



## Workshop Report

# Workshop Report: concepts and methods in the economics of nutrition – gateways to better economic evaluation of nutrition interventions

I. Lenoir-Wijnkoop<sup>1\*</sup>, M. J. C. Nuijten<sup>2</sup>, I. Gutiérrez-Ibarluzea<sup>3,4</sup>, J. Hutton<sup>5</sup>, M. J. Poley<sup>6</sup>, L. Segal<sup>7</sup>, J. L. Bresson<sup>8</sup>, E. van Ganse<sup>9</sup>, P. Jones<sup>10</sup>, L. Moreno<sup>11</sup>, S. Salminen<sup>12</sup> and D. Dubois<sup>13</sup>

<sup>1</sup>Danone Research, Scientific Affairs, Palaiseau, France

<sup>2</sup>Ars Accessus Medica, Amsterdam, The Netherlands

<sup>3</sup>Osteba, Basque Office for Health Technology Assessment, Health and Consumer Affairs Department, Basque Government, Vitoria-Gasteiz, Basque Country, Spain

<sup>4</sup>Nursing School of the Basque Health Service, Osakidetza, Vitoria-Gasteiz, Basque Country, Spain

<sup>5</sup>York Health Economics Consortium, Department of Health Sciences, University of York, York, UK

<sup>6</sup>Institute for Medical Technology Assessment, Erasmus University Rotterdam, Rotterdam, The Netherlands

<sup>7</sup>Health Economics and Social Policy Group, Division of Health Sciences, University of South Australia, Adelaide, SA, Australia

<sup>8</sup>Centre d'investigation Clinique, Hôpital Necker-Enfants Malades, Descartes University, Paris, France

<sup>9</sup>Pharmacoepidemiology, CHU-Lyon and UMR-5558, CNRS and Claude-Bernard Lyon 1 University, Lyon, France

<sup>10</sup>Richardson Centre for Functional Foods and Nutraceuticals, Nutrition Department, University of Manitoba, Winnipeg, MB, Canada

<sup>11</sup>Growth, Exercise, Nutrition and Development (GENUD) Research Group, University of Zaragoza, Zaragoza, Spain

<sup>12</sup>Functional Foods Forum, University of Turku, Turku, Finland

<sup>13</sup>PHARMED, Université Libre de Bruxelles, Brussels, Belgium

(Submitted 7 July 2012 – Final revision received 11 July 2012 – Accepted 12 July 2012 – First published online 5 September 2012)

### Abstract

Improving health through better nutrition of the population may contribute to enhanced efficiency and sustainability of healthcare systems. A recent expert meeting investigated in detail a number of methodological aspects related to the discipline of nutrition economics. The role of nutrition in health maintenance and in the prevention of non-communicable diseases is now generally recognised. However, the main scope of those seeking to contain healthcare expenditures tends to focus on the management of existing chronic diseases. Identifying additional relevant dimensions to measure and the context of use will become increasingly important in selecting and developing outcome measurements for nutrition interventions. The translation of nutrition-related research data into public health guidance raises the challenging issue of carrying out more pragmatic trials in many areas where these would generate the most useful evidence for health policy decision-making. Nutrition exemplifies all the types of interventions and policy which need evaluating across the health field. There is a need to start actively engaging key stakeholders in order to collect data and to widen health technology assessment approaches for achieving a policy shift from evidence-based medicine to evidence-based decision-making in the field of nutrition.

**Key words:** Nutrition economics: Health technology assessment: Preventive interventions: Cost-effectiveness: Public health guidance

Escalating healthcare costs have become a major concern for decision-makers, prompting development of innovative cost containment measures<sup>(1,2)</sup>. In Europe, health authorities have started to establish incentives for efficient healthcare

delivery by means of decentralisation of the healthcare decision-making process and implementation of market mechanisms<sup>(3)</sup>. Cost-effectiveness analysis has become common practice for informing reimbursement decisions for

**Abbreviations:** HRQL, health-related quality of life; HTA, health technology assessment; RCT, randomised clinical trial.

\* **Corresponding author:** I. Lenoir-Wijnkoop, email [irene.lenoir@danone.com](mailto:irene.lenoir@danone.com)

pharmaceuticals and other health technologies including devices<sup>(4)</sup>. Nutrition interventions tend to be excluded from these processes, although healthcare decision-makers have begun to realise that food plays an important role, not only in those already with disease, but also in the onset and evolution of lifestyle-related disorders. Indeed, improving health through better population nutrition may contribute to the cost-effectiveness and sustainability of healthcare systems. It is therefore essential to describe and quantify the costs and effectiveness of nutrition interventions, both the immediate costs of the intervention and downstream consequences, and to assess impacts for individuals, the healthcare system and society as a whole. The discipline of nutrition economics, currently being established, is relevant and timely for informing decision-making. First, this discipline helps to better inform health authorities and consumers on the harms of poor nutrition and on the benefits of making certain food choices. Second, the discipline is essential to governments in designing efficient public population-scaled interventions and educational campaigns. A third focus is on nutrition interventions delaying disease onset or progression. Finally, nutrition economics is also relevant for improving the nutritional quality of foods produced by industry.

To identify and explore the field of nutrition economics, a first expert meeting was held in February 2010. This exchange resulted in a consensus about the importance of defining this new area and led to the establishment of a first multidisciplinary approach to understanding the principles, relevance and particular characteristics of the field of nutrition economics<sup>(5)</sup>. A second meeting was held in Madrid, in October 2011 with the goal to investigate in detail a number of methodological concepts and issues. Nutrition interventions vary from specific individual treatments to broad public health measures, and therefore their evaluation requires a range of different approaches. They depend on involvement of the target audience in the decision to engage in the 'intervention', often without the support provided in adhering to a specific treatment on medical prescription. The feasibility of expressing the multidimensional impact of nutrition on the individual's quality of life in a single outcome measure has yet to be fully addressed. The need to enhance capacity in the evaluation of complex multi-component interventions formed the focus of the panel discussions reported below.

### Health economics and nutrition

Cost-effectiveness analyses aim to provide reliable, reproducible and verifiable insight into the effectiveness of an intervention, the costs of its implementation and the potential downstream savings. Cost-effectiveness analyses in nutrition interventions tend to rely heavily on health economic modelling, as a long-term follow-up is required to appropriately measure impacts, which invariably extend far beyond the periods of intervention. The challenges of a long-term follow-up are many, including handling of dropouts, study investment costs and changes in technology or society, which can render the original intervention or control context unrealistic. Nutrition interventions are often preventive; they

can be implemented at the population level or individually and employ various methods including health promotion, social marketing, consumer research, clinical consultation and financial incentives such as taxes, subsidies or regulations. Nutrition interventions cover the cycle from farm to fork and thus extend well beyond the health sector. Nutrition economics and the economic evaluation of nutrition interventions must therefore deal with a wide range of issues.

### Nutrition and health-related quality of life assessment

The concept of health-related quality of life (HRQL) is relevant to health-economic evaluations wherever quality of life impacts are expected, which will typically be the case with nutrition interventions. HRQL is a multidimensional concept and encompasses several aspects including (1) the person's functional status across various domains, such as physical, occupational and interpersonal, and (2) the person's appraisal of how his/her health affects his enjoyment or quality of life<sup>(6)</sup>. One proposed definition of HRQL is: 'the subjective perception of the impact of health status, including disease and treatment, on physical, psychological, and social functioning and wellbeing'<sup>(7)</sup>. However, this does not mean that it is a subjective measure. Indeed, a measurement instrument that is validated according to rigorous validity criteria can objectively assess subjective phenomena<sup>(8)</sup>. In contrast to traditional endpoints used in clinical trials, the responses to quality-of-life questionnaires directly reflect the subject's own perspective on his/her health status. The scope of HRQL measures is not limited to patients with defined symptomatic diseases, but can also be used in a general population setting. These measurements are valuable in providing preference-based 'utility values' used in economic evaluation studies. Several concepts<sup>(9,10)</sup>, techniques<sup>(11,12)</sup> and instruments<sup>(13,14)</sup> are available for assigning a utility value to a particular health state. Validated non-preference-based HRQL measures provide additional information on the subject's own viewpoint on health conditions and their management.

The principles of health economic evaluation apply to all health technologies. Thus, it makes sense to establish whether the existing methods provide reliable information on nutrition interventions, before addressing methodological problems specifically related to the field of nutrition. The different health outcome measures have in common that they ascribe the same weight regardless of who gains the benefit. Equity weighing is possible and has been used<sup>(15)</sup>, but this does not imply that fairness and equity in health is taken into account automatically<sup>(16)</sup>. Also, characteristics such as personality, cognitive dysfunction and psychological adaptation to illness may influence how a person responds to the items<sup>(17,18)</sup>. Notwithstanding the imperfections, these measures are very practical for decision-makers.

Other issues related to nutrition have remained largely unexplored until today. A nutrition intervention may operate very differently from drug treatment, and this needs to be addressed. Some existing paradigms require adjustment in order to include dimensions that are not captured using traditional measures. Food can serve in a context of prevention,

treatment, palliative care, etc., and this will inform the development of an appropriate endpoint model and condition the items to be measured.

A few more general considerations were discussed, in particular the need to consider the individual's satisfaction. It is important to have this dimension captured in the matrix for quality of life assessment in nutrition. A recent Food and Drug Administration Public workshop on Clinical Trial Outcome Assessments emphasised the need to define the context of use for validating outcome assessments: interestingly, the impact on general life concepts presented included productivity, health status, HRQL as well as satisfaction with health<sup>(19)</sup>. In addition, many subjects who are not diseased but have a known risk factor, e.g. a high LDL-cholesterol concentration or a low bone mineral density, will prefer not to take drugs to avoid being labelled as a patient or through fear of drug-related adverse effects<sup>(20)</sup>. The choice not to pursue medication is a component that is often not captured when assessing quality of life, partly because that target population is unlikely to enter a trial. Assessing the HRQL impact of prevention in a sub-healthy individual is extremely relevant in nutrition, since the awareness of being at risk for developing a disease might also affect quality of life<sup>(21)</sup>.

In summary, for comprehensive outcome measures for nutrition in a daily setting, the appropriate assessment tools have to be selected based on the context and the research question.

### Health technology assessment and decision-making

Health technology assessment (HTA) provides evidence and analysis for different levels of decision-making: micro – clinicians, meso – managers; and macro – policy makers. HTA seeks to provide health authorities and professionals with accessible and usable information to guide their decisions, whether these are used for advice on individual technologies or intended as guidelines for the management of health concerns and target populations. The scope of HTA needs to incorporate broad-ranging issues, including social values, legal concerns, ethical aspects and organisational issues, as well as clinical benefits and cost-effectiveness. The focus of a particular HTA will depend on the decision context – who needs the information and for what type of decision. Properly used, HTA helps to produce transparent, accountable and evidence-based decisions. However, HTA has been mainly associated with drug and medical device reimbursement decisions, where, in many countries, financial considerations of affordability may be as important as clinical and cost-effectiveness. Although a decision-making process in the field of nutrition economics will in general not involve reimbursement for individual products, interventions to change public awareness of, and attitudes to, nutrition will have a cost, which needs to be justified against other uses of health budgets. For example, in the case of initiatives to change eating patterns by introducing taxes on unhealthy or unbalanced food products, the consequences in terms of economic efficiency and social equity need to be carefully evaluated during the decision-making process.

Although the intention is to improve public health, the economic consequences of such taxation could induce an opposite effect or lead to increasing health inequalities<sup>(22,23)</sup>.

Another important consideration is the impact of policies which are primarily designed to meet non-health objectives, but which have a major effect on health. In the field of nutrition, there are clear links with agricultural policies. Reports from the European Commission indicate that the health impact of policies is often secondary to economic or regional policy interests<sup>(24)</sup> and support the idea that health is not necessarily considered in an appropriate manner in impact assessments<sup>(25)</sup>.

These factors offer an interesting opportunity for the application of the HTA evaluation framework in the field of nutrition economics, where equity and efficiency considerations may be equally important. The general population and decision-makers are not only interested in efficiency but also in equity in the distribution of health<sup>(26)</sup>. Current initiatives to apply comprehensive economic evaluation methods to public health interventions, including those in nutrition, should be continued<sup>(27)</sup>.

### The use of models in the nutrition arena

The use of models in economic evaluation combines different types of data sources to extend available information. Models can be used to simulate costs of trial modalities, to generalise trial results, to translate evidence from randomised clinical trials (RCT) into daily practice or to explore the potential value of additional evidence from empirical research. Several types of models can be used in the area of nutrition. One of them is the decision tree, comparing two or more health strategies. It defines intervention pathways and then links costs and outcomes to all the possible options. Another type of model is the Markov model, organised around health states rather than around pathways<sup>(28)</sup>. In this case, the data input will be based on probabilities of transitions between successive health states and specific costs and utilities associated with the various health states<sup>(29)</sup>. Still other modelling techniques that can be used in nutrition economics are methods that stem from epidemiology, such as the population attributable fraction and the potential impact fraction<sup>(30)</sup>. Modelling techniques usually extrapolate the available short-term evidence over time in order to estimate outcomes beyond the study period or to link intermediate endpoints to final outcomes. This approach represents a valuable contribution in decision-making processes that face the challenging task of achieving small but tangible modifications of dietary behaviour in order to reduce nutrition-related chronic health concerns on the long term<sup>(31)</sup>. The need for a long-term follow-up, in the general or in a healthy at-risk population, may be solved by extrapolation methods; these are not specifically related to nutrition, but more to underlying available evidence and relationships. A good illustration can be found in the North Karelia Project. In this Finish province, a major preventive project was launched in the early 1970s with the aim to reduce the high morbidity and mortality associated with CVD. The programme was a result of a petition by

representatives of the people, who were concerned about the data from national statistics<sup>(32)</sup>. The intervention, originally set up for a period of 5 years, became national and led in the late 1980s to an intensified action, when surveys showed that the reduction of blood cholesterol was levelling off. The dietary changes in Finland resulting from the intervention, i.e. changes in food supply and nutritional and lifestyle recommendations, have led to an 80% reduction in annual CVD mortality rates among the working-age population, and a major increase in life expectancy has been observed, as well as improvements in functional capacity and health<sup>(33,34)</sup>. Lifestyle study programmes<sup>(35)</sup>, cross-sectional surveys<sup>(36)</sup> and cohort studies<sup>(37,38)</sup> allow us to develop risk equations for disease progression that include the quality of the diet. The Australian longitudinal study on Women's Health illustrates the opportunity to explore dietary patterns and the relationship between diet and diverse health outcomes, including healthcare costs<sup>(39)</sup>. The foregoing discussion underlines that evidence requirements have to be fulfilled in two complementary ways: by clinical evidence from RCT and by epidemiological observations and national statistics.

### The quality of evidence

Healthcare guidance must be based on best available evidence<sup>(40,41)</sup>. It is not limited to the clinical situation; often the guidance is intended to other public agencies in the education and social service sectors or directly to individuals. In the case of therapeutic interventions, the properly conducted RCT is commonly recognised as the gold standard for clinical efficacy. This criterion relates to the issue of preferring internal validity to external validity<sup>(42)</sup>. The difficulty of using a RCT is its translation to the population level and linking results of clinical intervention trials with high internal validity in terms of treatment outcomes in routine practice<sup>(43)</sup>. This translation is especially challenging in nutrition because of more confounding variables and the greater difficulty in controlling nutritional factors when compared with pharmaceutical treatments.

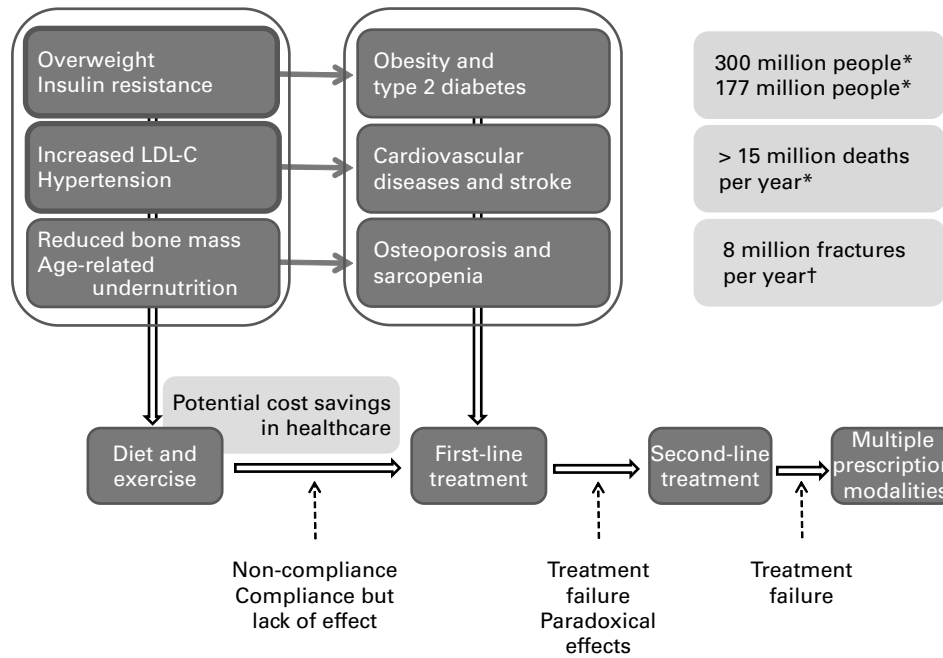
As previously mentioned<sup>(5)</sup>, the lifestyle setting and a need for high external validity justify the use of other types of evidence, such as cohort studies and other observational data. Clinical trial populations do not match the population likely to be treated with the study intervention. New methods and new developments have been produced, not as much related to the clinical effect, but more to the clinical relevance and final results on a totality of subjects<sup>(44)</sup>. It will be of great interest to translate this approach to the field of nutrition economics, where the final endpoint is the relevance for society. The issue is not restricted to defining the level of evidence but also includes translation of the evidence into public health guidance in terms of nutrition interventions, which raises the challenging issue of generalisability to daily practice. To move into the territory of another type of best evidence, a gradual strategy could be considered in order to obtain robust data. Such a strategy begins at the most serious end of a nutrition-related chronic health concern and then is gradually taken upwards. If an effect is observed, the cost of

doing so remains limited and when moving further and further up the intervention pathway, the population becomes larger. The research question needs of course to be correctly defined before starting the study and although individual effects might get smaller, the global impact on public health and healthcare expenditures is more likely to attain significance. The process of producing guidance based on the best available evidence is crucial to allow robust and accountable decision-making processes<sup>(45)</sup>. Nutrition should be no exception to this rule.

In recent years, the Grading of Recommendations Assessment, Development and Evaluation approach has been used as a system for rating quality of evidence and strength of recommendations. It is claimed to be explicit, comprehensive, transparent and pragmatic, and is increasingly being adopted by organisations worldwide<sup>(43)</sup>. The approach is mostly devoted to recommendations for clinical practice and has been applied to recommendations on individuals or health technologies<sup>(47)</sup>. However, this approach should also be tested in terms of its usefulness for public health interventions and modified accordingly if found to be insufficient.

### The importance of evidence-based guidance for nutrition

Clinical guidelines include the role of nutrition in the management of some metabolic diseases, for instance diabetes<sup>(48)</sup>, but do not routinely do so for other diseases where nutrition can be important. The incorporation of a new intervention modality into clinical guidelines depends on the evidence for the efficacy and safety of a new intervention. The recommendation in clinical guidelines is an important criterion for the choice of prescription modalities by healthcare providers, and if a new intervention strategy is not included in the clinical guidelines, healthcare professionals will be hesitant to apply it. If the guidelines advised consideration of diet and exercise before any drug prescription<sup>(49,50)</sup>, healthcare costs might be reduced (Fig. 1). In producing guidance, cost-effectiveness must also be considered. Escalating costs have resulted in a demand for cost-effectiveness data in the decision-making process. Therefore, interventions should be assessed on their cost-effectiveness *v.* standard practice before being included in guidelines<sup>(51)</sup>. Some countries have defined a cost-effectiveness threshold in terms of maximum cost per quality adjusted life year (QALY), which interventions must meet before being considered cost-effective and therefore reimbursable. The UK is the only European country to be explicit about the cost-effectiveness threshold it uses. The WHO has proposed thresholds on an arbitrary basis ([http://www.who.int/choice/costs/CER\\_thresholds/en/index.html](http://www.who.int/choice/costs/CER_thresholds/en/index.html)) and countries may seek to depart from these for various reasons. Countries may also seek to adopt a more complex approach that takes account of other factors such as the type of intervention, the target population, and the quality and certainty of evidence. In reality, in most countries, the health authorities seem to prefer to make decisions without defining clear thresholds or communicate them to the public domain, allowing considerable discretion for policy makers. It is still unclear what would constitute an appropriate cost-effectiveness threshold to apply in a lifestyle-oriented setting.



**Fig. 1.** Common conditions of ill health in the general population and treatment pathways – extension of nutritional strategies for managing many non-communicable diseases would considerably reduce healthcare expenditures. \*<http://www.who.int>; †<http://www.iofbonehealth.org> (accessed 17 May 2012). LDL-C, LDL-cholesterol.

### Discussion – the future agenda

Nutrition is an aspect of lifestyle and is subject to individual choice. Should society take it into consideration and more actively promote nutrition interventions that improve overall public health and thereby reduce healthcare costs? Should nutrition economics therefore be linked more closely to social values and would these be more relevant than in other fields of health economics? Identifying the concepts to measure and the context of use will be a key consideration in selecting and developing HRQL measurements for nutrition interventions. Satisfaction was frequently mentioned during the meeting and opposing views about the interest of including it in assessments were expressed. Some panel members argued that individual satisfaction is an important driver in motivating people and can therefore improve the impact of public health interventions. Others considered that was not the case, although they conceded that healthy food choices can be enjoyable and help in achieving changes in behaviour. At the moment, nutrition is generally not often taken into account by those seeking to reduce healthcare expenditures. This does not mean that nutrition should necessarily be included in the reimbursement system to attract the attention of decision-makers. By showing the outcomes of some of the measures and strategies already used<sup>(52–55)</sup>, the nutrition economic approach is likely to quickly gain interest among decision-makers. What is more, current strategies to address the issue of the ageing population and the consequent increasing demands on healthcare systems from the management of chronic diseases should recognise the value of interventions on lifestyle including nutrition. These interventions provide opportunities for societal organisations, healthcare providers and food businesses to develop new technologies

and products while using nutrition economic assessments to support their strategies.

At present, a major issue is to build up expertise within the clinical community to run trials in nutrition-related matters to obtain evidence that can support decisions on interventions and that provide good value for money. Most investigators are used to a very restrictive phase III-type RCT, but policy evaluations are of a different nature. So far, we have fallen short of carrying out more pragmatic trials in many areas where these would generate the most useful data. The hard work that was done in the evaluation of medical technologies, set up conceptually from the late 1960s onwards and developed simultaneously in different places, in the absence of electronic communication, resulted only 30 years later in the creation of dedicated structures, organisations and networks, e.g. IQWIG (Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen), HAS (Haute Autorité de Santé), NICE (National Institute for Health and Clinical Excellence), INAHTA (International Network of Agencies for Health Technology Assessment), EuroScan, EUnetHTA (European Network for Health Technology Assessment), and so on. This was the time needed to build up sufficient examples of its application and to show that the methodology actually is a valuable aid in health policy decision-making. The field of nutrition economics is now in a comparable situation of 'information gap period', and there is a need to start actively engaging key stakeholders to collect data, using measures that decision-makers will recognise. Within nutrition, some common metrics can be identified which allow us to judge the relative merits of clinically led interventions and public health advice. Then, as nutrition exemplifies all the types of interventions and policy which need evaluating across the

health field, the demonstration that many nutritional issues have not been dealt with correctly in the current context will further enable us to enrich the basic outcome data and to develop more relevant approaches. This may then give insights into ways in which the overall HTA paradigm can be widened and thus contribute to broadening out the concept of the social welfare function beyond simple incremental cost-effectiveness ratios and application of qualitative judgements on equity, as happens in current decision-making. This may further lead to interactions with policies from other sectors which have health implications through the medium of nutrition such as agricultural policy, food pricing and taxation.

It is time to change the paradigm from the micro-level of evidence-based medicine to evidence-based decision-making, including meso- and macro-levels, and to convince health authorities that there should be a policy shift by introducing up-to-date knowledge of the importance of nutrition. The authors welcome any feedback and suggestions for further substantiating the value of nutrition interventions in the optimisation of public health.

### Acknowledgements

All authors contributed to the workshop discussions. I. L.-W. drafted the manuscript and all authors had input into its final form. None of the authors declares a conflict of interest. I. L.-W. is employed by Danone Research.

### References

- Park M, Braun T & Carrin G (2007) *Technical Briefs for Policymakers*. WHO Department of Health Systems Financing No. 2. Geneva: World Health Organization.
- Ginsburg PB (2004) Controlling health care costs. *N Engl J Med* **351**, 1591–1593.
- World Health Organization & European Observatory on Health Systems and Policies Series (2005) *Purchasing to Improve Health Systems Performance* [J Figueras, R Robinson and E Jakubowski, editors]. Milton Keynes: Open University Press.
- Drummond MF, Dubois D, Garattini L, *et al.* (1999) Current trends in the use of pharmacoeconomics and outcomes research in Europe. *Value Health* **2**, 323–332.
- Lenoir-Wijnkoop I, Dapoigny M, Dubois D, *et al.* (2011) Nutrition economics: characterising the economic and health impact of nutrition. *Br J Nutr* **105**, 157–166.
- Fayers P & Bottomley A (2002) Quality of life research within the EORTC – the EORTC QLQ-C30. *Eur J Cancer* **38**, S125–S133.
- Leidy NK, Revicki DA & Genesté B (1999) Recommendations for evaluating the validity of quality of life claims for labeling and promotion. *Value Health* **2**, 113–127.
- FDA Guidance for Industry (2009) Patient-reported outcome measures: use in medical product development to support labeling claims. [www.fda.gov/downloads/Drugs/Guidance-ComplianceRegulatoryInformation/Guidances/UCM193282.pdf](http://www.fda.gov/downloads/Drugs/Guidance-ComplianceRegulatoryInformation/Guidances/UCM193282.pdf).
- Drummond M, Brixner D, Gold M, *et al.* (2009) Toward a consensus on the QALY. *Value Health* **12**, S31–S35.
- Cambridge, Harvard School of Public Health (1996) *The Global Burden of Disease: A Comprehensive Assessment of Mortality and Disability from Diseases, Injuries and Risk Factors in 1990 and Projected to 2020* [CJL Murray and AD Lopez, editors]. Cambridge, MA: Harvard School of Public Health.
- Torrance GW, Furlong W, Feeny D, *et al.* (1995) Multiattribute preference functions. Health Utilities Index. *Pharmacoeconomics* **7**, 503–520.
- Arnesen T & Trommald M (2005) Are QALYs based on time trade-off comparable? A systematic review of TTO methodologies. *Health Econ* **14**, 39–53.
- The EuroQol Group (1990) EuroQol – a new facility for the measurement of health-related quality of life. *Health Policy* **16**, 199–208.
- Richardson J, Iezzi A, Sihna K, *et al.* (2009) AQoL-7D (Vision) Instrument: Overview, survey results and utility algorithms. Monash University, Research Paper 2009 (45).
- World Bank & World Development Report (1993) *Investing in Health*. New York: Oxford University Press.
- Soares MO (2012) Is the QALY blind, deaf and dumb to equity? NICE's considerations over equity. *Br Med Bull* **101**, 17–31.
- Muldoon MF, Barger SD, Flory JD, *et al.* (1998) What are quality of life measurements measuring? *Br Med J* **316**, 542–545.
- Slevin ML, Plant H, Lynch D, *et al.* (1988) Who should measure quality of life, the doctor or the patient? *Br J Cancer* **57**, 109–112.
- Measurement in clinical trials: review and qualification of clinical outcome assessments, Public Workshop October 2011, White Oak, MD. <http://www.fda.gov/Drugs/NewsEvents/ucm276110.htm>
- Fried TR, Tinetti ME, Towle V, *et al.* (2011) Effects of benefits and harms on older persons' willingness to take medication for primary cardiovascular prevention. *Arch Intern Med* **171**, 923–928.
- Fidler C, Christensen TE & Gillard S (2011) Hypoglycemia: an overview of fear of hypoglycemia, quality-of-life, and impact on costs. *J Med Econ* **14**, 646–655.
- Nnoaham KE, Sacks G, Rayner M, *et al.* (2009) Modelling income group differences in the health and economic impacts of targeted food taxes and subsidies. *Int J Epidemiol* **38**, 1324–1333.
- Duffey KJ, Gordon-Larsen P, Shikany JM, *et al.* (2010) Food price and diet and health outcomes: 20 years of The CARDIA Study. *Arch Intern Med* **5**, 420–426.
- Observatory on Health Systems and Policies (2006) *Health in All Policies – Prospects and Potentials* [T Ståhl, M Wismar and E Ollila, *et al.*, editors]. [http://ec.europa.eu/health/archive/ph\\_information/documents/health\\_in\\_all\\_policies.pdf](http://ec.europa.eu/health/archive/ph_information/documents/health_in_all_policies.pdf)
- Ståhl T (2010) Is health recognised in the EU's policy process? An analysis of the European Commission's impact assessments. *Eur J Public Health* **2**, 176–181.
- Ubel PA, Baron J, Nash B, *et al.* (2002) Are preferences for equity over efficiency in health care allocation “all or nothing”? *Med Care* **38**, 366–373.
- NICE (2011) Supporting local investment in public health – using evidence on cost effectiveness, cost impact and return on investment to inform local commissioning. <http://www.nice.org.uk/media/737/C5/CostImpactSynopsis.pdf>
- Graves N (2006) Cost-effectiveness analyses and modelling the lifetime costs and benefits of health-behaviour interventions. *Chronic Illness* **2**, 97–107.
- Lenoir-Wijnkoop I, van Aalderen WM, Boehm G, *et al.* (2012) Cost-effectiveness model for a specific mixture of prebiotics in The Netherlands. *Eur J Health Econ* **13**, 101–110.

30. Lötters FJB, Lenoir-Wijnkoop I, Fardellone P, *et al.* (2012) Dairy foods and osteoporosis: an example of assessing the health-economic impact of food products. *Osteoporos Int* (epublication ahead of print version 16 June 2012).
31. Lotan Y, Buendia Jiménez I, Lenoir-Wijnkoop I, *et al.* (2012) Primary prevention of nephrolithiasis is cost-effective for a national health care system. *Br J Urol* (epublication ahead of print version 11 June 2012).
32. Puska P, Nissinen A & Tuomilehto J (1985) The community-based strategy to prevent coronary heart disease: conclusions from the ten years of the North Karelia project. *Ann Rev Public Health* **6**, 147–193.
33. Puska P (2009) Fat and heart disease: yes we can make a change – the case of North Karelia (Finland). *Ann Nutr Metab* **54**, S33–S38.
34. Puska P & Ståhl T (2010) Health in all policies – the Finnish initiative: background, principles, and current issues. *Annu Rev Public Health* **31**, 315–328.
35. Sesé MA, Jiménez-Pavón D, Gilbert CC, *et al.* (2012) Eating behaviour, insulin resistance and cluster of metabolic risk factors in European adolescents. The HELENA Study. *Appetite* **59**, 140–147.
36. Health Canada. (2006) *Canadian Community Health Survey, Cycle 2.2, Nutrition (2004) – A Guide to Accessing and Interpreting the Data*. Ottawa, ON: Health Canada. [http://www.hc-sc.gc.ca/fn-an/alt\\_formats/hpfb-dgpsa/pdf/surveill/cchs-guide-escs-eng.pdf](http://www.hc-sc.gc.ca/fn-an/alt_formats/hpfb-dgpsa/pdf/surveill/cchs-guide-escs-eng.pdf)
37. Duffey KJ, Steffen LM, Van Horn L, *et al.* (2012) Dietary patterns matter: diet beverages and cardiometabolic risks in the longitudinal Coronary Artery Risk Development in Young Adults (CARDIA) Study. *Am J Clin Nutr* **95**, 909–915.
38. Buckland G, Agudo A, Lujan L, *et al.* (2010) Adherence to a Mediterranean diet and risk of gastric adenocarcinoma within the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort study. *Am J Clin Nutr* **91**, 381–390.
39. Blumfield M, Hure A, MacDonald-Wicks L, *et al.* (2011) Disparities exist between national food group recommendations and the dietary intakes of women. *BMC Women's Health* **11**, 37.
40. Upshur REG (2003) Are all evidence-based practices alike? Problems in the ranking of evidence. *CMAJ* **169**, 672–673.
41. Tonelli MR (2001) The limits of evidence-based medicine. *Resp Care* **46**, 1435–1440.
42. Rothwell PM (2005) External validity of randomised controlled trials: “to whom do the results of this trial apply?”. *Lancet* **365**, 82–93.
43. Ioannidis JPA (2008) Some main problems eroding the credibility and relevance of randomized trials. *Bull NYU Hosp Joint Dis* **66**, 135–139.
44. Guyatt GH, Oxman AD, Kunz R, *et al.* (2008) Rating quality of evidence and strength of recommendations: what is “quality of evidence” and why is it important to clinicians? *BMJ* **336**, 995–998.
45. Rawlins M (2008). De Testimonio: on the evidence for decisions about the use of therapeutic interventions. The Royal College of Physicians of London Harveian Oration. <http://www.rcplondon.ac.uk/pubs/brochure.aspx?e=262>
46. Grading of Recommendations, Assessment, Development and Evaluation (GRADE) Working Group (2004) Grading quality of evidence and strength of recommendations. *BMJ* **328**, 1490.
47. Ibarгойen-Roteta N, Gutierrez-Ibarluzea I, Rico-Iturriz R, *et al.* (2010) The GRADE approach for assessing new technologies as applied to apheresis devices in ulcerative colitis. *Implement Sci* **16**, 48.
48. Nathan DM, Buse JB, Davidson MB, *et al.* (2006) Management of hyperglycemia in type 2 diabetes: a consensus algorithm for the initiation and adjustment of therapy: a consensus statement from the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetes Care* **29**, 1963–1972.
49. American Diabetes Association (2008) Clinical practice recommendations. Standards of medical care in diabetes – 2008. *Diabetes Care* **31**, Suppl. 1, S12–S54.
50. Agence Française de Sécurité Sanitaire des Produits de Santé (2006) *Traitement médicamenteux de l'ostéoporose post-ménopausique. Recommendations (Drug Treatment of Postmenopausal Osteoporosis. Recommendations)*. Saint-Denis: Agence Française de Sécurité Sanitaire des Produits de Santé.
51. Nuijten M, Renkens M, Kogels E, *et al.* (2011) The decision making process of payers: a pilot survey in The Netherlands. *ISPOR Connections* 8–9.
52. Plotnikoff GA (2003) Food as medicine – cost-effective health care? *Minnesota Med* **86**, 41–45.
53. McCarron DA & Heaney RP (2004) Estimated healthcare savings associated with adequate dairy food intake. *Am J Hypertens* **17**, 88–97.
54. Dalziel K & Segal L (2007) Time to give nutrition interventions a higher profile: cost-effectiveness of 10 nutrition interventions. *Health Prom Int* **22**, 271–283.
55. Doidge JC, Gospodarevskaya E & Segal L (2011) 7th Health Services & Policy Research Conference, Adelaide, SA, Australia.