

## Consulting Report November 2015

# Assessing trends in SMC Advice Decisions (October 2009- September 2015)

This report was  
initiated and funded  
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## Executive Summary

This report outlines trends in SMC advice decisions between October 2009 and September 2015. Specifically whether there are changes in the trends during a period of adoption of new policies by the SMC, namely the increasing use of modifiers when assessing cost effectiveness, the introduction of Patient and Clinical Expert (PACE) groups, and the increased use of patient access schemes.

The overall trend for SMC decisions show a steady increase in medicines being accepted for use with an associated decrease in decisions to not recommend use. Decisions to restrict use of medicines, to allow use in one subgroup of patients and not another relative to the scope of the appraisal, remain around the same level during the six year period.

Since October 2014, there has been an increase in the number of decisions on cancer medicines perhaps related to the increase in submissions using modifiers and PACE group's advice. Cancer medicines represent an important group of treatment and assessing trends for these provide further insight into SMC processes.

In the first year of operation of PACE SMC recommendations have not always been aligned with their deliberations. In the five instances, where PACE have made a strong recommendation for use of a medicine but SMC have not recommended use, it appears that the economic case outweighs these wider considerations. Research has suggested that the mean Incremental Cost Effectiveness Ratio (ICER) for medicines accepted by the SMC is approximately £30,000<sup>1</sup> and in three of the five instances the ICERs underlying the decisions were above £50,000 and in two instances there was significant uncertainty raised about the robustness of the economic case.

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<sup>1</sup> Charokopou, M, Majer, I, et.al. (2015) Which Factors Enhance Positive Drug Reimbursement Recommendation in Scotland? A Retrospective Analysis 2006–2013 *Value in Health* 18(2):284-91

The steady increase in patient access schemes (PAS) agreements and the upward trend in accepted decisions are a feature of the period under consideration.

## Background

Since 2002 the Scottish Medicines Consortium (SMC) has been publishing advice on the use of medicines based on clinical and cost-effectiveness criteria. From 2002 until September 2015 there have been 1,230 pieces of advice published. SMC aims to publish advice soon after launch of a new medicine or when additional indications, and/or new formulations are authorised in the market.

The process for assessing medicines is more streamlined for the SMC than NICE. They state that they “aim(s) to issue advice to NHS Scotland on all newly licensed medicines within 12 weeks of products being made available”<sup>2</sup>. This compares to more than a year for NICE<sup>3</sup>, albeit with some medicines receiving a decision in more rapid timeframes. The SMC also allow pharmaceutical companies to resubmit a medicine for consideration. Assessing medicines close to launch raises specific issues for Health Technology Assessment (HTA) processes, as some medicines will have a small or uncertain evidence base generated from their clinical trials. This in turn means that clinical and cost-effectiveness considerations can be challenging. Medicines more likely to face these challenges, such as those for cancer or orphan indications, are also perceived as test cases for assessing whether SMC is operating in a manner that supports the operation of the NHS in Scotland.

Acknowledging these issues, the process and methods used to reach decisions have evolved. This report examines trends in decisions where important recent changes have been made. These are the development and use of “modifiers”, the ability of companies to offer patient access schemes (PAS), and the introduction of Patient and Clinician Expert (PACE) groups.

“**Modifiers**” are characteristics about medicines that the SMC explicitly use to influence their deliberations, either by accepting a higher ICER or greater uncertainty<sup>4</sup>. Some of the modifiers potentially relevant are:

- End of life medicine: A medicine used to treat a condition at a stage that usually leads to death within three years with currently available treatments<sup>5</sup>.
- Orphan medicine: A medicine with European Medicines Agency designated orphan status (i.e. conditions affecting fewer than 2,500 people in a population of 5 million) or a medicine to treat an equivalent size of population irrespective of whether it has designated orphan status.

<sup>2</sup>[http://www.scottishmedicines.org.uk/Submission\\_Process/Submission\\_guidance\\_and\\_forms/Submission\\_Process\\_-\\_Submission\\_Guidance\\_and\\_Templates\\_for\\_Submission](http://www.scottishmedicines.org.uk/Submission_Process/Submission_guidance_and_forms/Submission_Process_-_Submission_Guidance_and_Templates_for_Submission) (accessed September 2015)

<sup>3</sup> See for example chart 16 Dashboard of NICE Technology Appraisals publication timeframes in OLS (2015) “Life Science Competitiveness Indicators”.

[https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/418305/BIS-15-249-life-science-competitiveness-indicators.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/418305/BIS-15-249-life-science-competitiveness-indicators.pdf)

<sup>4</sup>[http://www.scottishmedicines.org.uk/About\\_SMC/Policy\\_statements/SMC\\_Modifiers\\_used\\_in\\_Appraising\\_New\\_Medicines](http://www.scottishmedicines.org.uk/About_SMC/Policy_statements/SMC_Modifiers_used_in_Appraising_New_Medicines) (accessed September 20-15)

<sup>5</sup> SMC Guidance to Manufacturers for Completion of New Product Assessment Form (NPAF) Supplement on medicines for end of life and very rare conditions: June 2014. Although end of life is not explicitly listed in the SMC modifiers policy statement, they are used to “weight” the ICER

- Ultra-orphan medicine: A medicine used to treat a condition with a prevalence of 1 in 50,000 or less (or around 100 people in Scotland).
- Evidence of a substantial improvement in life expectancy (with sufficient quality of life to make the extra survival desirable). Substantial improvement in life expectancy would normally be a median gain of 3 months but the SMC assesses the particular clinical context in reaching its decision;
- Evidence of a substantial improvement in quality of life (with or without survival benefit);
- Evidence that a sub-group of patients may derive specific or extra benefit and that the medicine in question can, in practice, be targeted at this sub-group;
- Absence of other therapeutic options of proven benefit for the disease in question and provided by the NHS;
- Possible bridging to another definitive therapy (e.g. bone marrow transplantation or curative surgery) in a defined proportion of patients;
- Emergence of a licensed medicine as an alternative to an unlicensed product that is established in clinical practice in NHS Scotland as the only therapeutic option for a specific indication.

The SMC established a Task and Finish Group (T&FG) in 2013 to review the access to new medicines. The T&FG included representatives from key stakeholders, including clinicians, Patient Interest Groups, the pharmaceutical industry and the SMC Patient and Public Involvement Group (PAPIG). They agreed on the definition that SMC would use for End of Life (EoL) medicines and agreed that the brief given in relation to medicines for very rare conditions should encompass both orphan and ultra-orphan medicines<sup>6</sup>. Although the modifier denomination has been available since 2007, the use of modifiers have become more common only after 2012, precisely after the establishment of these common definitions.

Where initial deliberations suggest that the cost-effectiveness profile of a medicine means that it will not be accepted for use then a company may offer a PAS. A PAS is an agreement between a pharmaceutical company and NHS Scotland. It enables the company to reduce the value of the ICER through various means. The 2009 Pharmaceutical Price Regulation Scheme agreement lists the alternative methods for achieving this, grouped into financially and outcome based schemes<sup>7</sup>. The most common solution is to reduce the price paid by the NHS relative to list price for all or some of the medicines supplied. Although the 2009 PPRS explicitly discusses PAS in the context of NICE, it is a UK agreement and NHS Scotland has agreed an increasing number of those schemes per year since then.

**PACE** groups are a recent innovation, introduced in May 2014. They have been introduced to deal with medicines for end of life or orphan/ultra orphan conditions, in particular when considerations beyond cost-effectiveness might be relevant<sup>8</sup>. Eligible medicines are still evaluated by the New Drugs Committee (NDC) in the usual way. If they are not recommended, or accepted with restrictions, the pharmaceutical company that produces the medicine can ask for a PACE meeting. Membership of the group

<sup>6</sup> Assessment of medicines for end of life care and very rare conditions (orphan and ultra-orphan medicines) in Scotland, Report for the Cabinet Secretary for Health and Wellbeing, 20 December 2013.

<sup>7</sup> Department of Health, *The Pharmaceutical Price Regulation Scheme 2009* (2008), p15-16

<sup>8</sup> [http://www.scottishmedicines.org.uk/files/PACE/PACE\\_factsheet\\_FINAL\\_2.pdf](http://www.scottishmedicines.org.uk/files/PACE/PACE_factsheet_FINAL_2.pdf) (accessed September 2015)

comes from the following: expert advisers representing the patient and carer voice (nominated by Scottish Cancer Coalition, Rare Diseases UK or Genetic Alliance – up to three representatives per meeting); clinical expert advisers (nominated by clinical networks - up to three representatives per meeting); SMC Patient and Public Involvement Group member; SMC Public Involvement Team member; SMC New Drugs Committee member. The aim of this group is to provide additional patient and expert perspective to be considered by the NDC when assessing a medicine. This input includes explanation about how a medicine will be used in clinical practice, which may be different to the clinical evidence supplied, and the perceived value of the treatment from the perspective of key stakeholders. This group can make recommendations on the most appropriate use of the medicines in the Scottish NHS but this is not binding.

## Method

An excel spreadsheet was supplied by Pfizer Limited with data extracted for SMC decisions since March 2002. This was adapted by OHE into a datasheet with 26 variables capturing various characteristics about the medicine under consideration, the process followed, considerations made, and the outcome. All data in the original spreadsheet was validated using original source documentation. The additional variables were populated for the time period covered by the analysis and the data validated. A full list of the variables can be found in appendix A. The decision advice documents (DAD's), published in the SMC website, were used to elicit data. These describe process followed; clinical, cost effectiveness and other evidence considered; deliberations made; evidence provided by experts, patients and other consulted; and budget impact.

We did not attempt to identify the “decision ICER” representing the ICER that, given the published evidence, was deemed as the most plausible by the decision making committee. This can be a significant task<sup>9</sup> and was beyond the remit of this report. We have, however, looked at ICERs and cost-effectiveness considerations associated with decisions in five cases where PACE strongly recommended use of a medicines but SMC reached a decision not to recommend use.

Where annual data was presented, we converted it for the 12 months to September. This enabled us to show annual trends to September 2015 since PACE has been available since October 2014.

Because the focus was on the impact of recent use of the new processes and methods, we only considered data from the last six years (back to October 2009). This provides sufficient context to understand recent trends without too much historic data.

Some results are presented for all decisions, which include all types of SMC advice including those related to abbreviated and non-submissions. Most charts and tables

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<sup>9</sup> See for example Dakin. H, **Devlin N, Feng Y, Rice N, O’Neill P, Rice N** (2015) The Influence of Cost-Effectiveness and Other Factors on Nice Decisions, *Health Economics* 24:1256-1271

present trends for full submissions and re-submissions only since for those manufacturers are required to submit an economic model. They have to demonstrate that the medicine will either "provide additional health benefits that are valued by patients compared to current Scottish practice and that this is at a net cost to the NHS that offers acceptable value in relation to other uses of the same resources,"<sup>10</sup> or "offers equivalent levels of health benefit to patients at an equivalent or lower net cost to the NHS"<sup>11</sup>. For some issues we have presented trends in decisions for cancer medicines. This is both because cancer medicines are the most frequently assessed class of medicines since 2009. Their nature also means that they frequently have modifiers applied, PAS schemes used, and many instances of PACE being requested.

For the time period under consideration there were 370 full submissions and resubmissions.

This dataset was then used to produce descriptive statistics. It was beyond the scope of the exercise to apply econometric analysis to this dataset. Therefore we were not able to ascertain causality between the introduction of a policy and the decision outcomes following that.

## Results

The SMC decisions made since October 2009 are summarised in several descriptive charts to show if there are changes which could be related to the introduction of PACE and modifiers. Firstly, we analyse the trends according to the result of the decision: accepted, restricted, or not recommended. Given the relative importance of the submissions of cancer medicines, we present some trends for cancer medicines and its relationship to PACE decisions. Secondly, we analyse the trends in submissions for which there is a PAS agreement. Thirdly, we describe the trends in the use of modifiers since 2011/12.

And finally, we show whether the type of economic model is related to the decision outcome or not.

### Overall trends in SMC decisions

In the six year period from October 2009 to September 2015, the SMC received a total of 587 submissions for evaluation, of which 370 were full submissions or resubmissions. The number of annual full submissions/resubmissions ranges between 55 to 65, from 2009/10 to 2013/14, and increases to 85 during the last period 2014/15 (from October 2014 to September 2015).

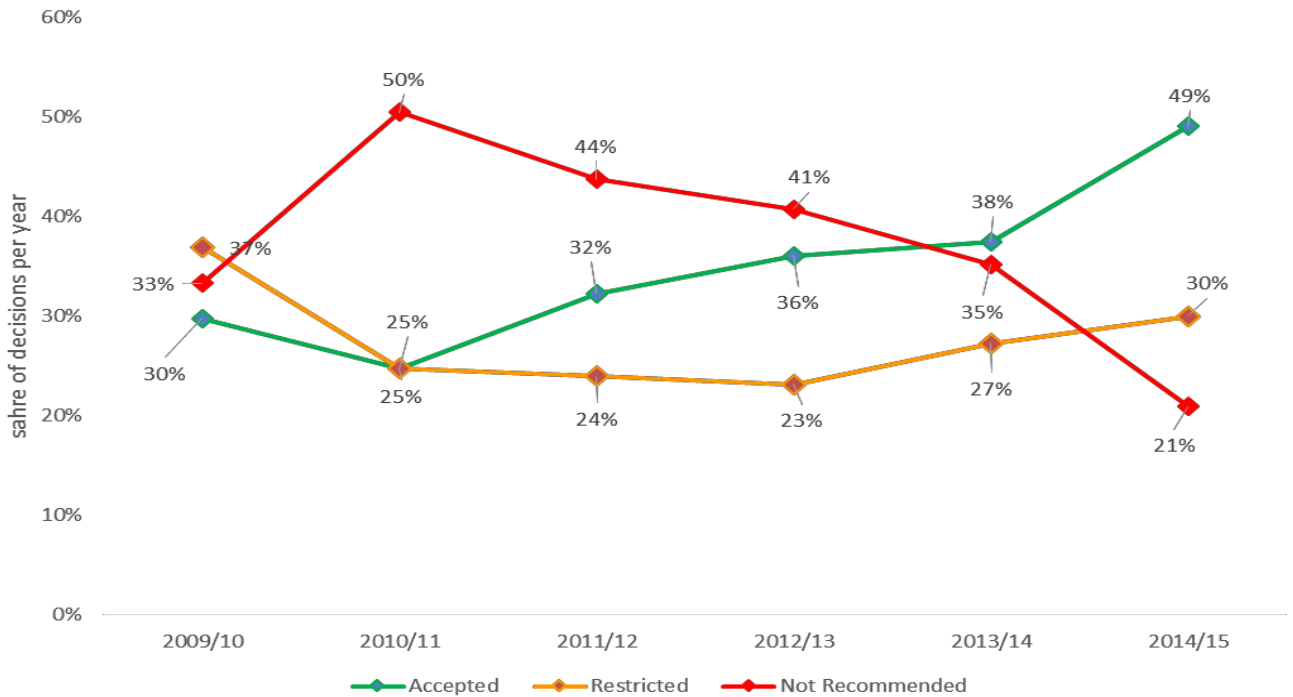
*Figure 1* plots trends in decisions for all SMC decisions. It shows a steady increase in the share of accepted for use decisions over the period from a low of 25% in 2010/11 to 49% in 2014/15. There is also a matching decrease in not recommended decisions

<sup>10</sup> Scottish Medicines Consortium (2014) Working with SMC – A Guide for Manufacturers [https://www.scottishmedicines.org.uk/files/submissionprocess/Working\\_with\\_SMC\\_July\\_2014.pdf](https://www.scottishmedicines.org.uk/files/submissionprocess/Working_with_SMC_July_2014.pdf)

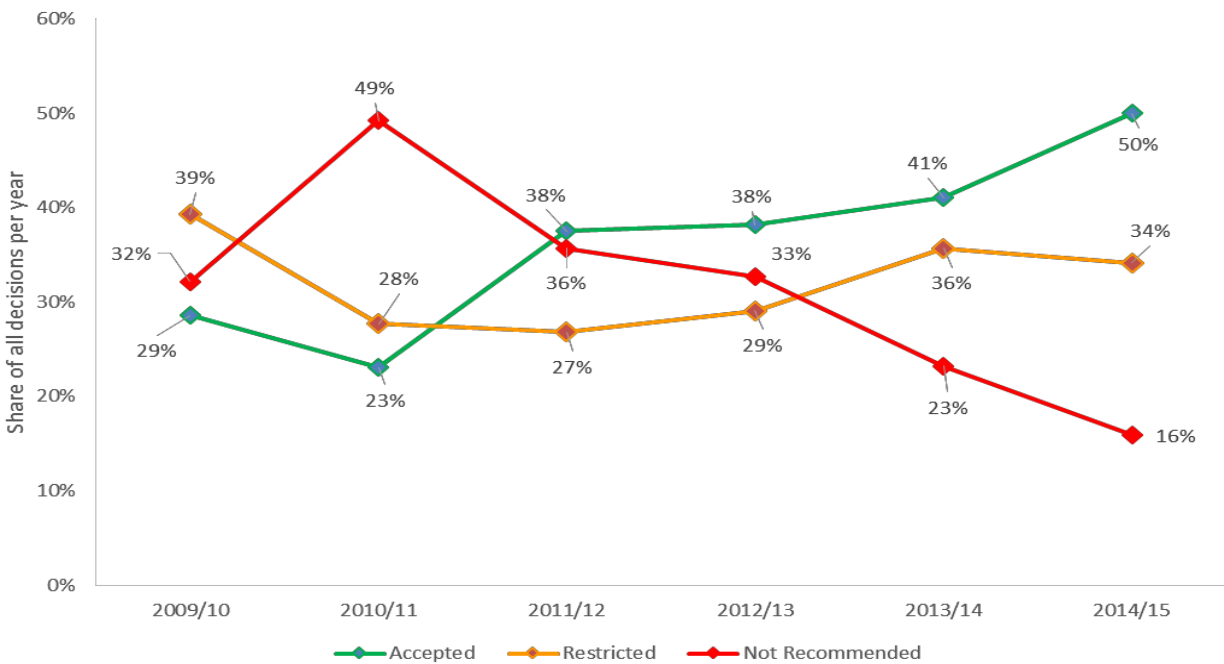
<sup>11</sup> Scottish Medicines Consortium (2014) *ibid*

down from 50% in 2010/11 to 21% in 2014/15 *Figure 2* shows a similar steady increase in acceptance rate from the lowest 23% in 2010/11 to a 50% in 2014/15. The highest rejection rate of 49% occurs in 2010/11 (32 not recommended decisions, of which 9 are for cancer medicines) and decreases to 16% in 2014/2015.

*Figure 1. Trends in SMC decisions - all decisions*



*Figure 2. Trends in SMC decisions - Full submissions and resubmissions*

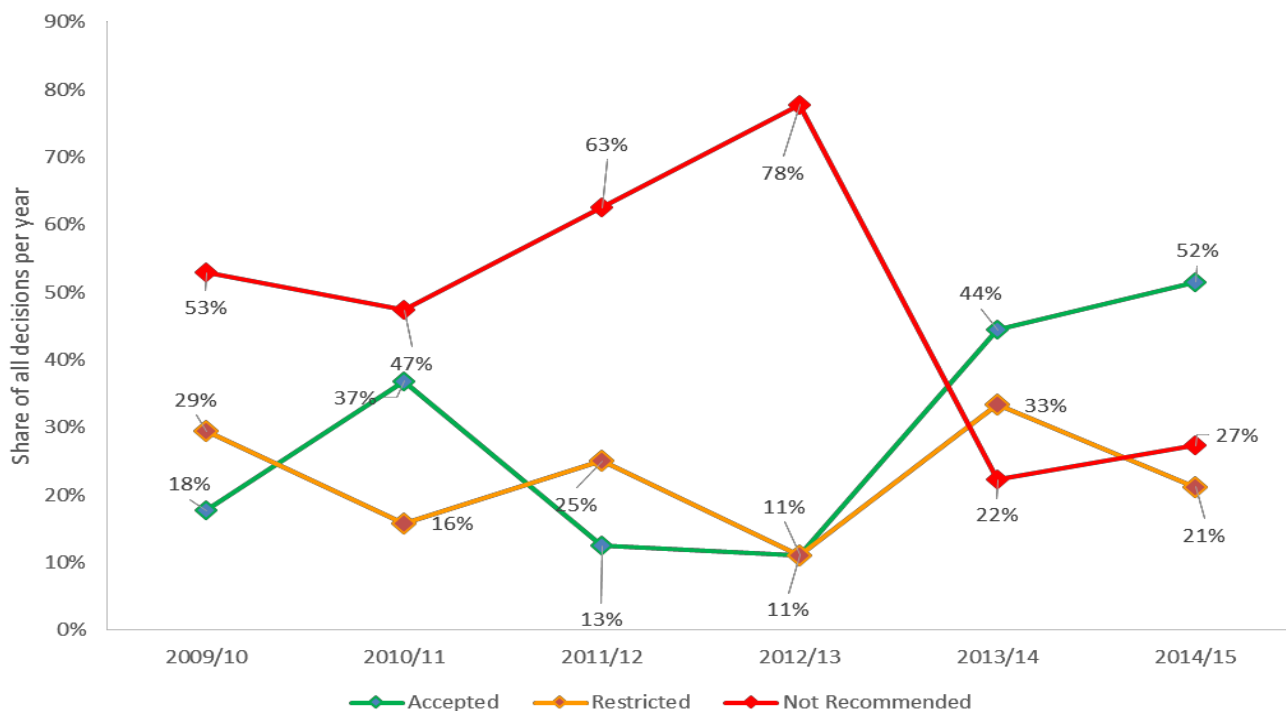


Nonetheless, the decisions on cancer medicines, which amount 112 decisions, cannot explain the overall trend. As shown in *Figure 3*, the rate of not recommended decisions



are greater in general for cancer medicines, especially during 2012/13 with a peak of 78% (7 medicines not recommended out of 9).

Figure 3. Trends in SMC decisions - Full submissions and resubmissions (Cancer Medicines)



**PACE**

The overall upward trend in acceptance is more pronounced between 2013-2014 and the last period 2014/15, coinciding with the introduction of PACE groups in October 2014 decisions. Figure 4 and Figure 5 confirm this increase in acceptance rate since the introduction of PACE up to a 50% from a prior five year average of 33%. The rate of not recommended medicines decreases from a 35% to a 16% given an almost stationary trend in the rate of restricted decisions.

Figure 4. Trends in all SMC decisions since introduction of PACE

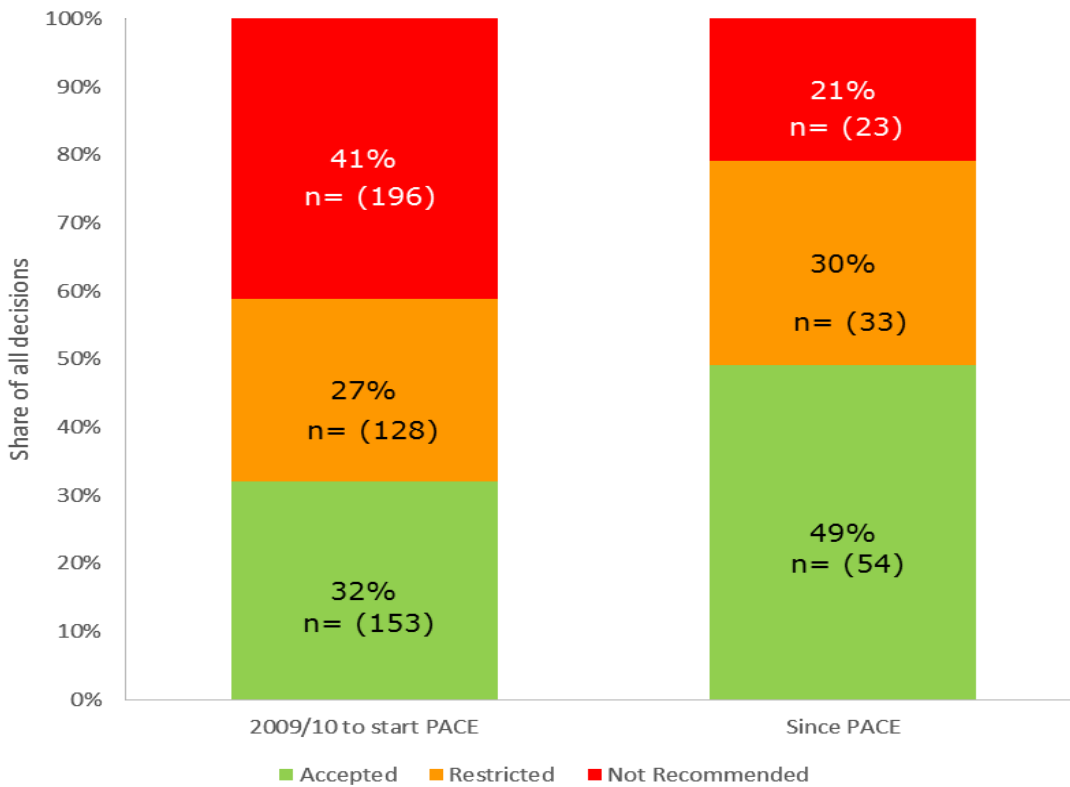
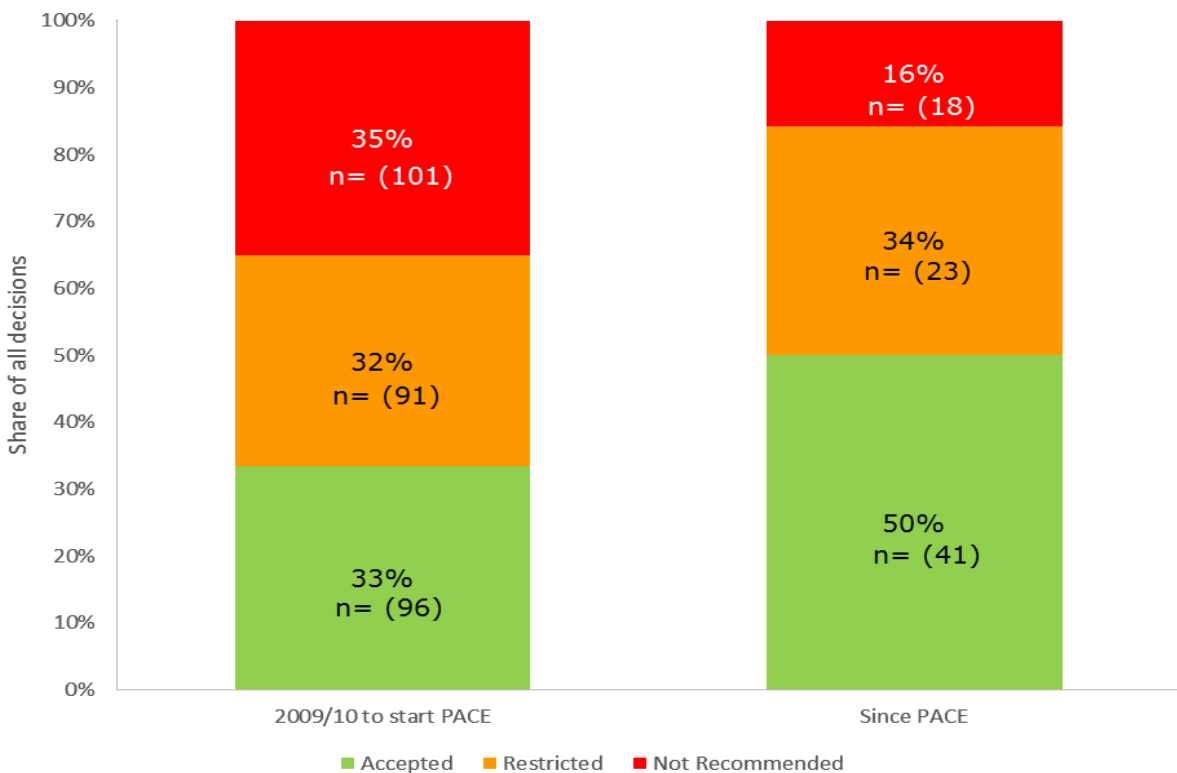


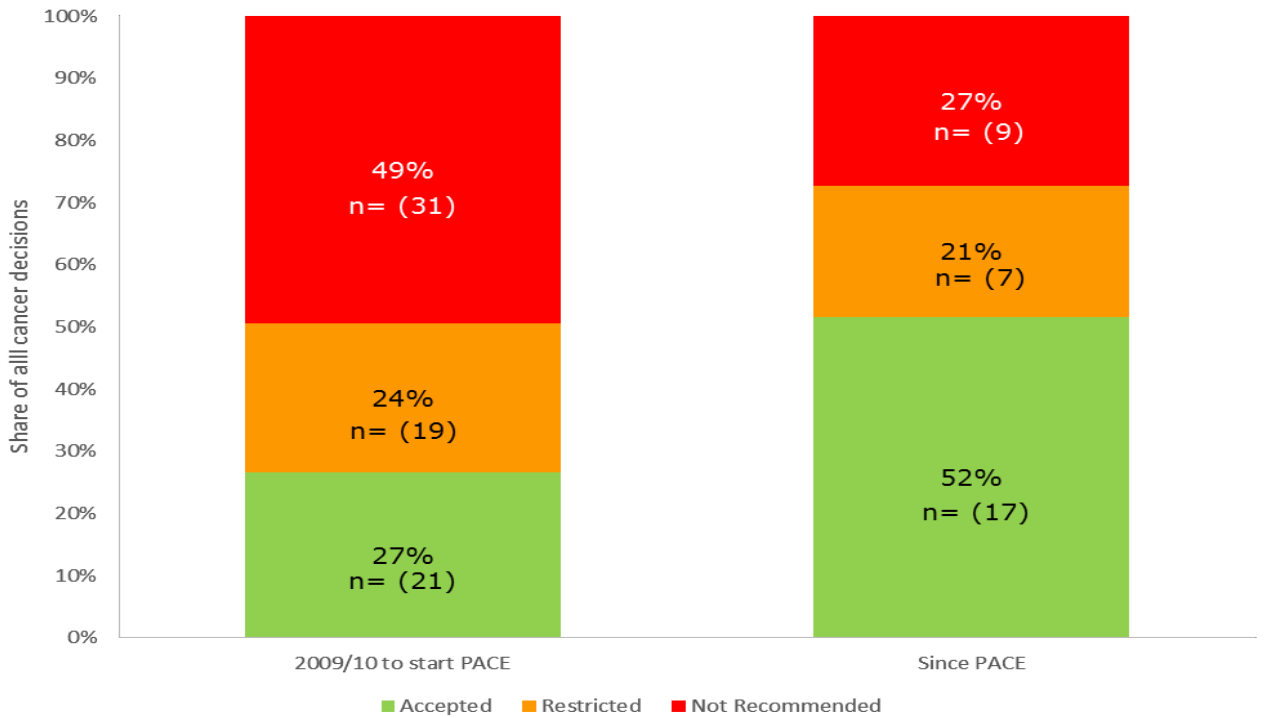
Figure 5. Trends SMC decisions since introduction of PACE (full submissions and resubmissions)



As shown in Figure 6, this upward trend in acceptance since the adoption of PACE is even more significant for cancer medicines, which represent a 40% of total full and resubmissions in 2014/15 versus 27% for the prior five year period (*Figure 7*).

*Figure 6. Trends SMC Cancer decisions since introduction of PACE*

*(full submissions and resubmissions)*



*Figure 7. Cancer medicines as a share of all full and resubmissions since introduction of PACE (full and resubmissions)*

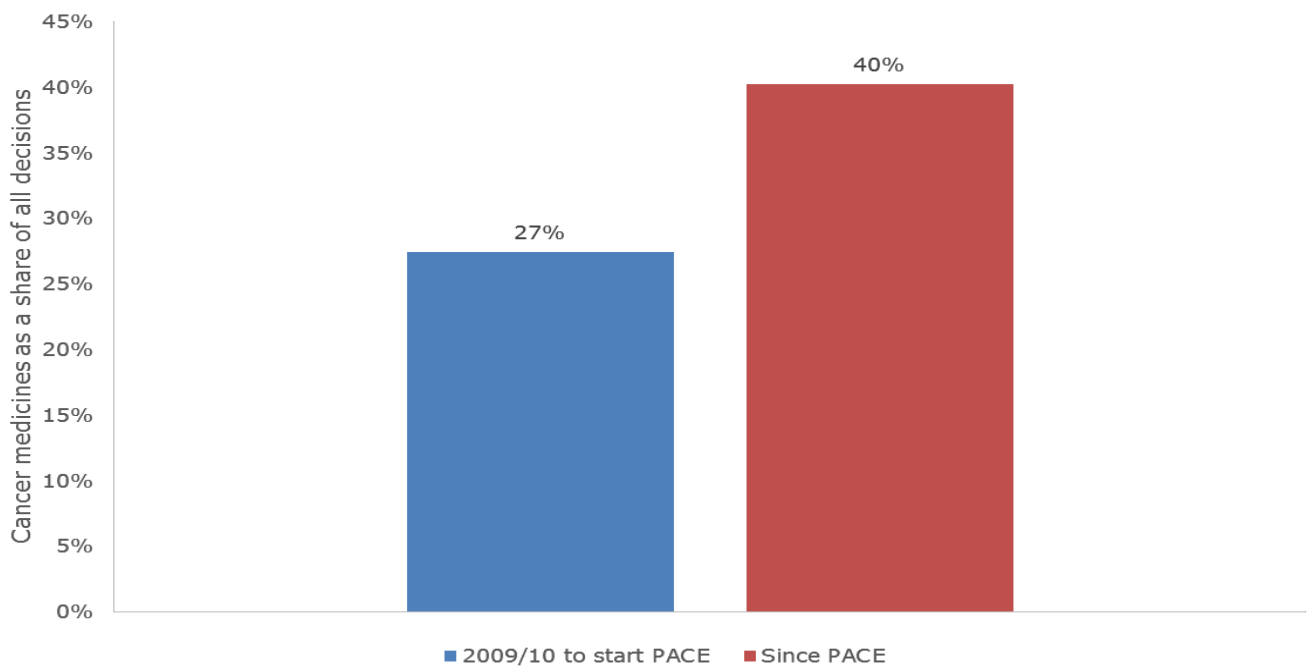
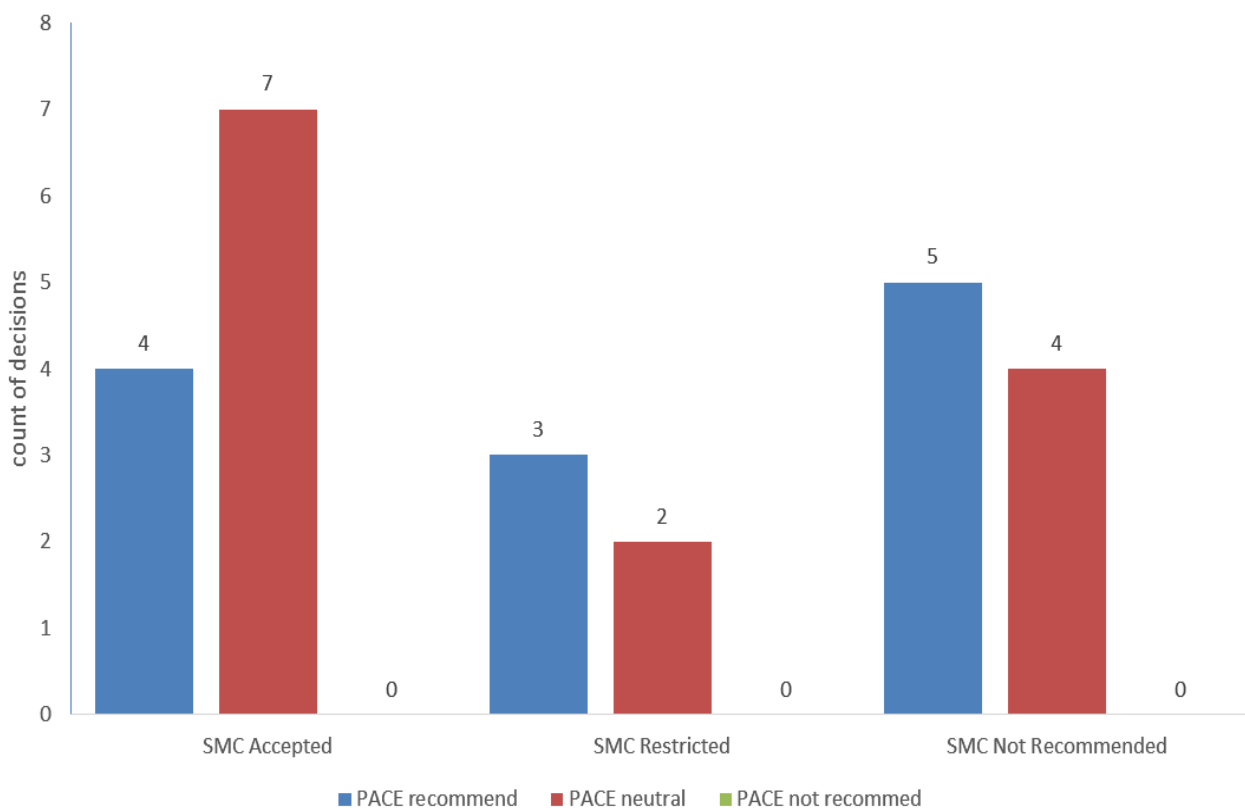


Figure 8 shows the distribution of PACE decisions versus the SMC decision outcome for cancer medicines. From a total of 33 cancer decisions in 2104/15, 25 decisions have been advised by PACE groups and 12 of them have been supported or recommended to the SMC for reimbursement, with no instances of the group not recommending use. However, the SMC did not always follow the recommendation of PACE groups, which are based on social burden of the disease rather than the cost-effectiveness ratio submitted by the manufacturer. Since the ICER ratio considered by the SMC was above the acceptable range of cost-effectiveness, five cancer medicines supported by PACE groups have received a negative decision by the SMC. Two of these five medicines showed an ICER over £100,000, one resulted in an ICER around £50,000, and the other two did not demonstrate the economic case. For the case of 4 cancer medicines with a neutral PACE but a negative SMC decision, the ICER was above £49,000. This compares with an estimated ICER for SMC of £30,000

Figure 8. PACE recommendation and SMC decision (cancer medicines)



### Trends in PAS agreements

As mentioned, PAS agreements have increasingly been offered by companies and accepted by NHS Scotland since 2009 (Figure 9 and Figure 10). Specifically, 31 decisions, out of the total 82 decisions, were agreed under a PAS in 2014/15 which averages an annual increase of five/six decisions over a five year period from the initial 4 PAS agreements in 2009/10. Figure 11 plots trends as a share of all decisions and shows the increasing trend to make use of PAS schemes since the 2009 PPRS. Although

the PPRS agreement provides scope for a number of types of arrangements all PAS agreements are discount schemes.

Figure 9. Number of PAS and no PAS for all decisions

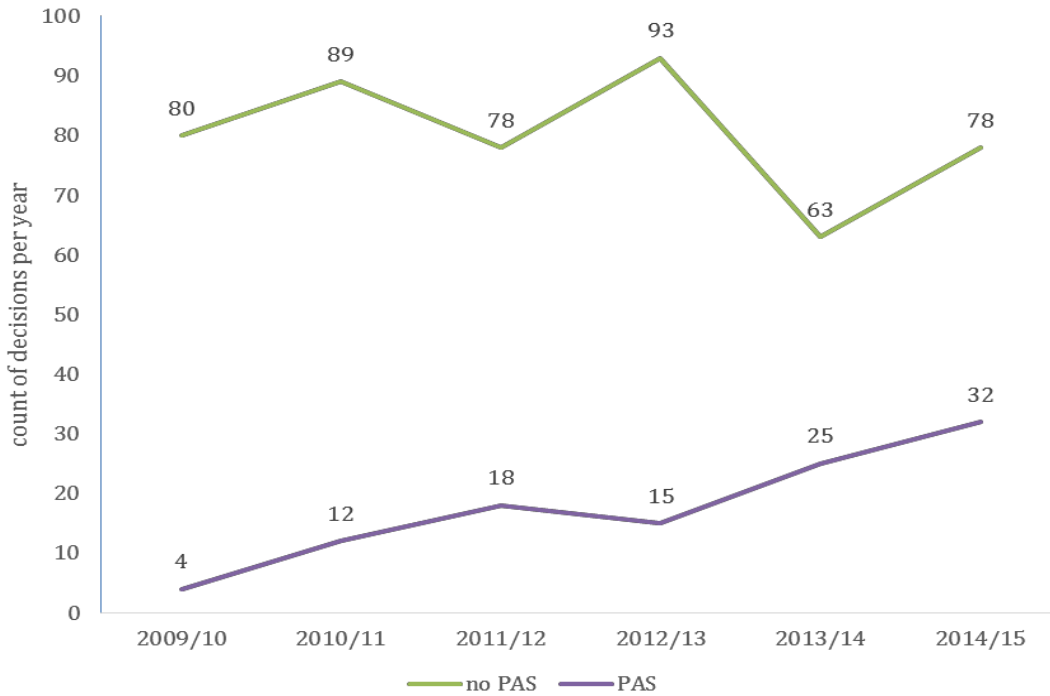


Figure 10. PAS and no PAS, count of decisions (full and resubmissions)

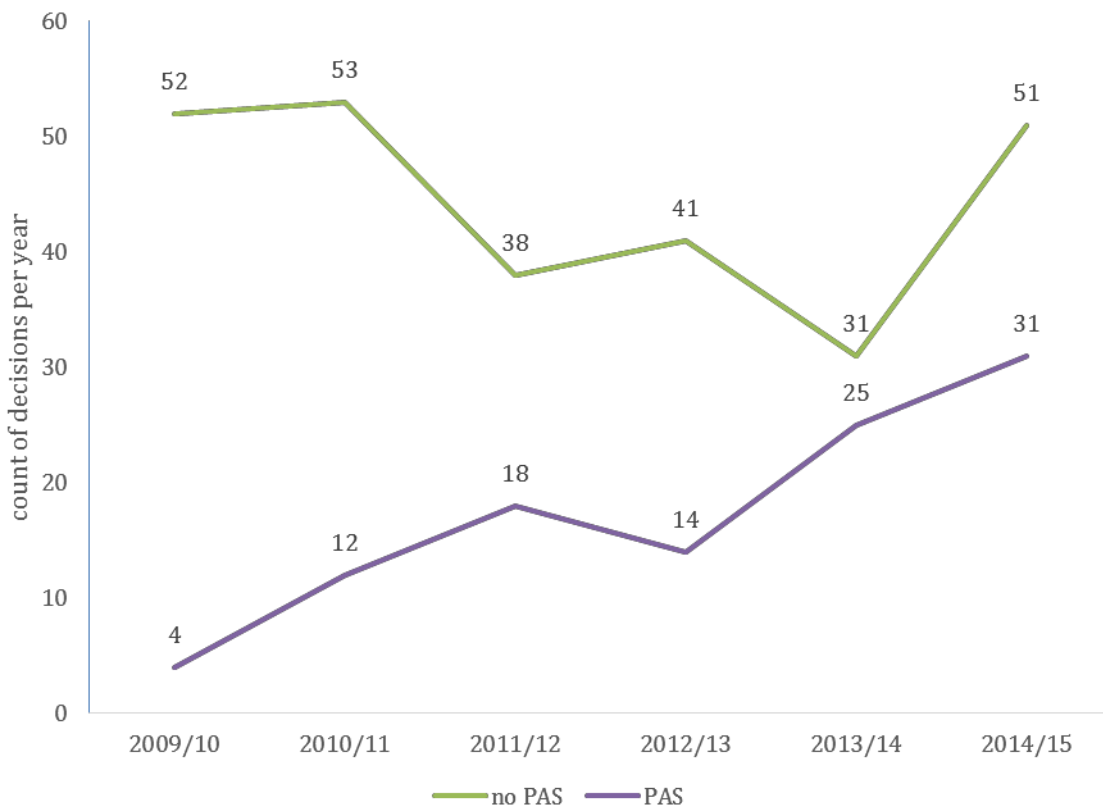
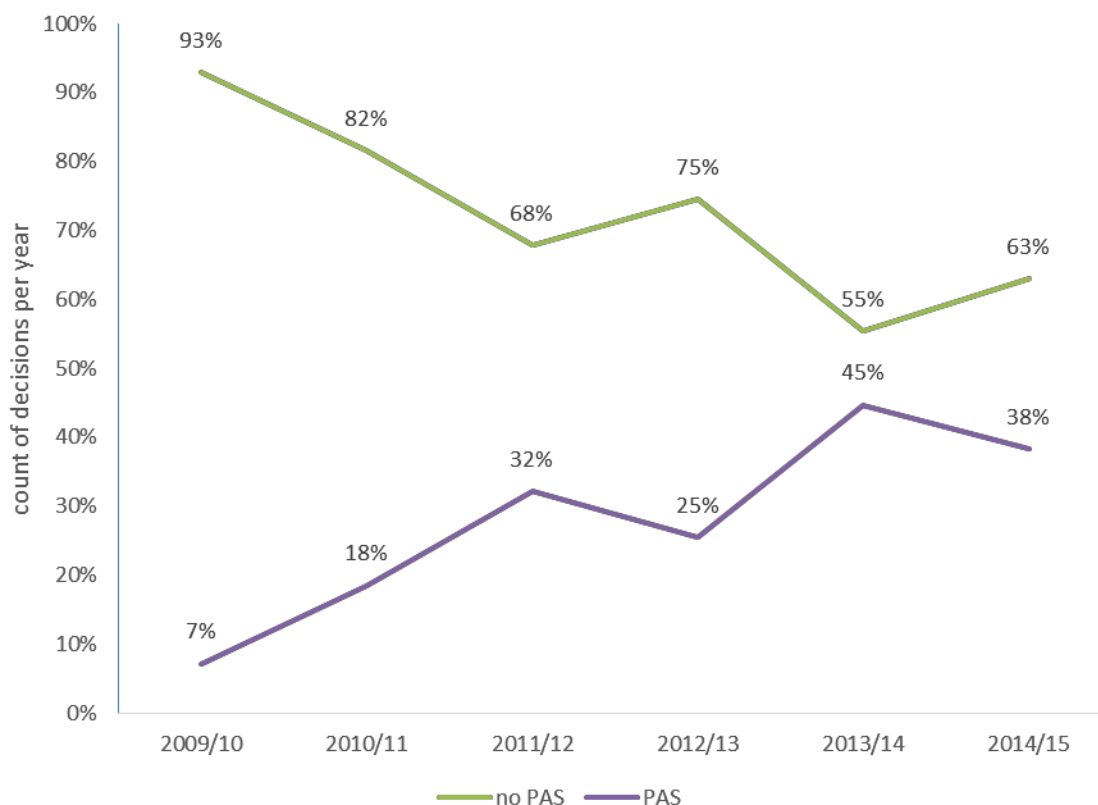
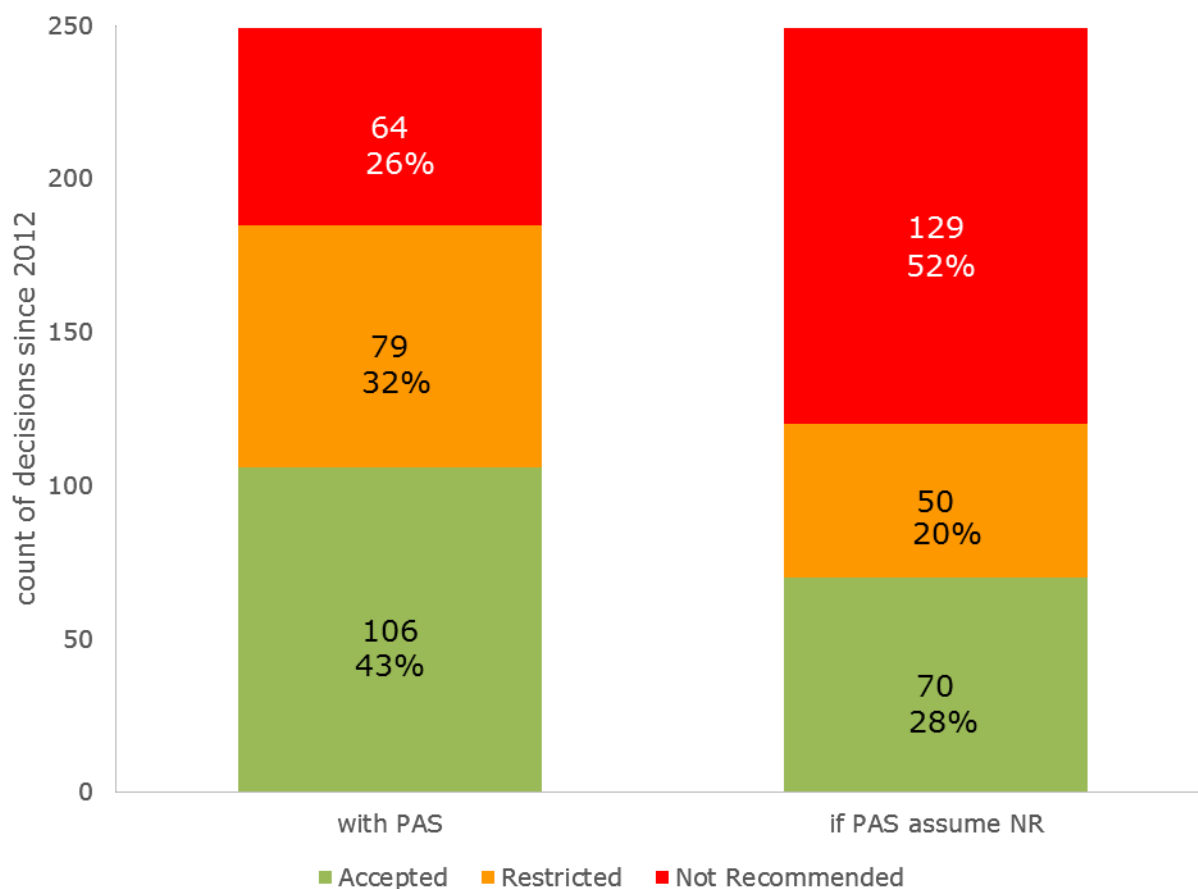


Figure 11. PAS and no PAS, share of decisions (full and resubmissions)



Since the PAS agreement improves the chances of accepted and restricted decisions by improving the economic case it is reasonable to assume that without a PAS in place the decision reached would be to not recommend use of the medicine. Figure 12 shows the decision outcome patterns if we replaced all medicine approved with a PAS were rejected. The second bar in this figure represents this hypothetical scenario to measure the impact of the PAS agreement by comparison with the actual decisions represented by the first bar. There have been 249 decisions in four years, since October 2011, of which 88 have followed a PAS agreement. The first bar of Figure 12 show that around a quarter of decisions were not recommended, and of those 88 decisions with PAS, there are 29 not recommended. But in the hypothetical scenario where all the 88 decisions with PAS are not recommended, the second bar shows the impact of PAS on the distribution of decisions; in the absence of PAS, in just over half of cases the decision reached would be to not recommend use.

Figure 12. For decisions since October 2011 if a PAS then assume not recommended (NR)- change in trends (full and resubmissions)



### Use of modifiers

Modifier characteristics have not been very common in submissions before 2012/13, but they have been introduced to support the case of many full submissions in 2014/15 with 33 submissions using modifiers out of a total of 82 full submissions. As Figure 13 and Figure 14 show, the most common modifier is the "End of life medicine", either on its own or in combination with orphan/ultra-orphan status. Most of the modifiers are used for cancer medicines. In 2014/15, of a total of 33 full submission with modifiers, 29 are for cancer medicines, and most of the full submissions using modifiers are accompanied of PACE group's advice (29 full submissions out of 33).

Figure 13. Use of modifiers by year (full and resubmissions)

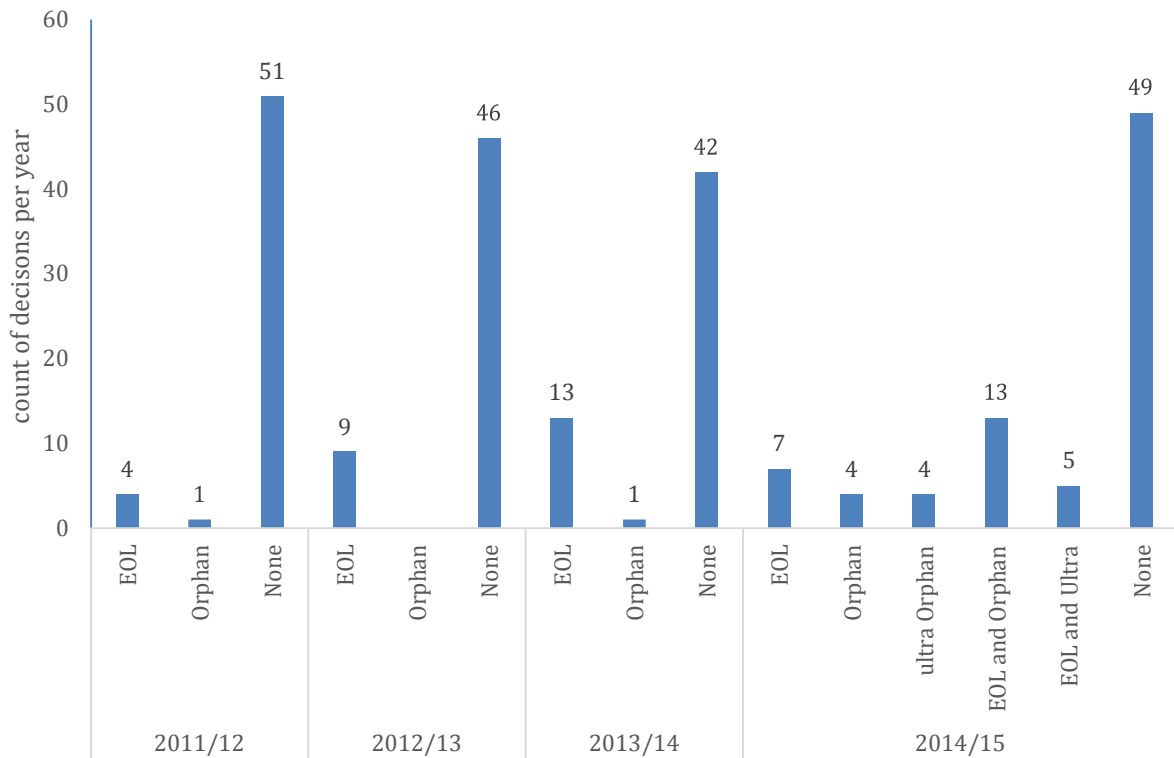
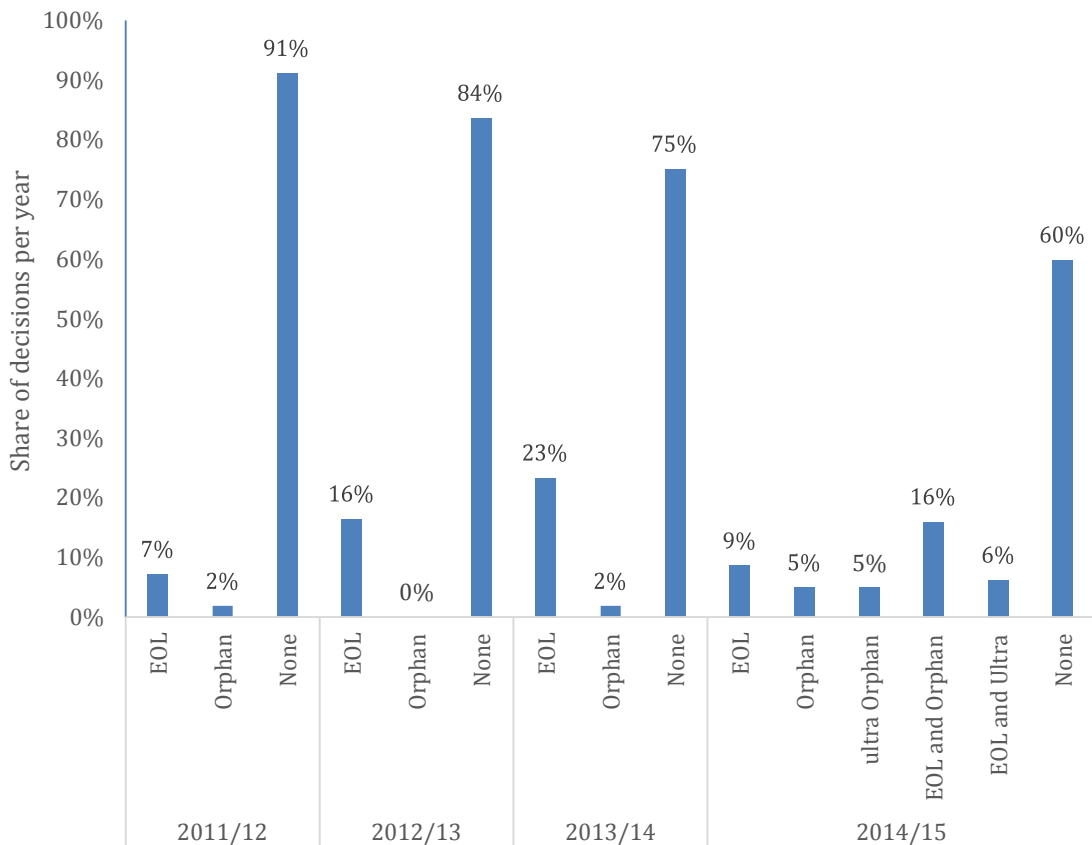


Figure 14. Use of modifiers by year (full and resubmissions)





As the use of modifiers has increased it is also the case that medicines that are assessed using modifiers have been more likely to receive a positive appraisal. Figure 15 shows this trend where among the few instances of the use of modifiers in 2010/11 none led to a medicines being accepted. By 2014/15 10 out of 33 medicines were not recommended following application of modifiers. This trend is clearer when looking at share of decisions (Figure 16) where accepted and restricted decisions increased from a share of 20% in 2010/11 to 70% in 2014/15.

Figure 15. Use of modifiers by count of decision outcome by year

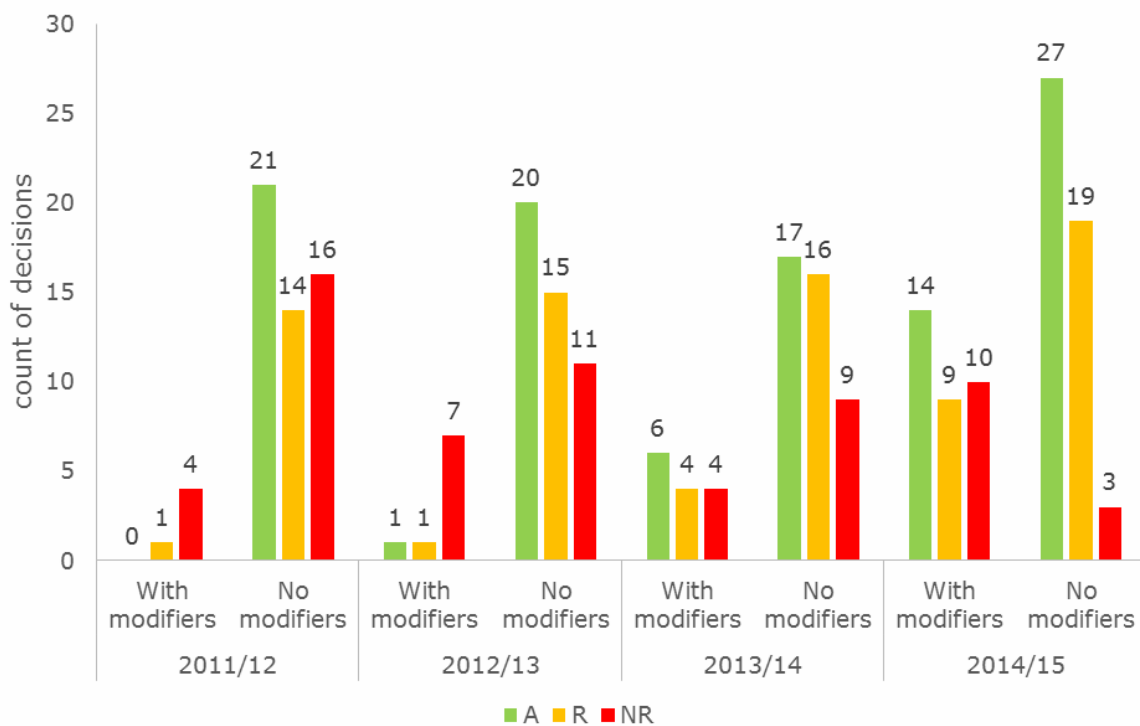
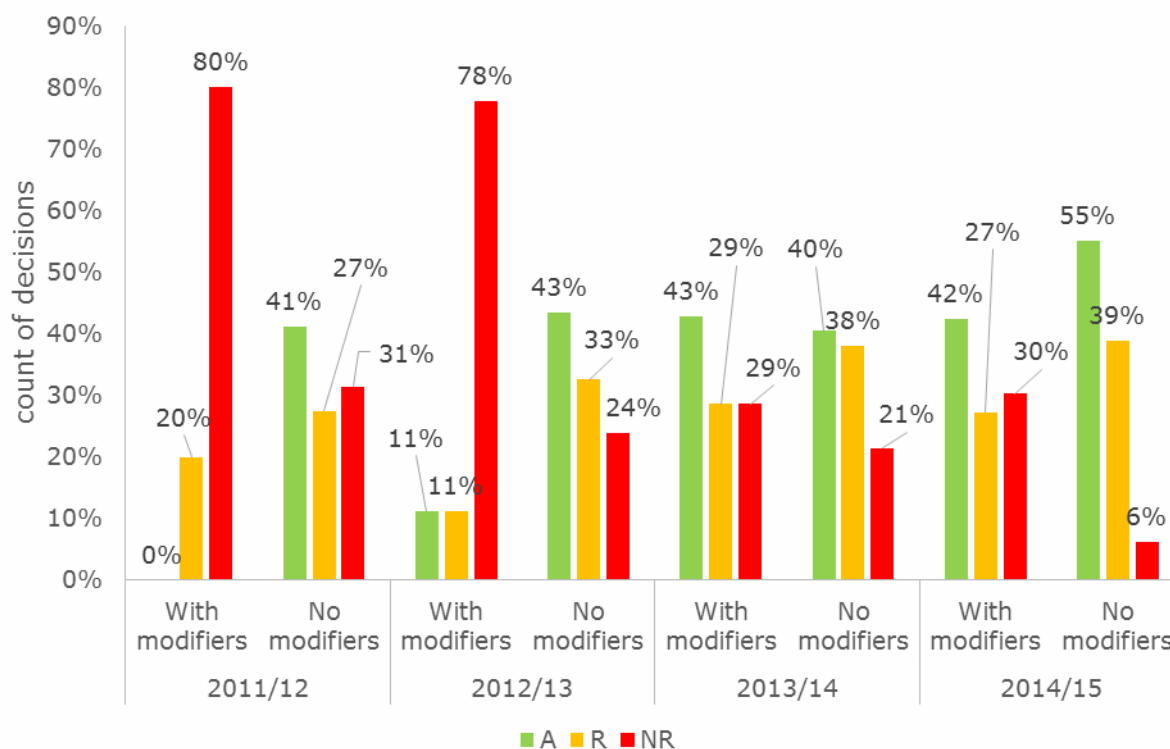


Figure 16. Use of modifiers by share of decision outcome by year



### Economic model used

Taking into account the 284 decisions made on full submissions since 2009/10, as represented in Figure 17 and Figure 18, the majority of them (178 full submissions) presented the economic case under a cost utility analysis, with the estimation of the cost-effectiveness ratio (ICER) for the base case analysis and also the analysis of uncertainty through sensitivity and/or scenario analysis. Cost minimisation analysis was presented in 84 full submissions, 8 full submission were strongly supported by both cost utility and cost minimisation analysis, and 14 decisions were made for full submission lacking an economic analysis. The rejections of all submissions lacking economic model, shows the importance of the cost effectiveness criteria in SMC decisions. Moreover, not recommended decisions, are more frequent relatively for cost utility models than for cost minimisation models. This is expected since a model of cost minimisation is allowed when the clinical effectiveness is already demonstrated as equivalent or dominant to comparators and the economic case only requires to demonstrate cost savings. Nonetheless, the SMC decided not to recommend 13 medicines where the model presented was only cost minimisation due to weakness of the clinical or economic case, based on comparators.

Figure 17. Decision outcome by economic modelling type, full submissions, since October 2009

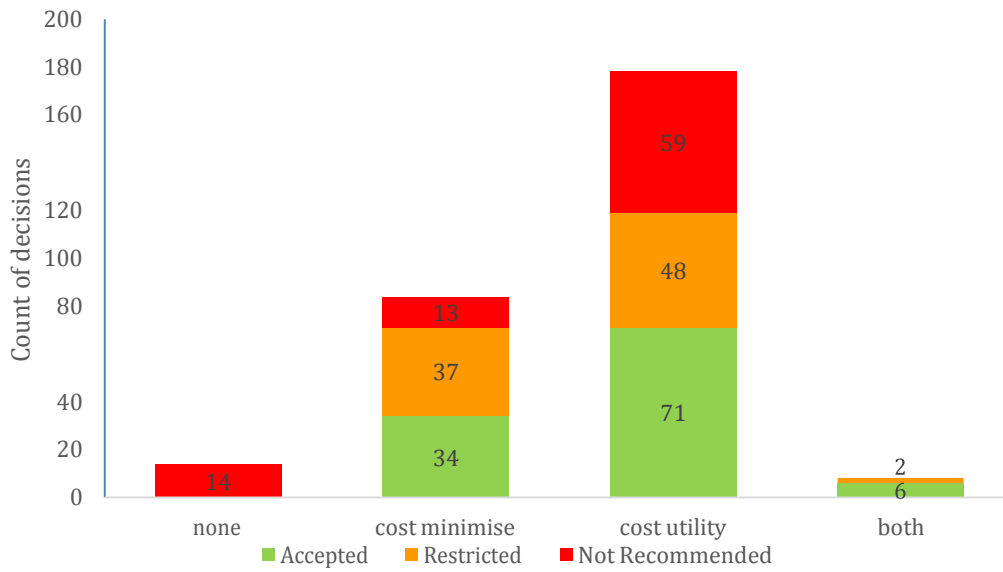
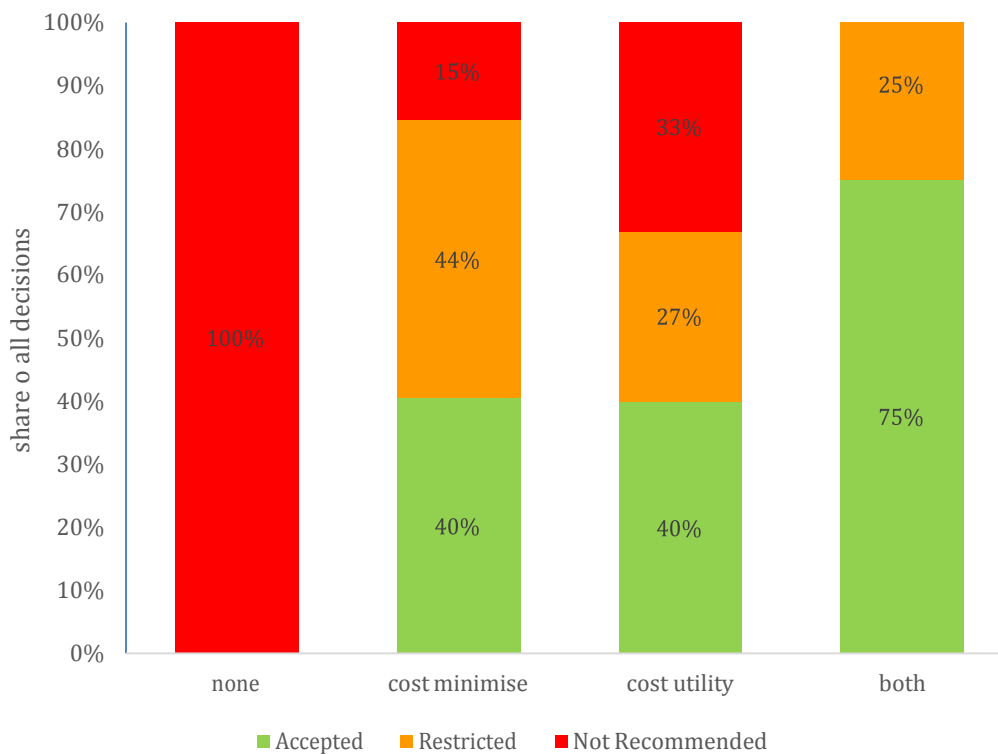


Figure 18. Decision outcome by economic modelling type - Full submissions since October 2009



## Conclusions

The evolution of SMC decisions during the last six years show an overall improvement in the access to new medicines, with a steady increase in the rate of submissions accepted versus a decrease in those not recommended.

The steady increase in the use of PAS agreements has facilitated greater flexibility for assessing the economic case for new medicines. This appears to contribute to the positive effect of the rate of accepted decisions.

The impact of the introduction of PACE groups has been more equivocal. There are clearly instances where the group's strong recommendations have been outweighed by other considerations. At present there is limited evidence, as PACE has only been in existence for a year. However, it would be interesting to see if a trend is established relating cost effectiveness evidence, including the ICER used in each decision, and the PACE group's recommendation.

Modifiers also appear to be associated with this trend of increasing numbers of accepted for use decisions.

It is beyond the scope of this report to suggest more than association between evolution of the processes for assessing medicines and the increase in the share of positive decisions. It would be interesting to undertake further study to assess these factors in the context of other clinical and economic considerations, notably the decision ICER.

## Appendix A – List of variables in the dataset

Variable	Brief description
<b>Number</b>	SMC guidance ID number
<b>Medicine</b>	INN name for the medicine
<b>Indication</b>	Indication under review
<b>BNF category</b>	Broad BNF category
<b>Company</b>	Company supplying evidence
<b>year</b>	Year guidance published
<b>Date</b>	Date guidance published
<b>Year9to9</b>	Year to September
<b>Type</b>	Guidance type (Full submission, Resubmission, Non Submission, Abbreviated Submission)
<b>Recommendation</b>	Decision reached by SMC (Accepted for use, Accepted for restricted use, not recommended for use)
<b>Economic Model</b>	Type of economic model used (Cost utility, Cost minimisation, both types)
<b>Model</b>	Code to identify model (CM=1, CU=2, CU+CM=3, No/missing=0)
<b>Comment re QALY</b>	SMC assessment of the quality of the cost effectiveness evidence supplied
<b>Budget Impact 1yr</b>	Manufacturer estimated cost of implementation for Scotland in the first year of use
<b>Budget Impact 5yr</b>	Manufacturer estimated cost of implementation for Scotland in year five of use
<b>Comment on Comparator</b>	Comparators for the treatment discussed by SMC
<b>Clinical Expert Reference</b>	Reported clinical expert clarification of the potential use of the medicine in NHS Scotland context
<b>PAS</b>	Whether a PAS was offered by the sponsor company
<b>PAS code</b>	Whether PAS offered (1 yes)
<b>PAPIG submission</b>	Which patient and public interest groups supplied statements or evidence
<b>Orphan Status</b>	Whether the medicine was considered to achieve orphan (2,500 per 5,000,000 population) or ultra-orphan (1 in 50,000 population)
<b>Modifiers</b>	Whether and which modifiers were identified
<b>modifer code</b>	1 = EOL, 2 = orphan, 3 = ultra-orphan, 4 = EOL and orphan, 5 = EOL and ultra-orphan
<b>PACE</b>	Whether PACE was requested (1 = yes)
<b>PACE recommendation</b>	recommend, not recommend, neutral (i.e. simply a description)
<b>Since PACE (1 yes)</b>	Dummy variable used to identify decisions since the introduction of PACE