This review is a synopsis from a recent symposium entitled “Update on Nutrition Research Methodologies” presented at the American College of Nutrition’s Annual Meeting in Orlando, in October 2009. The speakers provided an overview of new handheld and Web-based dietary assessment tools and their application to clinical and epidemiologic studies, identified key features and attributes for comparative effectiveness studies in nutrition, identified how to critique the literature on nutrition and dietary supplements and apply the principles of evidence-based reviews to their research, and examined the level of evidence needed to support the development of public health policy for nutrients and dietary supplements. Nutr Today. 2011;46(3):116–120

Dietary Intake Assessment Tools

Major impediments to the field of nutrition research are that eating behaviors are highly variable and difficult to measure and that the field has relied on self-reported methods. A number of new assessment tools are under development to make dietary intake assessment easier and more objective (Table 1). These tools aim to overcome the unique challenges encountered in large, population-based epidemiologic studies or clinical trials, which include the lack of affordable devices or software that ease respondent burden while providing accurate estimates of nutrient, food, and supplement intakes in often diverse populations. These new technologies for diet assessment are in different stages of development.

National Cancer Institute Automatic Self-administered 24-Hour Dietary Recall

The Automatic Self-administered 24-Hour Dietary Recall (ASA24) is a Web-based, automated, self-administered 24-hour dietary recall instrument developed by Subar and colleagues at the National Cancer Institute in collaboration with Baylor College of Medicine and the US Department of Agriculture (USDA). The system allows for probing (based on USDA’s automated multiple pass method), coding, and the calculation of dietary intakes using the USDA’s Food and Nutrient Database for Dietary Studies. It is easily updated with new Food and Nutrient Database for Dietary Studies releases. It is a highly interactive Web-based tool that uses an animated avatar to guide completion of a 24-hour diet recall using 11,100+ food images to estimate portion size. This tool is available at little to no cost to investigators, and a demonstration may be viewed at http://riskfactor.cancer.gov/tools/instruments/asa24/.
Improved measures of diet and physical activity have been developed through the National Institutes of Health’s (NIH’s) Genes, Environment, and Health Initiative (GEI). The GEI sought to develop new or refine existing technologies that were reliable and valid to measure dietary intake or physical activity in large-scale research studies (http://www.gei.nih.gov/exposurebiology/program/improved.asp). One project under development through GEI is the Food Intake Recording Software System, version 4 (FIRSt4), which aims to adapt the ASA24 intake software for children 8 to 13 years old. To do this, the FIRSt4 researchers are exploring several aspects of the child-computer interface: how children categorize foods, whether these categories will facilitate accuracy and speed of reporting, and whether pictures facilitate the accuracy of estimating portion sizes. In addition, researchers want to identify the age-appropriate use of the ASA24, both the adult and children versions, because of potential developmental, memory, or cognitive issues. A prototype is expected by fall 2011.

**Cellular Phone–Based Tools**

Two devices are under development that use cellular phone technology to collect food records. These tools will use photos or videos, voice recording, and/or text input to capture eating episodes, all captured via mobile phones. Software is being developed to automate the identification of foods and portions and calculate the nutrient and food intake. This software uses image processing techniques, voice recognition software, and various modeling techniques to process the captured images or recordings. Validation of new techniques prior to the release and use of these methodologies to ensure reproducibility and accuracy is key. Both devices will be evaluated under controlled conditions, and caloric intake values will be compared with those derived from doubly labeled water methodology—the criterion standard technique to determine energy intakes. They will also be evaluated in usability studies with free-living individuals.

**Comparative Effectiveness Trial Designs**

Comparative effectiveness research can be defined as an evaluation of the benefits and risks of different interventions for preventing, diagnosing, treating, and monitoring health conditions under real-world patient conditions. With the issuance of the recent Institute of Medicine (IOM) Report “Initial National Priorities for Comparative Effectiveness Research” and the US government’s allocation of $1.1 billion in February 2009 to support comparative effectiveness research, opportunities exist for nutritionists to explore this area of research. The IOM developed a list of 100 of the highest-priority research topics, of which 4 research areas are related to nutrition. The highest-priority ranking (50 priorities) was for health care delivery systems (Table 2).

**Table 1. Dietary Intake Assessment Methodologies**

<table>
<thead>
<tr>
<th>Methodology</th>
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<tbody>
<tr>
<td>Automated Self-administered 24-h Dietary Recall (ASA24)</td>
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<tr>
<td>Food Intake Recording Software System, version 4 (FIRSt4)</td>
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<tr>
<td>Mobile Food Intake Visualization and Voice Recognizer (FIVR)</td>
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<tr>
<td>Cellular phone and digital imaging</td>
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</table>

**Table 2. Institute of Medicine Research Areas in Nutrition**

<table>
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<th>Research Areas</th>
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<tr>
<td>Compare the effectiveness of school-based interventions involving meal programs, vending machines, and physical education, at different levels of intensity, in preventing and treating overweight and obesity in children and adolescents.</td>
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<tr>
<td>Compare the effectiveness of various strategies (eg, clinical interventions, selected social interventions [such as improving the built environment in communities and making healthy food more available, combined clinical and social interventions]) to prevent obesity, hypertension, diabetes, and heart disease in at-risk populations such as the urban poor and American Indians.</td>
</tr>
<tr>
<td>Compare the effectiveness of treatment strategies for obesity (eg, bariatric surgery, behavioral interventions, pharmacological treatment) on the resolution of obesity-related outcomes such as diabetes, hypertension, and musculoskeletal disorders.</td>
</tr>
<tr>
<td>Compare the effectiveness and cost-effectiveness of conventional medical management of type 2 diabetes in adolescents and adults, versus conventional therapy plus intensive educational programs or programs incorporating support groups and educational resources.</td>
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The Pounds Lost Trial was conducted to answer the crucial question of which macronutrient composition is best for long-term weight loss, as great controversy existed on this topic and no obvious patterns of study (eg, Mediterranean, low carbohydrate, or low fat) results favored a specific fat, carbohydrate, or protein content for weight loss. Limitations of earlier comparative trials of diets for weight loss suffered from a large percentage of dropouts, up to 50% and variability in the intensity of counseling delivered. Some studies lack a controlled intervention group. Also, for some studies, media attention and marketing of one of the diets under study may have created a bias among patients and/or investigators, threatening the validity of a study. The Pounds Lost Trial was a 2-year randomized clinical trial in 811 overweight adults to compare the effects on body weight of energy-reduced diets that differed in their targets for intake of macronutrients—low or high in fat, average or high in protein, or low or high in carbohydrates (Table 3), and otherwise followed recommendations for heart-healthy diet. Among the 80% of participants who completed the trial, the average weight loss achieved was 4 kg, and 14% to 15% of the participants had a reduction of at least 10% of their initial body weight. However, despite the intensive behavioral counseling in the study, participants had difficulty achieving the goals for macronutrient intake of their assigned group and tended to revert to their customary macronutrient intakes over time. It was demonstrated that the diets were equally successful in promoting and maintaining clinically meaningful weight loss over a 2-year period. The investigators confirmed that diets that are successful in causing weight loss can emphasize a range of macronutrient intakes, and these diets as well can have beneficial effects on cardiovascular disease risk factors and diabetes.\(^9,10\) The Pounds Lost Trial has demonstrated the usefulness of comparative effectiveness studies to rigorously evaluate multiple dietary regimens for weight loss.

### Systematic Review Methodology

Systematic review is a rigorous and transparent method to synthesize scientific evidence in which bias is minimized. The method was initially developed in medicine to inform clinical practice, support development of clinical practice guidelines and public health recommendations and policies, and identify research gaps and formulate scientific consensus statements. The use of systematic reviews for nutrition-related topics is more recent and has been endorsed by the Office of Dietary Supplements at the NIH, as well as other government entities, to help direct future research efforts (Table 4). Although systematic reviews are appearing with increasing frequency in the nutrition literature, there are unique challenges applying this approach to nutrition problems. Nutrition-related considerations include:

- baseline nutrient exposure,
- nutrient status,
- bioequivalence of bioactive compounds,
- bioavailability,
- multiple and interrelated biological functions,
- undefined nature of some interventions, and
- uncertainties in dietary intake assessment.

In addition, the methodological quality of the primary literature upon which the systematic reviews are based is often poor or inadequately reported and that these reviews often do not report information that is critical to interpret their findings or to replicate the study.

Standards are needed to improve the conduct and reporting of systematic reviews in nutrition. Current data in nutrition are often not robust, and improvements in design and conduct of studies, as well as additional empirical research and experience on how to perform and interpret findings, are needed. There is also a need to train more reviewers and to educate users in evidence-based methods in nutrition.\(^11\)

To this end, a number of standardized procedures have been developed to support a credible systematic review. A credible review begins by defining and refining the

### Table 3. Pounds Lost Trial: Diet Design

<table>
<thead>
<tr>
<th>Targeted Nutrient Levels</th>
<th>1. Low-fat (20%), average protein (15%), highest carbohydrate (65%)</th>
<th>2. Low-fat (20%), high protein (25%), carbohydrate (55%)</th>
<th>3. High fat (40%), average protein (15%), carbohydrate (45%)</th>
<th>4. High fat (40%), high protein (25%), lowest carbohydrate (35%)</th>
</tr>
</thead>
</table>

*Similar foods used for all diets but in different proportions.*

### Table 4. Nutrition-Related Systematic Reviews

- B vitamins and berries
- Ephedra
- Multivitamin/mineral supplements
- Omega-3 fatty acids
- Soy
- Vitamin D
question to be asked as it will be critical in performing the review. The “PICO” selection criterion is one such tool used to formulate a research question. The acronym PICO stands for patient, intervention, comparator, and outcome, and these 4 components are the essential elements of formulating a research question when undertaking a bibliographic search of evidence (Table 5). A well-constructed research question allows for the correct definition of which information, or evidence, is needed to solve the clinical research question. Articles are next identified and retrieved from suitable databases, and a quality assessment and critical appraisal of the study are conducted. Study selection or inclusion criteria are applied, and the data abstracted using a standardized format. Statistical methods are selected and applied based on the size of the data set. Results are interpreted and generalized to appropriate population groups based on the question under investigation. A number of systematic reviews on nutrition-related topics have been conducted and are available through the NIH Office of Dietary Supplements at http://ods.od.nih.gov and the Agency for Healthcare Quality at http://ahrq.gov (under Evidence Reports). In summary, evidence-based methods are useful and adaptable and can be applied to nutrition topics.

### Table 5. PICO Selection Criteria for Nutrition-Related Systematic Reviews

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<tr>
<td><strong>Population</strong></td>
<td>General healthy people with no known disorders</td>
</tr>
<tr>
<td></td>
<td>Studies that enrolled &lt;20% patients with common diseases allowed</td>
</tr>
<tr>
<td></td>
<td>For adverse effects of high intake, any population</td>
</tr>
<tr>
<td><strong>Intervention/exposure</strong></td>
<td>Observational studies: such as serum 25(OH)D or 1,25(OH)2D</td>
</tr>
<tr>
<td><strong>Comparator</strong></td>
<td>Dose relationship</td>
</tr>
<tr>
<td><strong>Outcome</strong></td>
<td>Outcomes selected by technical expert panel</td>
</tr>
<tr>
<td><strong>Study design</strong></td>
<td>Experimental/observational, duration, sample size</td>
</tr>
</tbody>
</table>

Using Evidence-Based Reviews to Provide a Signal for Updating Public Health Recommendations on Nutrients

How does a student or researcher examine the level of evidence necessary to support the development of public health policy for nutrients and dietary supplements? A 2007 IOM conference suggested that determining the need for a new nutrient review should be evaluated against criteria set a priori to provide a transparent and reproducible approach from which public health recommendations can emanate. In the past, when the IOM revised the Recommended Dietary Allowances (RDA), and more recently the Dietary Reference Intakes (DRI) (a general term for a set of reference values used to plan and assess nutrient intakes of healthy people) and when Health Canada revised the Recommended Nutrient Intakes, a review of all the nutrients and related substances with reference values was conducted regardless of whether relevant new research had become available. However, it is becoming increasingly apparent that different nutrients accrue data of clinical or public health importance at differing rates, and it then becomes important to determine when a nutrient rises to the top (provides a “trigger”) and is ripe for a new review. Using vitamin D as a case study to evaluate the intake requirements for vitamin D as related to optimal circulating 25-hydroxyvitamin D [25(OH)D] concentrations across life-stage and race-ethnicity groups of US and Canadian populations, Yetley and colleagues reviewed the published literature on vitamin D since the last DRI report of 1997. They used an a priori criterion of “significant, new, and relevant evidence” to determine if a new DRI review was warranted. The “significance” of new research was based on its scientific quality (eg, the type of study and quality rating scores). “New” studies were those unavailable to the 1997 IOM DRI committee. “Relevance” was determined by the availability of new information related to 4 key questions that are central to a future DRI review. The 4 questions for healthy populations were as follows:

1. What is the effect of circulating concentrations of 25(OH)D, as an indicator of vitamin D adequacy, on health outcomes?
2. What is the effect of vitamin D intakes on circulating concentrations of 25(OH)D?
3. What is the effect of vitamin D intakes on health outcomes?
4. What levels of vitamin D intakes are associated with adverse effects?

On the basis of the collective data (systematic review, 2 conferences and related activities), it was concluded that there appeared to be significant new and relevant scientific research related to the 4 key DRI questions, particularly for the elderly population. Overall, the new research adds to what we know about bone-related health outcomes and status regarding the role and function of vitamin D, and it also identified new health outcomes with respect to risk of falls and performance measures in the elderly. Potential new adverse effects (eg, increased risk of renal stones with supplemental intakes of 400 IU vitamin D3 and 1000 mg Ca per day in women aged 50–79 years and increased risk of some types of cancers) were also identified in this review. The review provided
additional information on dose-response between intakes and 25(OH)D and between 25(OH)D and several health outcomes. There are several possible effects of incorporating new research findings into the DRI deliberation process. It could provide increased or decreased confidence in current DRI values serving to reconfirm values with updated information. Revision of the DRIs may affect 1 or more life-stage groups because of the selection of different end points of interest, new data on dose-response relationships, change in type of reference value used, and possible changes in generalizing from studied to unstudied population groups. It is reasonable to suggest that further discussions will be needed to more fully delineate the range of criteria and procedures for deciding if and when other DRI nutrient reviews are warranted.

Future Research

A broad array of methodological advancements in the field of nutrition is driving a new era of nutrition research, not only for the nutrition scientist, but also for all health care professionals who seek to more fully understand or critically evaluate the role of nutrition in disease prevention and public health.

Rebecca Bortz Costello, PhD, is the director of Grants and Extramural Activities at the Office of Dietary Supplements, National Institutes of Health (NIH) in Bethesda, Maryland.

Catherine M. Loria, PhD, is with the Division of Population and Prevention Science, National Heart, Lung, and Blood Institute at the NIH.

Joseph Lau, MD, is professor of Medicine and Clinical Research at Tufts Medical School and adjunct professor at the Friedman School of Nutrition Science and Policy at Tufts University, Boston, Massachusetts.

Frank M. Sacks, MD, is professor of Cardiovascular Disease Prevention at the Department of Nutrition, Harvard School of Public Health, Boston, Massachusetts.

Elizabeth A. Yetley, PhD, is a senior nutrition scientist (retired) with the Office of Dietary Supplements, NIH.

None of the authors have any conflicts of interest to disclose.

Correspondence: Rebecca Bortz Costello, PhD, National Institutes of Health, 6100 Executive Blvd, 3801, Bethesda, MD (costellrb@od.nih.gov).

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REFERENCES