Dear Mr Cochrane

Thank you for your email of 30th April 2008 following the participation of the Scottish Medicines Consortium in the oral evidence session on the afternoon of 29th April.

I am very glad the Public Petitions Committee found our evidence useful in understanding the difficult issues around priority setting for cancer and indeed other medicines. I note the Committee’s additional questions which I will endeavour to answer below.

1. **NHS QIS recommends NICE guidelines to NHS Scotland. Why can SMC not do this given it undertakes an initial clinical assessment?**

NICE Multiple Technology Assessments (MTA) cover various treatment options for particular clinical diagnoses, for example, lung cancer or ischaemic heart disease. Some of the treatment options will be drug related but the NICE MTA will also cover other ‘non drug’ interventions such as angioplasty or radiotherapy and also other parallel inputs such as counselling, psychological support services or palliative care. While SMC has the skills to review recommendations related to drug therapy we would lack the expertise to review other issues and it therefore appears more appropriate for NHS QIS, with its wider skills base and remit, to review the whole NICE MTA guideline. NHS QIS may use individual SMC members or members of the SMC’s expert panel to comment on specific drug related issues within NICE assessments. SMC believes this is an appropriate way to handle the output from NICE – separate assessment of the ‘drug’ and ‘non-drug’ components of the advice would be inefficient and could lead to confusion.

2. **Do all NHS Boards have a joint formulary and how important is this?**

I am currently endeavouring to check on the situation with some of the smaller health boards but I can state categorically that the large Health Boards such as Greater Glasgow & Clyde, Lothian, Tayside, Lanarkshire, Ayrshire & Arran, Grampian and Highland certainly all have joint formularies. They are very important in co-ordinating prescribing across primary and secondary care and in providing access for clinicians to prescribing advice and details of approved medicines. There are slight differences in ethos between different formularies, some aiming to cover the majority of prescribing in both primary and secondary care with others opting for a list of ‘preferred’ drugs which the formulary management
group would regard as first or second choice in individual therapeutic areas. This difference in formulary ethos may account for different decisions as to adding drugs to formulary in different areas. I believe the local formulary ethos will be well understood by clinicians working in the local area.

3. **NHS QIS guidance, SMC advice and local formularies are intended to advise clinicians on the most clinical and cost effective treatments. However, ultimately clinicians have the freedom to prescribe what they want. How do you ensure they operate in an atmosphere of clarity and understanding and are not bombarded with too much guidance and advice?**

Area Drug and Therapeutics Committees (ADTCs) act as a conduit for advice to clinicians in both primary and secondary care. This helps to ensure that prescribers are not bombarded within the NHS in Scotland with excessive guidance and advice and possibly even conflicting information. Guideline development groups within the local Health Boards will usually work through their local Drug and Therapeutics Committee to ensure that locally developed guidelines are in line with prevailing ADTC advice which will, of course, itself be in line with SMC and NHS QIS decisions and advice. Prescribers do have other influences on their prescribing including recommendations from specialist societies and the influence of pharmaceutical industry advertising. The NHS has no control over these sources of advice but can at least make sure that the advice from within the NHS itself is focused and consistent.

4. **When will SMC publish its evaluation programme and how will that assist?**

The outcome of the SMC evaluation programme is due for publication in October 2008. In addition to reviewing the work of the SMC it will identify work to improve engagement with stakeholder organisations, develop further financial forecasting on the impact of new drug expenditure and the proposals for effective ongoing evaluation of the uptake of SMC advice.

5. **In terms of data collection, what precise data should be gathered; why; what is needed to put this in place and who needs what to make this happen?**

As I noted at the oral hearing, a project is already underway within the Information Services Division of National Services Scotland to bring together data on drug utilisation. This is going well in primary care, but at the present time within the secondary care setting data collection is limited and therefore the prospects for data analysis are poor. The key step forward in secondary care will be the introduction of a hospital electronic prescribing and medicines administration (HEPMA) system. This is currently in the throes of a procurement process and hopefully we will begin to see it rolling out across Scotland in the next three to five years. This will allow data on drug use to be linked to patient diagnosis and outcomes in secondary care and clearly will be of considerable benefit in monitoring the use, benefits and even side-effects of cancer chemotherapies and other interventions. SMC has representation on the steering group for this project and look forward to it moving forward soon.
In discussion with the committee a desire was expressed to learn more of the practicalities of the health economics analysis which the Scottish Medicines Consortium uses and in particular the use of the quality adjusted life year (QALY) approach. As we emphasised, this is an approach which is used internationally by bodies similar to SMC including NICE and, for example, in Canada and Australia.

For the Committee’s interest I have attached two briefing notes prepared by Dr Andrew Walker, used for briefing new members of the Scottish Medicines Consortium and its New Drugs Committee. The documents aim to explain, in an informal style, the reasons for QALY-type approach and how this is undertaken and analysed. I hope Committee members find these interesting and if, having reviewed them, there are any queries raised I would be happy to do my best to answer them either personally or with the help of my health economist colleagues.

Please thank the committee once again for their interest in the work of the Scottish Medicines Consortium.

With kind regards

Yours sincerely

[Signature]

Dr Kenneth R Paterson
Chairman
Economic evaluation – the whys and hows of applying it to new medicines
A Briefing Note for the Scottish Medicines Consortium
Dr. Andrew Walker, University of Glasgow

Why do we need to evaluate things from an economics point-of-view?
In an ideal world the only consideration for a new medicine would be whether it did more good than harm – for example if we knew it caused serious side-effects in 1-in-1,000 people, does it do enough good in the other 999 to make that risk acceptable?

Unfortunately we do not live in that ideal world. The facts are that many service improvements cost more and we do not have enough money to provide every health service to the standard we would ideally like. This means we have to decide which are worth funding and which are not.

New medicines very often involve an additional financial cost and even when we take account of the fact that they might reduce the need for other treatments they usually still cost more money overall. For example, SMC submissions to date show 76% involved a net cost, 8% were cost neutral and 16% were cost saving. (These are predictions by the pharmaceutical manufacturer).

In the last few years the funding available for the NHS has increased rapidly, so surely new services and new medicines should be more affordable? In fact, many primary care trusts in England and NHS boards in Scotland are struggling just to break even. The government has launched many new policy initiatives and these have used up a lot of the growth money so there is very little to spare.

In summary, the case for economic evaluation rests on the observation that there isn’t enough money to do everything we would like so we have to choose.

How do we choose?
There are many possible ways to choose which new medicines should be recommended to the NHS. We could choose the ones with the best clinical evidence, or the ones that saved lives, or we could refuse to fund any new medicine that cost over £5,000 per patient. (We could even prioritise them by listing their names in alphabetical order, but that might lead to an unseemly scramble to register the name “AAA Aardvark pain relief capsules”!)

If you look at each of these ways of choosing (except the last one!) in more detail, a more sensible way starts to emerge. Let’s start with the idea we should not fund some medicines because they are too expensive. That makes no sense because it doesn’t take account of how much good the medicine does. Supposing a pharmaceutical company developed a pill that cured all types of cancer: they could charge a lot for it because it would provide so much benefit. The high cost is justified if the benefit is high as well - in other words, we have to look beyond the purchase price to assess the overall value of
the new product. So we can’t make judgements on the basis of cost alone because it takes no account of what we get for the money.

So should we choose the medicines with the best clinical evidence? That would mean we could be fairly sure it did what was claimed for it, but this would ignore two things:

• first, it doesn’t take account of how much good the medicine does, and
• second, it does not take account of the cost. Just because we are not going to take account of the cost alone does not mean we can ignore it completely!

Suppose we have two medicines, medicine A which is cheap and does a lot of good but only has one clinical trial to support it and medicine B which does a small amount of good, is very expensive but has lots of trials. If we preferred medicine B just because it had more evidence we might not be able to fund medicine A. So we need to take account of the actual benefits the medicine will give us and its cost as well.

Finally, we could always favour medicines that have the potential to save life. But that doesn’t take account of either the cost of the medicine or the quality of life of people when their lives are saved and it also works against any disease that can make you very ill without actually killing you. For example, supposing medicine A gave someone with cancer a 1% chance of cure or medicine B could make a dramatic difference in the quality-of-life of hundreds of people who have severe symptoms just now. Would we always choose medicine A? Saving lives is an important objective of the health service but we have to bear in mind that other factors matter as well.

So where does that leave us?

Working through the above examples reveals that the key factors that have to be weighed up in reaching a judgement are:

(i) how much good will a new medicine do – an assessment of the advantages to patients in terms of living longer and reduced levels of symptoms and illness (better health-related quality of life) compared to the medicines currently used. These also have to be weighed against each other – how important is life-saving compared to quality-of-life enhancements?

(ii) how much harm the new medicine will do – through side-effects (adverse events), will the new medicine cause more symptoms or even (in extreme cases) kill patients? This needs to be quantified and set alongside the benefits.

(iii) how much does the new medicine cost – this should include any costs to identifying the patients who will benefit, the costs of explaining the treatment and any costs to giving the medicine (e.g. if the patient needs an intravenous drip), as well as costs of treating side-effects. The main interest is any costs over-and-above those already being incurred with existing treatments for the same condition.

(iv) any health care resources that are saved as a result of switching to a new treatment. For example, a more effective treatment might prevent a disease from progressing thus
avoiding the need for further treatment. The resources that would have been used are
now free to be used for other patients.

These are the key elements of an economic evaluation. When a new medicine is
available we would look at the costs and benefits from using the current treatment then
ask what difference the new medicine would make under each of the four headings
above: does it do more good? does it do more harm? does it cost more? does it save
resources?

**How do we pull all of these data together?**
Of the four factors above two are essentially about the health of the patient – they either
experience better health when the medicine works or their health is harmed where there
are side-effects. If we could combine these into a single measure we could estimate the
overall impact on health (or the net health gain); this is the main role for the QALY or
quality-adjusted life-year. This is a way of measuring the length of time someone will be
alive, weighted by a factor that reflects their quality-of-life during that time – it is
covered in much more detail in a later briefing note.

The other two factors are about resources and how they are used. There are additional
costs to the medicine and its administration and there might be some resources freed up
as a result of avoiding treatment for more advanced disease as a result so if we work out
the value of these we can estimate the overall additional cost (called the net cost).
Bringing these together we can reduce the four factors down to two the overall (or net)
impact on cost and the overall (or net) impact on health.

If we divide the net cost by the net health gain then we get an idea of the additional cost
of getting one more unit of good health (as measured in QALYs); this is the additional
cost per additional QALY gained (or “cost per QALY” for short). To get the most health
benefit we can from the health budget we should then choose the treatments (including
medicines) with the lowest cost per unit of health gain. Supposing we had a treatment for
diabetes that had a cost per QALY compared to current diabetes treatment of £2,000 and
a treatment for cancer that cost £20,000 per additional QALY compared to existing
cancer treatment. If we had a budget of £100,000 we could either get 50 QALYs from
funding the new diabetes treatment or 5 QALYs from funding the new cancer treatment.
We could then say the new diabetes treatment is more cost-effective than the new cancer
treatment.

**Are QALYs the whole story?**
No. There are several reasons for this:
- first, QALYs are a helpful but by no means perfect measure of health benefit. For
  example, there is no perfect way to judge changes in quality-of-life – that doesn’t
  mean we shouldn’t use them but people who make decisions should understand
  what has gone into the calculations. (This is discussed in more detail in the
  QALY briefing note).
- second, in some cases new medicines have equivalent effectiveness to existing
  treatments but might be cheaper either in terms of the cost of the medicine or
because they are easier to give to patients so save staff time. In this case, so long as we are happy that the new medicine is really as good as what we have now then it makes sense to choose the cheapest.

Note that the second point above is an example of cost-minimisation analysis, which is used when we know the benefits of two treatments are equal. The technique that uses the QALY as its outcome measure is called cost-utility analysis.

What should SMC and NDC members look out for?
On the basis of the analysis so far the things SMC members should bear in mind when reading a submission and economics review are as follows:

- When a manufacturer makes a submission that does not include an economic case the SMC has to decide whether this is justified. The economic view would be that the new medicine will involve additional costs and we do not know what we are going to get for our money; therefore, the economic case for the new medicine has not been proven. A variant on not submitting any economic evidence is when an economic evaluation IS included but it does not cover all the patients who might be eligible under the licence. In that case, from the economics point-of-view, the case for the product can only be supported for that specific patient group. We can’t assume that because a medicine is cost-effective in one group of patients then this will be true of all eligible patients.

- The new medicine has to be compared to the treatment it is most likely to replace. The main thing SMC should be interested in is the additional cost and the additional benefit compared to the way patients are managed at the moment. To take an extreme example, if a new medicine cost £200,000 we might doubt its cost-effectiveness, but we would not think it was so bad if the existing treatment cost £199,950 (or even £300,000!). It is crucial that the thing the new medicine is compared to is carefully chosen, however: one way in which a manufacturer might try to show their product in the best light is by comparing it to a treatment that is expensive and not very effective. So beware!

- The economic analysis might miss out some key costs and benefits. For example, experience suggests side-effects are often not included. Another example is when the submission reports the net cost per life-year saved, thereby missing out any quality-of-life effects.

- There will be times when SMC members in particular want to go against the economics advice to accept a medicine for use when it has either poor quality evidence of cost-effectiveness or has a high cost per QALY. There are grounds for doing this but everyone needs to bear in mind that when they accept something for use in the NHS in these circumstances there is a danger that funds will be directed away from other treatments with proven cost-effectiveness – this is the opportunity cost of the decision. The briefing note on cost per QALY
issues includes a table with health interventions that have a very low cost per QALY.

These are just some of the things members should be thinking about when economics issues are discussed. This has not covered the issue of what level of net cost per QALY gained is acceptable; that is the subject of another briefing note.

**Conclusion**

In summary, costs could be ignored in an ideal world but in the real world we need to take them into account. However, costs alone should not drive the decision: they should be balanced against health benefits, harms and savings. All of these should be compared to the existing treatment for the condition to show the additional costs and benefits of the new medicine. These should then be compared to other uses of the health budget. Economic evaluation is a way to draw all of the evidence relating to these issues into a single framework and guide decision-makers to the most economically efficient option. They are by no means obliged to choose this option, but if they do not they need to bear the opportunity cost in mind i.e. health benefits lost from services that will not now be funded.
QALYs: the measurement and valuation of health benefits
A Briefing Note for the Scottish Medicines Consortium
Dr Andrew Walker, University of Glasgow

Background
The essence of economic evaluation is to compare the costs and benefits of two or more alternative courses of action.

The principles of costing are relatively straightforward, although the practice is very varied. Net costs can be calculated by estimating costs minus future treatment avoided converted into a saving (negative cost). All the resource aspects can thus be captured in a single figure, the net cost of switching from the status quo to the proposed regime.¹

Most clinical trials have an aspect of the management of the disease as their endpoint e.g. reduction in cardiovascular events or reduction in a disease severity score. These suit licensing purposes in that they show the medicine has a statistically significant effect on a meaningful outcome compared to placebo (or another alternative).

The manufacturer of the medicine could simply take the clinical trial data and use this in their economic evaluation, estimating net costs and setting this against the proven difference in the primary outcome.

Sometimes this is enough e.g. when the new medicine is at least as beneficial and is cheaper. However, the SMC is usually trying to judge whether the “premium price” of a new medicine is justified by its additional benefits. The problem with using the primary outcome from the clinical trial is two-fold:

- First, it can be unclear what this means to the patient – for example, what does a 50% reduction in a dermatology score mean to the patient? Can they “do a Lazarus”? Or do they feel no better at all, even though some marker of their disease has changed?²

- Second, even if the first issue could be addressed (e.g. through interpretation by patient groups in their submission to SMC), there would still be a problem of judging cost-effectiveness in a consistent way. For example, suppose the SMC judged it was worth paying £1,000 per non-fatal cardiovascular event averted for one medicine, then the next submission asks for a judgement on whether it is worth paying £5000 for an extra three months of (possibly poor quality) life for patients with advanced cancer. How could SMC be sure its judgements were made on a comparable and open basis?

¹ It is actually a little more complicated than this, see briefing note on costing.
² For those who laughed at the attitude summed up in the phrase “The operation was a success but the patient died” the SMC equivalent usually comes in Section 5 on Clinical Effectiveness – “There was no obvious correlation between disease markers and broader quality-of-life measures.”
There are other problems with using RCTs as the basis for making judgements about effectiveness, of course, such as the sacrifice of external validity (i.e. generalisability) in the pursuit of internal validity (i.e. free from bias). Economists use modelling to try address this (see the modelling briefing note.)

**How QALYs are derived**

The Quality-Adjusted Life-Year is an attempt to address both of these issues at once. The foundation is the epidemiologist’s measure of a life-year: one person alive for one year is one life-year. At the risk of labouring the point, ten people alive for two years is 20 life-years and four people alive for five years is also 20 life-years.³ This is commonly used if we are measuring changes in length of life, or additional survival.

However, many medicines also affect quality-of-life (QoL)⁴ so we need a way to capture this. QALYs do this by applying a weighting to each period of time that reflects how good or bad a person’s QoL is during this time. The weighting is called a utility, hence the type of economic evaluation that uses the QALY as a benefit measure is called cost-utility analysis.

If the person is in full health then QoL is not a factor so the weight equals 1.0 (or 100%): in other words quality-adjusting makes no difference, life-years (LYs) and quality-adjusted life-years (QALYs) are exactly the same.

A disease that has a mild effect on QoL will have a weight, or utility, that is close to 1.0, so if I have a cold I might rate my QoL at 95% of normal, or 0.95. By the same argument, diseases that have a severe impact on QoL have a low weight, so somebody with advanced cancer might have a QoL that is 20% of normal.

This raises the question of what a weight of 0% means. This is the case when life-years are multiplied by a weight of 0.0 so the answer in QALYs will be 0. This is the case where a health state is so bad that it is equivalent to being dead. For some people, advanced cancer pain or advanced degenerative disease might have a weight of 0.0, or even a negative weight. In practice, these extreme values are very rare (thank goodness).

The following tables gives examples of values taken from the literature – the first table shows a range of health states and their utility values from specific studies. The third and fourth columns show who provided the value and what method was used to elicit them (these will be covered in more detail in a future briefing note).

<table>
<thead>
<tr>
<th>Health State</th>
<th>Utility</th>
<th>Valuer</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stable prostate carcinoma (asymptomatic)</td>
<td>0.92</td>
<td>Clinicians</td>
<td>Time Trade Off</td>
</tr>
</tbody>
</table>

³ This ignores discounting future effects to a present value, but that is another story.
⁴ Quality of Life is actually a far broader concept, extending well beyond what the NHS can affect. What we are thinking about here might better be described as Quality of Health – pain, immobility, etc. For consistency, however, I will stick with the more general term.
### Table of Health States, Utilities, and Valuers

<table>
<thead>
<tr>
<th>Health State</th>
<th>Utility</th>
<th>Valuer</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early progressive prostate carcinoma (moderate pain/fatigue)</td>
<td>0.83</td>
<td>Clinicians</td>
<td>Time Trade Off</td>
</tr>
<tr>
<td>Late progressive prostate carcinoma (severe pain/fatigue)</td>
<td>0.42</td>
<td>Clinicians</td>
<td>Time Trade Off</td>
</tr>
<tr>
<td>Insulin dependent diabetes mellitus</td>
<td>0.84</td>
<td>Clinicians</td>
<td>Time Trade Off</td>
</tr>
<tr>
<td>Untreated depression</td>
<td>0.31</td>
<td>Patients</td>
<td>Standard Gamble</td>
</tr>
<tr>
<td>Caregiver quality of life 6 months of standard care - demented patient</td>
<td>0.53</td>
<td>Relatives or Proxies</td>
<td>Time Trade Off</td>
</tr>
<tr>
<td>Mild schizophrenic symptoms</td>
<td>0.61</td>
<td>Clinicians</td>
<td>Standard Gamble</td>
</tr>
<tr>
<td>Moderate schizophrenic symptoms</td>
<td>0.36</td>
<td>Clinicians</td>
<td>Standard Gamble</td>
</tr>
<tr>
<td>Severe schizophrenic symptoms</td>
<td>0.29</td>
<td>Clinicians</td>
<td>Standard Gamble</td>
</tr>
<tr>
<td>Legal blindness for person &quot;poorly-adjusted&quot; after rehabilitation</td>
<td>0.36</td>
<td>?</td>
<td>Rating Scale</td>
</tr>
<tr>
<td>Legal blindness for person &quot;well-adjusted&quot; after rehabilitation</td>
<td>0.48</td>
<td>?</td>
<td>Rating Scale</td>
</tr>
<tr>
<td>Adult with profound deafness</td>
<td>0.59</td>
<td>Community, Patients</td>
<td>Health Utilities Index (HUI) 3</td>
</tr>
<tr>
<td>Severe multiple sclerosis (chronic progressive, non-ambulatory)</td>
<td>0.36</td>
<td>Community</td>
<td>Health Utilities Index (HUI) 1</td>
</tr>
<tr>
<td>Post-myocardial infarction (MI) in NYHA functional class I</td>
<td>1.00</td>
<td>Clinicians &amp; Patients</td>
<td>Health Utilities Index (HUI) 1</td>
</tr>
<tr>
<td>Post-myocardial infarction (MI) in NYHA functional class II</td>
<td>0.70</td>
<td>Clinician &amp; Patients</td>
<td>Health Utilities Index (HUI) 1</td>
</tr>
<tr>
<td>Post-myocardial infarction (MI) in NYHA functional class III/IV</td>
<td>0.50</td>
<td>Clinicians &amp; Patients</td>
<td>Health Utilities Index (HUI) 1</td>
</tr>
<tr>
<td>Minor stroke</td>
<td>0.75</td>
<td>Patients</td>
<td>Time Trade Off</td>
</tr>
<tr>
<td>Moderate stroke</td>
<td>0.39</td>
<td>Patients</td>
<td>Time Trade Off</td>
</tr>
<tr>
<td>Severe diarrhoea</td>
<td>0.81</td>
<td>Community</td>
<td>Time Trade Off</td>
</tr>
<tr>
<td>Dialysis</td>
<td>0.41</td>
<td>Patients</td>
<td>Time Trade Off</td>
</tr>
<tr>
<td>Partial incontinence</td>
<td>0.81</td>
<td>Clinicians</td>
<td>Time Trade Off</td>
</tr>
<tr>
<td>Complete incontinence</td>
<td>0.61</td>
<td>Clinicians</td>
<td>Time Trade Off</td>
</tr>
<tr>
<td>Prior to elective hip surgery with osteoarthritis</td>
<td>0.29</td>
<td>Patients</td>
<td>Time Trade Off</td>
</tr>
<tr>
<td>3 months post elective hip surgery with osteoarthritis</td>
<td>0.84</td>
<td>Patients</td>
<td>Time Trade Off</td>
</tr>
<tr>
<td>Below knee amputation</td>
<td>0.61</td>
<td>Community, Clinicians</td>
<td>Time Trade Off, Rating Scale</td>
</tr>
<tr>
<td>Above knee amputation</td>
<td>0.20</td>
<td>Community, Clinicians</td>
<td>Time Trade Off, Rating Scale</td>
</tr>
</tbody>
</table>

Another way to use these data would be with future SMC submissions when the manufacturer suggests a utility value for a health state – the “face validity” of that value could be checked by comparing it to the values in the table. Supposing a manufacturer of PPIs claims that having heartburn has a utility value of 0.2, for example; you could quickly see from the table that such a value would seem to be at odds with all the other values, as it is worse than having severe multiple sclerosis. To help with this “quick reference” role, the following table reorders the data with the “least ill” states first and then in descending order after that:

<table>
<thead>
<tr>
<th>Health State</th>
<th>Utility</th>
<th>Valuer</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 months post elective hip surgery with osteoarthritis</td>
<td>0.84</td>
<td>Patients</td>
<td>Time Trade Off</td>
</tr>
<tr>
<td>Below knee amputation</td>
<td>0.61</td>
<td>Community, Clinicians</td>
<td>Time Trade Off, Rating Scale</td>
</tr>
<tr>
<td>Above knee amputation</td>
<td>0.20</td>
<td>Community, Clinicians</td>
<td>Time Trade Off, Rating Scale</td>
</tr>
</tbody>
</table>
### Eliciting these values is NOT a precise science – there are different methods which ask people questions in different ways. The data in the table above are averages across groups of people – to give an idea of the spread of opinion the standard deviation should also be considered.

**Calculation of a QALY**
The calculation of a QALY gain might take several forms:

<table>
<thead>
<tr>
<th>Condition</th>
<th>Value</th>
<th>Source</th>
<th>Measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-myocardial infarction (MI) in NYHA functional class I</td>
<td>1.00</td>
<td>Clinicians &amp; Patients</td>
<td>Health Utilities Index (HUI) 1</td>
</tr>
<tr>
<td>Stable prostate carcinoma (asymptomatic)</td>
<td>0.92</td>
<td>Clinicians</td>
<td>Time Trade Off</td>
</tr>
<tr>
<td>Insulin dependent diabetes mellitus</td>
<td>0.84</td>
<td>Clinicians</td>
<td>Time Trade Off</td>
</tr>
<tr>
<td>3 months post elective hip surgery with osteoarthritis</td>
<td>0.84</td>
<td>Patients</td>
<td>Time Trade Off</td>
</tr>
<tr>
<td>Early progressive prostate carcinoma (moderate pain/fatigue)</td>
<td>0.83</td>
<td>Clinicians</td>
<td>Time Trade Off</td>
</tr>
<tr>
<td>Severe diarrhoea</td>
<td>0.81</td>
<td>Community</td>
<td>Time Trade Off</td>
</tr>
<tr>
<td>Partial incontinence</td>
<td>0.81</td>
<td>Clinicians</td>
<td>Time Trade Off</td>
</tr>
<tr>
<td>Minor stroke</td>
<td>0.75</td>
<td>Patients</td>
<td>Time Trade Off</td>
</tr>
<tr>
<td>Insulin dependent diabetes mellitus</td>
<td>0.70</td>
<td>Clinician &amp; Patients</td>
<td>Health Utilities Index (HUI) 1</td>
</tr>
<tr>
<td>Complete incontinence</td>
<td>0.61</td>
<td>Clinicians</td>
<td>Time Trade Off</td>
</tr>
<tr>
<td>Mild schizophrenic symptoms</td>
<td>0.61</td>
<td>Clinicians</td>
<td>Standard Gamble</td>
</tr>
<tr>
<td>Below knee amputation</td>
<td>0.61</td>
<td>Community, Clinicians</td>
<td>Time Trade Off, Rating Scale</td>
</tr>
<tr>
<td>Adult with profound deafness</td>
<td>0.59</td>
<td>Community, Patients</td>
<td>Health Utilities Index (HUI) 3</td>
</tr>
<tr>
<td>Caregiver quality of life 6 months of standard care - demented patient</td>
<td>0.53</td>
<td>Relatives/Proxies</td>
<td>Time Trade Off</td>
</tr>
<tr>
<td>Insulin dependent diabetes mellitus</td>
<td>0.50</td>
<td>Clinicians &amp; Patients</td>
<td>Health Utilities Index (HUI) 1</td>
</tr>
<tr>
<td>Legal blindness for person &quot;well-adjusted&quot; after rehabilitation</td>
<td>0.48</td>
<td>?</td>
<td>Rating Scale</td>
</tr>
<tr>
<td>Late progressive prostate carcinoma (severe pain/fatigue)</td>
<td>0.42</td>
<td>Clinicians</td>
<td>Time Trade Off</td>
</tr>
<tr>
<td>Dialysis</td>
<td>0.41</td>
<td>Patients</td>
<td>Time Trade Off</td>
</tr>
<tr>
<td>Moderate stroke</td>
<td>0.39</td>
<td>Patients</td>
<td>Time Trade Off</td>
</tr>
<tr>
<td>Legal blindness for person &quot;poorly-adjusted&quot; after rehabilitation</td>
<td>0.36</td>
<td>?</td>
<td>Rating Scale</td>
</tr>
<tr>
<td>Severe multiple sclerosis (chronic progressive, non-ambulatory)</td>
<td>0.36</td>
<td>Community</td>
<td>Health Utilities Index (HUI) 1</td>
</tr>
<tr>
<td>Untreated depression</td>
<td>0.31</td>
<td>Patients</td>
<td>Standard Gamble</td>
</tr>
<tr>
<td>Severe schizophrenic symptoms</td>
<td>0.29</td>
<td>Clinicians</td>
<td>Standard Gamble</td>
</tr>
<tr>
<td>Prior to elective hip surgery with osteoarthritis</td>
<td>0.29</td>
<td>Patients</td>
<td>Time Trade Off</td>
</tr>
<tr>
<td>Above knee amputation</td>
<td>0.20</td>
<td>Community, Clinicians</td>
<td>Time Trade Off, Rating Scale</td>
</tr>
</tbody>
</table>
First there could be a QoL impact only (no difference in survival). In terms of a picture this would look like this:

For example, if the patient would have lived for 10 years with a QoL valued at 0.5 and the medicine means they live for the same period with a QoL of 0.7 then the gain is 0.2 * 10 years = 2 QALYs.\(^5\) If the gain was only for the first five years, with the patient then “relapsing” to a QoL of 0.5, then the QALY gain would be 0.2 * 5 years = 1 QALY.

Second there could be an impact on QoL and length of life. In terms of a graph this might look like this:

Supposing a patient receiving the existing treatment would live two years with a QoL of 0.5. With the new medicine they would live for three years with a QoL of 0.7. During the first two years they have a QoL gain of 0.2, so that is 0.2 * 2 years = 0.4 QALYs.

\(^5\) In all of these examples I have ignored discounting of future effects, for simplicity.
They also get an additional life-year but their QoL is 0.7 so this is 0.7 * 1 year = 0.7 QALYs. Adding the two elements together 0.4 QALYs + 0.7 QALYs = 1.1 QALYs.

Do QALYs address the SMC’s problems?
Now we can go back to the two problems identified at the foot of page 1. QALYs address the question “What does this mean to the patient?” by asking manufacturers to convert the outcome measure from clinical trials into either a gain in length of life or a gain in QoL. Not only this, but they have to express QoL gain on the same scale that we use to measure across all diseases. Sometimes there is a suspicion that the disease-specific scales are calculated so that even quite modest changes in QoL produce a big change in the scale. QALYs “correct” for this by asking what this means on the common QoL weighting scale applied to all conditions. I would argue that while the QALY requires us to boil a person’s QoL down to a single number (which non-economists tend to find objectionable), it does that through the good intention of making the health gain that patients actually notice the centre-piece of the evaluation.

QALYs also add consistency to decision-making in that we are now using a common measure of benefit across all of the submissions seen by SMC. Rather than judging cost per non-fatal cardiovascular event averted and then cost per year of successful dermatology treatment, SMC is now presented with net cost per QALY gained for one medicine, then net cost per QALY gained for the next medicine. Of course, this is not the only factor in decision-making but it at least gives SMC the chance to be open and transparent in how it considered the economics element. However, it assumes a QALY is of equal value no matter how it is obtained or who gets it – this is open to debate.

Issues specific to a submission
In this section I have picked out the three questions I hope SMC members would consider in reviewing a submission.

Did this submission use QALYs? If not, was this justified (e.g. because the new medicine has lower cost and is at least as effective)?
In the past, SMC has felt that a new medicine with a major budget impact and an economic result of “cost per one-point reduction in disease-specific scale” had not provided sufficient information on value-for-money. Manufacturers have been clearly and consistently warned about this. You should be able to find information on this in the economic critique carried out by an SMC reviewer on the first page of the review.

If the submission used QALYs what were the QoL weights? Do these seem plausible?
QoL weights (or utilities) are subjective and will vary across patients. The figures in the submission will be an average value (although the variation around this average should also be presented and used in the sensitivity analysis6). You should be able to see these

---

6 The sensitivity analysis is the way economists assess the robustness of their results by changing the data used in the calculation to see under what circumstances their recommendation on cost-effectiveness will change.
in the manufacturer’s submission and find some comment on them in the economics reviewer’s critique in answer to questions 20 and 21.

To assess whether the utility values are plausible, try this “thought experiment”. Think about the health state that is being valued and what effect it would have on your QoL in terms of pain, anxiety, immobility, etc. Now suppose you were going to live in that state for ten years; how many of those ten years would you give up to have your full health restored? The worse the health state, the more years you should be prepared to give up. Suppose severe psoriasis has been valued at 0.6 or 60% of normal; this is equivalent to saying that you would be prepared to give up four years of the ten to be rid of it. This gives a very rough-and-ready way to “reality check” the utilities presented.

Is the analysis incremental?
The significance of this issue is that SMC is interested in the additional costs of the new medicine compared to the additional benefits (e.g. QALYs). Even if all the NHS can currently do is manage a patient’s symptoms, there is almost always some cost being incurred and some level of benefit. This makes some costs of new medicines less scary once we realise we are already paying for treatment (so the incremental cost is lower than the purchase price of the medicine would appear). However, it also means that seemingly impressive QALY gains from treatment might conceal that there is only a small advantage from what we already have. This means that we must focus on the incremental costs and incremental benefits – how much more are we willing to pay for more good health?

What is the net cost per QALY gained for this medicine? Is that acceptable or not?
You should be able to see the main result in the manufacturer’s submission or on the front page of the checklist.

From an analysis of the submissions to date, it is clear that SMC does not have a simple cost per QALY cut-off, such as £30,000. Almost all manufacturers submit quite low cost per QALY figures and the SMC’s job is to decide whether this estimate is broadly plausible or not: in general, the economists support the plausible ones and recommend rejection of the rest. This means that we have accepted submissions with a cost per QALY of around £25,000, and rejected submissions that promise a QALY gain and cost savings. We have done this because the former was based on a high-quality, transparent analysis whereas the latter was based on a poor-quality submission.

When New Drugs Committee of the SMC has asked for guidance on what is an acceptable cost per QALY, the economics review team have stated (i) we do not have an explicit upper limit, but (ii) the Committee might like to be aware of NICE guidance to manufacturers. To paraphrase this slightly, a cost per QALY up to £20,000 is acceptable so long as the economics case is robust. A cost per QALY between £20,000 and £30,000 needs some further justification, such as there being no alternative treatment for this condition. Cost per QALY in excess of £30,000 will come under intense scrutiny and may be rejected.

The issue that has probably forced SMC to think hardest about what is an acceptable cost per QALY (once we have accepted the quality of the economic case) is orphan drugs. Everyone acknowledges that this type of product will have a high cost per QALY. SMC
needs to consider under what circumstances this will be acceptable, given that any funding for orphan products diverts resources from other treatments. These issues are considered in more detail in the briefing note on cost per QALY values.

Some general issues
In this section I have selected three more general issues with using QALYs.

Are QALYs ageist?
The basis of the QALY is the life-year. Since older people have shorter life expectancy than young people, a measure based on ability-to-benefit such as the QALY may disadvantage older people because they have less LYs ahead of them. We certainly need to be aware of this but in practice interventions for older people do not seem to be systematically disadvantaged: for example, hip replacements, chiropody interventions, and screening for cancer for people in their 70s all have a low cost per QALY. (The cost per QALY briefing note includes a table of values for different services that demonstrates this point).

A refinement on this argument is that QALYs discriminate against diseases where the life-expectancy is very limited – for example, advanced cancer. It could be argued that the QALY does not adequately capture the value to the patient of even a few weeks of survival. This is an interesting area for further research.\(^7\)

Are QALYs a good measure of the objective of the NHS?
The QALY assumes the NHS should set its priorities so that we get as much health gain as possible. By focusing on ability-to-benefit as the basis for priority-setting (albeit in a trade-off with cost), QALYs have a potential ally in the “evidence-based medicine” approach. This raises at least two sets of issues:

(i) As a basis for priority-setting it ignores anything not captured by the QALY measure as described above. For example, it does not take account of how much need someone is in initially: QALYs only ask what difference an intervention can make and at what cost. QALYs thus do not take account of our natural, humane imperative to do something for people in extreme distress even if we realise that our efforts are probably futile. In a similar vein, some people think some treatments should be funded because even though they do little good, they might be the first treatment for a given unpleasant condition of any efficacy whatsoever. Finally, QALYs take no account of the “deservingness” of a patient group: for example, some people might believe people with a genetically-inherited condition deserve funding more than people who have a disease as a result of a lifestyle. This is why SMC needs to take a holistic view of the case for a new medicine, setting the QALY-based evidence in context (but not forgetting that every decision has an opportunity cost in terms of funds that will be diverted from other treatments that have a lower cost per QALY).

\(^7\) This argument has been used by manufacturers when facing a draft “not recommended” from NDC.
(ii) Some services have benefits that can’t be easily captured by QALYs. The most obvious example SMC has encountered are contraceptives. Thinking beyond the SMC, other types of benefit not captured by QALYs include factors relating to the process of care (such as continuity of care, inclusion in decision-making) and aspects of long-term care for older people (such as autonomy, dignity, etc.). There is also controversy over whether QALYs, originally designed for the acute hospital setting, are equally applicable in mental health care.

**Who should decide the values for the QoL weights?**

The SMC has received submissions that have used the following groups as sources for QoL weights: patients, doctors, the public, and the people completing the submission for the manufacturer. NICE argue that the NHS is a public service so it should be the values of the public that determine resource allocation. The problem is that you have to describe a health state to a sample of the public (the majority of whom might have no experience of it) and get them to value it. Research has shown that people’s valuations of a health state before and after they experience it are different, so asking people who have never had the condition is open to challenge. Put simply: if you were valuing the pain of childbirth, would you give an equal say to a woman who had experienced it and a man (even a “new” man)?? The use of doctors to value states can be defended on the grounds that they see a lot of different conditions (albeit at second hand) and hence they can put any given condition in context. However, QoL research consistently shows that when a patient, their doctor and their nurse answer the same questions about the patient’s health, nurses come much closer to matching the patient’s view. If we were to go down this route, the evidence-based approach would be to ask nurses, but that is quite rare. My personal view is that values derived from surveys of patients are the most credible because they have actually experienced the state. An objection is that if people know why they are answering questions they might have an incentive to exaggerate their illness and the size of any gains, but I am not aware of any evidence that this happens in practice. A more serious issue is whether the experience of illness changes people’s perceptions of good health (and states as bad as being dead) and hence they give different answers to “healthy” people. Another issue is what to do when patients are not competent to value their own health: notable groups that will come to the attention of the SMC include people with mental illness or children. In both these cases we may need to use proxy values, such as those of family or carers. In practice the SMC accepts utility values from a number of sources and assesses their plausibility.

**Summary**

This briefing note has attempted to set out the rationale and the basis for using the QALY in SMC decisions. It is not an exhaustive review of QALYs – for example, in the

---

8 Some mischievous people have argued that as each child born is equivalent to a gain of about 70-80 QALYs, then as a QALY-maximising NHS we should actually ban contraception!
interests of brevity, it has not reviewed the different ways to elicit QoL values from patients.  

The key points are:

- economics data based on primary outcomes from clinical trials are usually not good enough – SMC needs to know what the benefit means for the patient and to be able to make decisions in a consistent way
- QALYs combine changes in length of life and quality of life into a single measure, capturing arguably the most important benefits of the health service
- the net cost per QALY gained is a helpful way to summarise the economic differences between the status quo and a new treatment
- comparing this with the net cost per QALY for other treatments gives an idea of NHS-wide cost-effectiveness
- however, this is not the only criterion and SMC will weigh this evidence against other aspects of the decision, bearing in mind that every decision has an opportunity cost in terms of resources diverted from other care.

---

9 I am happy to provide further detail to those with a thirst for knowledge.