

interventions – and cost-effectiveness analysis is needed to do this.

A study by Skinner and Staiger, available as a National Bureau of Economics research report, looked at the rate of adoption of three highly cost-effective technologies for acute myocardial infarction (MI) – aspirin, beta-blockers and reperfusion. Now almost every hospital is using these to the full, but back in the 1980s and 1990s there was a period where hospitals adopted them at different rates.

Using regression analyses the study looks at the relationship between expenditures and outcomes for acute MI after the hospitals were stratified by their rate of adoption of these cost-effective technologies. The fastest-adopting quintile of hospitals have better outcomes than the slowest and – counter to the opinion that Dr Weinstein spoke of as being widespread in the US – there is a positive relationship between expenditures and outcomes in all the strata. So to cut costs and improve outcomes, hospitals would have had to adopt the cost-effective technologies more rapidly.

Another argument, one that the US Congress has decided to invest in, is that if we do more research on comparative effectiveness of health interventions we can identify the interventions that are useless, leaving enough money saved to pay for everything that is useful. The fact, Dr Weinstein explains, is that it is very hard to prove that something is useless. Randomised trials, if they are feasible, are not intended to prove a negative, and just because you cannot show that an intervention is better than its alternative it is very hard to show that it is exactly equivalent to the alternative. Most interventions do not lend themselves to randomised clinical trials and we have to rely on other sources of evidence, and it is very hard to prove beyond a reasonable doubt that an intervention is absolutely useless.

One argument backed by Dr Weinstein is that QALYs do not reflect everything that people care about in healthcare. For example, there may be value in some genetic testing that tells people what risks they face as they proceed through life, or what risks their child faces. Even if you cannot do anything about

it, there is the psychological value of knowing. Caring does not necessarily manifest itself in more QALYs but it is something that people value. Similarly, access to care, equity, and reducing disparities in society are things that people value but which do not reflect themselves in maximising QALYs.

Dr Weinstein was co-chair of the US Panel on Cost-effectiveness in Health and Medicine which reported to the US Government in the 1990s. One of the most important recommendations the panel made is that cost-effectiveness analysis is an aid to decision-making, not a complete procedure for making resource allocation decisions, because it cannot incorporate all the values relevant to such decisions. Dr Weinstein thought that NICE and Britain should be mindful of this, saying that ‘sometimes in one’s enthusiasm for the cost-effectiveness model – and I am certainly one of the enthusiasts – we need to temper that enthusiasm with the limitations and be mindful of the role that this type of analysis has among many other considerations – ethical, psychological and otherwise’.

Dr Weinstein posed a question - do the British take prescribed guidelines for cost-per-QALY modelling too seriously? The purpose of a model is to inform medical decisions and healthcare resource allocation. Modellers employ quantitative methods to gain qualitative insights. The purpose is not so much the number that comes out as to gain the qualitative insight. The tools of formal analysis are best employed to structure the clinical, epidemiological and economic evidence base in the service of better clinical practice decisions and public health priorities.

Finally, he noted that there is a role for deliberative processes through which individuals and stakeholders, including the general public, can get involved in conversations about how costs and benefits should be traded off against one and another, and with other ethical and psychological factors that people believe should go into decision-making.

## STANDING UP FOR ORPHANS



John Irwin  
Co-Chair ABPI Orphan Medicines  
Industry Group

### RARE DISEASES IN THE UK

2012 sees the publication of the UK’s first Plan for Rare Diseases. This represents an important landmark for the estimated 3.5 million patients in the UK believed to be living with a rare disease. This plan has been delivered in response to a commitment made in the response to the Council of the

European Union Recommendation on an action in the field of rare diseases (2009/C 151/02) to ‘establish and implement plans or strategies for rare diseases at the appropriate level ... in order to aim to ensure that patients with rare diseases have access to high quality care, including diagnostics, treatments, habilitation for those living with the disease and, if possible,

effective orphan medicines’.

A rare disease is defined by the European Union as one that affects fewer than 5 in 10,000 of the general population. There are between 6,000 and 8,000 known rare diseases and it is believed that 7 per cent of the population will be affected by a rare disease at some point in their lives. Seventy-five per cent of rare diseases affect children

and 30 per cent of rare disease patients die before their fifth birthday.

## MEDICINES FOR RARE DISEASES

Despite the fact that, collectively at least, rare diseases are 'common', there has historically been a dearth of medicines available to ameliorate the situation of those with such conditions. In 2000, the EU enacted orphan medicinal product (OMP) legislation (Regulation (EC) No 141/2000) to offer a package of economic incentives for the R&D and marketing of orphan medicines in recognition of the fact that 'patients with rare conditions should be entitled to the same quality of treatment as other patients'. Since 2000, over 600 medicines have been granted orphan designation, with just over 60 progressing to full European marketing authorisation. Of these, 51 per cent are for the treatment of diseases that affect fewer than 1 in 10,000 patients.

## THE AVAILABILITY OF ORPHAN MEDICINES IN THE UK

The EC regulation on orphan medicinal products has clearly stimulated the development of medicines for rare conditions that were previously untreatable, but how successful has this legislation been in increasing the actual availability of medicines for patients with rare disease in the UK?

In England, the majority, but not all, non-cancer rare diseases are defined within the National Specialised Services Definition Set (NSSDS). As a consequence of this, orphan medicines are frequently used in the management of conditions which are commissioned by

specialised commissioners either regionally, in Specialised Commissioning Groups (SCGs), or nationally, by the National Commissioning Group (NCG). The NCG only commissions services that generally impact upon fewer than 500 patients. Where medicines are used as part of a service commissioned by the NCG the medicine is paid for centrally. In contrast, where the medicine is used to treat a condition that is commissioned regionally by SCGs, Primary Care Trusts (PCTs) remain the ultimate payers.

The position of the National Institute for Health and Clinical Excellence (NICE) is that orphan medicines should be appraised in the same way as medicines for more prevalent diseases: although it does not appraise what it terms 'ultra orphan' medicines. However, since only technologies chosen through a topic selection process are referred to NICE, only 3 non-cancer orphan medicines have been appraised and recommended to date. The unintended consequence of the topic selection process has been 'NICE blight' for many orphan medicines in England. In the absence of NICE guidance, the decision of whether or not to pay for orphan medicines has fallen to Individual Funding Request panels considering case by case applications within individual PCTs. This can lead, and has led, to inconsistency in decision-making and geographic health inequalities.

In contrast, the Scottish Medicines Consortium (SMC) appraises all new medicines although it applies 'modifiers' to the cost-per-QALY approach. Despite the use of these 'modifiers', of the 46 orphan medicines appraised by the

SMC by May 2010, 18 were recommended, 17 rejected and 11 recommended for restricted use.

## FUTURE CHALLENGES AND OPPORTUNITIES

For patients who are suffering from serious, rare conditions for which no satisfactory treatment exists, undue delay of access to new medicines will always be unacceptable. It is however important that the use of OMPs is considered and a determination of their value to patients treated within the NHS made. The challenge is therefore in determining how both a *timely and appropriate* assessment of OMP value can be made. Judging on the SMC experience, it is evident that where a purely QALY-based approach to Health Technology Assessment (HTA) is applied to OMPs there is a high rate of rejection, but what's the alternative?

One development that represents a step in the right direction is the recent publication of a decision making framework by the Advisory Group for National Specialised Services (AGNSS).<sup>1</sup> This model has been designed to support decisions around which products, services or

technologies should be commissioned and paid for nationally. It evaluates the product against 12 core criteria organised into 4 domains with a holistic view taken across all criteria. (Figure 1)

Although as yet relatively untested, this approach does at least appear to represent a more holistic approach to the evaluation of medicines for rare disease. Unfortunately its application is currently restricted to OMPs that treat no more than 500 patients in England and its future, like that of AGNSS, is by no means certain.

As part of the reforms outlined within the Health Bill, the responsibility for the commissioning (and funding) of specialised services (and the medicines used as part of them) in England will transfer to the NHS Commissioning Board. This represents an opportunity finally to get it right for at least some patients with rare diseases. It is critical, however, that those of us with a stake maintain vigilance and ensure that patients with rare diseases get access to the medicines they need and deserve.

### Footnote

<sup>1</sup>[http://www.specialisedservices.nhs.uk/library/27/Introduction\\_to\\_AGNSS\\_Decision\\_Making\\_Framework.pdf](http://www.specialisedservices.nhs.uk/library/27/Introduction_to_AGNSS_Decision_Making_Framework.pdf)

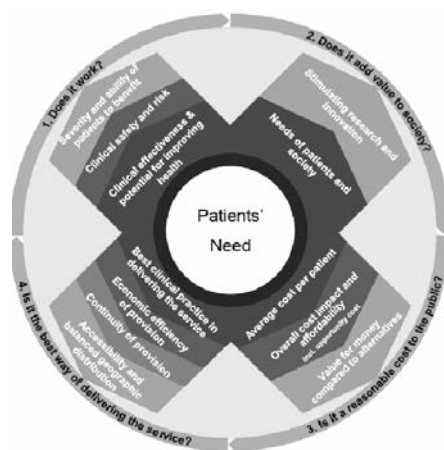


Figure 1: AGNSS Decision-Making Framework

