Journal of Evaluation in Clinical Practice
International Journal of Public Health Policy and Health Services Research

Journal of Evaluation in Clinical Practice ISSN 1365-2753

Bridging evidence and consensus methodology for inherited metabolic disorders: creating nutrition guidelines

Rani H. Singh PhD RD,[1] Fran Rohr MS RD LDN[2] and Patricia L. Splett PhD RD[3]

[1]Associate Professor, Department of Human Genetics, Emory University, School of Medicine and Director, Metabolic Nutrition Program, PD Southeastern NBS and Genetics Collaborative (Region 3), Atlanta, GA, USA
[2]Clinical Nutritionist, Children's Hospital Boston, Boston, MA, USA
[3]Evidence Analysis Consultant, Splett & Associates, LLC, Stanchfield, MN, USA

Keywords
consensus method, Delphi method, evidence-based, inborn error of metabolism, inherited metabolic disorder, nominal technique, nutrition, practice guidelines

Correspondence
Associate Prof. Rani H. Singh
Department of Human Genetics
Emory University
School of Medicine
Metabolic Nutrition Program
PD Southeastern NBS & Genetics
Collaborative (Region 3)
Atlanta, GA
USA
E-mail: rsingh@emory.edu

Accepted for publication: 17 August 2011

doi:10.1111/j.1365-2753.2011.01807.x

Abstract

Rationale, aims and objectives The management of many inherited metabolic disorders (IMDs) is dependent on nutrition intervention, but few clinical management guidelines for these uncommon disorders exist. Clinicians are forced to make nutrition treatment decisions using limited data. This results in clinical variations in both service and cost. We describe a method for establishing management guidelines to help clinicians treat patients with IMDs.

Methods The Southeast Newborn Screening and Genetics Collaborative (Region 3) convened a group of nine national experts in metabolic nutrition to determine the pertinent issues in the development of nutrition management guidelines for IMDs. These experts were trained in evidence analysis and examined established consensus techniques for guideline development.

Results The workgroup developed a multi-step process for guideline development known as the Delphi-Nominal Group-Delphi-Field Testing methodology, which includes a review of scientific and grey (unpublished) literature, a Delphi survey of practice, a nominal group meeting to clarify discrepancies, a formulation of recommendations and a second Delphi round to assess the degree of consensus with the proposed recommendations. External review and field testing are also built into the process.

Conclusion The evidence- and consensus-based method suggested for the development of nutrition management guidelines for IMDs will result in the production of consistent and accessible guidelines that can be created in a timely and cost-effective manner and offer a validated methodology to develop management guidelines for this field to optimize outcomes.

Introduction

Providing dietitians and clinicians with guidelines for nutrition management of multiple metabolic disorders is an urgent need. The ability to detect a wider array of conditions during newborn screening through the use of tandem mass spectrometry has resulted in the identification of more infants then in the past with inherited metabolic disorders (IMDs) [1]. With identification through newborn screening, clinicians have the unique but challenging opportunity for early detection and appropriate interventions to avoid or ameliorate adverse outcomes in patients with IMD.

For IMDs, the treatment guidelines must focus on nutrition intervention, which is basic to their management. However, nutrition treatment guidelines have not been created for most metabolic disorders and currently, only a consensus statement for one of the most common metabolic disorders, phenylketonuria (PKU) has been established [2], which is in need of updating due to new advances in the field. Similar work has been done in other disease areas, for example, diabetes mellitus [3]. While the appropriate course of treatment for pre-symptomatic patients is often unknown, the prospect of preventing the devastating effects of these diseases, including neurological consequences, is a motivating factor in developing pre-symptomatic nutrition treatment guidelines. Furthermore, there is a need to establish consistent and accessible nutrition treatment guidelines for existing symptomatic patients. With this in mind, we convened a workgroup to define a viable process for developing nutrition treatment guidelines for

IMDs using consensus techniques, developed in a systematic, transparent and rigorous manner. Herein, we describe our proposed method, which combines evidence-based review with a combination Delphi process and nominal group technique, followed by external review, field testing and revision.

Clinical practice guideline development is a systematic and transparent process of incorporating the best available evidence into sets of statements that can be designed to assist clinicians, patients and their families in making appropriate health care decisions when faced with specific clinical circumstances [3,4]. Ideally, guidelines are based on the review and synthesis of scientific evidence. Scientific evidence for clinical practice accumulates through laboratory research, case reports and clinical trials. Unfortunately, for IMDs, very little published evidence is available. Results from laboratory studies are often not reported to clinicians in a manner that would result in new approaches to treatment. Case reports can be useful, but many are not published or are not applicable across all patients. Finally, few clinical trials exist for IMDs because of the limited availability of subjects.

When research is lacking, the knowledge and experience of experts is the best evidence available. This expert knowledge can be assimilated into guidelines using consensus techniques. This process involves multiple steps, as described by Lomas [5], which include selecting the topic, picking the consensus group, providing background preparation, identifying information inputs, choosing a group judgment process, defining the criteria for recommendations and choosing a report preparation procedure and format.

Formal consensus techniques are structured methods in which a group of experts identify and rank the importance of issues surrounding a topic. The value of consensus-forming techniques is based on the premise that the considered opinion of a group of experts is more accurate than the opinion of an individual expert. Additionally, consensus techniques force the exposure of underlying assumptions, areas of conflict and uncertainty among experts, which allow debate and investigation to clarify the discrepant views. This debate may also expose topics for research and stimulate the production of primary evidence for guideline development. The techniques are usually multi-round processes with controlled feedback. The result is a summary of the group judgment expressed quantitatively with details about the extent of agreement [6].

Two of the most commonly used and/or adapted consensus techniques are the Delphi technique and the nominal group technique. Both have been used in the development of consensus guidelines for clinical practice. Variations of the Delphi technique have been used to produce treatment guidelines for disorders such as 3-methylcrotonyl coenzyme A (CoA) carboxylase deficiency, very long chain acyl-CoA dehydrogenase deficiency and intestinal Bechet's disease [7–9]. The nominal group technique has been used in developing guidelines for the treatment of gastroesophageal reflux in infants and children as well as other disorders [10–12]. Details of both techniques and the advantages and disadvantages of each are discussed below.

The Delphi technique, named after the ancient Greek oracle, was originally developed in the 1950s by RAND Corporation to obtain the most reliable consensus of expert opinion in a political/military setting [13]. The technique is an iterative process, which involves surveying a group of 12 or more geographically diverse experts by mail or electronically. The first round is an open-ended survey of expert panellists that determines the most pertinent issues related to that topic. The expert panellists then respond to a follow-up survey to rank the significance of the issues. With respect to clinical practice, this may involve ranking one or all of the following:

- priority of a treatment for use;
- appropriateness of a treatment for a condition or symptoms, and
- agreement with evidence-based clinical statements about a condition.

There is at least one additional follow-up survey where each panellist can view the mean ranking of the issues by the other panellists, and have the opportunity to modify their own response based on the group response [10,13–14]. All responses remain anonymous. A numerical scale such as a 5–9-point Likert scale is used to quantify the degree of consensus among the responses [15], enabling statistical analysis of the data.

The advantages of the Delphi technique are that a large group of experts can be included in the survey with a minimal time commitment and no travel and meeting costs. The panellists have time to thoroughly consider their responses, which can lead to better quality responses. In addition, the anonymity of the responses prevents participants from being unduly influenced by institutional loyalties or peer pressure as may happen in a face-to-face meeting. Disadvantages specific to the Delphi technique include the inability to control the survey response rate for each round and the lack of opportunity to discuss and clarify differences of opinion [14,16–17]. There is also a potential for bias in both the participant selection and survey development phases.

The nominal group technique was developed in 1971 by Van de Ven and Delbecq to provide a structured process for making decisions when dealing with controversial and complex issues [18]. It involves a facilitated meeting of a relatively small group of expert panellists (typically 9–12) to formulate ideas about a topic and come up with a group opinion as to the significance of these ideas [16,18–19]. Each panellist contributes an idea, which encourages a range of views to be presented. After contributing their ideas, the panellists have the opportunity to elaborate on and clarify these ideas through a facilitated discussion with the group.

For clinical guideline development, the ideas may involve treatments that have worked for a disorder or possible treatments that can be provided for a specific group of symptoms. Group members then privately rank the importance of and/or their agreement with these ideas. The facilitator summarizes the rankings for the group and the panellists then discuss the areas of disagreement or uncertainty. The panellists privately express their final views to the facilitator using a quantifiable ranking scale, and the facilitator summarizes the results from the group.

An advantage of the nominal group technique is that multidisciplinary panellists can explain their views to each other, allowing for broader insight and problem solving, which may lead to the panellists coming to a consensus sooner. Challenges of the nominal group technique include extensive planning required for the meeting and the time and travel costs involved. There is also the potential that the group discussion format may cause some panellists to be influenced by their peers. As with the Delphi technique, there is a potential for bias in panellist selection.

Some researchers have used a hybrid method that incorporates aspects of both the Delphi and the nominal group consensus techniques [5,7–8,20]. This allows the advantages of both methods to

be explored. These hybrid methods may be similar to the RAND/UCLA appropriateness method, which is not designed to force consensus, but draws from the Delphi method and the nominal group technique to determine the appropriateness and/or necessity of medical procedures for a given disorder or clinical situation. It starts with a literature review followed by a Delphi-type survey of experts to rank the benefit-to-harm ratio of medical procedures. A face-to-face meeting follows to discuss the areas of disagreement [21]. When extrapolated to a consensus-forming method, the advantage of using a Delphi survey prior to a face-to-face meeting is that areas of consensus and non-consensus can be exposed and therefore the nominal group discussion can promptly focus on the areas of disagreement or non-consensus.

Methods and materials

A group of nine national experts in metabolic nutrition were selected by the joint leadership of the Southeast Newborn Screening & Genetics Collaborative (Region 3) and Genetic Metabolic Dietitians International (GMDI), and convened to identify issues related to and steps towards the development of a process for creating consensus-based guidelines for rare disorders. These experts constitute the core group. Development of two sets of nutrition management guidelines related to fatty acid oxidation disorders was begun in collaboration with GMDI. The expert group was trained in the American Dietetic Association's (ADA) evidence analysis and guidelines development processes [22]. A facilitated face-to-face meeting was held to review the strengths and limitations of current consensus development methods, including both the Delphi and nominal group techniques.

The group concluded that existing methods alone were insufficient for their purposes and chose to draw on the strengths of existing methods to develop a new combined approach which would follow a Delphi-Nominal Group-Delphi-Field Testing (DNDF) methodology.

Results

A new methodology for a model for clinical guideline development incorporating the principles of both evidence-based and consensus-based techniques was created. The process is summarized in Fig. 1. The purpose of providing the proposed methodology is to lay the groundwork for these methods to be tested and employed in a clinical setting. For the purposes of this paper, we describe the process involved in creating the hybrid methodology.

Five workgroups were established to develop nutrition guidelines for amino acidopathies (including two groups specific to PKU and urea cycle disorders), fatty acid oxidation disorders and organic acidemias. Priority of disorders for guideline development was chosen by each workgroup based on results of a GMDI membership survey. A workgroup chairperson managed the development process at each step. The definition of roles of workgroup members are detailed in Table 1. Based on workgroup feedback, the following steps to the methodology were described.

Step 1: literature review

The proposed process will begin with a systematic review of published literature as well as 'grey literature', which would include unpublished communications, clinical guidelines, protocols and other resources relating to the nutrition management of the disorder of interest. For each IMD, important clinical questions will be determined and pertinent published articles will be obtained using a defined search strategy with specified keywords and inclusion/exclusion criteria. Simultaneously, there will be a systematic search for unpublished grey literature and clinical protocols that will include contacting organizations and institutions, searching conference proceedings and specifically requesting these documents via a LISTSERV of metabolic nutrition professionals. Once the workgroup chair approves the lists of published articles and unpublished documents obtained through the searches, each article and document will be abstracted and rated for quality by trained personnel using the ADA's Evidence Analysis Process. An adaptation of the review, abstraction and critical appraisal step was developed for grey literature and clinical protocols. A quality checklist was developed that incorporates the quality domains for evaluating practice guidelines developed by the Appraisal of Guidelines for Research and Evaluation (AGREE) Collaboration [23]. Following the search and appraisal of all pertinent published and unpublished information, each workgroup, led by the evidence synthesizer, will summarize the literature review and identify areas of uncertainty and practice variation. This process will be pilot tested for usability and reliability.

Step 2: initial Delphi round

The information obtained from the literature review will be used by the workgroups to formulate questions and/or clinical statements to be answered and ranked by a Delphi survey of experienced metabolic clinicians. The survey panels will include a doctor and a nutritionist identified by the principal investigators from each of the seven Health Resources and Services Administration (HRSA)-funded regional newborn screening (NBS) and genetics collaboratives. The panel will be sent the initial Delphi survey electronically. When the surveys are returned, the data will be compiled and analyzed to create preliminary recommendations for management of the disorder noting the areas of uncertainty.

Step 3: nominal group meeting

The treatment recommendations compiled from the first round of surveys and literature reviews will be presented to a group of expert panellists in the nominal group format. This expert panel will consist of two doctors, three dietitians and one academic researcher. At least one panellist will be included who does not practice at a metabolic centre (such as a primary care doctor). Also in attendance will be the workgroup chair, evidence synthesizer and writer to present information and observe the meeting, although they will not vote. A project consultant will facilitate the meeting. Participants will discuss and vote on their agreement with the preliminary recommendations as well as any identified areas of variability and disparity. Evidence will be presented relating to areas of uncertainty and panellists will vote again after hearing this evidence. The workgroup chair, evidence synthesizer, writer and project consultant will incorporate the recommendations from the meeting into a survey that will be designed to assess the level of agreement among clinicians regarding these recommendations.

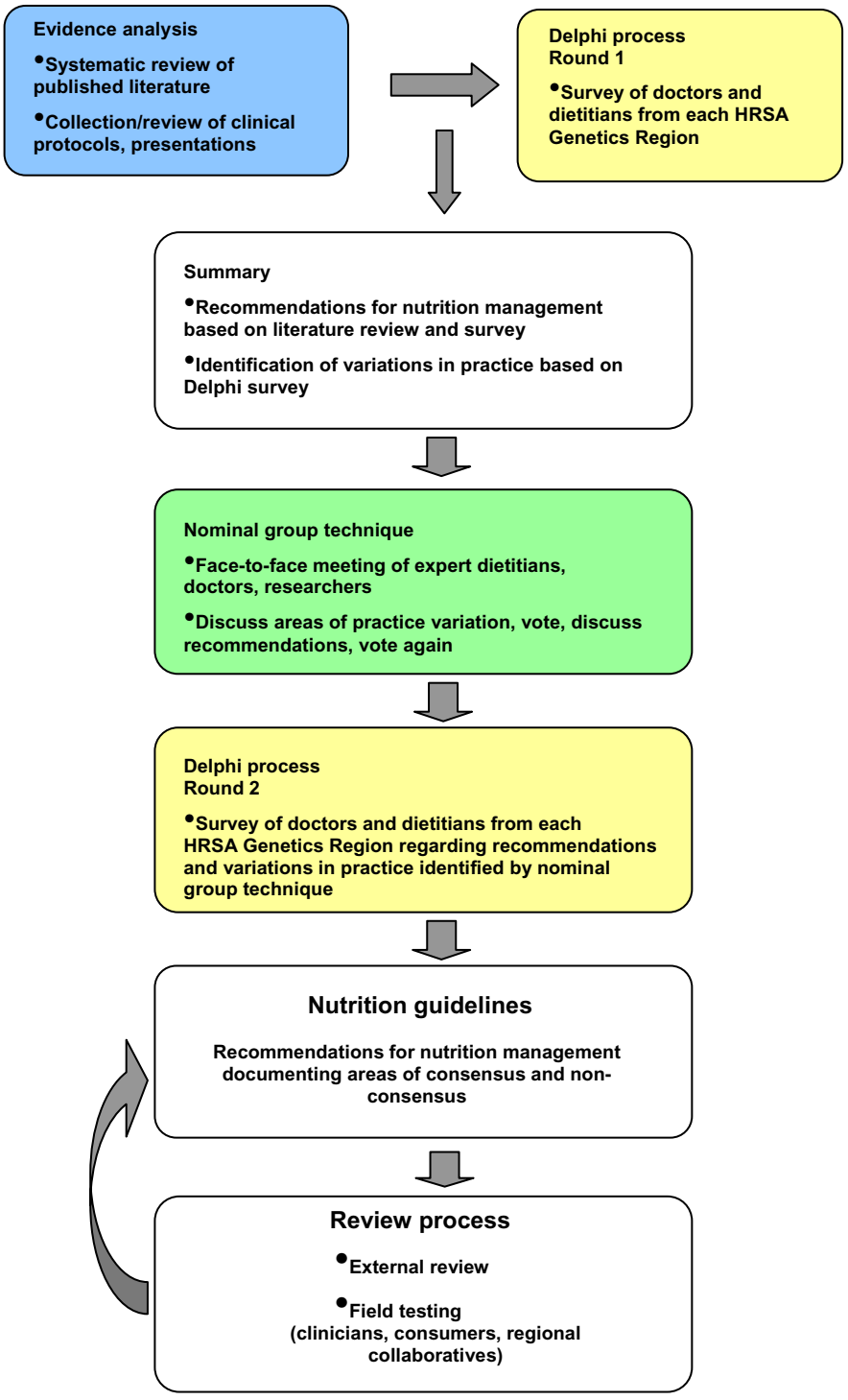

Figure 1 Flowchart of guidelines development process.

Step 4: second Delphi process

The resulting survey will be conducted via a second Delphi process. Surveys will be sent to the same group of panellists that responded to the first survey as well as two additional clinicians from each HRSA-funded region. Responses will be analyzed for consensus or lack of consensus and provided to the appropriate workgroup that will write the recommended guidelines.

Step 5: formal guideline writing

The guideline recommendations resulting from the consensus techniques will be integrated with the available scientific evidence to write formal guidelines for the nutrition management of the given disorder. The type and quality rating of the 'evidence' used in the formulation of each guideline will be identified and the strength of the recommendation noted according to the GRADE

Table 1 Definition of roles within the DNDF methodology for guidelines development

Role	Definition
Core group	Expert group who oversees guideline development and review process. Formally approves all guidelines before dissemination. Is appointed by the joint leadership of Southeast NBS & Genetics Collaborative (Region 3) and GMDI.
Workgroup	Comprised of 4–6 metabolic dietitians from clinical centres across the United States selected by application process. Established to develop the guidelines for each disorder.
Workgroup chairperson	Lead workgroup member who manages the development process at each step for a specific disorder. Makes final decision for the workgroup before submitting to core group in addition to providing input to overall process. A member of both a workgroup and the core group.
Evidence analyst	Workgroup members or other experts trained in the evidence analysis process and responsible for critiquing evidence reports (published articles and grey literature) and abstracting pertinent information.
Evidence synthesizer	Workgroup member who is selected to summarize information resulting from literature review, Delphi survey responses and nominal group recommendations. Works closely with the writer.
Writer	Workgroup member selected to write the guidelines based on literature reviews and consensus. Will also revise guidelines based on field testing. Works closely with the analyst.
Delphi survey panellist	Doctors and nutritionists who answer/rank questions and clinical statements formed by the workgroup. Those in first round of Delphi also participate in second round. Additional panellists are added to second round of survey. Each panellist is anonymous to each other.
Nominal group panellist	Doctors (specialists and primary care), nutritionists and academic researchers who meet in person to discuss and vote on their agreement of treatment recommendations (based on information compiled from literature review and first round Delphi survey).
External reviewer	Doctors, primary users, patients or parent groups who provide feedback to workgroups on each disorder.
Field tester	Workgroup member who tests guidelines by using the guidelines in patient management in a clinical setting.

system (Grading of Recommendations Assessment, Development and Evaluation) [20].

Step 6: guideline review

The completed guidelines will be submitted for review to workgroup chairs, other core group members and external reviewers. The external reviewers will include two doctors, two other primary users (one expert and one non-expert) and a representative patient or parent group for the disorder. A tool such as the AGREE Instrument will provide standard criteria for review and feedback from each respondent. Responses will be forwarded to workgroup chairs.

Workgroup members, who have not been involved in guideline writing (to avoid bias), will use the guidelines in patient management as a preliminary short-term field test.

Step 7: revision

Any revisions considered necessary, based on feedback from the reviewers and the preliminary field testing, will be made by the writer and workgroup chair. The final draft of the guidelines will be submitted to the core group for approval.

Step 8: guidelines disseminated/posted to the World Wide Web

The Nutrition Management Guidelines will be published on the HRSA and GMDI web sites for clinicians to use with their patients. Follow-up comments will be collected from these clinicians to determine the degree of implementation, usefulness and acceptance of the guidelines. Long-term goals will include measuring effectiveness of these guidelines as they relate to health outcomes.

Step 9: field testing and updating

Formal field testing will be conducted at each of the seven HRSA-funded regional NBS and genetics collaboratives, clinical centres and consumer groups to determine any practice issues that need to be incorporated into future revisions of the guidelines. The workgroup chair and GMDI members will convene every 2 years to review published evidence and guidelines, and revise them, if needed, in order to ensure that the most recent evidence is used in making clinical decisions.

Discussion

To ensure that clinicians have the best information readily available to them when treating a patient with an IMD, we have developed a systematic method to establish the Nutrition Management Guidelines for Inherited Metabolic Disorders. It is hoped that this method can be used by other groups to lead to a consensus statement regarding the nutrition management of children with IMDs. The method we have developed is a multi-step process that incorporates both the Delphi and nominal group consensus-forming techniques. Hutchings *et al*. compared the Delphi and nominal group techniques as methods for developing clinical guidelines for mental health treatment [24]. They found that consensus was greater using the nominal group technique but that the Delphi technique was more reliable. They concluded that a hybrid method would combine the advantages of both techniques. We have developed a hybrid of the two consensus techniques that follows a

Delphi Survey-Nominal Group Meeting-Delphi Survey-Field Testing (DNDF) methodology in order to take advantage of the best aspects of each technique.

The first steps in our methodology involve searching the published literature and contacting a large group of experts and organizations in order to identify current or previously used treatment procedures and nutrition interventions for a defined IMD. The initial Delphi survey will also provide an initial assessment of how closely clinicians agree on the importance and utility of identified procedures and interventions. The follow-up nominal group meeting will focus on areas of disagreement collected in the first Delphi survey. This meeting is significant because it allows a smaller group of experts to discuss and resolve inconsistencies and differences of opinions with regards to these treatments, which may result in the most appropriate interventions being recommended. The second Delphi survey allows for a larger group of experts to anonymously offer their opinions and indicate their level of agreement with the recommended management of the disorder, and enables quantifying the degree of consensus. External review and field testing will provide validation of the guidelines and allow for revisions to be made when results from clinical practice deviate from the guidelines. Our methodology builds in this process to occur every 2 years in order to generate sustainability of the effort.

Variation of this methodology was pilot tested with positive results for very long chain acyl-CoA dehydrogenase deficiency and medium chain acyl-CoA dehydrogenase deficiency, two of the fatty acid oxidation disorders. The results are posted on the GMDI web site and the preliminary results were reported at the 11th International Congress on Inborn Errors of Metabolism held in September 2009.

Developing evidence- and consensus-based guidelines in a transparent and rigorous manner requires a method that minimizes bias. Potentials for bias in consensus guideline development exist in the selection and presentation of scientific evidence, panel selection, the structure of the interaction between participants and the analysis phase [25]. Because scientific evidence is limited for treatment of many IMDs, a thorough search and assessment of the quality of the evidence available must include the grey literature. By using evidence analysis methods to include the ADA Evidence Analysis Process, the AGREE Instrument and the GRADE grid, our methodology addresses the potential for bias due to evidence quality and establish that the recommendations are feasible for practice [20,22–23].

In order to minimize the bias in the panel selection, survey participants and nominal group participants will be chosen to include a multifaceted group of geographically diverse doctors, dietitians and academic researchers from both large metabolic centres and smaller practices. This should ensure that multiple viewpoints are considered and avoid any bias introduced by the availability of resources to the panellists [16]. Others have cautioned that 'guidelines can be driven as much by "eminence" as by "evidence" ' [26]. Our method involves conducting a Delphi survey, where panellists are anonymous to each other, both before and after the nominal group meeting to help prevent any bias introduced because of the undue influence of prominent panellists and strong personalities. The nominal group meeting will help to minimize bias due to misunderstanding. Finally, our methodology attempts to avoid bias in the analysis phase by developing a well-designed survey and involving an increased number of respondents in the second Delphi survey stage. Further checks and balances are created by the external review as well as a commitment to reviewing the guidelines.

Although it is impossible to avoid all sources of bias, we believe the method we have developed will produce a realistic set of guidelines that can be combined with a clinician's clinical judgment and a patient's-values and expectations to determine the best course of action.

Conclusion

The guideline development and DNDF methodology presented here incorporates available scientific evidence with clinical expertise to produce evidence- and consensus-based guidelines for nutrition management of rare IMDs. Review and validation techniques are built into the process to ensure the guidelines remain up to date with currently accepted technology and practice. It is proposed that by using these guidelines, clinicians can manage patients with more certainty and less variability. Furthermore, the care and management of these patients can be then documented systematically and the outcomes tracked, creating evidence-based clinical data collected from multiple treatment centres that will be useful in validating and updating the guidelines. One approach being considered is a web-based template developed for data collection based on the findings using DNDF methodology for each disorder. Data collected from actual practices from identified centres will be used to compare and validate guideline recommendations. This process of field testing will enable determinations of future practice issues and revisions of the guidelines. Both the development and the implementation of the Nutrition Management Guidelines will expose specific priority research questions for the treatment of IMDs. The desired outcomes of these guidelines are listed in Table 2.

This method will not only make available much-needed guidelines for clinical practice in a manner that is timely, cost-effective,

Table 2 Desired outcomes of evidence- and consensus-based guidelines for nutrition management of inherited metabolic disorders

Desired outcomes
• Define evidence/consensus-based recommendations for nutrition management of patients with inherited metabolic disorders for use by metabolic dietitians in collaboration with doctor, other health care providers and members of the medical team
• Reduce variations in clinical practice and services across medical centres
• Guide practice decision that integrate medical and nutrition management/therapy
• Provide clinicians with criteria to make recommendations for nutrition management or recommend other treatments to achieve outcomes
• Define quality nutrition care based on patient's metabolic and/or genetic alteration
• Improve patient outcomes and clinician effectiveness
• Enhance patient quality of life, prevent untoward consequences and complications and reduce associated medical, educational and social costs

representing minimal bias, but also will offer a validated methodology to develop management guidelines for this field to optimize health outcomes of the patients.

Acknowledgements

These activities are supported by the Maternal and Child Health Bureau (Title V, Social Security Act), Grant #2-U22 MC010979, Health Resources and Services Administration, Department of Health and Human Services (HRSA)

These activities were developed in collaboration with doctors Southeastern Newborn Screening and Genetics Collaborative (Region 3) and Genetics Metabolic Dietitians International **(GMDI) Workgroup**
Kathryn Camp MS, RD, CSP
Cathleen Connolly RD, CSP, LD
Amy Cunningham MS, RD, LDN
Dianne Frazier PhD, MPH, RD
Shideh Mofidi MS, RD, CSP
Elizabeth Otwell MSPH
Fran Rohr MS, RD, LDN
Rani H. Singh PhD, RD, LD
Patricia L. Splett PhD, RD, FADA
Keiko Ueda MPH, RD, LDN

References

1. Schoen, E. J., Baker, J. C., Colby, C. J. & Trinh, T. T. (2002) Cost-benefit analysis of universal tandem mass spectrometry for newborn screening. *Pediatrics*, 110, 781–786.
2. Hellekson, K. L. (2001) NIH consensus statement on phenylketonuria. *American Family Physician*, 63 (7), 1430–1432.
3. Franz, M. J., Boucher, J. L., Green-Pastors, J. & Powers, M. A. (2008) Evidence-based nutrition practice guidelines for diabetes and scope and standards of practice. *Journal of the American Dietetic Association*, 108, S52–S58.
4. Frances, A., Kahn, D., Carpenter, D., *et al*. (1998) A new method of developing expert consensus practice guidelines. *The American Journal of Managed Care*, 4 (7), 1023–1029.
5. Lomas, J. (1991) Words without action? The production, dissemination, and impact of consensus recommendations. *Annual Review of Public Health*, 12, 41–65.
6. Rycroft-Malone, J. (2001) Formal consensus: the development of a national clinical guideline. *Quality in Health Care*, 10 (4), 238–244.
7. Arnold, G. L., Koeberl, D. D., Matern, D., *et al*. (2008) A Delphi-based consensus clinical practice protocol for the diagnosis and management of 3-methylcrotonyl CoA carboxylase deficiency. *Molecular Genetics and Metabolism*, 93 (4), 363–370.
8. Arnold, G. L., Van Hove, J., Freedenberg, D., *et al*. (2009) A Delphi clinical practice protocol for the management of very long chain acyl-CoA dehydrogenase deficiency. *Molecular Genetics and Metabolism*, 96 (3), 85–90.
9. Kobayashi, K., Ueno, F., Bito, S., *et al*. (2007) Development of consensus statements for the diagnosis and management of intestinal Behcet's disease using a modified Delphi approach. *Journal of Gastroenterology*, 42 (9), 737–745.
10. Vaneau, M., Chaby, G., Guillot, B., *et al*. (2007) Consensus panel recommendations for chronic and acute wound dressings. *Archives of Dermatology*, 143 (10), 1291–1294.
11. Rudolph, C. D., Mazur, L. J., Liptak, G. S., *et al*. (2001) Guidelines for evaluation and treatment of gastroesophageal reflux in infants and children: recommendations of the North American Society for Pediatric Gastroenterology and Nutrition. *Journal of Pediatric Gastroenterology and Nutrition*, 32 (Suppl. 2), S1–31.
12. Rolls, K. D. & Elliott, D. (2008) Using consensus methods to develop clinical practice guidelines for intensive care: the intensive care collaborative project. *Australian Critical Care*, 21 (4), 200–215.
13. Linstone, H. A. & Turoff, M. (eds) (1975) Delphi Method: Techniques and Applications. Reading, MA: Addison-Wesley.
14. Schmidt, K., Montgomery, L. A., Bruene, D. & Kenney, M. (1997) Determining research priorities in pediatric nursing: a Delphi study. *Journal of Pediatric Nursing*, 12 (4), 201–207.
15. Likert, R. A. (1932) A technique for measurement of attitudes. *Archives of Psychology*, 140, 44–53.
16. Raine, R., Sanderson, C. & Black, N. (2005) Developing clinical guidelines: a challenge to current methods. *BMJ*, 331 (7517), 631–633.
17. Hasson, F., Keeney, S. & McKenna, H. (2000) Research guidelines for the Delphi survey technique. *Journal of Advanced Nursing*, 32 (4), 1008–1015.
18. Van de Ven, A. H. & Delbecq, A. L. (1972) The nominal group as a research instrument for exploratory health studies. *American Journal of Public Health*, 62 (3), 337–342.
19. Jones, J. & Hunter, D. (1995) Consensus methods for medical and health services research. *BMJ*, 311 (7001), 376–380.
20. Guyatt, G. H., Oxman, A. D., Vist, G. E., *et al*. (2008) GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ*, 336 (7650), 924–926.
21. Fitch, K., Bernstein, S. J., Aguilar, M. S., *et al*. (2001) The RAND/UCLA Appropriateness Method User's Manual.
22. American Diabetic Association (2008) Evidence Analysis Manual: steps in the ADA Evidence Analysis Process. American Dietetic Association, Scientific Affairs and Research: Chicago, IL, Fall, 2008.
23. AGREE Collaboration (2001) The Appraisal of Guidelines for Research and Evaluation (AGREE) Instrument In. London: The AGREE Research Trust.
24. Hutchings, A., Raine, R., Sanderson, C. & Black, N. (2006) A comparison of formal consensus methods used for developing clinical guidelines. *Journal of Health Services Research and Policy*, 11 (4), 218–224.
25. Hutchings, A. & Raine, R. (2006) A systematic review of factors affecting the judgments produced by formal consensus development methods in health care. *Journal of Health Services Research and Policy*, 11 (3), 172–179.
26. Wong, R. C. & Favaloro, E. J. (2008) A consensus approach to the formulation of guidelines for laboratory testing and reporting of antiphospholipid antibody assays. *Seminars in Thrombosis and Hemostasis*, 34 (4), 361–372.

