | 59% |
| Ticagrelor | £25,097 | £18,922 | 12.75 | 8.10 | 6.28 | £261 | -0.16 | Dominated | £106,691 | 3 | 5% | 5% | 90% | 6% |
| **SA18: Minor bleeding costs set to GI bleed** | | | | | | | | | | | | | | |
| Clopidogrel | £23,191 | £17,425 | 13.05 | 8.29 | 6.42 | | | | £111,067 | 2 | 35% | 60% | 5% | 34% |
| Prasugrel | £23,283 | £17,495 | 13.09 | 8.31 | 6.44 | £70 | 0.02 | £4,189 | £111,331 | 1 | 60% | 35% | 5% | 59% |
| Ticagrelor | £23,394 | £17,772 | 12.76 | 8.10 | 6.28 | £276 | -0.16 | Dominated | £107,893 | 3 | 5% | 5% | 90% | 6% |
| **SA19: Major bleeding costs including intracranial bleeds (10%)** | | | | | | | | | | | | | | |
| Clopidogrel | £23,129 | £17,379 | 13.05 | 8.29 | 6.42 | | | | £111,086 | 2 | 36% | 60% | 5% | 35% |
| Prasugrel | £23,205 | £17,433 | 13.08 | 8.31 | 6.44 | £54 | 0.02 | £3,381 | £111,353 | 1 | 60% | 34% | 6% | 59% |
| Ticagrelor | £23,334 | £17,725 | 12.76 | 8.10 | 6.28 | £292 | -0.16 | Dominated | £107,923 | 3 | 5% | 6% | 89% | 6% |
| **SA20: Major bleeding costs including intracranial bleeds (20%)** | | | | | | | | | | | | | | |
| Clopidogrel | £23,087 | £17,351 | 13.05 | 8.29 | 6.42 | | | | £111,125 | 2 | 36% | 59% | 4% | 35% |
| Prasugrel | £23,159 | £17,403 | 13.08 | 8.31 | 6.44 | £52 | 0.02 | £3,424 | £111,377 | 1 | 58% | 35% | 6% | 58% |
| Ticagrelor | £23,292 | £17,698 | 12.76 | 8.10 | 6.28 | £295 | -0.16 | Dominated | £107,956 | 3 | 5% | 5% | 89% | 7% |
| **SA21: Intracranial bleeds set to 30% of major bleeds** | | | | | | | | | | | | | | |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Clopidogrel | £23,156 | £17,399 | 13.05 | 8.29 | 6.43 | | | | £111,103 | 2 | 37% | 59% | 5% | 36% |
| Prasugrel | £23,223 | £17,447 | 13.08 | 8.31 | 6.44 | £48 | 0.01 | £3,406 | £111,340 | 1 | 58% | 36% | 6% | 58% |
| Ticagrelor | £23,359 | £17,745 | 12.76 | 8.10 | 6.28 | £297 | -0.16 | Dominated | £107,921 | 3 | 5% | 5% | 90% | 6% |
| **SA22: Intracranial bleeds set to 40% of major bleeds** | | | | | | | | | | | | | | |
| Clopidogrel | £23,154 | £17,404 | 13.05 | 8.29 | 6.42 | | | | £111,049 | 2 | 37% | 58% | 5% | 36% |
| Prasugrel | £23,230 | £17,460 | 13.08 | 8.31 | 6.44 | £56 | 0.01 | £3,782 | £111,291 | 1 | 58% | 36% | 6% | 58% |
| Ticagrelor | £23,356 | £17,749 | 12.76 | 8.10 | 6.28 | £289 | -0.16 | Dominated | £107,887 | 3 | 5% | 6% | 89% | 6% |
| **SA23: Higher minor and major bleeding costs (intracranial 20%)** | | | | | | | | | | | | | | |
| Clopidogrel | £23,172 | £17,416 | 13.05 | 8.29 | 6.42 | | | | £111,066 | 2 | 37% | 59% | 5% | 36% |
| Prasugrel | £23,254 | £17,479 | 13.08 | 8.31 | 6.44 | £63 | 0.01 | £4,635 | £111,276 | 1 | 58% | 36% | 6% | 58% |
| Ticagrelor | £23,385 | £17,771 | 12.76 | 8.10 | 6.28 | £291 | -0.16 | Dominated | £107,852 | 3 | 5% | 6% | 90% | 6% |
| **Methods** | | | | | | | | | | | | | | |
| **SA24: Utilities not age-adjusted** | | | | | | | | | | | | | | |
| Clopidogrel | £23,147 | £17,394 | 13.05 | 10.75 | 8.27 | | | | £147,944 | 2 | 37% | 58% | 5% | 36% |
| Prasugrel | £23,207 | £17,437 | 13.07 | 10.78 | 8.28 | £43 | 0.02 | £2,510 | £148,242 | 1 | 57% | 36% | 7% | 57% |
| Ticagrelor | £23,342 | £17,733 | 12.75 | 10.50 | 8.08 | £296 | -0.20 | Dominated | £143,886 | 3 | 6% | 6% | 88% | 7% |
| **SA25: Discount rate 1.5%** | | | | | | | | | | | | | | |
| Clopidogrel | £23,079 | £20,274 | 13.05 | 8.29 | 7.39 | | | | £127,456 | 2 | 36% | 59% | 5% | 35% |
| Prasugrel | £23,150 | £20,334 | 13.08 | 8.31 | 7.40 | £60 | 0.02 | £3,464 | £127,743 | 1 | 59% | 35% | 6% | 59% |
| Ticagrelor | £23,273 | £20,538 | 12.76 | 8.10 | 7.22 | £204 | -0.18 | Dominated | £123,871 | 3 | 5% | 6% | 89% | 6% |

*Abbreviations: CE = cost effective; disc. = discounted; Incr. = incremental; NMB = net monetary benefit; QALY = quality-adjusted life years; £20K = a threshold of £20,000 per QALY gained; £30K = a threshold of £30,000 per QALY gained.*
*Note: SA11 is for the UA/NSTEMI population only and so does not appear in this table. Incremental costs and QALYs are versus the comparator with the next lowest costs (the previous line in the table) unless that option has been ruled out by extended dominance in which case they are compared to the option with the lowest costs (the first line in the table).*

**Table 56: Sensitivity analyses results for scenario 2: UA/NSTEMI population (probabilistic analysis, per person results)**

| Intervention | Mean lifetime costs undisc | Mean lifetime costs disc | Mean life years | Mean lifetime QALYs Undisc | Mean lifetime QALYs disc | Incr. cost | Incr. QALYs | ICER | NMB (£20k) | Rank at £20k | % CE at £20k | % Rank 2nd at £20k | % Rank 3rd at £20k | % CE at £30k |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Base case analysis** | | | | | | | | | | | | | | |
| Clopidogrel | £19,359 | £14,874 | 12.95 | 8.21 | 6.44 | | | | £113,936 | 2 | 38% | 60% | 2% | 37% |
| Prasugrel | £19,403 | £14,914 | 12.97 | 8.22 | 6.45 | £39 | 0.01 | £4,525 | £114,071 | 1 | 60% | 37% | 4% | 59% |
| Ticagrelor | £19,810 | £15,386 | 12.78 | 8.10 | 6.36 | £472 | -0.09 | Dominated | £111,732 | 3 | 2% | 4% | 94% | 4% |
| **Baseline risks** | | | | | | | | | | | | | | |
| **SA1: Stroke baseline risks adjusted based on PLATO** | | | | | | | | | | | | | | |
| Clopidogrel | £16,947 | £13,170 | 12.98 | 8.26 | 6.47 | | | | £116,325 | 2 | 37% | 61% | 2% | 36% |

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Prasugrel | £16,987 | £13,208 | 13.00 | 8.28 | 6.48 | £38 | 0.01 | £4,266 | £116,464 | 1 | 60% | 36% | 4% | 60% |
| Ticagrelor | £17,435 | £13,706 | 12.81 | 8.15 | 6.39 | £497 | -0.09 | Dominated | £114,131 | 3 | 3% | 4% | 94% | 4% |
| **SA2: Include baseline risk adjustment** | | | | | | | | | | | | | | |
| Clopidogrel | £18,726 | £14,427 | 12.96 | 8.22 | 6.45 | | | | £114,525 | 2 | 37% | 61% | 2% | 36% |
| Prasugrel | £18,765 | £14,462 | 12.98 | 8.24 | 6.46 | £35 | 0.01 | £4,082 | £114,662 | 1 | 60% | 36% | 4% | 60% |
| Ticagrelor | £19,188 | £14,946 | 12.79 | 8.11 | 6.36 | £484 | -0.09 | Dominated | £112,307 | 3 | 2% | 4% | 94% | 4% |
| **SA3: Reduce SMR for ACS/Reinfarction by 20%** | | | | | | | | | | | | | | |
| Clopidogrel | £20,995 | £15,850 | 14.14 | 8.92 | 6.87 | | | | £121,558 | 2 | 37% | 60% | 3% | 36% |
| Prasugrel | £21,040 | £15,890 | 14.16 | 8.94 | 6.88 | £39 | 0.01 | £4,181 | £121,708 | 1 | 60% | 37% | 4% | 60% |
| Ticagrelor | £21,425 | £16,349 | 13.96 | 8.81 | 6.78 | £460 | -0.10 | Dominated | £119,287 | 3 | 3% | 4% | 93% | 4% |
| **Treatment effects** | | | | | | | | | | | | | | |
| **SA4: Stroke treatment effect excluded** | | | | | | | | | | | | | | |
| Clopidogrel | £19,303 | £14,837 | 12.96 | 8.21 | 6.44 | | | | £114,003 | 2 | 39% | 59% | 2% | 38% |
| Prasugrel | £19,384 | £14,905 | 12.97 | 8.23 | 6.45 | £68 | 0.01 | £7,888 | £114,108 | 1 | 58% | 37% | 5% | 59% |
| Ticagrelor | £19,723 | £15,323 | 12.78 | 8.11 | 6.36 | £418 | -0.09 | Dominated | £111,864 | 3 | 3% | 4% | 94% | 4% |
| **SA5: Ticagrelor's stroke treatment effect not included** | | | | | | | | | | | | | | |
| Clopidogrel | £19,408 | £14,912 | 12.95 | 8.21 | 6.44 | | | | £113,896 | 2 | 37% | 60% | 2% | 36% |
| Prasugrel | £19,451 | £14,950 | 12.97 | 8.23 | 6.45 | £38 | 0.01 | £4,028 | £114,046 | 1 | 61% | 35% | 4% | 61% |
| Ticagrelor | £19,828 | £15,399 | 12.78 | 8.10 | 6.36 | £449 | -0.09 | Dominated | £111,758 | 3 | 2% | 4% | 94% | 4% |
| **SA6: Prasugrel's stroke treatment effect not included** | | | | | | | | | | | | | | |
| Clopidogrel | £19,366 | £14,879 | 12.96 | 8.21 | 6.44 | | | | £113,932 | 2 | 41% | 57% | 2% | 38% |
| Prasugrel | £19,444 | £14,945 | 12.97 | 8.22 | 6.45 | £66 | 0.01 | £7,675 | £114,039 | 1 | 57% | 40% | 4% | 58% |
| Ticagrelor | £19,825 | £15,397 | 12.78 | 8.10 | 6.36 | £452 | -0.09 | Dominated | £111,748 | 3 | 2% | 4% | 94% | 4% |
| **SA7: Rivaroxaban treatment effect included (current practice usage)** | | | | | | | | | | | | | | |
| Clopidogrel | £19,360 | £14,879 | 12.96 | 8.21 | 6.44 | | | | £113,960 | 2 | 40% | 58% | 2% | 39% |
| Prasugrel | £19,382 | £14,899 | 12.97 | 8.22 | 6.45 | £20 | 0.01 | £2,980 | £114,072 | 1 | 58% | 38% | 4% | 58% |
| Ticagrelor | £19,791 | £15,374 | 12.78 | 8.10 | 6.35 | £475 | -0.09 | Dominated | £111,721 | 3 | 2% | 4% | 94% | 3% |
| **SA8: Rivaroxaban treatment effect included (100% usage)** | | | | | | | | | | | | | | |
| Prasugrel | £19,346 | £14,874 | 12.97 | 8.22 | 6.45 | | | | £114,075 | 2 | 7% | 88% | 5% | 4% |
| Ticagrelor | £19,760 | £15,353 | 12.78 | 8.10 | 6.36 | £479 | -0.09 | Dominated | £111,761 | 3 | 0% | 5% | 95% | 0% |
| Clopidogrel | £20,372 | £15,809 | 13.19 | 8.36 | 6.55 | £456 | 0.20 | £8,915 | £115,237 | 1 | 93% | 7% | 0% | 96% |
| **SA9: Dyspnoea included in analysis** | | | | | | | | | | | | | | |
| Clopidogrel | £19,322 | £14,846 | 12.95 | 8.21 | 6.44 | | | | £113,982 | 2 | 37% | 61% | 2% | 36% |
| Prasugrel | £19,362 | £14,882 | 12.97 | 8.23 | 6.45 | £36 | 0.01 | £4,070 | £114,122 | 1 | 60% | 36% | 4% | 60% |
| Ticagrelor | £19,780 | £15,364 | 12.78 | 8.10 | 6.36 | £482 | -0.09 | Dominated | £111,783 | 3 | 2% | 4% | 94% | 4% |
| **Intervention costs** | | | | | | | | | | | | | | |
| **SA10: Clopidogrel 300mg loading dose** | | | | | | | | | | | | | | |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Clopidogrel | £19,326 | £14,851 | 12.96 | 8.21 | 6.44 | | | | £113,958 | 2 | 38% | 60% | 2% | 37% |
| Prasugrel | £19,369 | £14,889 | 12.97 | 8.22 | 6.45 | £38 | 0.01 | £4,356 | £114,095 | 1 | 59% | 37% | 4% | 59% |
| Ticagrelor | £19,780 | £15,365 | 12.78 | 8.10 | 6.36 | £476 | -0.09 | Dominated | £111,754 | 3 | 2% | 3% | 94% | 4% |
| **SA11: UA/NSTEMI prasugrel arm receiving clopidogrel loading dose** | | | | | | | | | | | | | | |
| Clopidogrel | £19,388 | £14,897 | 12.95 | 8.21 | 6.44 | | | | £113,879 | 2 | 36% | 62% | 2% | 35% |
| Prasugrel | £19,431 | £14,935 | 12.97 | 8.22 | 6.45 | £38 | 0.01 | £4,023 | £114,031 | 1 | 62% | 35% | 4% | 61% |
| Ticagrelor | £19,840 | £15,410 | 12.78 | 8.10 | 6.35 | £475 | -0.09 | Dominated | £111,685 | 3 | 2% | 4% | 94% | 4% |
| **SA12: Treatment duration based on TRITON TIMI** | | | | | | | | | | | | | | |
| Clopidogrel | £19,331 | £14,854 | 12.96 | 8.21 | 6.44 | | | | £113,973 | 2 | 36% | 61% | 3% | 35% |
| Prasugrel | £19,371 | £14,889 | 12.97 | 8.23 | 6.45 | £34 | 0.01 | £3,674 | £114,126 | 1 | 61% | 35% | 3% | 61% |
| Ticagrelor | £19,738 | £15,321 | 12.78 | 8.10 | 6.36 | £433 | -0.09 | Dominated | £111,819 | 3 | 3% | 4% | 94% | 4% |
| **SA13: Treatment duration based on PLATO** | | | | | | | | | | | | | | |
| Clopidogrel | £19,330 | £14,853 | 12.95 | 8.21 | 6.44 | | | | £113,932 | 2 | 34% | 63% | 3% | 34% |
| Prasugrel | £19,359 | £14,876 | 12.97 | 8.22 | 6.45 | £23 | 0.01 | £2,413 | £114,101 | 1 | 62% | 33% | 4% | 62% |
| Ticagrelor | £19,630 | £15,213 | 12.78 | 8.10 | 6.35 | £337 | -0.09 | Dominated | £111,873 | 3 | 3% | 4% | 93% | 4% |
| **SA14: Treatment duration DAPT specific** | | | | | | | | | | | | | | |
| Clopidogrel | £19,359 | £14,871 | 12.95 | 8.21 | 6.44 | | | | £113,903 | 2 | 37% | 61% | 2% | 36% |
| Prasugrel | £19,404 | £14,912 | 12.97 | 8.22 | 6.45 | £40 | 0.01 | £4,505 | £114,042 | 1 | 60% | 36% | 4% | 60% |
| Ticagrelor | £19,798 | £15,371 | 12.78 | 8.10 | 6.35 | £459 | -0.09 | Dominated | £111,709 | 3 | 3% | 4% | 94% | 4% |
| **SA15: Treatment duration full year** | | | | | | | | | | | | | | |
| Clopidogrel | £19,328 | £14,856 | 12.95 | 8.21 | 6.44 | | | | £113,929 | 2 | 39% | 59% | 2% | 37% |
| Prasugrel | £19,381 | £14,904 | 12.97 | 8.22 | 6.45 | £48 | 0.01 | £5,118 | £114,067 | 1 | 59% | 37% | 4% | 59% |
| Ticagrelor | £19,840 | £15,430 | 12.78 | 8.10 | 6.35 | £526 | -0.10 | Dominated | £111,631 | 3 | 2% | 3% | 94% | 4% |
| **Event costs** | | | | | | | | | | | | | | |
| **SA16: Percentage stroke social care costs publicly funded - 30%** | | | | | | | | | | | | | | |
| Clopidogrel | £18,471 | £14,271 | 12.95 | 8.21 | 6.44 | | | | £114,515 | 2 | 36% | 62% | 2% | 35% |
| Prasugrel | £18,518 | £14,313 | 12.97 | 8.22 | 6.45 | £43 | 0.01 | £4,310 | £114,670 | 1 | 61% | 35% | 4% | 61% |
| Ticagrelor | £18,932 | £14,788 | 12.78 | 8.10 | 6.36 | £475 | -0.09 | Dominated | £112,334 | 3 | 3% | 4% | 94% | 4% |
| **SA17: Percentage stroke social care costs publicly funded - 70%** | | | | | | | | | | | | | | |
| Clopidogrel | £20,341 | £15,551 | 12.95 | 8.21 | 6.44 | | | | £113,260 | 2 | 37% | 61% | 2% | 36% |
| Prasugrel | £20,386 | £15,589 | 12.97 | 8.23 | 6.45 | £38 | 0.01 | £3,984 | £113,414 | 1 | 61% | 36% | 4% | 60% |
| Ticagrelor | £20,788 | £16,061 | 12.78 | 8.10 | 6.36 | £472 | -0.09 | Dominated | £111,060 | 3 | 3% | 4% | 94% | 4% |
| **SA18: Minor bleeding costs set to GI bleed** | | | | | | | | | | | | | | |
| Clopidogrel | £19,420 | £14,921 | 12.96 | 8.21 | 6.44 | | | | £113,894 | 2 | 37% | 61% | 3% | 35% |
| Prasugrel | £19,475 | £14,970 | 12.97 | 8.23 | 6.45 | £50 | 0.01 | £5,015 | £114,042 | 1 | 61% | 35% | 4% | 61% |
| Ticagrelor | £19,878 | £15,439 | 12.78 | 8.10 | 6.36 | £468 | -0.09 | Dominated | £111,714 | 3 | 2% | 4% | 94% | 4% |
| **SA19: Major bleeding costs including intracranial bleeds (10%)** | | | | | | | | | | | | | | |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Clopidogrel | £19,372 | £14,886 | 12.95 | 8.21 | 6.44 | | | | £113,903 | 2 | 37% | 61% | 3% | 36% |
| Prasugrel | £19,418 | £14,926 | 12.97 | 8.22 | 6.45 | £41 | 0.01 | £4,252 | £114,053 | 1 | 61% | 36% | 3% | 61% |
| Ticagrelor | £19,831 | £15,403 | 12.78 | 8.10 | 6.36 | £477 | -0.09 | Dominated | £111,732 | 3 | 2% | 4% | 94% | 4% |
| **SA20: Major bleeding costs including intracranial bleeds (20%)** | | | | | | | | | | | | | | |
| Clopidogrel | £19,343 | £14,866 | 12.96 | 8.21 | 6.44 | | | | £113,941 | 2 | 38% | 60% | 2% | 36% |
| Prasugrel | £19,388 | £14,906 | 12.97 | 8.22 | 6.45 | £40 | 0.01 | £4,434 | £114,082 | 1 | 60% | 36% | 4% | 59% |
| Ticagrelor | £19,800 | £15,383 | 12.79 | 8.10 | 6.36 | £477 | -0.09 | Dominated | £111,766 | 3 | 3% | 4% | 94% | 4% |
| **SA21: Intracranial bleeds set to 30% of major bleeds** | | | | | | | | | | | | | | |
| Clopidogrel | £19,396 | £14,902 | 12.96 | 8.21 | 6.44 | | | | £113,934 | 2 | 38% | 60% | 3% | 37% |
| Prasugrel | £19,439 | £14,940 | 12.97 | 8.23 | 6.45 | £38 | 0.01 | £4,465 | £114,067 | 1 | 60% | 37% | 3% | 60% |
| Ticagrelor | £19,855 | £15,420 | 12.78 | 8.10 | 6.36 | £480 | -0.09 | Dominated | £111,751 | 3 | 2% | 4% | 94% | 4% |
| **SA22: Intracranial bleeds set to 40% of major bleeds** | | | | | | | | | | | | | | |
| Clopidogrel | £19,422 | £14,927 | 12.95 | 8.21 | 6.44 | | | | £113,854 | 2 | 38% | 59% | 3% | 37% |
| Prasugrel | £19,470 | £14,970 | 12.97 | 8.22 | 6.45 | £43 | 0.01 | £4,766 | £113,990 | 1 | 60% | 37% | 4% | 59% |
| Ticagrelor | £19,880 | £15,445 | 12.78 | 8.10 | 6.36 | £475 | -0.09 | Dominated | £111,682 | 3 | 2% | 4% | 94% | 4% |
| **SA23: Higher minor and major bleeding costs (intracranial 20%)** | | | | | | | | | | | | | | |
| Clopidogrel | £19,407 | £14,914 | 12.96 | 8.21 | 6.44 | | | | £113,892 | 2 | 38% | 60% | 2% | 37% |
| Prasugrel | £19,458 | £14,961 | 12.97 | 8.22 | 6.45 | £47 | 0.01 | £5,707 | £114,010 | 1 | 60% | 37% | 4% | 59% |
| Ticagrelor | £19,870 | £15,436 | 12.78 | 8.10 | 6.36 | £475 | -0.09 | Dominated | £111,692 | 3 | 3% | 4% | 94% | 4% |
| **Methods** | | | | | | | | | | | | | | |
| **SA24: Utilities not age-adjusted** | | | | | | | | | | | | | | |
| Clopidogrel | £19,407 | £14,913 | 12.95 | 10.76 | 8.37 | | | | £152,496 | 2 | 38% | 59% | 3% | 36% |
| Prasugrel | £19,446 | £14,947 | 12.97 | 10.77 | 8.38 | £35 | 0.01 | £3,301 | £152,673 | 1 | 59% | 36% | 5% | 59% |
| Ticagrelor | £19,860 | £15,426 | 12.78 | 10.61 | 8.26 | £478 | -0.12 | Dominated | £149,776 | 3 | 3% | 5% | 92% | 5% |
| **SA25: Discount rate 1.5%** | | | | | | | | | | | | | | |
| Clopidogrel | £19,328 | £17,154 | 12.95 | 8.21 | 7.36 | | | | £130,012 | 2 | 37% | 60% | 3% | 35% |
| Prasugrel | £19,372 | £17,195 | 12.97 | 8.22 | 7.37 | £41 | 0.01 | £3,813 | £130,184 | 1 | 60% | 36% | 4% | 61% |
| Ticagrelor | £19,782 | £17,637 | 12.78 | 8.10 | 7.26 | £442 | -0.11 | Dominated | £127,592 | 3 | 3% | 4% | 93% | 4% |

*Abbreviations: CE = cost effective; disc. = discounted; Incr. = incremental; NMB = net monetary benefit; QALY = quality-adjusted life years; £20K = threshold of £20,000 per QALY gained; £30K = a threshold of £30,000 per QALY gained.*
*Note: Incremental costs and QALYs are versus the comparator with the next lowest costs (the previous line in the table) unless that option has been ruled out by extended dominance in which case they are compared to the option with the lowest costs (the first line in the table).*

**Table 57: Sensitivity analyses results for scenario 3: STEMI population (probabilistic analysis, per person results)**

| Intervention | Mean lifetime | Mean lifetime | Mean life years | Mean lifetime | Mean lifetime | Incr. cost | Incr. QALYs | ICER | NMB (£20k) | Rank at £20k | % CE | % Rank 2nd | % Rank | % CE at £30k |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|

| | costs undisc | costs disc | | QALYs Undisc | QALYs disc | | | | | | at £20k | at £20k | 3rd at £20k | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Base case analysis** | | | | | | | | | | | | | | |
| Clopidogrel | £23,101 | £17,362 | 13.05 | 8.29 | 6.42 | | | | £111,091 | 3 | 0% | 0% | 100% | 0% |
| Prasugrel | £23,996 | £17,983 | 13.57 | 8.62 | 6.67 | £620 | 0.25 | £2,469 | £115,495 | 1 | 96% | 4% | 0% | 95% |
| Ticagrelor | £24,331 | £18,413 | 13.36 | 8.48 | 6.57 | £430 | -0.10 | Dominated | £112,994 | 2 | 4% | 96% | 0% | 5% |
| **Baseline risks** | | | | | | | | | | | | | | |
| **SA1: Stroke baseline risks adjusted based on PLATO** | | | | | | | | | | | | | | |
| Clopidogrel | £19,756 | £15,022 | 13.08 | 8.36 | 6.47 | | | | £114,378 | 3 | 0% | 0% | 100% | 0% |
| Prasugrel | £20,440 | £15,499 | 13.60 | 8.69 | 6.72 | £477 | 0.25 | £1,871 | £118,998 | 1 | 96% | 4% | 0% | 95% |
| Ticagrelor | £20,829 | £15,959 | 13.39 | 8.56 | 6.62 | £460 | -0.10 | Dominated | £116,452 | 2 | 4% | 96% | 0% | 5% |
| **SA2: Include baseline risk adjustment** | | | | | | | | | | | | | | |
| Clopidogrel | £21,816 | £16,396 | 13.17 | 8.38 | 6.48 | | | | £113,219 | 3 | 0% | 0% | 100% | 0% |
| Prasugrel | £22,624 | £16,957 | 13.69 | 8.72 | 6.73 | £561 | 0.25 | £2,223 | £117,709 | 1 | 96% | 4% | 0% | 95% |
| Ticagrelor | £22,989 | £17,405 | 13.48 | 8.58 | 6.63 | £448 | -0.10 | Dominated | £115,203 | 2 | 4% | 96% | 0% | 5% |
| **SA3: Reduce SMR for ACS/Reinfarction by 20%** | | | | | | | | | | | | | | |
| Clopidogrel | £24,767 | £18,329 | 14.18 | 8.97 | 6.83 | | | | £118,226 | 3 | 0% | 0% | 100% | 0% |
| Prasugrel | £25,723 | £18,983 | 14.74 | 9.33 | 7.09 | £654 | 0.26 | £2,471 | £122,865 | 1 | 95% | 4% | 0% | 94% |
| Ticagrelor | £26,036 | £19,402 | 14.51 | 9.18 | 6.98 | £419 | -0.11 | Dominated | £120,278 | 2 | 5% | 95% | 0% | 6% |
| **Treatment effects** | | | | | | | | | | | | | | |
| **SA4: Stroke treatment effect excluded** | | | | | | | | | | | | | | |
| Clopidogrel | £23,152 | £17,392 | 13.05 | 8.29 | 6.43 | | | | £111,111 | 3 | 0% | 0% | 100% | 0% |
| Prasugrel | £24,074 | £18,034 | 13.57 | 8.62 | 6.68 | £641 | 0.25 | £2,541 | £115,517 | 1 | 96% | 4% | 0% | 94% |
| Ticagrelor | £24,252 | £18,340 | 13.36 | 8.49 | 6.57 | £306 | -0.10 | Dominated | £113,150 | 2 | 4% | 96% | 0% | 6% |
| **SA5: Ticagrelor's stroke treatment effect not included** | | | | | | | | | | | | | | |
| Clopidogrel | £23,029 | £17,307 | 13.05 | 8.29 | 6.42 | | | | £111,193 | 3 | 0% | 0% | 100% | 0% |
| Prasugrel | £23,919 | £17,923 | 13.57 | 8.62 | 6.68 | £616 | 0.25 | £2,450 | £115,606 | 1 | 96% | 4% | 0% | 94% |
| Ticagrelor | £24,129 | £18,255 | 13.36 | 8.49 | 6.57 | £332 | -0.10 | Dominated | £113,230 | 2 | 4% | 96% | 0% | 6% |
| **SA6: Prasugrel's stroke treatment effect not included** | | | | | | | | | | | | | | |
| Clopidogrel | £23,098 | £17,354 | 13.05 | 8.29 | 6.42 | | | | £111,144 | 3 | 0% | 0% | 100% | 0% |
| Prasugrel | £24,019 | £17,995 | 13.57 | 8.62 | 6.68 | £641 | 0.25 | £2,543 | £115,543 | 1 | 96% | 4% | 0% | 95% |
| Ticagrelor | £24,330 | £18,407 | 13.36 | 8.48 | 6.57 | £412 | -0.10 | Dominated | £113,061 | 2 | 4% | 96% | 0% | 5% |
| **SA7: Rivaroxaban treatment effect included (current practice usage)** | | | | | | | | | | | | | | |
| Clopidogrel | £23,162 | £17,406 | 13.06 | 8.29 | 6.43 | | | | £111,101 | 3 | 0% | 0% | 100% | 0% |
| Prasugrel | £24,026 | £17,999 | 13.57 | 8.62 | 6.67 | £593 | 0.25 | £2,399 | £115,452 | 1 | 96% | 4% | 0% | 94% |
| Ticagrelor | £24,366 | £18,433 | 13.36 | 8.48 | 6.57 | £435 | -0.10 | Dominated | £112,965 | 2 | 4% | 96% | 0% | 6% |
| **SA8: Rivaroxaban treatment effect included (100% usage)** | | | | | | | | | | | | | | |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Prasugrel | £24,038 | £18,008 | 13.57 | 8.62 | 6.68 | | | | £115,514 | 1 | 83% | 13% | 3% | 79% |
| Ticagrelor | £24,370 | £18,436 | 13.36 | 8.48 | 6.57 | £428 | -0.10 | Dominated | £113,010 | 3 | 1% | 22% | 77% | 1% |
| Clopidogrel | £24,724 | £18,740 | 13.49 | 8.56 | 6.64 | £305 | 0.06 | Dominated | £113,969 | 2 | 16% | 65% | 20% | 20% |
| **SA9: Dyspnoea included in analysis** | | | | | | | | | | | | | | |
| Clopidogrel | £23,108 | £17,362 | 13.05 | 8.29 | 6.42 | | | | £111,102 | 3 | 0% | 0% | 100% | 0% |
| Prasugrel | £24,003 | £17,982 | 13.57 | 8.62 | 6.68 | £620 | 0.25 | £2,462 | £115,519 | 1 | 96% | 4% | 0% | 95% |
| Ticagrelor | £24,341 | £18,415 | 13.36 | 8.48 | 6.57 | £433 | -0.10 | Dominated | £113,023 | 2 | 4% | 96% | 0% | 5% |
| **Intervention costs** | | | | | | | | | | | | | | |
| **SA10: Clopidogrel 300mg loading dose** | | | | | | | | | | | | | | |
| Clopidogrel | £23,108 | £17,365 | 13.05 | 8.29 | 6.42 | | | | £111,118 | 3 | 0% | 0% | 100% | 0% |
| Prasugrel | £24,012 | £17,992 | 13.57 | 8.62 | 6.68 | £627 | 0.25 | £2,481 | £115,544 | 1 | 96% | 4% | 0% | 95% |
| Ticagrelor | £24,337 | £18,415 | 13.36 | 8.48 | 6.57 | £422 | -0.10 | Dominated | £113,033 | 2 | 4% | 96% | 0% | 5% |
| **SA12: Treatment duration based on TRITON TIMI** | | | | | | | | | | | | | | |
| Clopidogrel | £23,091 | £17,351 | 13.05 | 8.29 | 6.42 | | | | £111,103 | 3 | 0% | 0% | 100% | 0% |
| Prasugrel | £23,980 | £17,965 | 13.57 | 8.62 | 6.68 | £613 | 0.25 | £2,425 | £115,549 | 1 | 96% | 4% | 0% | 95% |
| Ticagrelor | £24,284 | £18,363 | 13.36 | 8.48 | 6.57 | £398 | -0.10 | Dominated | £113,065 | 2 | 4% | 96% | 0% | 5% |
| **SA13: Treatment duration based on PLATO** | | | | | | | | | | | | | | |
| Clopidogrel | £23,101 | £17,356 | 13.05 | 8.29 | 6.42 | | | | £111,134 | 3 | 0% | 0% | 100% | 0% |
| Prasugrel | £23,986 | £17,964 | 13.57 | 8.62 | 6.68 | £608 | 0.25 | £2,415 | £115,563 | 1 | 95% | 4% | 0% | 94% |
| Ticagrelor | £24,178 | £18,255 | 13.36 | 8.48 | 6.57 | £290 | -0.10 | Dominated | £113,190 | 2 | 5% | 95% | 0% | 6% |
| **SA14: Treatment duration DAPT specific** | | | | | | | | | | | | | | |
| Clopidogrel | £23,111 | £17,367 | 13.05 | 8.29 | 6.42 | | | | £111,129 | 3 | 0% | 0% | 100% | 0% |
| Prasugrel | £24,016 | £17,995 | 13.57 | 8.62 | 6.68 | £628 | 0.25 | £2,488 | £115,548 | 1 | 96% | 4% | 0% | 95% |
| Ticagrelor | £24,331 | £18,407 | 13.36 | 8.48 | 6.57 | £413 | -0.10 | Dominated | £113,054 | 2 | 4% | 96% | 0% | 5% |
| **SA15: Treatment duration full year** | | | | | | | | | | | | | | |
| Clopidogrel | £23,085 | £17,348 | 13.05 | 8.29 | 6.42 | | | | £111,126 | 3 | 0% | 0% | 100% | 0% |
| Prasugrel | £23,984 | £17,973 | 13.57 | 8.62 | 6.68 | £625 | 0.25 | £2,477 | £115,547 | 1 | 96% | 4% | 0% | 95% |
| Ticagrelor | £24,382 | £18,465 | 13.36 | 8.48 | 6.57 | £492 | -0.10 | Dominated | £112,974 | 2 | 4% | 96% | 0% | 5% |
| **Event costs** | | | | | | | | | | | | | | |
| **SA16: Percentage stroke social care costs publicly funded - 30%** | | | | | | | | | | | | | | |
| Clopidogrel | £21,375 | £16,193 | 13.05 | 8.29 | 6.42 | | | | £112,303 | 3 | 0% | 0% | 100% | 0% |
| Prasugrel | £22,159 | £16,740 | 13.57 | 8.62 | 6.68 | £547 | 0.25 | £2,173 | £116,790 | 1 | 96% | 4% | 0% | 95% |
| Ticagrelor | £22,516 | £17,182 | 13.36 | 8.48 | 6.57 | £441 | -0.10 | Dominated | £114,286 | 2 | 4% | 96% | 0% | 5% |
| **SA17: Percentage stroke social care costs publicly funded - 70%** | | | | | | | | | | | | | | |
| Clopidogrel | £24,834 | £18,530 | 13.05 | 8.29 | 6.42 | | | | £109,945 | 3 | 0% | 0% | 100% | 0% |
| Prasugrel | £25,836 | £19,220 | 13.57 | 8.62 | 6.68 | £690 | 0.25 | £2,732 | £114,307 | 1 | 96% | 4% | 0% | 95% |
| Ticagrelor | £26,157 | £19,647 | 13.36 | 8.48 | 6.57 | £426 | -0.10 | Dominated | £111,801 | 2 | 4% | 96% | 0% | 5% |

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **SA18: Minor bleeding costs set to GI bleed** | | | | | | | | | | | | | | |
| Clopidogrel | £23,107 | £17,367 | 13.05 | 8.29 | 6.43 | | | | £111,136 | 3 | 0% | 0% | 100% | 0% |
| Prasugrel | £24,028 | £18,010 | 13.58 | 8.62 | 6.68 | £643 | 0.25 | £2,547 | £115,544 | 1 | 96% | 4% | 0% | 95% |
| Ticagrelor | £24,345 | £18,425 | 13.36 | 8.49 | 6.57 | £415 | -0.10 | Dominated | £113,050 | 2 | 4% | 96% | 0% | 5% |
| **SA19: Major bleeding costs including intracranial bleeds (10%)** | | | | | | | | | | | | | | |
| Clopidogrel | £23,115 | £17,371 | 13.05 | 8.29 | 6.42 | | | | £111,086 | 3 | 0% | 0% | 100% | 0% |
| Prasugrel | £24,012 | £17,992 | 13.57 | 8.62 | 6.67 | £621 | 0.25 | £2,464 | £115,506 | 1 | 96% | 4% | 0% | 95% |
| Ticagrelor | £24,346 | £18,422 | 13.36 | 8.48 | 6.57 | £430 | -0.10 | Dominated | £113,006 | 2 | 4% | 96% | 0% | 5% |
| **SA20: Major bleeding costs including intracranial bleeds (20%)** | | | | | | | | | | | | | | |
| Clopidogrel | £23,138 | £17,386 | 13.05 | 8.29 | 6.42 | | | | £111,091 | 3 | 0% | 0% | 100% | 0% |
| Prasugrel | £24,040 | £18,011 | 13.58 | 8.62 | 6.68 | £625 | 0.25 | £2,475 | £115,521 | 1 | 97% | 3% | 0% | 96% |
| Ticagrelor | £24,370 | £18,438 | 13.36 | 8.48 | 6.57 | £427 | -0.10 | Dominated | £113,004 | 2 | 3% | 97% | 0% | 5% |
| **SA21: Intracranial bleeds set to 30% of major bleeds** | | | | | | | | | | | | | | |
| Clopidogrel | £23,136 | £17,388 | 13.05 | 8.29 | 6.42 | | | | £111,057 | 3 | 0% | 0% | 100% | 0% |
| Prasugrel | £24,032 | £18,008 | 13.57 | 8.62 | 6.67 | £620 | 0.25 | £2,471 | £115,457 | 1 | 96% | 4% | 0% | 95% |
| Ticagrelor | £24,369 | £18,440 | 13.36 | 8.48 | 6.57 | £432 | -0.10 | Dominated | £112,971 | 2 | 4% | 96% | 0% | 5% |
| **SA22: Intracranial bleeds set to 40% of major bleeds** | | | | | | | | | | | | | | |
| Clopidogrel | £23,137 | £17,386 | 13.05 | 8.29 | 6.42 | | | | £111,104 | 3 | 0% | 0% | 100% | 0% |
| Prasugrel | £24,027 | £18,002 | 13.57 | 8.62 | 6.68 | £616 | 0.25 | £2,457 | £115,502 | 1 | 96% | 4% | 0% | 94% |
| Ticagrelor | £24,362 | £18,433 | 13.36 | 8.48 | 6.57 | £430 | -0.10 | Dominated | £113,005 | 2 | 4% | 95% | 0% | 6% |
| **SA23: Higher minor and major bleeding costs (intracranial 20%)** | | | | | | | | | | | | | | |
| Clopidogrel | £23,103 | £17,366 | 13.05 | 8.29 | 6.42 | | | | £111,106 | 3 | 0% | 0% | 100% | 0% |
| Prasugrel | £24,017 | £18,005 | 13.57 | 8.62 | 6.68 | £639 | 0.25 | £2,532 | £115,513 | 1 | 96% | 4% | 0% | 95% |
| Ticagrelor | £24,341 | £18,424 | 13.36 | 8.48 | 6.57 | £419 | -0.10 | Dominated | £113,025 | 2 | 4% | 96% | 0% | 5% |
| **Methods** | | | | | | | | | | | | | | |
| **SA24: Utilities not age-adjusted** | | | | | | | | | | | | | | |
| Clopidogrel | £23,147 | £17,389 | 13.05 | 10.76 | 8.27 | | | | £148,025 | 3 | 0% | 0% | 100% | 0% |
| Prasugrel | £24,041 | £18,008 | 13.57 | 11.19 | 8.60 | £619 | 0.33 | £1,896 | £153,933 | 1 | 96% | 4% | 0% | 95% |
| Ticagrelor | £24,382 | £18,443 | 13.36 | 11.01 | 8.46 | £435 | -0.13 | Dominated | £150,810 | 2 | 4% | 96% | 0% | 5% |
| **SA25: Discount rate 1.5%** | | | | | | | | | | | | | | |
| Clopidogrel | £23,086 | £20,282 | 13.05 | 8.29 | 7.39 | | | | £127,448 | 3 | 0% | 0% | 100% | 0% |
| Prasugrel | £23,977 | £21,038 | 13.57 | 8.62 | 7.68 | £756 | 0.29 | £2,583 | £132,545 | 1 | 96% | 4% | 0% | 95% |
| Ticagrelor | £24,315 | £21,423 | 13.36 | 8.48 | 7.56 | £385 | -0.12 | Dominated | £129,746 | 2 | 4% | 96% | 0% | 5% |

*Abbreviations: CE = cost effective; disc. = discounted; Incr. = incremental; NMB = net monetary benefit; QALY = quality-adjusted life years; £20K = a threshold of £20,000 per QALY gained; £30K = a threshold of £30,000 per QALY gained.*

*Note: SA11 is for the UA/NSTEMI population only and so does not appear in this table. Incremental costs and QALYs are versus the comparator with the next lowest costs (the previous line in the table) unless that option has been ruled out by extended dominance in which case they are compared to the option with the lowest costs (the first line in the table).*

**Table 58: Sensitivity analyses results for scenario 3: UA/NSTEMI population (probabilistic analysis, per person results)**

| Intervention | Mean lifetime costs undisc | Mean lifetime costs disc | Mean life years | Mean lifetime QALYs Undisc | Mean lifetime QALYs disc | Incr. cost | Incr. QALYs | ICER | NMB (£20k) | Rank at £20k | % CE at £20k | % Rank 2nd at £20k | % Rank 3rd at £20k | % CE at £30k |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Base case analysis** | | | | | | | | | | | | | | |
| Clopidogrel | £19,374 | £14,890 | 12.96 | 8.21 | 6.44 | | | | £113,893 | 3 | 0% | 1% | 99% | 0% |
| Prasugrel | £19,774 | £15,175 | 13.25 | 8.40 | 6.58 | £286 | 0.14 | £1,979 | £116,493 | 1 | 98% | 2% | 0% | 97% |
| Ticagrelor | £20,262 | £15,701 | 13.12 | 8.32 | 6.52 | £526 | -0.06 | Dominated | £114,727 | 2 | 2% | 98% | 1% | 3% |
| **Baseline risks** | | | | | | | | | | | | | | |
| **SA1: Stroke baseline risks adjusted based on PLATO** | | | | | | | | | | | | | | |
| Clopidogrel | £17,014 | £13,219 | 12.98 | 8.26 | 6.47 | | | | £116,265 | 3 | 0% | 0% | 100% | 0% |
| Prasugrel | £17,328 | £13,445 | 13.28 | 8.45 | 6.62 | £226 | 0.15 | £1,554 | £118,954 | 1 | 98% | 2% | 0% | 97% |
| Ticagrelor | £17,823 | £13,971 | 13.15 | 8.37 | 6.56 | £525 | -0.06 | Dominated | £117,189 | 2 | 2% | 98% | 0% | 3% |
| **SA2: Include baseline risk adjustment** | | | | | | | | | | | | | | |
| Clopidogrel | £18,642 | £14,364 | 12.96 | 8.22 | 6.45 | | | | £114,611 | 3 | 0% | 1% | 99% | 0% |
| Prasugrel | £19,015 | £14,631 | 13.26 | 8.41 | 6.59 | £267 | 0.14 | £1,841 | £117,243 | 1 | 98% | 2% | 0% | 97% |
| Ticagrelor | £19,508 | £15,159 | 13.13 | 8.33 | 6.53 | £528 | -0.06 | Dominated | £115,474 | 2 | 2% | 98% | 0% | 3% |
| **SA3: Reduce SMR for ACS/Reinfarction by 20%** | | | | | | | | | | | | | | |
| Clopidogrel | £20,968 | £15,834 | 14.14 | 8.93 | 6.87 | | | | £121,608 | 3 | 0% | 1% | 99% | 0% |
| Prasugrel | £21,399 | £16,137 | 14.46 | 9.13 | 7.02 | £303 | 0.15 | £1,983 | £124,359 | 1 | 98% | 2% | 0% | 96% |
| Ticagrelor | £21,876 | £16,657 | 14.33 | 9.04 | 6.96 | £520 | -0.07 | Dominated | £122,536 | 2 | 2% | 98% | 0% | 4% |
| **Treatment effects** | | | | | | | | | | | | | | |
| **SA4: Stroke treatment effect excluded** | | | | | | | | | | | | | | |
| Clopidogrel | £19,400 | £14,903 | 12.95 | 8.21 | 6.44 | | | | £113,915 | 3 | 0% | 0% | 100% | 0% |
| Prasugrel | £19,811 | £15,197 | 13.25 | 8.40 | 6.59 | £294 | 0.14 | £2,032 | £116,513 | 1 | 98% | 2% | 0% | 96% |
| Ticagrelor | £20,223 | £15,662 | 13.12 | 8.32 | 6.52 | £465 | -0.06 | Dominated | £114,818 | 2 | 2% | 98% | 0% | 4% |
| **SA5: Ticagrelor's stroke treatment effect not included** | | | | | | | | | | | | | | |
| Clopidogrel | £19,284 | £14,820 | 12.96 | 8.21 | 6.44 | | | | £114,019 | 3 | 0% | 1% | 99% | 0% |
| Prasugrel | £19,681 | £15,103 | 13.25 | 8.40 | 6.59 | £283 | 0.14 | £1,958 | £116,623 | 1 | 98% | 2% | 0% | 97% |
| Ticagrelor | £20,108 | £15,580 | 13.13 | 8.32 | 6.53 | £477 | -0.06 | Dominated | £114,921 | 2 | 2% | 98% | 0% | 3% |
| **SA6: Prasugrel's stroke treatment effect not included** | | | | | | | | | | | | | | |
| Clopidogrel | £19,351 | £14,867 | 12.95 | 8.21 | 6.44 | | | | £113,944 | 3 | 0% | 1% | 99% | 0% |
| Prasugrel | £19,762 | £15,161 | 13.25 | 8.40 | 6.59 | £294 | 0.14 | £2,036 | £116,539 | 1 | 98% | 2% | 0% | 97% |
| Ticagrelor | £20,240 | £15,679 | 13.13 | 8.32 | 6.52 | £518 | -0.06 | Dominated | £114,786 | 2 | 2% | 98% | 1% | 3% |
| **SA7: Rivaroxaban treatment effect included (current practice usage)** | | | | | | | | | | | | | | |
| Clopidogrel | £19,398 | £14,906 | 12.96 | 8.21 | 6.44 | | | | £113,917 | 3 | 0% | 1% | 99% | 0% |

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Prasugrel | £19,775 | £15,171 | 13.25 | 8.40 | 6.58 | £265 | 0.14 | £1,867 | £116,492 | 1 | 98% | 2% | 0% | 96% |
| Ticagrelor | £20,267 | £15,700 | 13.13 | 8.32 | 6.52 | £529 | -0.06 | Dominated | £114,737 | 2 | 2% | 97% | 1% | 4% |
| **SA8: Rivaroxaban treatment effect included (100% usage)** | | | | | | | | | | | | | | |
| Prasugrel | £19,791 | £15,183 | 13.25 | 8.40 | 6.58 | | | | £116,503 | 1 | 92% | 7% | 1% | 87% |
| Ticagrelor | £20,279 | £15,709 | 13.12 | 8.32 | 6.52 | £526 | -0.06 | Dominated | £114,738 | 3 | 1% | 24% | 76% | 1% |
| Clopidogrel | £20,463 | £15,872 | 13.19 | 8.36 | 6.55 | £163 | 0.03 | Dominated | £115,195 | 2 | 8% | 70% | 23% | 12% |
| **SA9: Dyspnoea included in analysis** | | | | | | | | | | | | | | |
| Clopidogrel | £19,360 | £14,875 | 12.95 | 8.21 | 6.44 | | | | £113,904 | 3 | 0% | 1% | 99% | 0% |
| Prasugrel | £19,759 | £15,159 | 13.25 | 8.40 | 6.58 | £284 | 0.14 | £1,965 | £116,513 | 1 | 98% | 2% | 0% | 97% |
| Ticagrelor | £20,250 | £15,688 | 13.12 | 8.32 | 6.52 | £529 | -0.06 | Dominated | £114,748 | 2 | 2% | 97% | 1% | 3% |
| **Intervention costs** | | | | | | | | | | | | | | |
| **SA10: Clopidogrel 300mg loading dose** | | | | | | | | | | | | | | |
| Clopidogrel | £19,366 | £14,882 | 12.95 | 8.21 | 6.44 | | | | £113,929 | 3 | 0% | 1% | 99% | 0% |
| Prasugrel | £19,769 | £15,169 | 13.25 | 8.40 | 6.59 | £288 | 0.14 | £1,983 | £116,541 | 1 | 98% | 2% | 0% | 97% |
| Ticagrelor | £20,253 | £15,692 | 13.12 | 8.32 | 6.52 | £522 | -0.06 | Dominated | £114,769 | 2 | 2% | 98% | 1% | 3% |
| **SA11: UA/NSTEMI prasugrel arm receiving clopidogrel loading dose** | | | | | | | | | | | | | | |
| Clopidogrel | £19,382 | £14,890 | 12.95 | 8.21 | 6.44 | | | | £113,905 | 3 | 0% | 1% | 99% | 0% |
| Prasugrel | £19,777 | £15,172 | 13.25 | 8.40 | 6.58 | £282 | 0.15 | £1,942 | £116,524 | 1 | 98% | 1% | 0% | 97% |
| Ticagrelor | £20,270 | £15,702 | 13.12 | 8.32 | 6.52 | £530 | -0.06 | Dominated | £114,751 | 2 | 2% | 98% | 1% | 3% |
| **SA12: Treatment duration based on TRITON TIMI** | | | | | | | | | | | | | | |
| Clopidogrel | £19,341 | £14,861 | 12.95 | 8.21 | 6.44 | | | | £113,930 | 3 | 0% | 1% | 99% | 0% |
| Prasugrel | £19,734 | £15,140 | 13.25 | 8.40 | 6.58 | £279 | 0.15 | £1,919 | £116,556 | 1 | 98% | 2% | 0% | 97% |
| Ticagrelor | £20,185 | £15,628 | 13.13 | 8.32 | 6.52 | £488 | -0.06 | Dominated | £114,819 | 2 | 2% | 98% | 1% | 3% |
| **SA13: Treatment duration based on PLATO** | | | | | | | | | | | | | | |
| Clopidogrel | £19,366 | £14,877 | 12.96 | 8.21 | 6.44 | | | | £113,938 | 3 | 0% | 0% | 100% | 0% |
| Prasugrel | £19,750 | £15,147 | 13.25 | 8.40 | 6.59 | £270 | 0.14 | £1,866 | £116,557 | 1 | 97% | 2% | 0% | 96% |
| Ticagrelor | £20,097 | £15,533 | 13.13 | 8.32 | 6.52 | £386 | -0.06 | Dominated | £114,929 | 2 | 3% | 97% | 0% | 4% |
| **SA14: Treatment duration DAPT specific** | | | | | | | | | | | | | | |
| Clopidogrel | £19,374 | £14,888 | 12.95 | 8.21 | 6.44 | | | | £113,918 | 3 | 0% | 1% | 99% | 0% |
| Prasugrel | £19,779 | £15,177 | 13.25 | 8.40 | 6.59 | £290 | 0.15 | £1,997 | £116,529 | 1 | 98% | 2% | 0% | 97% |
| Ticagrelor | £20,251 | £15,688 | 13.12 | 8.32 | 6.52 | £510 | -0.06 | Dominated | £114,770 | 2 | 2% | 98% | 1% | 3% |
| **SA15: Treatment duration full year** | | | | | | | | | | | | | | |
| Clopidogrel | £19,340 | £14,862 | 12.95 | 8.21 | 6.44 | | | | £113,941 | 3 | 0% | 1% | 99% | 0% |
| Prasugrel | £19,745 | £15,153 | 13.25 | 8.40 | 6.58 | £290 | 0.14 | £2,008 | £116,544 | 1 | 99% | 1% | 0% | 97% |
| Ticagrelor | £20,296 | £15,741 | 13.12 | 8.32 | 6.52 | £589 | -0.06 | Dominated | £114,714 | 2 | 1% | 98% | 1% | 3% |
| **Event costs** | | | | | | | | | | | | | | |
| **SA16: Percentage stroke social care costs publicly funded - 30%** | | | | | | | | | | | | | | |

| | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Clopidogrel | £18,472 | £14,268 | 12.96 | 8.21 | 6.44 | | | | £114,571 | 3 | 0% | 1% | 99% | 0% |
| Prasugrel | £18,836 | £14,530 | 13.25 | 8.40 | 6.59 | £261 | 0.14 | £1,810 | £117,198 | 1 | 98% | 2% | 0% | 97% |
| Ticagrelor | £19,326 | £15,055 | 13.13 | 8.32 | 6.52 | £526 | -0.06 | Dominated | £115,439 | 2 | 2% | 98% | 1% | 3% |
| **SA17: Percentage stroke social care costs publicly funded - 70%** | | | | | | | | | | | | | | |
| Clopidogrel | £20,245 | £15,482 | 12.95 | 8.21 | 6.44 | | | | £113,323 | 3 | 0% | 1% | 99% | 0% |
| Prasugrel | £20,676 | £15,787 | 13.25 | 8.40 | 6.58 | £306 | 0.14 | £2,111 | £115,912 | 1 | 98% | 2% | 0% | 97% |
| Ticagrelor | £21,169 | £16,318 | 13.12 | 8.32 | 6.52 | £531 | -0.06 | Dominated | £114,143 | 2 | 2% | 97% | 1% | 3% |
| **SA18: Minor bleeding costs set to GI bleed** | | | | | | | | | | | | | | |
| Clopidogrel | £19,358 | £14,878 | 12.96 | 8.21 | 6.44 | | | | £113,942 | 3 | 0% | 1% | 99% | 0% |
| Prasugrel | £19,773 | £15,177 | 13.25 | 8.40 | 6.59 | £299 | 0.15 | £2,055 | £116,551 | 1 | 98% | 2% | 0% | 97% |
| Ticagrelor | £20,251 | £15,693 | 13.13 | 8.32 | 6.52 | £517 | -0.06 | Dominated | £114,783 | 2 | 2% | 98% | 1% | 3% |
| **SA19: Major bleeding costs including intracranial bleeds (10%)** | | | | | | | | | | | | | | |
| Clopidogrel | £19,374 | £14,888 | 12.96 | 8.21 | 6.44 | | | | £113,904 | 3 | 0% | 1% | 99% | 0% |
| Prasugrel | £19,774 | £15,173 | 13.25 | 8.40 | 6.58 | £285 | 0.14 | £1,970 | £116,516 | 1 | 98% | 2% | 0% | 97% |
| Ticagrelor | £20,262 | £15,699 | 13.13 | 8.32 | 6.52 | £526 | -0.06 | Dominated | £114,748 | 2 | 2% | 98% | 1% | 3% |
| **SA20: Major bleeding costs including intracranial bleeds (20%)** | | | | | | | | | | | | | | |
| Clopidogrel | £19,377 | £14,889 | 12.95 | 8.21 | 6.44 | | | | £113,897 | 3 | 0% | 1% | 99% | 0% |
| Prasugrel | £19,781 | £15,177 | 13.25 | 8.40 | 6.58 | £288 | 0.15 | £1,982 | £116,516 | 1 | 98% | 2% | 0% | 98% |
| Ticagrelor | £20,266 | £15,702 | 13.12 | 8.32 | 6.52 | £524 | -0.06 | Dominated | £114,738 | 2 | 2% | 98% | 0% | 2% |
| **SA21: Intracranial bleeds set to 30% of major bleeds** | | | | | | | | | | | | | | |
| Clopidogrel | £19,388 | £14,899 | 12.95 | 8.21 | 6.44 | | | | £113,876 | 3 | 0% | 1% | 99% | 0% |
| Prasugrel | £19,787 | £15,184 | 13.25 | 8.40 | 6.58 | £285 | 0.14 | £1,975 | £116,474 | 1 | 99% | 1% | 0% | 97% |
| Ticagrelor | £20,277 | £15,711 | 13.12 | 8.32 | 6.52 | £527 | -0.06 | Dominated | £114,718 | 2 | 1% | 98% | 1% | 3% |
| **SA22: Intracranial bleeds set to 40% of major bleeds** | | | | | | | | | | | | | | |
| Clopidogrel | £19,374 | £14,886 | 12.96 | 8.21 | 6.44 | | | | £113,942 | 3 | 0% | 1% | 99% | 0% |
| Prasugrel | £19,770 | £15,168 | 13.25 | 8.40 | 6.59 | £282 | 0.14 | £1,961 | £116,537 | 1 | 98% | 2% | 0% | 96% |
| Ticagrelor | £20,259 | £15,695 | 13.13 | 8.32 | 6.52 | £527 | -0.06 | Dominated | £114,776 | 2 | 2% | 97% | 1% | 4% |
| **SA23: Higher minor and major bleeding costs (intracranial 20%)** | | | | | | | | | | | | | | |
| Clopidogrel | £19,355 | £14,877 | 12.95 | 8.21 | 6.44 | | | | £113,914 | 3 | 0% | 1% | 99% | 0% |
| Prasugrel | £19,766 | £15,172 | 13.25 | 8.40 | 6.58 | £296 | 0.14 | £2,041 | £116,517 | 1 | 98% | 2% | 0% | 97% |
| Ticagrelor | £20,247 | £15,692 | 13.12 | 8.32 | 6.52 | £519 | -0.06 | Dominated | £114,756 | 2 | 2% | 97% | 1% | 3% |
| **Methods** | | | | | | | | | | | | | | |
| **SA24: Utilities not age-adjusted** | | | | | | | | | | | | | | |
| Clopidogrel | £19,387 | £14,894 | 12.95 | 10.76 | 8.37 | | | | £152,571 | 3 | 0% | 0% | 100% | 0% |
| Prasugrel | £19,785 | £15,177 | 13.25 | 11.01 | 8.56 | £283 | 0.19 | £1,496 | £156,078 | 1 | 97% | 3% | 0% | 96% |
| Ticagrelor | £20,276 | £15,706 | 13.13 | 10.90 | 8.48 | £529 | -0.08 | Dominated | £153,920 | 2 | 3% | 97% | 0% | 4% |
| **SA25: Discount rate 1.5%** | | | | | | | | | | | | | | |

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|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Clopidogrel | £19,345 | £17,171 | 12.95 | 8.21 | 7.36 | | | | £129,980 | 3 | 0% | 0% | 100% | 0% |
| Prasugrel | £19,742 | £17,513 | 13.25 | 8.40 | 7.53 | £341 | 0.17 | £2,039 | £132,988 | 1 | 98% | 2% | 0% | 97% |
| Ticagrelor | £20,232 | £18,021 | 13.12 | 8.32 | 7.45 | £509 | -0.07 | Dominated | £131,040 | 2 | 2% | 98% | 0% | 3% |

*Abbreviations: CE = cost effective; disc. = discounted; Incr. = incremental; NMB = net monetary benefit; QALY = quality-adjusted life years; £20K = a threshold of £20,000 per QALY gained; £30K = a threshold of £30,000 per QALY gained.*
*Note: Incremental costs and QALYs are versus the comparator with the next lowest costs (the previous line in the table) unless that option has been ruled out by extended dominance in which case they are compared to the option with the lowest costs (the first line in the table).*

# 4 Discussion

## 4.1 Summary of results

Due to inconsistency in the 1-year clinical treatment effect data, three scenarios using different sets of clinical data were undertaken in the cost effectiveness analysis. The three scenarios utilise the following data to inform the 1 year relative treatment effects in the model (all scenarios use the 30 day NMA to inform the relative treatment effects 0 to 30 days in the model):

1. Ticagrelor vs clopidogrel (meta-analysis); prasugrel vs clopidogrel (meta-analysis)
2. Prasugrel vs clopidogrel (meta-analysis); ticagrelor versus prasugrel (ISAR-REACT 5)
3. Ticagrelor vs clopidogrel (meta-analysis); ticagrelor versus prasugrel (ISAR-REACT 5)

The DAPT option that was most cost effective varied depending on the clinical data used to inform the 1 year relative treatment effects. Ticagrelor was the most cost effective DAPT option, for STEMI and UA/NSTEMI, when data from studies comparing prasugrel to clopidogrel and ticagrelor to clopidogrel (and not ISAR-REACT 5) were used to inform the relative treatment effects at 1 year in the model (data scenario 1). Prasugrel was the most cost effective DAPT option, for STEMI and UA/NSTEMI, when data comparing ticagrelor and prasugrel from ISAR-REACT 5 were incorporated (data scenarios 2 and 3). Ticagrelor had the highest costs in all scenarios and ACS subgroups but only had the highest QALYs in scenario 1. In scenarios 2 and 3 prasugrel had lower costs than ticagrelor and the highest QALYs. Clopidogrel had the lowest costs in all scenarios.

There was low uncertainty in scenarios 1 (ticagrelor cost effective 93%/86%) and 3 (prasugrel cost effective 96%/98%). There more uncertainty in scenario 2 (prasugrel cost effective 58%/60%, clopidogrel 37%/38%). In addition, conclusions about which DAPT option was the most cost effective were unchanged in a range of sensitivity analyses around baseline risks, treatment effects, event costs and intervention costs in all three scenarios. The exception being when rivaroxaban use after ACS was incorporated alongside clopidogrel with 100% usage (and not alongside prasugrel or ticagrelor). In this exploratory sensitivity analysis, clopidogrel (incorporating rivaroxaban) became the most cost effective option in scenarios 1 and 2, although not in scenario 3 where prasugrel remained the most cost effective option. However, note that when rivaroxaban use was based on an estimate of current practice, conclusions did not differ from the base case analyses.

## 4.2 Limitations and interpretation

**Baseline risks in 1 year decision tree**

In the model we aimed to use baseline risks based on UK audit data in order to reflect real world risks for people with ACS. As discussed in the methods, the ideal source of baseline risks for the model would have been to undertake a bespoke analysis of national audit data linked with mortality and HES data as this would allow calculation of probabilities that matched the decision tree exactly, for example the probability of reinfarction 31 days to 1 year given you did or did not have an event 0 to 30 days, but this was not feasible within guideline development time constraints. Published audit data analyses were therefore used in the model and probabilities 31 days to 1 year were assumed to be independent of events experienced 0 to 30 days.

As the baseline risks were to populate the clopidogrel arm, it was ideal that the data was obtained from people in England who underwent PCI and were taking clopidogrel. One of the limitations was that the data for baseline risks was not solely people taking clopidogrel. For example, the mortality data was taken from BCIS audit from 2011/12 and clopidogrel use was 77.8% for STEMI and 98.5% for UA/NSTEMI. The use of clopidogrel in the UA/NSTEMI

population was very high, but the use was lower for STEMI. Although this was a limitation, the committee agreed that this was reasonable. Firstly, it was noted that people taking clopidogrel in more recent audit data may not be a good representation of the average population, for example, they have a higher bleeding risk due to age. Therefore, the committee agreed using the data from 2011/12 was a good balance between having a majority of people on clopidogrel and being relevant to current practice.

As described in section 2.3.2.1, the baseline risk data for stroke (in both STEMI and UA/NSTEMI) and reinfarction (only in STEMI) was for all events instead of non-fatal events. This may overestimate the number of people that are alive with an event at the end of the decision tree and entering the Markov model. This has implications as the health states for post-reinfarction and post-stroke result in higher costs and lower quality of life. In order to address this a sensitivity analysis was undertaken using lower probabilities for these events and this did not impact conclusions.

The committee noted that the mortality rates for UA/NSTEMI appeared lower than might be expected. However, it was agreed that this was due to the fact this analysis only included the PCI population, and it is those who are medically managed that might have a higher mortality rate. This was reinforced by the analysis of audit data undertaken in CG94 which showed that people that underwent PCI had a lower mortality rate. Also, the most recent BCIS audit report for 2017/18 showed that the 30-day mortality rate was 1.6% for people with UA/NSTEMI that underwent PCI which is very similar to the 1.79% used in the model.

Another limitation was that there was no recent data for reinfarction for the UA/NSTEMI population, and therefore the previous MINAP analysis that was conducted for the UA/NSTEMI NICE Guideline CG94 was used. This is based on data from 2005 to 2007 and may not be as reflective of current practice. However, everyone in the analysis would have been taking clopidogrel and therefore the committee felt this was a reasonable source to use. Also, the analysis only reported reinfarction at 1 year, and an assumption had to be made about the reinfarction rate at 30 days. In order to obtain this rate, the relationship between 31 days and 1 year reinfarction rates from a Swedeheart analysis and the PLATO trial was obtained. These showed a similar relationship and the committee agreed this was a reasonable way to obtain the 30 day reinfarction rate.

The source of baseline risk for stroke did not report 1-year event rates for either STEMI or UA/NSTEMI. Therefore, a similar approach had to be taken to obtain the relationship between 31 day and 1 year event rates. The relationship observed in the Swedeheart audit and PLATO trial were both discussed but as they were quite different, the committee agreed to use the relationship from the Swedeheart audit in the base case and to test using the data from the PLATO trial in a sensitivity analysis; and this did not impact conclusions.

There was no data available for minor and major bleeds from a UK audit. As a result, data from the PLATO RCT was used as it was considered the trial that was closest to UK practice. One limitation was that the PLATO trial included CABG related bleeding in their major and minor bleeding outcomes, and did not report non-CABG related bleeding for minor bleeds. As a result, assumptions had to be made about the relationships between major and minor bleeds, as well as the relationship between 31 day and 1 year bleeding events. The committee acknowledged this was a limitation, however, considered this to be the best available estimate.

**Treatment effects**

The treatment effects used in the model were obtained from the network meta-analysis (30 day data) and pairwise meta-analyses (1 year data) undertaken as part of guideline development (see Evidence report A and NMA report).

The RCTs that informed treatment effects varied in terms of their ACS population with some conducted in the overall ACS population and some in a particular ACS subtype (STEMI or

UA/NSTEMI). They also varied in terms of management strategy with some only including people receiving PCI and others including all management strategies. It was considered appropriate by the committee to assume that relative treatment effects were consistent and that combining ACS data together provided the best estimate of treatment effects. This may have limitations as it can be said that STEMI and UA/NSTEMI differ clinically, for example, STEMI is a medical emergency requiring urgent treatment. Although they may differ with regards to some clinical aspects, the committee reviewed the clinical evidence stratified by subtype (STEMI or UA/NSTEMI) and also by management approach (PCI or medically managed) and agreed that treatment effects were sufficiently consistent. It was therefore deemed appropriate to combine these to get the best estimate of treatment effects. This approach has been undertaken by other clinical reviews and in randomised controlled trials, for example the PLATO trial assessed the overall ACS population.

The NMA of 30-day outcomes included 14 RCTs; however, there were some limitations of the RCTs included. Firstly, the TRITON-TIMI 38 trial did not report 30 day outcomes for the overall ACS population and only reported 30 day outcomes for the STEMI population. This trial was the largest RCT comparing prasugrel and clopidogrel in over 13,000 patients, but the sub-analysis of the STEMI population only included over 3,000 patients. The committee considered this study significant for the comparison of prasugrel versus clopidogrel; therefore the absence of a large number of participants was considered a limitation of the NMA. Another RCT that was not included in the NMA as 30 day data was not available and was considered a significant study was the ISAR-REACT 5 trial. This study was conducted in over 3,000 participants and was considered a very important trial comparing ticagrelor and prasugrel. The studies included in the NMA for the ticagrelor vs prasugrel comparison were conducted on a smaller number of participants in comparison to the ISAR-REACT 5 (n = 1,698 versus 4,016 respectively); therefore not including this study was considered a limitation of the 30 day outcome data from the NMA. Note however that both ISAR-REACT 5 and the full TRITON-TIMI 38 population data are incorporated into the model as part of the 1 year relative treatment effects.

Another limitation was studies used to inform relative treatment effects did not always report both 30 day and 1 year treatment effects, resulting in different studies contributing to the 30 day and 1 year relative treatment effects used in the model. The committee considered the data available at 1 year to be the most complete however it was not possible to obtain a single set of consistent treatment effects incorporating all available data at 1 year due to the there being a high level of inconsistency across the ‘direct’ and ‘indirect’ estimates of effect in the evidence network which meant NMA was considered unreliable. As a result, the economic analysis had to utilise data from two sides of the network at one given time, resulting in 3 alternative base case scenarios, in order to explore the impact of the inconsistency in the clinical evidence on cost effectiveness conclusions. The alternative base case scenarios resulted in different conclusions; the inconsistency in the data was therefore an important issue to consider when interpreting the results.

The sensitivity analyses conducted which incorporated rivaroxaban use as an adjunctive therapy post-ACS alongside clopidogrel showed that conclusions could be affected. As rivaroxaban is only currently indicated alongside clopidogrel, a recommendation for one of the other antiplatelets could preclude rivaroxaban’s use, therefore an exploratory analysis was undertaken where treatment effects of rivaroxaban were incorporated into the model to see if this would impact results. However, there were limitations associated with this analysis. As the use of low dose rivaroxaban post-ACS is not part of the scope of this update a systematic review of the clinical evidence was not undertaken and treatment effects were based on the ATLAS-TIMI trial as used in the NICE TA. The treatment effects reported in the ATLAS-TIMI trial were hazard ratios at 24 months. As treatment effects were not reported at the specific time points of interest (30 days and 1 year) it was assumed that treatment effects remained constant. The committee agreed this was a reasonable approach for this exploratory sensitivity analysis. The available data also relates a longer time point than was considered in this analysis, however, the study showed that on average rivaroxaban was

taken for 13 months, therefore applying these at 1 year was considered reasonable. The BNF also states 12 months as the usual duration. The committee noted that only a small number of people are prescribed low dose rivaroxaban and clopidogrel after ACS in practice and the assumption about the proportion of people on clopidogrel that would receive rivaroxaban affected conclusions. When based on an estimate of current usage the conclusions from the base case analyses were not changed, however when it was assumed everyone received rivaroxaban post-ACS conclusions changed in scenarios 1 and 2, but not 3. National audits do not collect data on rivaroxaban use and current usage was estimated using prescription data but this was not available by indication. It was also highlighted at consultation that some recent studies have combined rivaroxaban with prasugrel and ticagrelor. The use of rivaroxaban was not part of this guideline update and so this issue was not examined by the committee, however if rivaroxaban could equally be used alongside any DAPT option, this sensitivity analysis may not be relevant as the DAPT option recommended may not affect the use of low dose rivaroxaban post-ACS.

There was uncertainty around including the treatment effects of stroke in the model as it was unclear if there were differences between treatments and because stroke affects a small number of people. There was some uncertainty in the treatment effect estimates as some trials reported no events or only a very small number of events. It was acknowledged that stroke events have high costs associated with them and therefore a small number of events could impact costs considerably and also have a large impact on QALYs. However, this was tested in a sensitivity analysis by removing the treatment effects of stroke from the analysis to see if this impacted results. Conclusions did not differ from the base case analyses in these sensitivity analyses.

**Events beyond one year**

Data was not identified about risks of stroke or reinfarction in an ACS population beyond one year and so it was assumed that the rate beyond one year would be the same as that between 31 days and 1 year. It can be considered a limitation that there was no real world data available for the rate of reinfarction or stroke beyond one year to inform this decision. However, this is an approach that was used in other ACS models and the committee agreed it was a reasonable assumption.

The model did not allow for repeat events after 1 year and only allowed people in the no further event health state to have a reinfarction or stroke, and if they had one event they could not have the other event too. This can be considered a limitation as this does not reflect the real world as people can experience repeat reinfarctions and stroke. However, this was considered to be a reasonable simplification for modelling purposes as there is limited data available to model repeat events beyond one year and would require making too many assumptions. In addition, this was taken into account when selecting health state cost data where costs incorporating downstream events were used if possible.

It was considered that the mortality transition probabilities could be over or underestimating death in the model. The study used to obtain the SMRs for the no further event, reinfarction and post-reinfarction health states was for people with a myocardial infarction, and not just PCI. It was thought that this could potentially overestimate the mortality rates. Also, the study analysed mortality for people who have had their first myocardial infarction separately to those with a second myocardial infarction. The data for those that had their first myocardial infarction was used for the no further event health state in the model, however, some of these people being modelled would have had a previous myocardial infarction, therefore this could be underestimating mortality for this group. It was considered that despite these limitations, this was a good source of data and being able to utilise different SMRs for the no further event and reinfarction/post-reinfarction health states was important. Lastly, it was discussed that the SMRs from the study would include death from any cause, therefore this would include people who are dying from having a stroke. As a result, this could overestimate the number of people dying in each cycle, as the ACS SMRs have not been

adjusted to account for the fact that people with a stroke is being captured separately. A sensitivity analysis was conducted where the SMRs for the ACS health states (no further event, reinfarction and post-reinfarction) were reduced by 20% and this did not impact conclusions. In order to further test whether mortality in the model was accurate, the 5-year survival rate for STEMI was calculated and compared to the reported 5 year survival rate in a study by Brogan 2017[5] for people with STEMI that underwent PCI. Results were similar, with the study reporting that 87% of people survive 5 years and the model showing that 85% survived 5 years.

**Intervention costs**

Intervention costs for those alive were calculated to take account of average treatment duration. However, this information is not collected in national audits and this varied between clinical studies used in the analysis. However, sensitivity analyses were undertaken using different assumptions and this did not impact conclusions.

**Event costs**

There were some assumptions made in relation to the costs. Firstly, the costs associated with ACS and applied to everyone were obtained from a study which reported the cost of myocardial infarction for people who were receiving lipid modifying therapy. Although this is not the exact population being modelled, the committee agreed that whether you are taking lipid modifying treatment before an event should not impact the treatment you receive for having a myocardial infarction, and therefore the costs should not be impacted. These costs were applied to both the STEMI and UA/NSTEMI population. It was noted that as unstable angina is not classified as a myocardial infarction, this could be overestimating the costs associated with these people. However, the committee agreed that as the model looked at people undergoing PCI, the downstream management and resource use would be similar to those with myocardial infarction and therefore this was considered a reasonable approach.

The costs associated with stroke were obtained from SSNAP data, which was considered the most reliable source of UK stroke data. However, some assumptions were made around the social care costs. As the SSNAP costs included both publicly and non-publicly funded social care costs, these had to be adjusted to ensure only the costs incurred to the NHS and personal social services were included. The percentage that was publicly funded was not reported; therefore an assumption had to be made. The committee agreed it was reasonable to follow the assumption made in an analysis by the Stroke Association which indicated that 50% of social care costs were publicly funded. This was also explored in a sensitivity analysis where 30% and 70% of these costs were assumed to be publicly funded, and this did not impact conclusions.

The costs of major and minor bleeding were based on what the committee considered were relevant NHS reference costs. For minor bleeds, the cost of an emergency admission was used. Although it was noted that minor bleeds may not require medical interventions, it was discussed that people experiencing a minor bleed may feel anxious as they have just had an ACS event, and therefore seek medical help. The costs associated with an emergency admission were used in a previous NICE technology appraisal, and the committee considered this a reasonable cost. There was variation in what other models in the areas had used to cost minor bleeds, and as a result a sensitivity analysis was conducted which costed a gastrointestinal bleed without interventions, and this did not impact conclusions. Major bleeds were costed as gastrointestinal bleeds with interventions, and gastrointestinal bleeds without interventions with a high comorbidity score (5+). It was discussed that major bleeding can also include intracranial bleeds; however, gastrointestinal bleeds were more common in this population. Sensitivity analyses were conducted which included intracranial bleeds in the costs of a major bleed, and these did not impact conclusions.

## 4.3 Generalisability to other populations or settings

The relative treatment effects used in the model were for the overall ACS population and therefore included people who were not invasively managed. Also, the same relative treatment effects were applied to the STEMI and UA/NSTEMI populations. The committee considered the pairwise meta-analyses stratified by condition and management approach, as well as the evidence for all ACS, and considered it was reasonable to assume that relative treatment effects were consistent and combining all the evidence provided the best estimate of treatment effects. To account for the fact that event rates may differ by subgroup, different baseline risks were used for the STEMI and UA/NSTEMI populations, and therefore absolute event rates were different.

The committee acknowledged that the people recruited to randomised controlled trials are generally younger and/or lower risk than the overall ACS population. However, this was partially addressed in the model by using baseline risks associated with real world ACS PCI population in order to estimate real world absolute event rates with the different treatment options. Although noting these issues, the committee agreed that it was appropriate to use the available clinical effectiveness and cost effectiveness evidence to make recommendations for the whole ACS PCI population,

## 4.4 Comparisons with published studies

The economic literature review results are detailed in full in Evidence report A. Five published economic evaluations were included in the review. Two compared ticagrelor, prasugrel and clopidogrel, two compared ticagrelor and clopidogrel, one compared prasugrel and clopidogrel and one compared ticagrelor and prasugrel. One of the analyses that compared ticagrelor and clopidogrel is not relevant to this analysis as it looked at people with ACS that were medically managed, therefore, this is not included in this discussion.

One published economic evaluation (NICE TA236)[39] compared ticagrelor with clopidogrel in the overall ACS population (invasive and non-invasive management) using a probabilistic decision analytic model. The new analysis for the guideline takes a similar approach as it was conducted from a UK NHS and personal social services perspective and used a decision tree to model first year events and a Markov model for long term extrapolation, with the same health states. The analysis found that ticagrelor had higher costs and QALYs and was cost effective with an ICER of £3,805 per QALY gained. In this new analysis, if excluding prasugrel, ticagrelor is cost effective in comparison to clopidogrel in scenarios 1 and 3 which incorporate the studies directly comparing ticagrelor and clopidogrel (but not in scenario 2 which doesn't). The QALY gain between ticagrelor and clopidogrel is similar in this analysis for scenarios 1 and 3 compared to the NICE TA, however, the incremental costs are higher. It is likely this is due to the costs used in the current analysis being higher than the costs used in NICE TA236. For example, the Markov model costs for the no further event health state was £217 compared to £943 in the new analysis. The reinfarction health sate cost was similar however the post-reinfarction health state cost was £1,415 in the new analysis but only £285 in NICE TA236. The post-stroke health sate had a similar cost, however, the stroke health state costs in NICE TA236 was £13,084 compared to £18,522 in the new analysis. As more people were alive with ticagrelor compared to clopidogrel in scenarios 1 and 3, this means that more costs would have been accrued over time. Due to higher costs being used and more people being alive in the ticagrelor arm, this would have contributed to the higher difference in incremental costs and result in higher incremental cost effectiveness ratios. The same study also conducted an analysis comparing ticagrelor and prasugrel, however, this was based on an indirect comparison of ticagrelor versus prasugrel as there were no published trials at the time that had compared ticagrelor and prasugrel. The results from that analysis found that ticagrelor was cost effective compared to prasugrel, with an ICER of £3,482 per QALY gained. This is consistent with scenario 1 in the new analysis that also found ticagrelor to be cost effective compared to prasugrel using studies that compared

prasugrel and ticagrelor with clopidogrel. However, it differs considerably to scenarios 2 and 3 in the current analysis undertaken for this guideline that showed that ticagrelor was dominated by prasugrel in scenario 2 and 3 when 1 year data from ISAR-REACT 5 comparing ticagrelor and prasugrel were incorporated. The results are similar for scenario 1 but differ considerably to scenarios 2 and 3 due to the fact similar data is used in this analysis as scenario 1 but scenarios 2 and 3 utilised new head to head data for prasugrel and ticagrelor which showed that prasugrel was more effective in comparison to ticagrelor.

Greenhalgh 2015[15] conducted an economic evaluation of prasugrel versus clopidogrel in people with ACS undergoing PCI and was the evidence review group report for NICE TA317. This analysis split the ACS population in to four subgroups which included STEMI with and without diabetes and UA/NSTEMI with and without diabetes. Prasugrel was found to be cost-effective in comparison to clopidogrel, with an ICER of £6,687 per QALY gained for people with STEMI and without diabetes, £1,643 for people with STEMI and diabetes, £4,679 for people with UA/NSTEMI without diabetes and was dominant (higher QALYs and lower costs compared to clopidogrel) for the UA/NSTEMI group with diabetes. These results are consistent with the results in this analysis if excluding ticagrelor in terms of prasugrel being cost-effective compared to clopidogrel. One difference between this analysis and the new analysis is the cost of prasugrel. The NICE TA317 used a pack price of £47.56 and this cost has significantly decreased. This analysis reported higher lifetime costs across all subgroups in comparison to the new analysis. A breakdown of the costs showed that the no further event and reinfarction health state costs were similar, however, the costs associated with stroke over the lifetime were higher in this analysis compared to the new analysis. This may be due to the analysis separating stroke in to disabling and non-disabling stroke, and having a higher cost associated with disabling stroke over a long period of time. Another contributing factor could be the fact that the start age in the analysis was lower and therefore people were alive for a longer period of time and therefore accruing more costs. Despite the higher lifetime costs, incremental costs were similar, apart from the UA/NSTEMI with diabetes group, where prasugrel resulted in less costs. The lifetime QALYs were also higher across all subgroups in this analysis compared to the new analysis. This could be due to the new analysis for the guideline having a higher start age and therefore having a lower life expectancy, which would accrue less QALYs. Also, Greenhalgh 2015 did not apply a lower quality of life to those who had a second myocardial infarction, and this could further explain the differences in the lifetime QALY estimates. Incremental QALYs were lower in scenario 1 and 2 of the new analysis than in this analysis. This is likely to be largely due the 1 year relative treatment effect for mortality used in these scenarios being 1 in the new analysis and less than 1 in this analysis. Conversely, they were generally higher in scenario 3 where there is a greater mortality relative risk at 1 year than in this analysis.

Two economic evaluations conducted a three-way analysis of ticagrelor, prasugrel and clopidogrel. Abdel-Qadir 2015[1] conducted an analysis from a Canadian healthcare perspective and found that ticagrelor had the highest costs and QALYs followed by prasugrel and then clopidogrel. Prasugrel was extendedly dominated by ticagrelor and the ICER for ticagrelor versus clopidogrel was £6,556 per QALY gained. This analysis was based on data collected in three randomised controlled trials, two of which compared ticagrelor and clopidogrel (DISPERSE-2 and PLATO) and one which compared prasugrel to clopidogrel (TRITON-TIMI 38). Therefore, this analysis did not include head-to-head data for ticagrelor versus prasugrel. The analysis reported higher lifetime QALYs compared to the new analysis, and this is due to the utility values being much higher than the values used in the new analysis. For example, the no further event health state utility value was 0.91 compared to 0.84. Also, the analysis did not indicate whether quality of life was age-adjusted, and this could contribute to the analysis having higher QALYs. The sensitivity analysis conducted in the new analysis for the guideline where utilities were not age-adjusted also resulted in higher QALYs. Incremental QALYs were similar to scenario 1 in the new analysis which used similar data. The lifetime costs were also higher and the incremental cost between ticagrelor and prasugrel was lower. Wisloff 2015[62] was the second three-way analysis which was conducted from a Norwegian healthcare perspective. This analysis found that ticagrelor had

the highest costs and QALYs followed by prasugrel and then clopidogrel. The ICER for prasugrel versus clopidogrel was £6,107 per QALY gained and the ICER for ticagrelor versus prasugrel was £6,210 per QALY gained and ticagrelor was the most cost-effective option. The lifetime QALYs were higher in this analysis compared to the new analysis, however the paper did not give details of what utility values were used. The difference in lifetime costs between the treatments was much bigger than the incremental costs in the new analysis, but due to the absence of detail regarding costs in the study, it is unclear why. The results from these three-way analyses are generally similar to scenario 1 in the new analysis undertaken as part of guideline development, but very different to scenarios two and three. The main reason for these differences is because they did not have head-to-head data for ticagrelor and prasugrel, and the new head-to-head data shows that prasugrel is more effective than ticagrelor, which resulted in the new analysis having higher QALYs associated with prasugrel in scenarios 2 and 3 that use this data.

## 4.5 Conclusions

This analysis found that the DAPT option that was most cost effective varied depending on the clinical data used to inform 1-year relative treatment effects. Ticagrelor (plus aspirin) was the most cost effective option for STEMI and UA/NSTEMI in data scenario 1 which used data from studies comparing prasugrel to clopidogrel and ticagrelor to clopidogrel (and not ISAR-REACT 5). Prasugrel (plus aspirin) was the most cost effective option in data scenarios 2 and 3, which both utilised data directly comparing ticagrelor and prasugrel from ISAR-REACT 5.

## 4.6 Implications for future research

There have been various economic evaluations looking at the cost effectiveness of dual-antiplatelet therapy. This is the first UK analysis which has included the results from the ISAR-REACT 5 trial, which is the first large randomised controlled trial comparing ticagrelor and prasugrel. Due to the uncertainty around the applicability of the ISAR-REACT 5 trial to a UA/NSTEMI population in the UK, it would be beneficial to conduct a UK study in this population undergoing PCI, comparing ticagrelor and prasugrel.

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