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**Multiple Criteria Decision Analysis for Value
Based Assessment of New Medical Technologies:
A Conceptual Framework**

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Working Paper No.33/2013

First published in March 2013 by:
LSE Health
The London School of Economics and Political Science
Houghton Street
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British Library Cataloguing in Publication Data. A catalogue record for this publication is available from the British Library
ISSN 2047-8879

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Acknowledgements

This is a paper written under the auspices of ADVANCE_HTA, a research project funded by the European Commission's Framework Programme 7 for Research. The paper does not express the views of the European Commission.

Abstract

Assessing the value of new medical technologies may require new approaches that take into account a more comprehensive set of parameters than the incremental cost/QALY. It is argued that MCDA can fulfil this role and has the potential to be methodologically superior to the currently used approaches mainly because of receiving input from multiple, and seemingly relevant criteria or parameters, thus forming a more holistic approach to assessing overall value. Inclusion, scoring and weighting of these parameters would be based on the expertise and opinion of a much wider spectrum of stakeholders involved, thus aiming to achieve an optimal balance across different, and probably opposing, interests. The MCDA score reflecting the overall value of a new medical technology would then be linked to coverage and/or pricing decisions. Coverage decisions could adopt a value for money approach that considers both value and cost of options based on an enhanced cost-effectiveness paradigm. Alternatively, for price-setting purposes, a pre-determined link between scores and prices would be needed; however, such a link would be country- and context-specific for each assessment case. Either way, any coverage and/or pricing decision would need to reflect the value as received by the different stakeholders and in relation to a wide range of criteria.

Keywords: multiple criteria decision analysis; value-based pricing; cost effectiveness; medical technology; pharmaceuticals; HTA

JEL classification: H43, I13, I18

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1. Background

Technological advancements in combination with higher life expectancy, higher patient expectations, and increased prevalence of chronic diseases, have led to significant increases in public spending on pharmaceuticals, which, on average account for 17% of total health expenditure or about 1.6% of GDP across OECD countries (OECD, 2012). Given the resources governments and health systems can spend on healthcare, the pathway to optimal resource allocation passes through cost containment and efficiency improvement policies.

At the other end of the spectrum scientific advances often require significant risk-taking and research and development (R&D) investment and are usually rewarded via the intellectual property system. Although patent-induced monopolies may be associated with market inefficiency (Baker and Chatani, 2002; Hollis, 2004) they have been accepted as a necessary trade-off for social welfare enhancement through the advance of scientific innovation.

The above create a crucial trade-off in achieving a balance between the potentially conflicting interests of health policy and industrial policy goals, or static efficiency (optimal allocation at a point in time) and dynamic efficiency (efficient allocation over time) respectively (Sloan and Hsieh, 2007; McGuire et al, 2009).

2. Transition to a Value Based Pricing Framework

An increasing proportion of new medicines are associated with a high monetary cost but also with a high degree of uncertainty on their additional value. In the context of value assessment for new medical technologies, current Health Technology Assessment (HTA) approaches examine the clinical efficacy of new medicines in combination with or without their cost-effectiveness, while increasingly incorporating real world post-marketing authorisation evidence, to incorporate comparative effectiveness and efficiency (Kanavos et al, 2010). However, these approaches are limited by significant subjectivity in the process of criteria selection for interpreting evidence and determining value, including what metrics to use for measuring efficacy/effectiveness, what types of costs to consider, and, very importantly, how to account for other key factors relating to overall value.

The value of new medical technologies is multi-dimensional and not strictly limited to clinical benefit and monetary cost. Many important factors affecting value such as the burden of disease the treatment addresses, aspects of the treatment's innovation level, and its wider socioeconomic implications are not adequately reflected in the assessment process. Many of these value parameters are not always considered, and when they are it is only on an

implicit and non-systematic manner; thus the methodological framework these value assessment approaches are adopting is incomplete and at best partial.

Following a number of criticisms of the current system of pharmaceutical regulation (OFT, 2007; Kennedy, 2009; DH, 2010) the UK government announced a public consultation in 2010, suggesting for the introduction of a new system of value based pricing (VBP) when the current PPRS agreement expires and inviting interested groups to submit views on the design of a new system that should “reflect the value of medicines and deliver best health outcomes for the people of the UK” (DH, 2010, p.6; Cabinet Office, 2010). The rationale was that the new system should take into account drugs’ real value to patients along their trajectory, thus providing better value for money for the NHS, stronger incentives for socially desirable R&D and creating a more stable and sustainable investment environment (OFT, 2007; DH, 2010).

It was suggested that in addition to drugs’ incremental (quality-adjusted) therapeutic benefit (e.g. Quality Adjusted Life Years gained), relative to its incremental cost that currently many HTA approaches consider, other parameters related to burden of illness, therapeutic innovation and improvement, and wider societal benefits should also be explicitly incorporated in the assessment process. It was proposed that the cost-effectiveness threshold of the new medicines should be somehow weight-adjusted in order to reflect any of these additional elements, implying a higher range of threshold for medicines which tackle diseases with higher burden of illness, that demonstrate greater therapeutic innovation, and with wider societal benefits (DH, 2010); the rationale for assigning such a weighting system was subsequently contested by NICE due to methodological issues and double-counting considerations (NICE, 2011).

The consultation that ensued on the subject attracted significant attention and received 188 responses (DH, 2011) from a variety of stakeholders. Some among them suggested or implied the use of multi-criteria decision analysis (Kanavos et al, 2011; NICE, 2011) as a means of providing an enhanced analytical framework for the assessment of value. The Government response to the consultation confirmed that there was a clear majority supporting a transition towards VBP, and that it intends to better define how to represent value (DH, 2011).

It is clear that a central aim of more recent approaches to value, including VBP, is to incorporate other factors into the valuation scheme. Multiple conflicting interests that need to be balanced out when placing a new medical technology on the market act as an additional reason why a wider perspective and assessment are needed. No such “holistic” value based assessment framework has been successfully created yet.

3. Aggregating value categories into a composite metric of overall value: different approaches

In order to capture the debate around different value parameters and their incorporation into a single metric that reflects overall value, different approaches exist, notably, a deliberative method, the net benefit approach, the weighted QALY approach and multiple criteria decision analysis.

Deliberative methods are commonly described as a hybrid between consultation and research and aim to involve the public in decision-making in a meaningful way; they include citizens' juries, consensus conferences, deliberative workshops, deliberative polling and deliberative mapping (Yetim, 2009; Myant and Urquhart, 2009). While in some ways similar to qualitative research methods (e.g. focus groups), they provide an opportunity for participants to find out more about a topic, consider relevant evidence and discuss this evidence with other participants before presenting their view. While deliberative methods provide opportunities for the public to consider different options and make more informed decisions than is possible from traditional consultation methods, they suffer from significant disadvantages such as biases, lack of robust sampling strategies, and applicability of the results, among others (Myant and Urquhart, 2009).

The net-benefit approach avoids the interpretation and statistical problems related to the incremental cost effectiveness ratio and implies a number of advantages (Zethraeus et al, 2003). First, traditional statistical methods can be used for confidence-interval estimation and hypothesis testing. Second, calculation of the optimal sample size and the power of the study are facilitated allowing the correlation between costs and effects to vary within and between patient groups. Third, the use of a Bayesian approach to cost-effectiveness analysis is facilitated. Fourth, a formal relation between cost-effectiveness acceptability curves and statistical inference is provided. Finally, the net-benefit approach gives the Fieller's limits of the confidence interval for the incremental cost-effectiveness ratio in the cost-effectiveness plane. However, the net benefit approach has significant challenges, which may limit its general applicability; for example, it is difficult to estimate certain elements of value in monetary terms; in addition, there may be social/political unease with assigning a monetary value to health.

The weighted QALY approach uses QALYs as the single measure of value, which is up-rated or down-rated with the use of weights to account for the elements of value. As already discussed, this can be a useful approach when the QALYs are a good (and proportional)

measure of value for the other elements (such as severity of the patient's condition, etc.), nevertheless, not all elements of value can be measured directly in terms of QALYs gained (e.g. degree of innovation).

In the context of Multiple Criteria Decision Analysis (MCDA), elements of value can be measured and scored in their natural units or through constructed scales, quantitatively or qualitatively, and weights are assigned to reflect criteria's importance when combining them. This methodology may signal a departure from the cost per QALY gained approach and the cost-effectiveness threshold would potentially need to be recalculated into cost per additional point (where the point is the aggregated unit of value, possibly encompassing QALYs and any other measures involved). However, this approach may provide a more comprehensive account of value parameters, greater transparency in how multiple criteria are explicitly valued, weighted, and aggregated, and a more inclusive approach to stakeholder views on value.

In turn, we are exploring how MCDA could offer an alternative method of valuing new medical technologies.

4. Developing an MCDA Framework for Value Based Assessment of new medical technologies

Decision analysis can provide an alternative way of measuring and eliciting value. In particular, MCDA "is both an approach and a set of techniques, with the goal of providing an overall ordering of options" by looking at the extent to which a set of objectives are achieved (Dodgson et al, 2009, p.46). It is a way of analysing complex situations characterised by a mix of objectives and does so by disaggregating a complex problem into simpler components, measuring the extent to which certain options achieve the objectives, weighting these objectives, and re-assembling the components to show a comprehensible overall picture (Raiffa, 1968; Dodgson et al, 2009).

MCDA methodologies have been suggested for use in public services (Dodgson et al, 2009), including transport (Pearman et al, 1989; DETR, 1998). MCDA has been used, on an experimental basis, in order to assess the benefit-risk (clinical) profile of new medicines for the purpose of regulatory approval during marketing authorisation stage by the European Medicines Agency (Phillips et al, 2011) and others (Walker and Cone, 2004). Its use has also been suggested in health care and value assessment in HTA (Devlin and Sussex, 2011) also offering a conceptual framework (Goetghebeur et al, 2008).

The robustness in terms of the multiplicity of criteria that can be assigned to assess value, the flexibility in terms of the differential weights that can be applied to the different criteria, and the encompassing nature in terms of stakeholder inclusion suggest that MCDA can be applied in medical technology value assessment. Still, technical and methodological questions remain related to the details of the assessment process, including (a) the criteria of value that should be considered, (b) how can the weightings of the different elements be determined, (c) what should the involvement be of stakeholders and (d) how would the derived value translate into coverage and/or pricing decisions for the technology assessed.

Although a variety of MCDA methodologies exist, the process of MCDA includes a number of common stages as follows (Dodgson et al, 2009): (a) establishing the decision context by defining the aims of the MDCA, and who the decision makers and other key stakeholders are; (b) identifying the relevant options; (c) identifying the objectives and criteria that reflect the value associated with the consequences of each option; (d) “scoring” the value associated with the performance of each option against the criteria; (e) “weighting” each of the criteria to reflect their relative importance to the decision; (f) combining scores and weights for each option to derive the overall value; (g) examine the results; and (h) conducting a sensitivity analysis of the results to test the influence of changes in scores or weights.

4.1. The decision context

For the purpose of value-based assessment (VBA) of pharmaceuticals, the decision context could adopt a societal point of view that aims to maximise social welfare. Since MCDA would form a framework for the pricing of future and already marketed drugs, options (i.e. different drug candidates) might not altogether be known beforehand but would be introduced on a rolling basis.

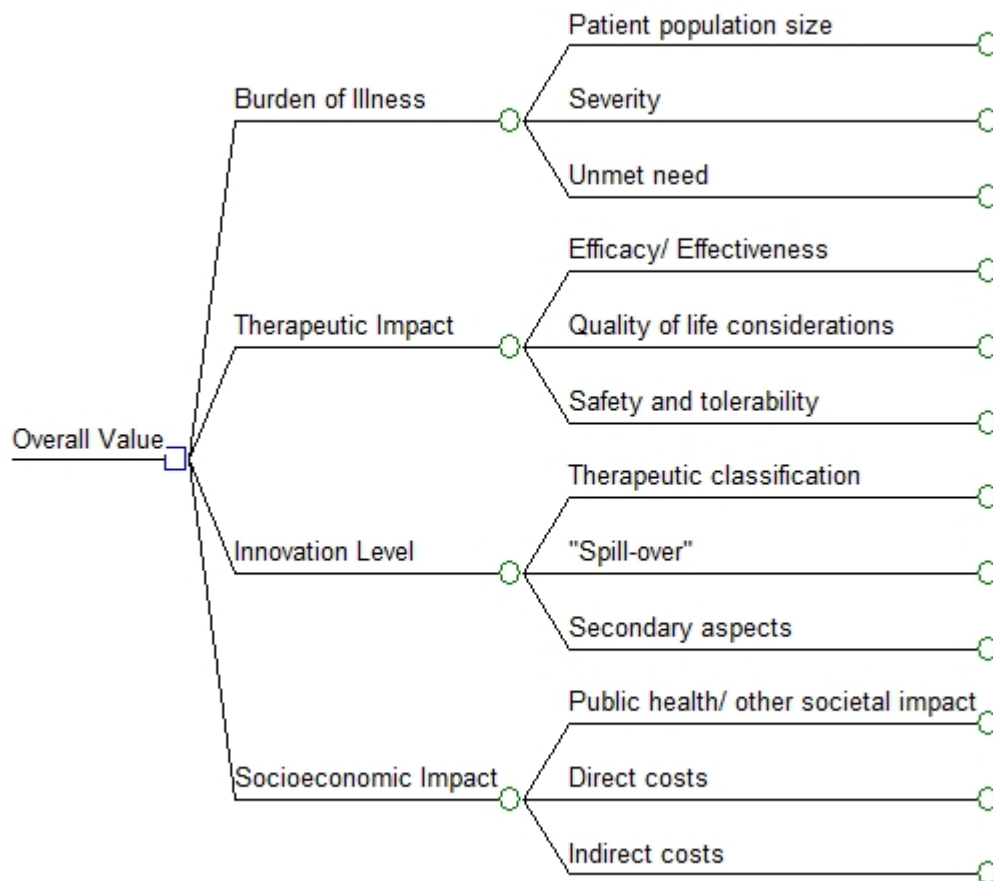
4.2. Deciding on criteria for value assessment

Possibly the most fundamental step affecting the MCDA model would be to decide on the criteria for which the drugs would be scored against. These criteria, or grading parameters, would represent factors that are important when assessing the “value” of a drug in a VBA context, and would be chosen through a literature review, possibly accompanied by experts’ opinions collected through questionnaires and/or group meetings.

They would include several drug – disease vital characteristics that could be divided in 4 main clusters: (a) burden of illness, (b) therapeutic impact, (c) innovation level, and (d) socioeconomic impact. These clusters would form the higher or top-level criteria groups

where the most important trade-offs take place, made up from a number of more specific lower or sub-level criteria whose hierarchical representation would take the form of a value decision tree, such as ValueVector™, as shown in Figure 1.

Figure 1
ValueVector™: An MCDA tree for Value Based Assessment of new medical technologies ^{(1),(2)}



Notes: ⁽¹⁾ ValueVector™ is a value framework based on MCDA principles developed by the authors of this paper.

⁽²⁾ This figure provides a brief account for ValueVector™; for further information please enquire with the authors.

Source: The authors.

“Burden of illness” would include criteria related to the size of the patient population being affected, the severity of the disease and the current unmet clinical need. “Therapeutic impact” would include clinical criteria mainly associated with the efficacy/effectiveness (e.g. direct and clinically meaningful endpoints including quality of life benefits, indirect and surrogate endpoints) and the safety and tolerability (adverse drug events and contra-indications) of the treatment; essentially, these criteria would rate technologies based on whether they provide significant added therapeutic benefit or a cure, moderate therapeutic benefit or modest therapeutic benefit. “Innovation level” criteria would classify the technology based on the nature of innovation it incorporates (e.g. whether it is breakthrough or a follow-on); it could also consider its Anatomical Therapeutic Chemical classification, the existence of any “spill-over” innovation effects, and other non-typical secondary types of innovation. Finally, “socioeconomic impact” would refer to any broader societal public health benefits and the impact on direct and indirect costs, including non-medical costs and loss of productivity, both for patients and carers.

In structuring and exemplifying the clusters and the specific criteria in ValueVector™, we ensure that the resulting model is parsimonious and that the criteria and the dimensions considered are not overlapping with each other.

4.3. Assigning scores for each option

The second most influential step after deciding on the criteria would be assigning the expected consequences for each criterion attribute (e.g. % of population affected by the disease, for the population size criterion) - on the X-axis, with a numerical “preference” or “utility” relative score - on the Y-axis, thus creating “value-functions” that can be used to convert criteria consequences into scores that are comparable. Typically, such a scale could range from 0 to 100, where 0 would represent “a real or hypothetical least preferred option”, and 100 would represent “a real or hypothetical most preferred option”, thus more preferred options would score higher and less preferred options would score less. Each option would subsequently be scored against each criterion, yielding the corresponding “preference” scores.

“Value-functions”, either in linear or non-linear form, could be constructed using key stakeholder and expert (e.g. clinical professionals, public health specialists, government officials, HTA regulators, industry representatives, and patient advocates) opinions collected through facilitated workshop(s) or study session(s) as part of “decision conferences” (Phillips 2007; Walker et al., 2011; Phillips et al., 2011). Such an approach that uses the judgment of

expert(s) to associate a value number, possibly in a 0–100 range, with the attribute’s input (performance) of that criterion is known as direct rating (Dodgson et al., 2009); alternatively, if it is difficult to directly allocate scores, perhaps because the criterion is weakly defined or it reflects a complex concept, indirect scoring approaches could also be used such as the bisection method and various difference methods (Belton and Stewart, 2002).

4.4. Assigning weights to each criterion

The next most important step would be assigning a weight on each criterion, reflecting its relative importance to the overall valuation of the drug. For example, in terms of the “burden of illness” cluster of criteria, if severity of the disease was to be considered twice as important as that of population size and unmet need, then a relative weight of 0.5 would be assigned to the former, and a relative weight of 0.25 would be assigned to the two latter respectively.

In practice, this could involve a swing weighting or trade-off method, possibly implemented in combination with a “nominal-group technique”, according to which key stakeholders (as mentioned above) decide on the relative contribution of each criterion, perhaps through a paired-comparison process if many criteria are existent (Belton and Stewart, 2002; Dodgson et al., 2009; Walker et al., 2011).

4.5. Producing a value index by combining individual scores and weights

Assuming that criteria are mutually preference-independent from each other, and given that uncertainty does not formally need to be built into the model, a linear additive model procedure could be used for individual criteria scores and their relative weights to be combined through a weighted average of scores to produce “total value” (Keeney and Raiffa, 1976; Dodgson et al., 2009; Phillips et al., 2011). Other more advanced types of modelling procedures also exist that could be applied depending on the model’s assumptions, allowing the weighted scores of the different criteria to interact with each other in a more complex manner, other than in a simple additive fashion (Keeney and Raiffa, 1976).

Results would be examined, validated, and sensitivity analysis would be conducted to test the impact of different possible scores or weights on the overall value of the drug, thus testing inputs vagueness and possibly helping to resolve any existing disagreements between the various stakeholders.

4.6. Applying the methodology more widely and linking value assessment to coverage and/or pricing decisions.

The result of such an MCDA would subsequently give evidence of the overall value of each drug option. Depending on the context of the health care system and the respective pricing and reimbursement policies in place, such a value metric could be applied in two possible ways: to inform either coverage/reimbursement decisions, or the price setting mechanism.

Under the former application, a rational way forward could be to adopt a “value for money” or cost-effectiveness approach that takes into account the MCDA value scores and the costs of the corresponding options. Such a cost-effectiveness ranking of options would inform decision makers on how to most efficiently allocate resources by prioritising drugs with the best “value for money”.

Under the latter application, drug candidates could be priced according to their value by setting a link between MCDA value index scores and the corresponding prices. In practice this could take place through the application of comparative price rules, translating MCDA scores differences between the competing products into a pricing scale, most likely in combination with the development of a price index. The actual price differences would depend on the available health care and pharmaceutical budgets of the country per se, and possibly on other surrounding factors associated with the pricing and reimbursement system in place.

5. Conclusion

A new approach is needed for assessing the value of new medical technologies that takes into account a more comprehensive set of parameters than just the incremental cost per unit of additional therapeutic benefit. Such an approach could be conceptually and methodologically superior to the current HTA approaches mainly because of examining multiple, and seemingly necessary, criteria thus forming a “holistic” approach of complete assessment. In turn, inclusion, scoring and weighting of these parameters should be based on the expertise and opinions of a full spectrum of key stakeholders, thus trying to achieve an optimum balance across all the different, and possibly opposing, interests. A value index reflecting the overall value of a new medical technology could then be used to inform evidence-based coverage and/or pricing decisions thus helping to achieve an optimal allocation of resources.

In conclusion, by developing an appropriate MCDA methodological framework for the context of HTA, the total value of new medical technologies could be transparently assessed using a clear, comprehensive, and explicit set of criteria. The results could then be applied as

a tool for consistent decision making that aims to maximise efficiency in resource allocation while improving health outcomes and sustaining future innovation.

References

1. Baker D, Chatani N. (2002) Promoting Good Ideas on Drugs: Are Patents the Best Way? The Relative Efficiency of Patent and Public Support for Bio-Medical Research. Center for Economic and Policy Research. Accessed 24 April 2012, via: http://www.cepr.net/documents/publications/promoting_good_ideas_on_drugs.htm.
2. Belton V, Stewart TJ. (2002) Multiple criteria decision analysis: an integrated approach. Dordrecht: Kluwer.
3. Cabinet Office (2010) The Coalition: our programme for government. HM Government. Accessed 24 April 2012, via: http://www.cabinetoffice.gov.uk/sites/default/files/resources/coalition_programme_for_government.pdf.
4. Department of Health, The (2010) A new value-based approach to the pricing of branded medicines: A consultation. Accessed 24 April 2012, via: http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/document/digitalasset/dh_122793.pdf.
5. Department of Health, The (2011) A new value-based approach to the pricing of branded medicines: Government response to consultation. Accessed 24 April 2012, via: http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_128404.pdf.
6. DETR (1998) A New Deal for Transport: Better for Everyone (The Government's White Paper on the Future of Transport) The Stationery Office, p 133.
7. Devlin NJ, Sussex J. (2011) Incorporating Multiple Criteria in HTA: Methods and Processes. Office of Health Economics. Accessed 24 April 2012, via: <http://www.ohe.org/publications/article/incorporating-multiple-criteria-in-hta-methods-and-processes-8.cfm>.
8. Dodgson J, Spackman M, Pearman A, Phillips L. (2009) Multi-criteria Analysis: A Manual. Department for Communities and Local Government. Accessed 24 April 2012, via: <http://www.communities.gov.uk/documents/corporate/pdf/1132618.pdf>.
9. Goetghebeur MM, Wagner M, Khoury H, Levitt RJ, Erickson LJ, Rindress D. (2008). Evidence and Value: Impact on DEcisionMaking – the EVIDEM framework and potential applications. *BMC Health Services Research*, 8:270.
10. Hollis A. (2004). An Efficient Reward System for Pharmaceutical Innovation. Accessed 24 April 2012, via: <http://www.who.int/intellectualproperty/news/Submission-Hollis6-Oct.pdf>
11. Kennedy I. Appraising the value of innovation and other benefits. A short study for NICE. July 2009.
12. Kanavos P, Manning J, Taylor D, Schurer W, Checchi K. (2010) Implementing value-based pricing for pharmaceuticals in the UK. 2020health.

13. Kanavos P, Casson M, Nicod E. (2011) A new value-based approach to the pricing of branded medicines: a consultation. LSE Health.
14. Keeney RL, and Raiffa H. (1976) *Decisions with Multiple Objectives: Performances and Value Trade-Offs*, Wiley, New York.
15. McGuire A, Raikou M, Kanavos P. (2009) Pricing pharmaceuticals: Value based pricing in what sense? *Eurohealth*; 14 (2), 3-6.
16. Myant K, Urquhart G. (2009). *Deliberative Methods*. Scottish government social research group social science methods series. Accessed 4 February 2013 via: <http://www.scotland.gov.uk/Resource/Doc/175356/0091392.pdf>
17. National Institute for Health and Clinical Excellence (NICE). (2011) Value Based Pricing: Response to the Department of Health consultation. Accessed 24 April 2012, via: <http://www.nice.org.uk/media/D7E/05/NICEVBPConsultation.pdf>
18. OECD (2012), OECD Health Data 2012 – Frequently Requested Data. Accessed March 2013, via: www.oecd.org/els/health-systems/OECDHealthData2012FrequentlyRequestedData_Updated_October.xls
19. Office of Fair Trading (2007) The Pharmaceutical Price Regulation Scheme [Online]. Accessed 24 April 2012, via: http://www.offt.gov.uk/shared_offt/reports/comp_policy/oft885.pdf
20. Pearman AD, Mackie PJ, May AD, Simon D. (1989) The use of multi-criteria techniques to rank highway investment proposals, in A.G. Lockett and G. Islei (eds.) *Improving Decision Making in Organisations*, Springer Verlag, Berlin, pp. 157–65.
21. Phillips LD. (2007) Decision Conferencing. In Edwards W., Miles R.F., and Von Winterfeldt (Eds.), *Advances in decision analysis: from foundations to applications*. Cambridge: CUP.
22. Phillips LD, Fasolo B, Zafiropoulos N, Beyer A. (2011) Is quantitative benefit–risk modelling of drugs desirable or possible? *Drug discovery today: technologies*; 8 (1). e3-e10.
23. Raiffa H. (1968) *Decision analysis: Introductory lectures on choices under uncertainty*. Reading, MA: Addison-Wesley.
24. Sloan F.A., and Hsieh C. (2007) *Introduction, in: Incentives, Competition, and Cost-Benefit Analysis in International Perspective*, Edited by Sloan F.A., and Hsieh C., Cambridge University Press.
25. Walker S., and Cone M. (2004) *Benefit–Risk Assessment: Summary Report of the workshop on The Development of a Model for Benefit–Risk Assessment of Medicines Based on Multi-Criteria Decision Analysis*. CMR International Institute for Regulatory Science.

26. Walker S. et al. (2009) Measuring benefit and balancing risk: strategies for the benefit–risk assessment of new medicines in a risk-averse environment. *Clin Pharmacol Ther*; 85, 241–246.
27. Walker S. et al. (2011) Refining the benefit–risk framework for the assessment of medicines: valuing and weighting benefit and risk parameters, *Clin Pharmacol Ther*; 89, 179–182.
28. Yetim F. (2009). A deliberation theory-based approach to the management of usability guidelines. *Informing Science: the International Journal of an Emerging Transdiscipline*, Vol. 12; accessed 19 February 2013 via: <http://www.inform.nu/Articles/Vol12/ISJv12p073-104Yetim519.pdf>.
29. Zethraeus N, Johannesson M, Jönsson B, Löthgren M, Tambour M. (2003). Advantages of using the net-benefit approach for analysing uncertainty in economic evaluation studies. *Pharmacoeconomics*. 21(1):39-48.

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