Policy in Economic Analysis of Nutrition Interventions
Session 3 Summary

Session 3 Moderators: Dr. Johanna Dwyer, Senior Nutrition Scientist, Office of Dietary Supplements, NIH
Dr. Robert Russell, Special Expert, Office of Dietary Supplements, NIH

The final session focused the role of health economics in health policy, health regulation, and health care service delivery.

Supporting Congressional Decision Making on Nutritional Policy
Susan Offutt, Chief Economist, Government Accountability Office

The role of GAO, which is part of the legislative branch of government, is to make government more efficient, effective, ethical, equitable, and responsive. GAO examines federal nutrition programs to support congressional decisions on nutrition policy.

Examples of GAO evaluations of nutrition interventions include a report on ways to use electronic benefit transfers in SNAP to increase fruit and vegetable consumption. GAO also examined nutrition education delivery in schools when Congress considered reauthorizing the school nutrition program under the Farm Bill. GAO has reported on how the FDA has implemented food labeling requirements and how the increased information in food labels affects food choices. Unfortunately, better nutritional information did not bring about desired behavior changes, and research needs to identify the reasons for this failure. GAO also has reported on successful efforts to reduce childhood obesity.

Economic analyses of nutrition interventions involve understanding food choices in all of the environments in which people choose what to eat. Few cost-effectiveness studies have taken place in these community environments. Better data on food consumption and food choice behavior are needed to design effective policies.

A more sophisticated model of food choice architecture is needed. Although peoples' incomes influence their food choices, prices and income alone do not completely explain food choices. Insights from behavioral economics might help researchers better understand food choices, and this enhanced understanding could lead to better nutrition policies and outcomes.

Health Economics in Planning, Evaluation, and Policy Research at the Department of Health and Human Services
Laina Bush, Office of the Assistant Secretary for Planning and Evaluation, U.S. Department of Health and Human Services

The DHHS Office of the Assistant Secretary for Planning and Evaluation (ASPE) advises the DHHS Secretary on policy development in health, disability, aging, human services, and science. ASPE functions include policy analysis and development; policy research, evaluation, and data collection; policy and program planning; and policy implementation. The office has 124 experts

in economics and other disciplines. Detailed information on ASPE projects is available at http://www.hhs.gov/aspe.

In 2007, ASPE and several other organizations sponsored a workshop, Nutritional Risk Assessment, to explore issues and challenges faced by nutritionists. Issues addressed include the strengths and challenges of using various risk-assessment approaches to inform dietary and nutritional recommendations, using risk-assessment approaches to evaluate standards for nutrient intake and the relationship of diet and nutrition to chronic disease risk, and identifying next steps to make progress in these areas.

ASPE also identified barriers to the adoption of previous versions of the U.S. Department of Agriculture's Dietary Guidelines for Americans in support of developing the 2010 guidelines. The most commonly cited barrier among at-risk subpopulations was the high cost or perceived high cost of food. The most successful interventions to promote guideline adoption targeted narrow dietary problems and addressed only one or two barriers for each subpopulation.

Other ASPE nutrition-related activities include:

- Exploring the adaptation of adult-based guidelines for children. Although at least 100 child-focused studies support the use of the dietary guidelines for children, evidence is lacking on the health effects of whole grains, potassium, and certain fats on children. More studies are also needed on the impact of following the dietary guidelines on children's short- and long-term health.
- Creating a model to estimate the budgetary and public health impact of the FDA's food import screening activities and determine the effects of reallocating examination resources to food safety.
- Developing a model of the potential costs and savings associated with prevention services as part of health reform. Researchers are determining whether restricting coverage to evidence-based services and whether targeting specific populations makes a difference.

Using Economic Analysis in Food and Drug Administration Nutrition Interventions
Dr. David Zorn, Center for Food Safety and Applied Nutrition, FDA

Economic analysis brings social science and human behavior into decision making. It provides quantification of exposures, behavior changes, and health effects, and provides an estimate of the opportunities and consequences involved in applying interventions on the large scale. U.S. federal regulatory agencies have been required to carry out economic analyses of various regulations since the 1970s, under a series of laws and executive orders.

Basic requirements for economic analyses of federal regulations include identifying the need for regulation, identifying regulatory options, and estimating the costs and benefits of options. The elements of effective regulatory analysis include: (1) addressing a public health problem, (2) explaining why regulation is the best way to address the problem, (3) providing regulatory options for addressing the problem, (4) identifying specific changes in the behavior of all affected, (5) determining cost changes in behavior, (6) identifying the effectiveness of changes in behavior, (7) determining the value of the reduction in the public health problem, and (8)

identifying variability and uncertainty in estimates. Regulatory analysis has a very narrow purpose. It is informing (not deciding or advertising) regulatory (not clinical practice) policy (sufficient for law and decision making). A regulatory analysis needs to be an honest evaluation of a regulation to inform decision making. It is only one input in the decision making process. Examples of FDA economic analyses of major nutrition regulations include nutrition labeling (1993), folic acid fortification (1996), and *trans* fat labeling (2003).

The FDA estimates costs based on an engineering cost model for product changes, the cost of negative health consequences, and the cost for consumers and producers of behavioral changes. Benefit estimation at FDA is a product of the number of illnesses prevented, number of QALYs saved per illness prevented, and monetary value of a statistical life year. Several approaches are available for estimating willingness to pay to reduce risk and these different approaches result in a wide range of estimates.

Many FDA projects involve estimates of the effects of food labeling. The consumer studies experts in FDA's Center for Food Safety and Applied Nutrition estimate how much labeling affects consumers' food choices.

Labeling regulations can influence product formulation, as demonstrated by the experience with *trans* fat labeling. When products are reformulated to improve a set of products' overall nutrition profile, the nutrition intake even of consumers who do not use nutrition labeling improves.

FDA has conducted economic analyses of nutrition interventions:

- The standardized "Nutrition Facts" labeling on food packaging and established standards for and authorized nutrient content claims and health claims. FDA estimated that these standards prevented 39,000 cases of coronary heart disease and cancer and saved 13,000 lives as a result over a 20-year period, resulting in 81,000 life-years saved. Monetized benefits totaled $3.6 billion.
- FDA required the reporting of *trans* fat amounts on food labels and authorized a *trans*-fat-free claim. The rule will prevent an estimated 600 to 1,200 heart attacks and 250 to 500 deaths annually, resulting in 2,000–4,000 life-years saved annually. The annual monetized benefits associated with this rule total $1–2 billion. Many more products have been reformulated to remove *trans* fats than anticipated in these estimates.
- FDA regulations required the fortification of enriched grain products with folic acid to prevent NTDs. When the rule was published in 1996, economists estimated that it would prevent 25–125 NTDs and 5–30 deaths per year, with annual monetized benefits of $220–$700 million. Subsequent studies have shown a much larger effect.

How Medicare Develops National Coverage Policy
Dr. Louis Jacques, Office of Clinical Standards and Quality, Centers for Medicare and Medicaid Services

Medicare is a national program that health insurance companies administer in 15 U.S. regions. The Medicare Modernization Act of 2003 stipulates that after the Medicare program issues a draft decision, it must publish its final version within 9-12. During this period, the Medicare

program offers two 30-day public comment periods; one is required by law for any proposed decision and one occurs whenever Medicare opens a decision. Medicare must make its final decision public no later than 60 days following the close of the mandated public comment period. This is challenging because, in some cases, CMS receives more than 6,000 public comments and all public comments must be catalogued and responded to.

Medicare rarely makes decisions regarding nutrition-related matters because Congress has not identified most nutritional interventions as insurance benefits under Medicare. Rather, Medicare beneficiaries typically self-administer nutritional interventions or obtain over-the counter nutrition supplements on their own.

The challenges that are common in the comparative analysis of nutritional and other health interventions include using secondary health outcomes from clinical trials done primarily to address other questions, weighing public input and other important but methodologically weaker factors in decisions, the sensitivity of recommendations to changes in inputs, and addressing uncertainties about the consequences of adopting a particular strategy.

The Grades of Recommendation, Assessment, Development and Evaluation Approach for Incorporating Resource Use into Clinical Guidelines
Dr. Gordon H. Guyatt, McMaster University

Over the past two decades, guideline panels have begun to rate the quality of medical evidence and the strength of health-related recommendations, including nutritional recommendations, to provide informative summaries for consumers. Virtually every clinical organization in the United States has not only produced its own guidelines, but has also developed its own system for grading its recommendations, as have many national and international organizations. These myriad systems create much confusion.

Ten years ago, an international group of methodologists and guideline developers began to create a common international system, Grades of Recommendation, Assessment, Development and Evaluation (GRADE), to grade evidence quality and recommendation (Figure 2). The GRADE rating system is described in detail in a 2008 issue of the *British Medical Journal.*[1]

In the past few years, more than 50 organizations have adopted the GRADE approach. The U.S. Preventive Services Task Force, an independent panel that systematically reviews effectiveness evidence and develops recommendations for clinical preventive services, uses many elements of the GRADE approach but continues to use its own system.

Figure 2. Grades of Recommendation, Assessment, Development and Evaluation (GRADE)

Quality of the Evidence

Study Design	Quality of Evidence	Lower if	Higher if
Randomised trial →	High	Risk of bias - 1 Serious - 2 Very serious Inconsistency - 1 Serious - 2 Very serious Indirectness - 1 Serious - 2 Very serious Imprecision - 1 Serious - 2 Very serious Publication bias - 1 Likely - 2 Very likely	Large effect + 1 Large + 2 Very large Dose response + 1 Evidence of a gradient All plausible confounding + 1 Would reduce a demonstrated effect or + 1 Would suggest a spurious effect when results show no effect
	Moderate		
Observational study →	Low		
	Very low		

Strength of Recommendations

Determinants of strength of recommendation	
Factor	**Comment**
Balance between desirable and undesirable effects	The larger the difference between the desirable and undesirable effects, the higher the likelihood that a strong recommendation is warranted. The narrower the gradient, the higher the likelihood that a weak recommendation is warranted
Quality of Evidence	The higher the quality of evidence, the higher the likelihood that a strong recommendation is warranted
Values and preferences	The more values and preferences vary, or the greater the uncertainty in values and preferences, the higher the likelihood that a weak recommendation is warranted
Costs (resource allocation)	The higher the costs of an intervention- that is, the greater the resources consumed- the lower the likelihood that a strong recommendation is warranted

The two topics evaluated by GRADE are: (1) the *quality* of a body of evidence (i.e., the extent to which there is confidence that the estimates are adequate to support a decision), which is rated as high, moderate, low, or very low; and (2) the *strength* of a recommendation, which is graded as strong or weak. Randomized trials start as high-quality evidence, but limitations, including risk of bias, inconsistency, indirectness, imprecision, and publication bias, may lower their quality ratings. Observational studies start as low-quality evidence, but factors such as very large effects or a dose-response relationship may increase their quality ratings. The output of the GRADE evaluation is an evidence profile, which permits different ratings of quality of evidence for different outcomes, and presents the best estimates of relative and absolute effects.

Resource use is considered an outcome in GRADE. Because of the complexity of its assessment, some clinical guideline panels choose not to consider resource use. When a panel does decide to consider resource use, GRADE's approach is to identify the viewpoint (that is, costs to whom, since different payers bear the costs across and within societies), label the important resource use items, find relevant evidence, evaluate the quality of the evidence, and value resources in terms of cost. As with other outcomes, a systematic review is needed that includes the quality of the evidence and a summary of findings. Also, both resource use and costs are documented. Quality issues may arise, just as with other outcomes, and directness often is a major issue. Costs vary more than other outcomes, and even when resource use is the same, the implications and opportunity costs differ in different jurisdictions.

GRADE defines the *strength* of recommendations as the degree of confidence that the desirable effects of adhering to a recommendation outweigh the undesirable effects. In the case of "strong" recommendations, the benefits clearly outweigh the downsides, or vice versa for weak recommendations. The strength of recommendations may be downgraded if the *quality* of evidence is low or the desirable and undesirable consequences are closely balanced. Values and preferences are important when making tradeoffs, especially with regard to costs. It is important that guideline panels make their values and preferences explicit.

The Role of Economic Analysis in Funding Decisions for Health Care Interventions in Canada

Dr. Doug Coyle, University of Ottawa

In Canada, reviews of health care technologies for funding decisions use economic analysis, and economists now play a prominent role on the committees that make policy decisions. Economic analysis in decision making in health care has begun to widen beyond its established role in pharmaceuticals, although this is still its major use.

Provincial drug formulary decisions are facilitated by the work of the Common Drug Review (CDR), which examines new drugs to help provincial drug benefit plans make decisions about which drugs to cover. Manufacturers and drug plans submit requests for a CDR review. These requests must include all of the information needed to evaluate whether an intervention is worthwhile, including efficacy, effectiveness, and safety data; an economic evaluation; a budget impact analysis; the product monograph; information on disease prevalence and pricing; and a letter indicating that the product can be supplied.

The Canadian Expert Drug Advisory Committee (CEDAC) uses CDR reports to make recommendations to drug plans. CEDAC considers safety and efficacy, therapeutic advantages and disadvantages compared with those of available therapies, and cost-effectiveness in recommending whether drug plans should cover a drug. After CEDAC issues its recommendation to drug plans, some provinces conduct their own economic evaluation. For example, the Ontario Committee to Evaluate Drugs considers the same kinds of evidence as the CDR to evaluate drugs considered by CDR and other drugs.

The National Institute for Health and Clinical Excellence Approach to Assessing the Clinical Effectiveness and Cost-Effectiveness of Health Care Interventions
Dr. Michael F. Drummond, University of York

The United Kingdom's National Institute for Health and Clinical Excellence (NICE) is part of the U.K. National Health Service (NHS) and was created in 1999 to provide an evidence-based approach to evaluating the clinical effectiveness and cost-effectiveness of new medical technologies and procedures. NICE issues guidance to the NHS on the use of health care interventions, assesses new treatment methods and procedures, and evaluates clinical guidelines and public health interventions.

NICE assesses interventions systematically by conducting scoping exercises, reviewing submissions from the technology's key sponsors, and independently reviewing the published evidence. Based on these activities, NICE issues guidance to the NHS and then monitors and reviews the implementation of this guidance.

The clinical data and the economic modeling that NICE systematically reviews tend to be of higher quality than the actuarial analyses, which are only performed at the end of the review process and are not always done well. Many NICE evaluations do not consider indirect costs because of technical problems, although doing so would be desirable. These problems include uncertainty about how to measure productivity losses due to illness. Failure to consider indirect costs is rarely a major impediment to implementing NICE recommendations.

When NICE first announces plans to study an innovation, it issues a call to a broad list of stakeholder groups, including professional organizations and patient advocacy groups. In addition, every NICE committee includes a patient representative. However, patient recommendations may be overruled by budgetary considerations in NICE decisions.

NICE has evaluated many nutritional interventions over the past decade. Unfortunately, the evaluations have concluded that no evidence exists to support these interventions' use. However, a NICE review did result in a recommendation (but not a mandate) that health professionals should consider using omega-3 fatty acid ethyl esters in patients within 3 months after a MI who are not consuming 7 g of omega-3 fatty acids per week by dietary means.

NICE makes decisions for public health evaluations by examining the intervention types, how relevant they are to NHS costs, and how strong the evidence is. Recommendations about very broad interventions that the health care sector is not solely responsible for implementing, such as interventions involving exercise, rely primarily on goodwill for implementation because funding

is rarely available to implement them. The NHS tends to follow NICE's recommendations regarding medical interventions, such as vaccinations, more rigidly. The NHS enforces guidance regarding nutritional interventions, such as nutrient supplementation for certain populations, if the evidence is very strong. However, the evidence for nutritional intervention is often weak; in these cases, NICE words its guidance less definitively, saying, for example, that "clinicians may consider" a specific course of action.

The negative recommendations of NICE tend to be followed more rigidly in a cost-containment environment than the positive ones. Enforcement of coverage decisions is always problematic but it is easier in specialist than primary care. Primary care physicians who follow NICE guidance closely in their prescribing receive incentives.

Some of the issues raised by NICE's experience that are relevant in the United States are the importance of clear authority, rigorous assessments of medical technologies and procedures, extensive stakeholder involvement in these reviews, and transparency in decision-making about these technologies and procedures.

Approaches to Economic Evaluation at German Agencies for Health Technology Assessment

Dr. Uwe Siebert, University for Health Sciences, Medical Informatics and Technology; Harvard Medical School

The German Agency for Health Technology Assessment at the German Institute of Medical Documentation and Information (DIMDI) examines a wide range of technologies. Unlike NICE, DIMDI produces many health technology assessment reports from the societal rather than the payer's perspective because DIMDI's assessments are intended for all stakeholders, including the general public. DIMDI has not assessed or analyzed dietary supplements.

The German government established the Institute for Quality and Efficiency in Health Care (IQWiG) in 2004 as an independent foundation. Its technology assessments are primarily intended for the German Federal Joint Committee, which issues directives to safeguard medical service provision. IQWiG examines all types of technologies, although it has focused on expensive new drugs and special problems.

IQWiG recently began to conduct economic evaluations. An international expert panel prepared draft guidelines for economic evaluations at IQWiG and, after extensive external reviews, hearings, revisions, and pilot studies, the institute established a framework for these analyses. IQWiG compares new technologies undergoing assessment with existing technologies for a given indication, not across the health care system.

IQWiG conducts economic evaluations of new health technologies only if a benefit assessment shows that the new technology is superior to existing ones. IQWiG operates within the specific disease with no unique cost threshold. IQWiG generates an efficiency frontier, or range of expected return and standard deviation combinations available from efficient asset portfolios, and then compares the costs and benefits of a new technology within that framework.

Although IQWiG is not required to calculate costs per QALYs gained (for comparisons across diseases), IQWiG might recommend using QALYs within a disease to synthesize the evidence on different issues, such as the new technology's benefits and harms. The Federal Joint Committee has not established a WTP value or price per QALY that cannot be exceeded, and the German Ministry of Health has concluded that excluding drugs with costs above a fixed uniform threshold value from reimbursement is not permissible.

IQWiG encourages modeling to extrapolate cost beyond clinical trials to a relevant time horizon, consider prognostic implications, if necessary, and summarize multidimensional benefits.

Conclusions

One next step suggested at the workshop was for ODS to focus on the unique methodological issues related to studying dietary supplements, such as considering the impact of third-party payments for dietary supplements instead of out-of-pocket funding. Other possible directions include using value information analysis (described by Dr. Weinstein) to help guide prioritization and next steps. An epidemiological approach would be a useful alternative to standard regression analyses by controlling for time-dependent confounding when the confounders are a cause of the exposure and outcome.

Studying economic issues related to nutrition interventions in chronic disease would also be valuable; these issues are difficult to understand and are largely unexplored. ODS's nutrition intervention evaluations must account for other potential health effects that require a great deal of data and modeling. The office should also take into account the implications of having different providers treat obesity and other chronic diseases on costs and effectiveness.

ODS will apply the lessons from this workshop in its mission areas and work with other federal agency partners to consider the implications of these lessons in its planning. ODS will identify economic analyses of ongoing and planned studies, especially those that are directly related to dietary supplements and those that are more broadly relevant to nutrition interventions for chronic disease prevention. ODS also plans to form partnerships with federal agencies to advance research in this area, and it welcomes input on areas that need investment and options for moving forward.

[1] Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ. 2008;336:924-926.