



Bridging Discovery and Delivery

Micronutrient Forum Global Conference
Addis Ababa, Ethiopia, 2–6 June 2014



Micronutrient
FORUM



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Foreword

Bridging Discovery and Delivery

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The Micronutrient Forum (MN Forum) – like its predecessor, the Iron and Vitamin A Consultative Groups – has long been a strong convener of academics, policy makers, and program implementers with an interest in learning and sharing evidence and programmatic experiences related to micronutrients. The 2014 Micronutrient Forum meeting in Addis Ababa, Ethiopia, marked the revival and revitalization of the MN Forum and brought together 1,000 participants from 65 countries across the globe.

Providing updates and insights

With the theme of “Bridging Discovery and Delivery”, the conference aimed to bring together academics, practitioners, policy makers, program developers and evaluators, and others with a common interest in micronutrients.

The dual objective was to provide updates to those who rely on the evidence base to guide their work, and to provide insights to the academic community and those involved in research on the critical gap areas relevant for policy making and practice. Looking beyond the traditional nutrition focus, the conference placed particular emphasis on creating linkages across sectors relevant to ensuring adequate supply, access, and utilization of micronutrient-rich foods, such as agriculture, social protection and food security, while ensuring a continued focus on nutrition-specific interventions such as fortification and supplementation, through the health and other sectors.

Ethiopia: An exemplary commitment to nutrition

Ethiopia was chosen as the venue for the Micronutrient Forum’s 2014 Global Conference for many reasons, not least of which was to showcase the country’s exemplary commitment to nutrition through multi- and inter-sectoral collaborations. Conference delegates were honored by a stirring address by Her Excellency First Lady Roman Tesfaye during the opening ceremonies, along with opening remarks from Ethiopia’s Minister of Health, Dr. Kesetebirhan Admassu.

In a special session, representatives of the Federal Government of Ethiopia provided details of their approach to identifying and systematically addressing malnutrition. This approach is laid out in a revised National Nutrition Program document (2013–2015), now signed by nine governmental ministries. This program has been informed by the findings from the nationally and regionally representative Food Consumption Survey. The presentation highlighted how the results of that survey were used to develop the national fortification plan, regionally relevant complementary feeding guidelines, and calcium supplementation for pregnant women. Plans for, and initial findings from, the ongoing National Micronutrient Survey were also presented. This survey will be used to improve planning for, and targeting of, micronutrient programs. Finally, Ethiopia’s participation in adapting and implementing a high-level Cost of Hunger Survey was highlighted, as was the fact that Ethiopia is one of the first countries in Africa to do so.

Conference themes

The conference program was organized around four themes:

The first theme related to the **Epidemiology of Micronutrients**. Sessions in this theme provided updates on the magnitude and distribution of micronutrient deficiencies globally. Methods to better track progress – including the development of new biomarkers and methods of assessment in surveys, research, and program evaluations – were also addressed.

The **Biology of Micronutrients and Intervention Efficacy and Effectiveness** were addressed in the second theme. Sessions in this theme provided updates on the latest scientific evidence related to micronutrients, including intervention design, efficacy and program effectiveness, but also the causes and consequences of inadequate micronutrient nutrition, including risks associated with deficiency as well as excess intake of micronutrients.

Scaling up micronutrient interventions was addressed in the third theme, bringing in experiences from around the globe. Sessions presented frameworks for successfully scaling up interventions and for coordination and integration with other sectors. Specific challenges and issues commonly faced by program designers and implementers were discussed; examples included securing financing, developing costed scale-up plans for micronutrient programs, innovations in program monitoring and surveillance, among many others.



Lynnette Neufeld, GAIN and Chair of Micronutrient Forum Steering Committee, welcomes attendees during the opening plenary session.

The fourth theme, new to this meeting, focused on the **Enabling Environment**. As the name implies, sessions focused on multiple factors that might facilitate or impede progress in nutrition, from resource availability and mobilization to ethics and policy change, among many others. The fourth theme included many panel discussions, creating ample opportunity for dialogue among panelists and with the audience.

Iron: A case study

The case of one key micronutrient, iron, was woven through the four programmatic themes with the objective of highlighting particular challenges and opportunities related specifically to iron, but relevant more broadly for the entire field of micronutrients. The individuals we assess and attempt to influence through the many nutrition interventions live in intricate biological, social, and cultural systems and interact with complex health and food systems. The Integration to Implementation for iron sessions took the conference participants through iron and its risks and benefits within biological systems, across the four themes discussed above, ending with policy and programmatic implications, all with a focus on understanding the nature and implications of this complexity.

“The Integration to Implementation for iron sessions took the conference participants through iron and its risks and benefits within biological systems, with a focus on understanding the nature and implications of this complexity”

In the following pages, you will find a recount of the key findings that were presented at the Micronutrient Forum 2014, and, to the extent possible, some of the lively and thought-provoking discussion that occurred there. Clearly, it is impossible to capture all the exciting science updates, program experiences, and policy-making implications that were presented and discussed, but we hope that you will find these proceedings useful, and we look forward to seeing you in 2016 at the next Micronutrient Forum.

“I to I”:

Integration to Implementation

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The global nutrition context

The global nutrition context is becoming increasingly complex, with continuing pandemics of infections and exploding epidemics of obesity and non-communicable diseases (NCDs), all superimposed on an evolving environment of food insecurity, nutrition transition and climate change. This complexity requires us to see nutrition as more than a mere question of “too much or too little.” Our ability to respond to this complexity demands an integrated approach that acknowledges the continuum of science and effort required to develop and implement evidence-informed clinical and population-based guidance, standards of care, and programs.

Integrating nutrition: A “biological systems” approach

The complexity of the nutrition and health relationship calls for a view of nutrition within the context of a host of different processes (digestion, absorption, transport, etc.) and biological systems (immune, neurological, etc.) such that perturbations at any point in these processes or systems can have an impact on nutrition and vice versa. The relationship between nutrition and health is reciprocal and must be viewed in that context to enable the development of safe and effective interventions. Additionally, a deeper appreciation of nutrition from a systems’ perspective will enable us to identify better tools (biomarkers) to further explore nutrition both in terms of its role in health and as an outcome of interventions.

Integrating nutrition: A “health systems” approach

Just as patients access the health systems via diverse entry points, so does a need exist to fully integrate an appreciation of the importance of nutrition at all levels in order to ensure safe and efficacious interventions and standards of care. Similarly, as countries grapple with the complex food and nutrition landscape, a conversation is needed between technical agencies, academic/research leaders, funders, implementing agencies, NGOs, the private sector, and also with country-level stakeholders and relevant agencies on how best to implement existing and new guidelines/programs to address the role of food/nutrition in health promotion and disease prevention. There is a need for a “systems approach” that includes both biological systems and those systems within the public infrastructure intended to provide service. A full integration of nutrition as both a biological and a programmatic construct is required throughout all components of the clinical and population-based care and service continuum.

“I to I”: Overarching goals

In an attempt to develop a conceptual framework for such an effort and to begin this conversation, the *Integration to Implementation*, or “I to I” concept, was developed. Its overarching goals are to:

- Address specific aspects of the biology of nutrition as it pertains to individual clinical or population level challenges;
- determine what is needed (e.g. research gaps, new tools,



Ken Brown (Bill & Melinda Gates Foundation and Micronutrient Forum Steering Committee Member), Saskia Osendarp (Micronutrient Initiative) and other delegates at the 2014 Micronutrient Forum Global Conference.

new approaches/interventions) to address the challenge based on realities on the ground;

- foster a meaningful dialogue between countries, implementing agencies, the private sector, donors, and civil society; and
- initiate a process to develop effective strategies that integrates an appreciation of the evolving science of nutrition with the attributes of all the stakeholders, leading to successful implementation.

In application, “I to I” is intended to identify cases that exemplify how to responsively move the science forward with an appreciation of the relevant contextual issues, along with how best to utilize the respective resources of different agencies/organizations to reach a common goal.

“I to I” within the 2014 Micronutrient Forum Global Conference

For **Track 1**, this involved examining how the evidence to be used to support current guidelines, policies and programs is, or should be, collected. This included a discussion of the biological relevance and utility of tools available to generate relevant data.

Discussions within **Track 2** centered on the evidence base for safe and effective interventions to address both nutritional insufficiency and excess in the context of complex health issues including infectious and NCDs, and their treatment.

The overarching theme of “I to I” is to determine through dialogue with key players in the development, delivery and monitoring chain where crucial obstacles lie. **Track 3** therefore featured presentations of the experiences of individual countries with specific initiatives aimed at addressing key public health concerns.

Track 4 focused on engaging the players from different sectors and understanding the challenges (and opportunities) faced to bring these sectors together to work in partnership while highlighting the specific needs of micronutrients within the broader nutrition agenda. “I to I” was presented as an approach that fosters the creation of an enabling environment.

Glossary of Acronyms



Local musicians provide entertainment during the conference gala.

Acronym	Complete Name Term
µg	Microgram
A4NH	Agriculture for Nutrition and Health
ANC	Antenatal Care
ANM	Auxiliary Nurse Midwife
BCC	Behavior Change Communication
BCG	Bacillus Calmette-Guérin
BCI	Behavior Change Intervention
BMGF	Bill & Melinda Gates Foundation
BMVA	Breast Milk Vitamin A
BOND	Biomarkers of Nutrition for Development
CDC	Centers for Disease Control and Prevention, USA
CGIAR	Formerly, the Consultative Group on International Agricultural Research
CMAM	Community-Based Management of Acute Malnutrition
CO	Corn Oil
CSAS	Centric Systematic Area Sampling
CSIRO	Commonwealth Scientific and Industrial Research Organization
CVD	Cardiovascular Diseases
CVIVA	Center for Vitamins and Vaccines
DALY	Disability-Adjusted Life Year
DBS	Dried Blood Spot
DD	Dietary Diversity

DFID	Department For International Development, UK
DID	Difference-In-Difference
ECD	Early Child Development
ED	Euclidean Distance
E-HFP	Enhanced-Homestead Food Production
ENAM	Enhancing Child Nutrition Through Animal Source Food Management
ENOUGH	Essential Nutrient for Optimal Underpinning of Growth and Health
EPHI	Ethiopian Public Health Institute
ETH Zurich	Swiss Federal Institute of Technology Zurich
EU	European Union
FACT	Fortification Assessment Coverage Tool
FANTA	Food and Nutrition Technical Assistance Project
FAO	Food and Agriculture Organization
FFI	Food Fortification Initiative
FoNSE	Food and Nutrition Society of Ethiopia
GAIN	Global Alliance for Improved Nutrition
GIS	Geographical Information System
GMP	Good Manufacturing Practice
Hb	Hemoglobin
HBV	Hepatitis B Virus
HC	Health Committee
HIES	Household Income and Expenditure Survey
HKI	Helen Keller International
HKI's ARCH Project	Helen Keller International's Assessment and Research on Child Feeding Project
I to I	Integration to Implementation
IAEA	International Atomic Energy Agency
ICCIDD Global Network	International Council for Control of Iodine Deficiency Disorders Global Network
ICDDR,B	International Centre for Diarrheal Disease Research, Bangladesh
ICN2	Second International Conference on Nutrition
ID	Iron Deficiency
IDA	Iron Deficiency Anemia
IDD	Iodine Deficiency Disorders
IFA	Iron Folic Acid
IFPRI	International Food Policy Research Institute
IMMPaCt	Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials
INACG	International Nutritional Anemia Consultative Group
IRR	Internal Rate of Return
IUNS	International Union of Nutritional Sciences
IVACG	International Vitamin A Consultative Group
IYCF	Infant and Young Children Feeding
IYCN	Infant and Young Children Nutrition

Acronym	Complete Name Term	Acronym	Complete Name Term
LGUs	Local Government Units	S3M	Simple Spatial Survey Method
LNS	Lipid-Based Nutrient Supplements	SAM	Severe Acute Malnutrition
LQAS	Use of Lot Quality Assurance Sampling	SBN	SUN Business Network
M&E	Monitoring and Evaluation	SEANUTS	Southeast Asian Nutrition Surveys
MAM	Moderate Acute Malnutrition	SGA	Small-For-Gestational Age
Mama SASHA	Mama Sweet-potato Action for Security and Health in Africa	SI	Stimulation Index
MDG	Millennium Development Goal	SMP	School Meal Program
mg	Milligrams	SP	Sulphadoxine/Pyrimethamine
MGM	Mothers Group Meetings	SPRING	Strengthening Partnerships, Results, and Innovations in Nutrition Globally
MI	Micronutrient Initiative	STARD	Standards for Reporting of Diagnostic
miRNA	MicroRNA	SUN	Scaling Up Nutrition
MN	Micronutrient	TI	Thymic Index
MN Forum	Micronutrient Forum	TNO	Netherlands Organization for Applied Scientific Research
MNP	Micronutrient Powder	TRECs	T-Cells and T-Cell Receptor Excision Circles
MOH	Ministry of Health	TT	Tetanus Toxoid
MoHP	Ministry of Health and Population	UN	United Nations
MoPH	Ministry of Public Health	UNAIDS	Joint United Nations Programme on HIV/AIDS
MoRES	Monitoring Results for Equity System	UNICEF	United Nations Children's Fund
MT	Metric Tonnes	USAID	United States Agency for International Development
MUAC	Mid-Upper Arm Circumference	USDA, ARS	United States Department of Agriculture, Agricultural Research Service
NCD	Non-Communicable Diseases	USI	Universal Salt Iodization
NeoVitA	Neonatal Vitamin A Supplementation for Improving Child Survival	VA	Vitamin A
NGO	Non-Governmental Organisation	VAS	Vitamin A Supplementation
NICHD	National Institute of Child Health and Human Development	VMD	Vitamin and Mineral Deficiencies
NIH	National Institutes of Health	WB	World Bank
NTBI	Non-Transferrin-Bound Iron	WFP	World Food Programme
NVAS	Neonatal Vitamin A Supplementation	WHO	World Health Organization
OFDA	Office of U.S. Foreign Disaster Assistance	WIFA	Weekly Iron and Folic Acid
OFSP	Orange-Flesh Sweet-potato	WIFS	Weekly Iron and Folic Acid Supplementation
OPV	Oral Polio Virus		
OR	Operational Research		
ORS	Oral Rehydration Salts		
OWL	Older Women Leaders		
ppm	Parts Per Million		
PPP	Public-Private Partnership		
QA/QC	Quality Assurance/Quality Control		
RCT	Randomized Controlled Trial		
RNA	RiboNucleic Acid		
RDA	Recommended Daily Allowance		
REACH	Renewed Effort Against Child Hunger and Undernutrition		
ROC	Receiver Operating Curves		
RRI	Rapid Results Initiative		

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Key Contributors to These Proceedings

The below key contributors played a major role in developing the content for these conference proceedings, and their efforts are hereby acknowledged with sincere gratitude. This document captures the highlights and key messages of a wide-ranging program whose content often had multiple contributors, and it is regrettably not possible to acknowledge every single one. Our

sincere thanks nevertheless go out to everyone who helped to make the Micronutrient Forum Global Conference 2014 such a success. The spirit of their work is present in these pages, even if their names are not individually recorded.

An extensive selection of conference material is available at www.micronutrientforum.org.



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About the Micronutrient Forum

The Micronutrient Forum (MN Forum) serves as a global catalyst and convener for sharing expertise, insights and experience relevant to micronutrients in all aspects of health promotion and disease prevention, with special emphasis on the integration of nutrition actions across relevant sectors. The primary objective of the MN Forum is to foster dialogue among the research, policy, clinical, program and private sector communities to facilitate the translation of evidence for policy and program planning and to inform research needs and priorities based on evidence gaps to support programs.

The MN Forum was first established in 2006, merging the International Nutritional Anemia Consultative Group (INACG) and the International Vitamin A Consultative Group (IVACG). Funding for these groups and this transition was provided by the United States Agency for International Development. These two groups brought to the MN Forum more than 30 years of global experience in research, policy and program issues related to iron and vitamin A. Two highly successful MN Forum global meetings were held, in 2007 in Istanbul and in 2009 in Beijing.

Following a transition period with no active MN Forum, a group of individuals with common interests in diverse issues related to micronutrients met in 2011 to review the purpose and viability of the MN Forum. An assessment conducted on the MN Forum in 2011 reported the need for its continuation due to its perceived usefulness as a means for exchanging scientific, programming and policy information on micronutrients among scientists and public health professionals. It recommended that future MN Forum groups should continue their focus on effective scaling up of programs and improved biomarkers, monitoring and evaluation, and multi-sector integration of micronutrient activities.

The resulting, revitalized, MN Forum is built on a broad foundation of technical and financial support. Leadership is provided by a Steering Committee of approximately 17 individuals actively involved in issues related to micronutrients from academia and diverse normative, policy and implementing organizations across the globe. Coordination is provided by a Secretariat currently hosted at the Micronutrient Initiative in Ottawa, Canada.

We are extremely grateful to the Micronutrient Initiative for hosting the Secretariat of the Micronutrient Forum and to the Bill & Melinda Gates Foundation for providing us with a conference grant; without the support of both, the 2014 Conference would never have taken place. Our thanks go likewise to our donors and sponsors for their great generosity and vision, and also to the Local and International Steering Committees and the Program Working Group Chairs and Members who worked so hard to develop the conference program. Last but by no means least, we would like to thank all the delegates who made the journey to Addis Ababa to share their knowledge, insights and experiences with us.

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www.youtube.com/watch?v=pLG5XVFAC9g

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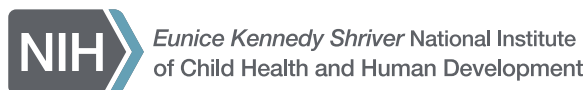
Founding Donors

The revitalization of the Micronutrient Forum has been made possible thanks to the generous contributions of our Founding Donors. The Founding Donors are organizations which have invested in the revival of the MN Forum by making onetime or ongoing financial and in-kind contributions. These contributions permitted the formation of the Steering

Committee, the development of the strategic plan, all of the start-up activities necessary for the planning and organization of the 2014 meeting as well as contributions to the meeting itself. The Micronutrient Forum would not have been possible without these generous contributions, for which we are extremely grateful.

**BILL & MELINDA
GATES** *foundation*

The Micronutrient Forum would also like to acknowledge the support of the **Centers for Disease Control and Prevention**



Sponsors

The Sponsors of the 2014 Micronutrient Forum Global Conference provided funds for the many expenses related to the meeting itself. In addition, the funds from our sponsors enabled us to bring many speakers and participants from

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Track 1 Measuring and Interpreting Information on Micronutrient Intake, Status and Program Coverage

Introduction

Kenneth Brown

Bill & Melinda Gates Foundation,
Seattle, WA, USA

The major goals of this track were:

- a) To provide an update on new methods for the assessment of nutritional status (involving dietary assessment, biochemical assessment, measurement of biomarkers, and functional assessment); and
- b) to provide a global update on the prevalence of micronutrient deficiency.

The discourse at the conference itself revealed the inadequacies of our current picture of the micronutrient status of populations around the world. Few developing countries are collecting and reporting reliable and timely measurements of nutritional status, and the global community is not yet devoting adequate attention and resources to make this data collection and analysis possible.

Micronutrient status and program coverage

An important point made by participants in this track is the necessity of collecting and analyzing concurrent data for both micronutrient status and program coverage, which is essential to ensure that the programs being delivered are **a)** actually targeting the populations that are micronutrient deficient, and **b)** appropriately designed to improve their micronutrient status.

The need for more effective biomarkers

Another major theme of this track was the inadequacy of some of the biomarkers that are currently being used to assess micronutrient status. Reliable data are essential for effective and well-targeted programs, and the global nutrition community needs more field-friendly and accurate biomarkers that are reliable even in the presence of inflammation and other potential confounding factors. New biomarkers based on a systems biology approach that makes use of novel techniques such as metabolomics could be one way to fill this gap.



The plenary room at the opening of the 2014 Micronutrient Forum Global Conference.

The presentations, posters and plenary discussions of this track reflect the complexity of these issues, the most recent advances made in biomarker development, and areas for further research and expanded resource allocation.

1.1 Plenary Sessions: Development and Evaluation of Novel Biomarkers of Micronutrient Status (Part 1 and 2)

Coordinator | Moderator: Daniel Raiten

Pediatric Growth and Nutrition Branch,
Eunice Kennedy Shriver National Institute
of Child Health and Human Development (NICHD),
National Institutes of Health (NIH),
Bethesda, MD, USA

Terms of Reference

What do we mean by “biomarker”?

“Biomarkers are characteristics that are objectively measured and evaluated as indicators of normal biological processes, pathogenic processes, or pharmacologic responses to therapeutic intervention.”

*The Biomarkers Consortium, Foundation for the NIH
(official NIH definition)*

What is a “nutritional biomarker”?

“Biomarkers of nutrition may reflect exposure, status (where an individual or population sits relative to accepted standard), function (reflecting either the role of a nutrient within a biological system, e.g. function as a cofactor for a given enzyme or a function directly impacted by nutrient, e.g. vision and vitamin A), and effect (response to an intervention).”

The Biomarkers of Nutrition for Development (BOND) project

Why do we need biomarkers?

Individual level:

- Clinical diagnosis and treatment
- Monitoring response to treatment
- Research, e.g. understanding homeostatic mechanisms

Population level:

Nutrition survey

- Identify populations at risk of deficiency
- Design effective and efficient interventions
- Monitor and evaluate impact of interventions

*Nicola Lowe, International Institute
of Nutritional Sciences and Food Safety Studies,
University of Central Lancashire, UK*

Making effective use of biomarkers

“The ability to develop evidence-based clinical guidance and effective programs and policies to achieve global health promotion and disease prevention goals depends on the availability of valid and reliable data. With specific regard to the role of food and nutrition in achieving those goals, relevant data are developed with the use of biomarkers that reflect nutrient exposure, status, and functional effect. A need exists to promote the discovery, development, and use of biomarkers across a range of applications. In addition, a process is needed to harmonize the global health community’s decision making about what biomarkers are best suited for a given use under specific conditions and settings.”¹

The overarching theme of these sessions was to present current research on biomarker development and use for exploring new directions in biomarker discovery. To cover the breadth of the topic, two sessions were conducted on successive days.

Part 1

This session began with an overview of the summary of the Biomarkers of Nutrition for Development (BOND) Phase I Expert Panel reviews presented by Daniel Raiten.

The first six nutrients covered by BOND were iodine, iron, zinc, folate, vitamin A and vitamin B₁₂. In addition to the conclusions of the Expert Panel reviews, Dr. Raiten presented conclusions of deliberations about how best to implement



Measuring child mid-upper arm circumference in Rajasthan – not a biomarker, but an important indicator of growth.

these recommended biomarkers with particular focus on low-resource settings. He also included a brief review of discussions about current and new technologies and platforms that might be employed in the implementation of these biomarkers, including dried blood spot (DBS), microarray/multiplex platforms, microfluidics using paper-based platforms, and acoustic-fluidics.

Establishing the validity and reliability of new diagnostics tests

Sant-Rayn Pasricha, Nossal Institute for Global Health, University of Melbourne, presented an overview of issues associated with establishing the validity and reliability of new diagnostics tests. He focused specifically on the issues of sensitivity, specificity, predictive values, likelihood ratios, Receiver Operating Curves (ROC), reference ranges and statement – Standards for Reporting of Diagnostic (STARD) Accuracy. The latter consists of a checklist of 25 items and a flow chart used to improve the quality of studies of diagnostic accuracy. As a case study application of these concepts, Dr. Pasricha summarized results from his analysis of the utility of hepcidin as a biomarker of iron. He demonstrated the effectiveness of hepcidin to not only detect iron deficiency but also distinguish iron deficiency anemia from anemia of inflammation.

The diagnostic utility of proxy markers of serum retinol concentration

Elise Talsma, Wageningen University, summarized the result of her study of the diagnostic utility of proxy markers of serum

retinol concentration, including retinol binding protein (RBP), transthyretin concentration, transthyretin: RBP molar ratio and retinol concentration by fluorescence. Ms. Talsma concluded that transthyretin and RBP are useful biomarkers for identifying children with vitamin A deficiency.

Zinc supplementation RCT

Barbara Stoecker, Oklahoma State University, followed with the results of a zinc supplementation randomized control trial (RCT) conducted in rural southern Ethiopia. Specifically, the study focused on evaluating potential new biomarkers of zinc, including mRNA abundance of ZnT1, ZIP3, 4 & 8. The study utilized samples from adult women after 23 days of zinc supplementation (~20 mg/d). Dr. Stoecker concluded that supplementation significantly decreased ZIP 4 and ZIP 8 mRNA abundance and increased plasma zinc concentrations after 23 days of Zn supplementation.

Simplified approaches for estimating vitamin A stores and β -carotene bioconversion

Majorie Haskell, University of California, presented on behalf of Georg Lietz and Michael Green on simplified approaches for estimating vitamin A stores and β -carotene bioconversion in humans. She focused on such new methodologies as – LC/MS/MS analysis of stable isotope retinoids, and concluded that use of ^{13}C stable isotopes can help determination of full body vitamin A stores at three days and that LC/MS/MS would allow fast, accurate and easy determination of ^{13}C stable isotopes. This technology can be made field-friendly by replacing complex compartmental mathematical modeling with simple equations.

The interpretation of iron, zinc and vitamin A biomarkers

The session concluded with a presentation by Ryan Wessells, University of California, about the interpretation of iron, zinc and vitamin A biomarkers in the context of asymptomatic malaria infection. She presented the results of a study conducted in Burkina Faso in children aged 6–23 months and concluded that interpretation of biomarkers of iron and vitamin A status are impacted after adjusting for systemic inflammation in the presence of asymptomatic malaria. By contrast, plasma zinc concentrations are not similarly impacted. Dr. Wessells suggested that a need exists for additional research to more fully understand the effects of infection and inflammation on biomarker selection and performance, as well as an increased effort to discover and develop new biomarkers that are not resistant to these effects in order to more specifically distinguish nutritional micronutrient status from the effects of concurrent inflammation/disease.

Part 2

Ian Darnton-Hill, session chair, provided context by summarizing the presentations and discussions from [Part 1](#). In addition to the presenters, the session had a panel of respondents including Yiwu He (Bill & Melinda Gates Foundation, Seattle, WA, USA) and Michael Fenech, who opened by acknowledging the efforts of programs like BOND in stimulating new research in discovery, development and implementation.

The value of systems biology approaches for developing new micronutrient biomarkers

The first presentation, provided by Bas Kremer (TNO, Metabolomics Center, Zeist, Netherlands), focused on the value of systems biology approaches for developing new micronutrient biomarkers. He emphasized that systems thinking is a more inclusive approach that incorporates nutrition, health and disease processes, as well as consideration of physical, social and behavioral factors, all of which have a potential to alter gene expression. Dr. Kremer provided a systems model of gene-environment interactions and discussed how the Essential Nutrients for Optimal Underpinning of Growth and Health (ENOUGH) consortium is promoting a systems approach to global nutrition activities. He concluded by advocating greater harmonization and support for data sharing so as to identify better and more physiologically relevant biomarkers, and suggested that the use of multi-marker panels should be a target in efforts to move this agenda forward.

The potential of the “omic” approaches to develop new micronutrient biomarkers

Michael Fenech (CSIRO [Commonwealth Scientific and Industrial Research Organization], Food and Nutritional Sciences, Adelaide, South Australia, Australia) focused on the potential of the various “omic” approaches to develop new micronutrient biomarkers. Dr. Fenech presented a model of the “nucleo-centric” view of ageing and highlighted the role of malnutrition (over- or under-nutrition) in increasing DNA damage. He focused on the epigenetic changes that occur throughout the lifecycle starting from gametogenesis through to old age, and how a myriad of factors – from environmental toxin exposure to maternal and fetal nutrition, dietary methyl donors, alcohol and stress, among many others – play a role in epigenetic events. He then discussed MicroRNA (miRNA) and how the alterations in miRNA expression may underlie many diseases, including cancer. He touched on how proteomics can be exploited in the effort to identify new biomarkers of micronutrients and other relevant functional domains.

The value of stable isotope techniques for the assessment of micronutrient bioavailability / status

Cornelia Loechl, International Atomic Energy Agency (IAEA), presented a brief review of the value of stable isotope techniques for the assessment of micronutrient bioavailability and status. She provided an overview of IAEA’s work in nutrition, noting that IAEA’s motivation is to use isotopic techniques to develop and evaluate interventions to combat malnutrition in all its forms. Dr. Loechl highlighted the various uses of stable isotope techniques, including body composition, total energy expenditure, and micronutrient bioavailability with particular reference to IAEA’s focus on vitamin A, iron and zinc. These techniques offer the advantage of being non-invasive, suitable for all ages, and applicable in community settings. Dr. Loechl highlighted examples of micronutrient bioavailability studies conducted in Senegal, Thailand, Rwanda and India. She concluded by emphasizing another focal point of IAEA activity: capacity development. In that context, she introduced the IAEA Technical Cooperation Program and IAEA Coordinated Research Program, as well as regional designated centers in Botswana, Morocco and the IAEA Collaborating Center for Nutrition in Bangalore, India, as examples of IAEA’s global commitment to capacity development.

References

1. Daniel J Raiten, Sorrel Namaste ´, Bernard Brabin et al, Biomarkers of Nutrition for Development: Building a Consensus, *Am. J. Clin. Nutr.* 2011; 94 (suppl): 633S–50S.

1.2 Plenary Session: Update on the Prevalence, Risk Factors and Spatial Distribution of Micronutrient Deficiency and Excess

Coordinator | Moderator: Roland Kupka

UNICEF, New York, NY, USA

Presenters

Mark Myatt

Brixton Health, Llawryglyn, Powys, UK

Use of simple spatial survey methods to assess the spatial distribution of risk of micronutrient deficiency, program targeting efficiency, and program coverage

Abstracts selected for oral presentations:

Grant Aaron

Global Alliance for Improved Nutrition, (GAIN), Geneva, Switzerland

Assessing coverage of targeted and large-scale fortification programs: development of a fortification assessment coverage tool (FACT)

Panam Parikh

FrieslandCampina Innovation, BN, Amersfoort, Netherlands

Effect of demographic variables on 25(OH)D level and on the risk of vitamin D insufficiency in SEANUTS countries

Mario Capanzana

Food and Nutrition Research Institute, Taguig City, Philippines

Zinc status of Filipinos by serum zinc level: 7th National Nutrition Survey, Philippines 2008

Banda Ndiaye

Micronutrient Initiative, Dakar, Senegal

Distribution of iron, vitamin A and zinc deficiencies in children and women in Senegal

Ascertaining the needs of at-risk groups

Effective nutrition programs need to be able to characterize at-risk groups, intervention coverage, and how these two overlap. Such knowledge is even more important in the context of growing disparities among and within nations with regard to nutrition and other health-related indicators. Furthermore, it is important for the nutrition community to have better survey data on key nutrients such as zinc and vitamin D.

Even though nutrition surveys with traditional cluster designs are able to adequately determine characteristics of the study population at a specific time, they are limited to providing estimates over very large areas, often thousands of square kilometers. Such lack of spatial resolution is an important limiting factor if the variable of interest, such as program coverage, varies substantially over the estimation area.

“New methodologies are allowing us to better ascertain the nutritional needs of the most vulnerable”

New methodologies are now emerging beside the traditional population-based surveys. These allow us to better measure the characteristics of sub-sections of the overall population of a given country or region, and thus to better ascertain the nutritional needs of the most vulnerable groups within those populations. Two of these are the Centric Systematic Area Sampling (CSAS) method and the Simple Spatial Survey Method (S3M). While requiring further testing before they can be widely rolled out, these two methodologies could offer benefits if used alongside the traditional ones – which, in their turn, could be made more effective than in the past and thus could deliver improved data.

The CSAS and S3M methods

The CSAS method allows for the estimation and mapping of coverage with geographic precision and provides information about barriers to program access. The method uses a grid to identify communities to sample, and is simple to understand and implement. The S3M is an adaptation of the CSAS method

and employs improved spatial sampling and more effective use of data. It uses a triangular irregular network with highly efficient use of samples. Both methods have been developed for use in the community-based management of acute malnutrition among children, but provide opportunities for micronutrient and other public health interventions.

Fortification programs in Rajasthan, India

As an illustration of such an application, the S3M tool has been used to assess the coverage of targeted and large-scale fortification programs in the state of Rajasthan, India. In this state, limited information was available about the program coverage of staple food fortification. In a statewide survey, different fortification vehicles were assessed among women with children aged 0–24 months. Using S3M, the study evaluated the household coverage of Atta wheat flour. Even though the consumption of Atta wheat flour was high (83.3%), the amount of fortifiable and fortified wheat flour (7.2% and 6.2%, respectively) was low. As per the S3M design employed, no household lived further than 32 km away from the sampling point. The application showed that S3M is a practical and useful survey methodology for programs and that it allows for the creation of fine-scale geographical maps.

Vitamin D deficiency in Southeast Asia

Vitamin D has well-described functions in calcium metabolism, but its role in cell growth, neuromuscular and immune function, and reduction of inflammation, has only recently been recognized. Nevertheless, there is limited data on the prevalence of vitamin D deficiency in Southeast Asia. The Southeast Asian Nutrition Surveys (SEANUTS) consortium assessed levels of 25-hydroxyvitamin D (25OH)D in children > 2 years in Indonesia, Malaysia, Thailand, and Vietnam. The prevalence of vitamin D deficiency ((25OH)D < 25 nmol/L) was low except in Vietnam (11.1%). However, there was high prevalence of insufficient vitamin D concentrations (25 nmol/L ≤ 25(OH)D level < 50 nmol/L), ranging from 31.7% in Thailand to 44.0% in Indonesia. Vitamin D concentrations were not related to reported sunshine exposure, which may have been subject to misclassification. Dietary vitamin D intake was not assessed due to non-availability or incomplete data in local food composition tables. In aggregate, the data indicate that vitamin D deficiency is a public health problem among children in Southeast Asia.

Zinc deficiency in the Philippines

In the Philippines, zinc deficiency is likely to be a public health problem, but no data on serum zinc levels were available. The 7th national nutrition survey in the Philippines followed a multi-stage stratified sampling design to assess national serum zinc levels' among the entire age range (age > 6 months to > 60 years), including pregnant and lactating women. Using generally accepted indicators, the mean prevalence of zinc deficiency in all population groups combined was 30%. Among children 6 months–5 years and 6–12 years, the prevalence was 21.6% and 30.8%, and 21.5% and 39.7%, respectively, among pregnant and lactating women. In sum, zinc deficiency is highly prevalent among the Philippine population.

Micronutrient deficiencies in Senegal

In Senegal, the importance of micronutrient deficiencies is well recognized, but there was insufficient data to adequately characterize their prevalence and to adjust deficiency control programs. To obtain such data, Senegal conducted a national household-based survey in 2010. In children aged 12–59 months, the prevalence of hemoglobin < 110 g/L was 62%, while that of low serum zinc (< 65 µg/dL and < 57 µg/dL for morning and afternoon samples) was 67%. Deficiencies among women of reproductive age were also high. Estimates were elevated among the most vulnerable, and often overlapped. Disease control and micronutrient interventions should be considered developmental priorities by Senegalese decision-makers.



Participation was uniformly high throughout the conference.

1.3 Plenary Session: Assessment of Program Coverage Indicators in Relation to the Distribution of Micronutrient Deficiency

Coordinator: Grant Aaron

Global Alliance for Improved Nutrition (GAIN)
Geneva, Switzerland

Moderator: Sherry Tanumijardjo

University of Wisconsin-Madison, WI, USA

Summary of presentation 1

Keith Lividini

HarvestPlus, Washington DC, USA

Indicators of coverage for achieving effectiveness in cost-effectiveness studies

In order to achieve maximum effectiveness from food-based nutrition interventions, the appropriate coverage indicators need to be examined for proper planning. For this reason, reach, coverage and effective coverage were distinguished in this analysis. Reaching a high proportion of the population alone will not guarantee effectiveness: vehicles must cover those with inadequate intakes and must be consumed in sufficient quantity to change micronutrient intake and when fortified or biofortified with additional micronutrients.

The consumption module from the Bangladesh Household Income and Expenditure Survey (HIES) 2005 was used to estimate the reach, coverage and effective coverage of wheat flour (for fortification) and rice (for biofortification) after simulating the additional zinc intake from proposed fortification and biofortification levels. While both rice and wheat flour demonstrated high reach and coverage, only rice achieved high effective coverage due to the magnitude of consumption of the vehicle among those with inadequate zinc intake. Moreover, the coverage of wheat flour was lowest where inadequate zinc intake was highest (Barisal). Examining not only the change in the prevalence of inadequate micronutrient intake but also the micronutrient intake gap both before and after simulation of the intervention is essential to understanding the relationship between consumption and micronutrient intake status.

Summary of presentation 2

Reina Engle-Stone

University of California, Davis, CA, USA

Predicted impact of large-scale fortification on adequacy of vitamin A intakes among women and young children in Cameroon: Simulations using nationally representative 24-h recall data

Dietary intake data (for example, from 24-hour recalls) can be used to simulate the impact of different food fortification scenarios on the adequacy of micronutrient intakes. This information can be used to inform fortification program decisions, such as selecting appropriate vehicles and fortification levels (as per WHO guidelines).

Results from simulations using nationally representative 24-h recall data from Cameroon suggest that fortification will improve adequacy of vitamin A intakes among both women and young children (1–4 ys of age), but the potential impact varies regionally, depending on the baseline prevalence of inadequacy and the distribution of consumption of fortifiable foods. Fortification with high levels of vitamin A and/or with multiple vehicles would also increase the prevalence of retinol intakes above the UL, depending on the food vehicle and the population subgroup. Examination of total nutrient intakes and the distribution of fortified food consumption (rather than mean food intake alone) explains the differential effects of different fortification scenarios on the prevalence of inadequate and excessive intakes.

Summary of presentation 3

Steve Vosti

University of California, Davis, CA, USA

An economic optimization tool for micronutrient interventions in Cameroon

The need for, and effectiveness of, specific micronutrient interventions can vary over space and time for given countries. This presentation focused on a tool that aims to help countries formulate and manage cost-effective vitamin A intervention programs.



A young girl is measured as part of the studies conducted in Nepal.

The tool has three components: **a)** A nutrition model that estimates the effective coverage of alternative vitamin A interventions; **b)** a cost model that estimates the costs of alternative vitamin A interventions; and **c)** an economic optimization model that finds the most cost-effective interventions for meeting effective coverage targets for vitamin A across three regions in Cameroon, over a 10-year planning time horizon. Significant cost savings for Cameroon are possible by adopting vitamin A intervention strategies that vary spatially and over time. These cost savings are much larger than the estimated data collection and research costs associated with developing the vitamin A planning tool.

Summary of presentation 4

Kevin Sullivan

Centers for Disease Control and Prevention
and Emory University, Atlanta, GA, USA

The Micronutrient Survey Manual

A new manual on performing cross-sectional surveys to assess micronutrients is being jointly developed by the Centers for Disease Control and Prevention, World Health Organization, UNICEF, and the Micronutrient Initiative. The current version is called *Indicators and Methods for Cross-Sectional Surveys of Vitamin and Mineral Status of Population*, and the newer version will be called the *Micronutrient Survey Manual*. The manual will cover the many aspects of assessing micronutrient status and interventions for iodine, iron, folate, vitamin A, zinc, and anemia.

Summary of presentation 5

Kuong Khov

Institut de Recherche pour le Développement, Phnom Penh,
Cambodia and University of Copenhagen, Denmark

What is the right indicator to evaluate the impact of interventions? Examples from a rice fortification trial in Cambodia

Large-scale programs often use simple and robust proxy indicators for evaluation purposes. Little is known about whether the use of these proxy indicators might lead to erroneous conclusions regarding the impact of programs.

In the FORISCA-UltraRice+NutriRice trial in Cambodia, fortified rice was introduced through the World Food Programme school meal program (SMP). A wide range of impact indicators collected during the study was explored to test the usefulness of two proxy indicators (anemia and stunting), which are associated with micronutrient status for program evaluation.

The trial established that proxy indicators did not reflect the impact of the interventions, and that the interventions sometimes have opposing effects: benefit for one outcome, harm for other outcome. However, micronutrient status is significantly improved as result of intervention. Thus it is recommended that proxy indicators might not be enough for evaluating interventions. The impact on real health problems (cognition/morbidity) should be assessed; overall impact needs to be assessed/balanced using several different direct indicators which might show opposing effects; a more in-depth understanding of the causes of health problems is needed; and the constraints of proxy indicators need to be identified.



Track 2

Effects of Micronutrient Interventions on Indicators and Functional Outcomes

Introduction

Lindsay Allen

USDA, ARS Western Human Nutrition Research Center University of California, Davis, CA, USA

Updating the evidence from efficacy and effectiveness trials

The main goal of this track was:

- to update the evidence from efficacy and effectiveness trials evaluating how interventions affect nutritional status, health and other functional outcomes (impact in programmatic conditions, measured by program evaluations).

Topics were prioritized based on both knowledge of new evidence that was available, and of controversies that remain to be resolved. For example, recent evidence has emerged that programs providing iron supplements to young children could increase the risk of mortality and/or morbidity, especially in those who were not iron-deficient initially. Much research has been subsequently focused on this question, and this was presented in the plenary session on the risks and benefits of iron interventions and their implications for iron status assessment.

Another important question is whether pregnancy outcome, including reduction of low birth weight and later stunting, is better if women are provided with multiple micronutrient sup-

A technician performs an ultrasound on a pregnant woman in Vietnam as part of the PRECONCEPT trial to assess the impact of preconception micronutrient supplementation on maternal and child outcomes.





A mother being interviewed as part of a field study in Bangladesh.

plements vs. the current recommendation for folic acid plus iron supplements. Likewise, an important question is whether programs to deliver multiple micronutrients improve the growth and short- and/or longer-term development of young children, and the most effective way to deliver these micronutrients. These issues were presented in the plenary session on micronutrient interventions to prevent fetal growth retardation and stunting.

Iodine deficiency has long been recognized as a serious problem and universal salt iodization to be the basic approach for prevention of this problem in vulnerable populations. The session on iodine interventions presented an update on both the functional benefits of iodine programs – including improved pregnancy outcome and child development – and the need to consider other approaches, such as supplementation, for delivering iodine in some situations.

Folate and vitamin B₁₂ have emerged as two other important micronutrients to consider delivering in intervention programs. Thus the session on interventions to improve folate and vitamin B₁₂ status reviewed the current status of information on vitamin B₁₂ deficiency, and whether there are potential risks of providing folic acid programs to population groups with a high prevalence of B₁₂ deficiency or where anti-malarial drugs work through their anti-folate properties. The session on vitamin A supplementation of the newborn provided an update on the recent trials designed to resolve the inconsistent previous evidence about whether giving high-dose vitamin A supplements to newborn infants would reduce infant mortality and/or morbidity, and to evaluate their effect on the function of their immune system.

“An important question is whether pregnancy outcome is better if women are provided with multiple micronutrient supplements”

2.1 Determining the Risks and Benefits of Iron Interventions, Recommended Assessment Methods and the Need for Individual Assessment

Richard Hurrell

Institute of Food, Nutrition and Health,
ETH Zurich, Switzerland

Laura Murray-Kolb

The Pennsylvania State University,
University Park, PA, USA; and Johns Hopkins
Bloomberg School of Public Health,
Baltimore, MD, USA

Sant-Rayn Pasricha

John Radcliffe Hospital, University of Oxford, UK;
and University of Melbourne, Australia

Lynnette Neufeld

Global Alliance for Improved Nutrition (GAIN),
Geneva, Switzerland

Introduction

Anemia is responsible for approximately 8.8% of the world's Years Lived with Disability, with the burden focused on low- and middle-income countries, especially in South and South East Asia, sub-Saharan Africa and parts of Latin America. Recent estimates suggest that the worldwide anemia prevalence is 43%, 29% and 38% in children <5 years, non-pregnant women of reproductive age, and pregnant women, respectively, with approximately half of the anemia being attributable to iron deficiency (ID).

Iron deficiency anemia (IDA) can be treated or prevented by iron supplementation or by the iron fortification of foods. A critical recent issue has been the safety of iron supplementation to children living in settings where malaria infection is endemic, as there are concerns that iron may exacerbate malaria. However, IDA has been identified as a risk factor for poor child development, and failure to prevent or treat could lead to many children not reaching their full cognitive potential. With the aim of better informing policy, the four presentations in this session were designed to help find consensus regarding the risks and benefits of iron interventions in malaria-endemic areas, including their efficacy and safety, and new approaches to assess iron status.



Taking blood samples to assess micronutrient status during a rice fortification trial in Cambodia.

Functional effects of anemia and iron deficiency and of iron interventions in pregnancy, infancy, and childhood

Laura Murray-Kolb

Dept. of Nutritional Sciences, The Pennsylvania State University, University Park, PA, USA; and Dept. of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

In order to make the best decisions regarding policy, we need to understand the effects of iron supplementation on functional outcomes such as cognition, in addition to the more traditional hematological outcomes that have been used hitherto. Results from animal studies reveal a clear relation between iron status and neurobiology such that myelination, metabolic activity, morphology, and monoamines are altered by ID. Furthermore, we know that these effects vary by timing, severity, and duration of the insult, and that recovery is dependent on time and dose of supplementation. Results from human studies reveal lower mental development and motor test scores, differences in socio-emotional behavior and alterations in neurophysiology in infants with IDA vs. iron-sufficient infants. However, most supplementation trials report persistent differences between groups, even after correction of the deficiency. Findings in toddlers and school-aged children reveal a relation between iron status and cognition, with supplementation reversing the negative effects of the ID.

The long-term functional effects of iron supplementation during gestation have received less attention, as have the effects of ID in women of reproductive age. However, emerging studies reveal relations between maternal iron status and subsequent child behavior/cognition, with iron supplementation altering the findings. In addition, iron supplementation trials in women of reproductive age reveal relations between iron status and cognition/affect in these women, with the negative effects of the deficiency being reversed by supplementation. Finally, there is evidence to suggest that iron status in a woman of reproductive age alters the manner in which she interacts with her children, which has implications for child development.



A woman receives iron folic acid during a post-natal check-up at a health center in Mirpur, Dhaka (Bangladesh).

“Emerging studies reveal relations between maternal iron status and subsequent child behavior/cognition, with iron supplementation altering the findings”

Although the research across age groups reveals a relationship between iron status and cognition/behavior, the specifics of this relationship and an understanding of the effects of iron supplementation are still needed. Studies need to utilize the correct outcomes; the timing of both testing and supplementation needs to be considered; and the research team needs to include individuals with expertise in administering the tests and interpreting the findings. The goal is to set policies that will provide optimal benefit while preventing harm. In order to do so, we require a clear understanding of the risks of ID, as well as the benefits (and risks) of iron supplementation.

Efficacy, benefits, risks and confounders of using iron to prevent or treat anemia

Richard Hurrell

Institute of Food, Nutrition and Health,
ETH Zurich, Switzerland

The two strategies commonly used to treat or prevent IDA are iron supplementation and iron fortification. Iron supplementation is usually given in high doses without food, whereas iron fortification is given at much lower doses with food. Cereal staples, condiments and complementary foods are commonly fortified with iron at an industrial level, and iron-containing micronutrient mixtures can be added to porridges for young children at the household level. In the absence of infections, such interventions will improve iron status and can successfully be used to prevent or treat IDA.

In the presence of infections, however, the normal immune response is for hepcidin to prevent iron entering the plasma, either from enterocytes leading to decreased iron absorption, or from macrophages, leading to an interruption of red cell iron recycling and the anemia of inflammation. In malaria-endemic areas, the high prevalence of anemia can be due to both the anemia of inflammation and IDA. As the inflammation decreases iron absorption, this has led to the suggestion that iron interventions may not be effective in malaria-endemic areas. Both fortification and supplementation, however, have been shown to be efficacious in improving iron status, indicating that the iron needs for erythropoiesis overrule the inhibition of iron absorption due to inflammation. Whereas supplementation may also decrease the prevalence of anemia, the lower iron levels used in fortification may not, and the anemia of inflammation may persist.

Iron supplementation can intensify malaria infections in the absence of malaria surveillance and good health care. While the mechanism is not entirely clear, it is thought to be modulated via non-transferrin-bound iron (NTBI), formed when the rate of iron entering the plasma is greater than the binding potential of transferrin, or via the formation of reticulocytes, the young red blood cell favored for plasmodium merozoite infection. Iron supplementation increases NTBI, and can also increase hemoglobin and thus reticulocytes. Because of the much lower iron doses with food fortification, iron fortification does not increase NTBI and, in malaria-endemic areas, iron-fortified foods have



A doctor uses a toy to distract a child while his colleague takes a blood sample as part of the Grow Smart project to examine the impact of micronutrient and early learning interventions on child micronutrient status and development in Andhra Pradesh, India.

been reported not to increase hemoglobin. There is also no evidence that iron-fortified foods increase the incidence or intensity of malarial infections. However, there is only one large-scale study investigating this issue, and this study found no influence of an iron-fortified micronutrient powder on malaria incidence. This study, as others, did observe less malaria in subjects with anemia, perhaps due to less reticulocyte formation, indicating that it may be beneficial to eliminate ID and the risk of poor cognitive development but to remain anemic as a protection against malaria. In summary, iron fortification is both efficacious and safe in malaria-endemic areas, but it would still be wise to use the lowest iron dose that will lead to an improved iron status.

“Iron fortification is both efficacious and safe in malaria-endemic areas, but it would still be wise to use the lowest effective iron dose”

New approaches to understanding iron status in the presence of inflammation

Sant-Rayn Pasricha

MRC Human Immunology Unit, Weatherall Institute of Molecular Medicine, John Radcliffe Hospital, University of Oxford, UK; and Melbourne School of Population and Global Health, Faculty of Medicine, Dentistry and Health Sciences, University of Melbourne, Australia

Evolving insights into the molecular regulation of iron metabolism can potentially inform policy. Plasma iron levels are regulated via the action of hepcidin, a liver-derived hormone which acts to prevent cellular export of iron from intestinal cells and macrophages via its interaction with the sole cellular iron export protein, ferroportin. Thus, both iron absorbed from the intestine and macrophage iron (recycled from senescent erythrocytes) are withheld from plasma (and erythropoiesis) when hepcidin levels are high, while iron absorption is facilitated and plasma iron maintained when hepcidin levels are suppressed. Hepcidin is increased by iron stores and directly by inflammation, and is suppressed by erythropoiesis and iron deficiency. Thus, measurement of hepcidin levels may combine assessment of iron stores, inflammation and erythropoietic iron needs into a single measure.

“Measurement of hepcidin levels may combine assessment of iron stores, inflammation and erythropoietic iron needs into a single measure”

In Gambian children with post-malarial anemia or IDA, we found that hepcidin levels were the best correlate of erythrocyte iron incorporation and that they predicted erythrocyte iron incorporation exceeding 20% ($AUC^{ROC} = .90$). In two cross-sectional populations of pre-school children in rural communities in The Gambia and Tanzania ($n=1313$), hepcidin predicted iron deficiency ($AUC^{ROC} = .85$) and among anemic individuals distinguished between ID and anemia of inflammation ($AUC^{ROC} = .89$). Hypothetical pre-screening of the population with hepcidin prior to supplementation using a cut-off of 5.5ng/mL would reduce the number of children receiving iron in this population to just 27.5%, and would see 77.2% of the children who were ID and 79.9% of the children who were IDA receive iron, while preventing 86.3% and 79.7% of children with anemia of inflammation and malaria parasitemia from receiving iron. Beyond diagnostics, the hepcidin-ferroportin provides important insights into iron physiology. Specifically, humans have evolved to exclude iron from the plasma during infection, probably to withhold iron from pathogens. This insight should provoke a re-evaluation of approaches that provide iron supplementation unless the expected benefits are well understood and the potential risks (infectious and otherwise) are considered and managed.

Program implications: Do we have consensus? What are we recommending?

Lynnette Neufeld

Global Alliance for Improved Nutrition (GAIN),
Geneva, Switzerland

In reflecting on the implications of the role of iron and the potential risks and benefits associated with supplementation, it is important to remember that our understanding of nutrition will continue to evolve, and that, inevitably, our better understanding of biology and our constantly changing environment may lead to apparent contradictions and the need to modify recommendations and policies.

Our lack of consensus can limit the ability to obtain the commitment needed for nutrition in countries, and it is our challenge as the nutrition community to find a way to reach consensus when possible and ways to communicate better when consensus cannot be reached in a manner that does not undermine our credibility.

Being very clear in what we are seeking consensus about can help that. To respond to the implications and whether we have consensus on the topics listed in this symposium, it is helpful to break down the questions we are asking. These are as follows:

1. *Is there a consensus that there are functional consequences of insufficient iron intake in infants and at other ages and life stages?* Yes. For example, iron is essential for brain development, and infants and possibly other age groups who do not have sufficient iron in their diets suffer from diverse cognitive impairments.
2. *Is there a consensus that iron interventions (supplementation, fortification) improve functional outcomes in individuals with insufficient iron intake/iron deficiency?* Yes.
3. *Is there consensus that iron deficiency should be prevented?* Yes, but consensus exists only around the use of food-based interventions such as fortified foods. No consensus exists around supplementation.
4. *Are there risks associated with supplementation as an approach to prevent or treat iron deficiency?* Yes, consensus exists that there are risks in malaria-endemic areas, and possible elsewhere, but no consensus exists around whether those risks outweigh the benefits, or whether we need to target programs.

“It is our challenge
as the nutrition community
to find a way to reach
consensus when possible”

By definition, iron deficiency treatment programs require targeting. They may also miss the critical period for brain development if inadequate iron intake goes undetected for some time. At the moment, we have no individual level indicator that is specific to iron deficiency (i.e. not affected by infection and/or inflammation). Ferritin and serum transferrin receptor can be adjusted for infection/inflammation, and hepcidin shows some promise, but is not ready for use in population-based programs. More importantly, all methods for individual-level screening require regular contact of individuals through a health system and infrastructure and supplies for sample analysis – two conditions that cannot currently be met in many of the countries where deficiency prevails.

Population-level targeting could increase the proportion of those provided with iron who would benefit from it and thus may help balance the ratio of benefits and risks. Populations for targeted programs can be identified by indicators such as economic status and region, which predict risk of inadequate intakes. Many programs have successfully been targeted using such criteria. A formal risk-benefit analysis would be helpful to resolve these issues and move the dialogue forward.

2.2 Plenary Session: Micronutrient Interventions to Prevent Fetal Growth Retardation and Stunting

Coordinator: Parul Christian

Department of International Health,
Johns Hopkins Bloomberg School of Public Health
Baltimore, MD, USA

Moderator: Sisay Sinamo

Nutrition Advisor, East Africa Region,
World Vision International,
Addis Ababa, Ethiopia

Presenters

Parul Christian

Department of International Health,
Program in Human Nutrition, Bloomberg School
of Public Health, Johns Hopkins University, USA
*Update on micronutrient deficiencies implicated
in poor pregnancy outcomes and childhood stunting:
Evidence for impact, mechanisms and implications
for interventions*

Kathryn Dewey

Program in International and Community Nutrition,
University of California, Davis, USA
*Efficacy of LNS for prevention of fetal growth restriction
and stunting*

Sophie Moore

MRC Human Nutrition Research,
Cambridge, UK
*Impacts of perinatal micronutrient interventions
on later health and development of young children*

Micronutrient deficiencies affect over two billion women and young children worldwide. These deficiencies have wide-scale implications for survival, health, and function across the life span, but specifically during the critical first 1,000 days.

This session provided an overview of the global burden of individual and multiple micronutrient deficiencies and their effects on birth outcomes, fetal growth, and growth in the first two years of life. It also provided an overview of current evidence regarding the effects on linear growth and stunting brought about by fortified lipid-based nutrient supplements (LNS) given to women during pregnancy, or to infants and young children.

Also reviewed was the evidence of the impact of perinatal micronutrient interventions on the later health and development of young children. Data were summarized from existing published systematic reviews and meta-analyses, as well as from recently completed but as yet unpublished trials. The following results were highlighted in these presentations.

Iron-folic acid and multiple micronutrient supplementation

With regard to fetal growth and birth outcomes, daily antenatal iron supplementation (with/without folic acid) enhances fetal growth and reduces the risk of low birth weight and small-for-gestational age (SGA) birth.

“There is sufficient evidence to consider replacing iron-folic acid with a multiple micronutrient supplementation”

Trials (n=15) comparing daily multiple micronutrient supplementation vs. iron-folic acid show a modest but additional significant improvement in birth weight, plus reductions in low birth weight and SGA. A recent trial completed in Bangladesh showed a significant reduction in preterm birth, stillbirth and low birth weight, accompanied by a reduction in infant mortality in girls, although not in boys. Routine antenatal iron-



The 2014 Micronutrient Forum Global Conference generated intense discussion of the key challenges and opportunities confronting the global nutrition community today.



An infant being measured as part of the field studies conducted in Bangladesh.

folic supplementation continues to be policy in many low-to-middle-income countries. There is sufficient evidence to consider replacing iron-folic acid with a multiple micronutrient supplementation in these settings.

Calcium supplementation

Calcium supplementation is recommended in countries where calcium intakes are low, with a view to reducing the risk of pre-eclampsia/eclampsia. There is limited evidence for preschool micronutrient interventions in influencing postnatal growth, and routine prophylactic micronutrient supplementation in children does not seem to be indicated at present.

Lipid-based nutrient supplements (LNS)

With regard to lipid-based supplements, in four trials, prenatal LNS increased birth size by a modest amount compared to iron-folic acid, with larger effects observed in more vulnerable women. Results of postnatal trials using LNS compared to non-intervention or controls have been heterogeneous, with some showing reductions in stunting but most showing modest to no effects on linear growth. Differences in study design, composition and quantity of LNS used, age at baseline, duration of intervention, and prevalence of non-nutritional constraints on growth response may explain this heterogeneity. LNS is a promising, food-based strategy for preventing fetal growth restriction and stunting. Further evaluation is needed of interventions that combine several approaches for reduction of stunting, including control of pre- and post-natal infection.

“LNS are a promising strategy for reducing stunting”

Long-term effects on health and development

Published studies of single, combined or multiple micronutrient interventions in pregnancy, with follow-up on offspring health and development, were also reviewed. Although some benefits are noted – especially with prenatal iron supplementation and cognitive function – no consistent effects were observed between the different trials of single, combined or multiple micronutrients on offspring health and developmental outcomes. Differences in age at follow-up, disease risk between population groups, rates of cohort attrition, along with the heterogeneity in formulation and timing of interventions, may explain these differences.

There is limited, though inconsistent, evidence to support the long-term benefit of micronutrient supplementation during pregnancy. The existing knowledge base will be strengthened through further follow-up of existing trials in pregnancy and by the standardization of protocols (in pregnancy and follow-up). Follow-up of the ongoing trials of peri-conceptional micronutrient supplementation will also be critical to this field of research.

2.3a Update on Current Issues in Iodine Interventions

Coordinator: Michael Zimmermann

ETH Zurich, Zurich, Switzerland

Moderator: Pieter Jooste

Medical Research Council, Cape Town, South Africa

Presenters

Nancy Aburto

United Nations World Food Programme, Rome, Italy

A systematic review of the effects of salt iodization in populations

Pattanee Winichagoon

Mahidol University, Bangkok, Thailand

Randomized control trial on efficacy of iodine supplementation in pregnancy: A multi-center trial in Thailand and South India

Michael Zimmermann

ETH Zurich, Zurich, Switzerland

Randomized control-led trial on efficacy of iodine supplementation with iodized oil during infancy in Morocco: Indirectly through maternal supplementation in lactation vs. direct newborn supplementation

Vincent Assey

Ministry of Health and Social Welfare, Tanzania

Monitoring iodine programs and issues of iodine excess

Karim Bougma

McGill University, Montreal, Quebec, Canada

Iodine and other nutritional predictors of infant and young child development: Results from a cluster randomized trial in Amhara, Ethiopia / Iodine and other nutritional predictors of preschool-aged children's development in Amhara, Ethiopia

Sonja Hess

University of California, Davis, California, USA

Iodine status of young Burkinabe children receiving small-quantity lipid-based nutrient supplements and iodized salt

Despite the progress of iodized salt programs in many areas of the world, over a third of the global population remains iodine deficient. The most vulnerable groups are pregnant women and their newborns, and iodine deficiency is the leading cause of preventable mental retardation worldwide. Even mild-to-moderate iodine deficiency during pregnancy can increase the risk of neuromotor and cognitive impairment in the offspring. Although iodine deficiency control programs should focus on pregnancy and infancy, assessment of iodine status in these target groups is difficult because iodine requirements are only poorly defined, and methods for monitoring iodine status have not been rigorously established, particularly for iodine excess. Because of this, concerns have been raised over whether iodized salt programs provide adequate iodine to children and adults, but do not cover the higher needs of the pregnant woman, the fetus and the newborn. The ability to better define iodine status, and the impact of iodine deficiency, during these critical life stages is urgently needed.

“It is urgently necessary to better define the iodine needs of pregnant women, fetuses and newborns”

Nancy Aburto, from the World Food Programme, Rome, Italy, opened the session and presented the WHO-sponsored systematic review of the benefits of salt iodization in populations. Dr. Arbutto reported that, although the risk of bias was high, the effect estimates were large and consistent across a vast number of studies implemented in diverse contexts in all regions of the world. This should increase confidence that iodized salt is an effective intervention for the prevention of iodine deficiency disorders (IDD).

The next presentation was by Pattanee Winichagoon (Mahidol University, Bangkok, Thailand), who discussed iodine

requirements in pregnancy and a recent randomized controlled trial (RCT) on the efficacy of iodine supplementation in pregnancy in Thai women. Winichagoon concluded that oral iodine supplementation of mildly iodine-deficient pregnant women was: **a)** Safe; **b)** effective in increasing iodine intakes into the adequate range; and that it **c)** resulted in a small but significant decrease in postpartum thyroiditis.

This was followed by a presentation by Michael Zimmermann ((ETH Zurich, Zurich, Switzerland) of a RCT determining the efficacy of iodized oil supplementation during infancy in Morocco, comparing supplementation indirectly through maternal supplementation during lactation with direct newborn supplementation. The study presented indicates that, in regions of moderate-to-severe iodine deficiency without effective salt iodization, lactating women who receive one dose of 400 mg iodine as oral iodized oil soon after delivery can provide adequate iodine to their infants through breast milk for at least six months, enabling the infants to achieve euthyroidism. Direct supplementation is less effective in improving infant iodine status.

The final main speaker was Vincent Assey (Ministry of Health and Social Welfare, Dar es Salaam, Tanzania), who discussed monitoring of iodine programs and issues of iodine excess, with new data from a large multicenter international study examining the value of using dried blood spot thyroglobulin to assess both iodine deficiency and excess in children.

Studies on the impact of iodized salt on infants

Two country examples of studies, focused on assessing the impact of iodized salt on infants, were presented.

Karim Bougma (McGill University, Montreal, Canada) described intervention trials in Ethiopia looking at the effect of iodized salt on child growth and cognition, concluding that iodized salt improved children's mental development both directly and indirectly by its effect on growth.



Salt iodization in Pemba island, Zanzibar

Sonja Hess (University of California, Davis, California) presented findings of recent studies on the iodine status of young Burkinabe children who received LNS while exposed to iodized salt. Dr. Hess explained that, although the majority of household salt samples contained iodine above the target of 30 ppm, provision of iodine in LNS significantly reduced the percentage of children with abnormally low t₄ (thyroxine) concentrations at 18 months.

Major positive benefits for populations

The session concluded with an overall agreement that iodized salt and iodine supplements have major positive benefits for populations, including pregnant women, children and infants, although better methodology for assessing iodine status and its impact is still required.

2.3b Optimizing Iodine Status in the Context of Salt Reduction Strategies

The following summary of the above-titled session was provided by **Roland Kupka**, New York, NY, USA

The session was chaired by **Laurence Grummer-Strawn**, CDC/Chair, ICCIDD Global Network



USI expert Teshome Desta poses a question during a plenary session.

Iodine deficiency is the most common cause of preventable mental impairment worldwide and is effectively prevented by iodizing all salt for human and animal consumption.¹ Salt is the preferred vehicle for the delivery of iodine for a number of reasons, including that it is one of the few commodities consumed by virtually everyone and in stable quantities, iodization technology is easy to implement and the addition of iodine is inexpensive and does not affect color, taste, or odor. Globally, salt is the only fortification vehicle that is consistently able to reach the groups with the highest risk of iodine deficiency, including the rural poor.

According to the World Health Organization (WHO),² cardiovascular diseases (CVD) are the leading global cause of death, and dietary salt/sodium intake has been implicated as a CVD risk factor. In a recent systematic review,³ a reduction in adult sodium intake significantly reduced blood pressure. Decreased sodium intake had no significant adverse effect on blood lipids, catecholamine levels, or renal function. Higher sodium intake was also associated with increased risk of stroke, stroke mortality, and coronary heart disease. The benefits of reducing sodium intake were deemed to be of substantial public health benefit.

Global recommendations for salt and iodine intake

To combat the public health problems of cardiovascular disease and iodine deficiency, the WHO and partner agencies have issued global recommendations. The WHO recommends to reduce sodium intake to < 2 g/day (5g salt/day) in adults (and equivalent amounts in children after differences in energy intakes are taken into account).⁴ Furthermore, WHO and UNICEF recommend universal salt iodization (USI) as the main strategy to achieve the elimination of IDD.⁵

Maintaining iodine intake while cutting salt intake

Given that both strategies concern salt, it is important that the concurrent implementation of both strategies is compatible in theory and practice. In 2007, a WHO expert consultation recognized the coherence between the policy of reducing salt consumption to prevent NCDs and the policy of universal salt iodization to eliminate iodine deficiency disorders. The meeting concluded that the policies for salt iodization and reduction of salt to less than 5 g/day are compatible, cost-effective and of great public health benefit. In 2013, an expert consultation demonstrated the potential to synergize both programs by promoting their commonalities and complementarities. The consultation concluded that such synergies can be achieved if there is **a)** full implementation of universal salt iodization, **b)** effective implementation of salt reduction policies including regulation of salt levels in processed foods, and **c)** an increase made in iodine levels in salt as salt intakes are decreased. Modelling exercises indicate that as salt intake falls, iodine intakes will be highly context and country-specific. This emphasizes the importance of careful monitoring of iodine status as salt reduction efforts advance.

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2.4 Plenary Session: Update on Interventions to Improve Folate and B₁₂ Status, and Homocysteine

Coordinator: Lindsay Allen

USDA, ARS Western Human Nutrition
Research Center, Davis, California, USA

Moderator: Klaus Kraemer

Sight and Life, Basel, Switzerland, and
Johns Hopkins Bloomberg School
of Public Health, Baltimore, MA, USA

Presenters

Lisa Rogers

World Health Organization, Geneva, Switzerland
*WHO process to establish blood folate concentrations
for folate-preventable congenital anomalies*

Lindsay Allen

USDA, ARS Western Human Nutrition
Research Center, Davis, California, US
*Update on vitamin B₁₂: Biomarkers, and effects
of interventions on function*

Himangi Lubree

KEM Hospital Research Centre, Pune, India
*Vitamin B₁₂ and folic acid interventions and risk
of later metabolic disease*

Alexis Nzila

King Fahd University in Dhahran, Saudi Arabia
*Interactions between anti-malarials and
folic acid supplementation during pregnancy*

Alex Brito

McGill University, Montreal, Quebec, Canada
*Sensory Peripheral nerve function in
Chilean elderly consuming folic acid fortified flour:
Relationship to plasma folate and a novel
combined biomarker of B₁₂ status*

One of the most prevalent micronutrient deficiencies in the world

This was the first time that vitamin B₁₂ and folate were included in the program of the Micronutrient Forum. Lindsay Allen, from the USDA, ARS Western Human Nutrition Research Center in Davis, California, introduced this session by showing that vitamin B₁₂ deficiency is one of the most prevalent micronutrient deficiencies in the world, because it affects all age groups and both males and females. It is almost always caused by a low intake of animal source foods; it does not require a strict vegetarian diet to develop poor vitamin B₁₂ status.

“Low vitamin B₁₂ status is
almost always caused by a low intake
of animal source foods”

Vitamin B₁₂ status is usually assessed by measuring serum vitamin B₁₂ concentrations. Other common measures include plasma holotranscobalamin, methylmalonic acid and homocysteine. However these measures typically give inconsistent diagnoses of vitamin B₁₂ deficiency. For this reason a new biomarker of vitamin B₁₂ status called “combined B₁₂” or “cB₁₂” has been developed based on a formula that includes two or more of the four usual assays. Preliminary evidence, discussed by Alex Brito in this session, suggests that cB₁₂ is a more sensitive predictor of changes in peripheral nerve conduction when elderly people with poor vitamin B₁₂ status are supplemented with the vitamin.

Vitamin B₁₂ status in pregnancy is a concern because deficiency during this period has been associated with increased risk of neural tube defects, low fetal storage of the vitamin and low breast-milk concentrations in lactation with subsequent impairment of infant development. Maternal supplementation with vitamin B₁₂ during pregnancy and through three months of lactation in Bangladesh increased levels of maternal, colostrum and infant antigens in response to H1N1 vaccine.

Other speakers also noted that vitamin B₁₂ deficiency may impair immune function and that more work is needed on this topic. Levels of vitamin B₁₂ in colostrum and breast milk are



The 2014 Micronutrient Forum Global Conference attracted delegates from many countries and offered opportunities for many “bridging” conversations.

much lower in deficient mothers, and may be reasonable indicators of population vitamin B₁₂ status; concentrations vary greatly across population groups depending on usual consumption of animal source foods. Maternal and infant serum vitamin B₁₂ concentrations are relatively strongly positively correlated throughout the period of lactation. Maternal vitamin B₁₂ supplementation in lactation slowly increases the concentration in milk.

Early folate or vitamin B₁₂ deficiency as risk factors for the later onset of metabolic disease

Himangi Lubree, from the KEM Hospital Research Centre in Pune, India, discussed the evidence that early folate or vitamin B₁₂ deficiency could be risk factors for the later onset of metabolic disease, especially diabetes. India has the largest number of people affected by undernutrition, and the largest number with diabetes. Compared to the white population in the UK, diabetes onset in India occurs 10 years sooner and at a substantially lower body mass index.

At age four years, children with a birthweight around 2.5 kg had higher fasting serum glucose and insulin concentrations than those weighing > 3 kg at birth. In urban Pune a 2001 study found almost half of adults were vitamin B₁₂ deficient with high plasma homocysteine and methylmalonic acid, whilst folate deficiency was relatively uncommon. However, higher maternal red cell folate was associated with higher birthweight and fewer small for gestational age deliveries. Importantly, mothers in the highest tertile for red cell folate and the lowest tertile for serum vitamin B₁₂ produced children with the strongest indications of early metabolic disease (insulin resistance) at six years of age.

In another Indian study, pregnant women who had a combination of vitamin B₁₂ deficiency with serum folate in the upper two tertiles of values had double the risk of gestational diabetes. Intervention trials are currently being conducted by the Pune team, evaluating the effects of vitamin B₁₂ supplementation from pre-conception through pregnancy on birth outcomes, developmental, metabolic and epigenetic outcomes.

Defining blood folate concentrations for folate-preventable congenital abnormalities

Lisa Rogers from the World Health Organization, described the recent WHO process that is defining blood folate concentrations for folate-preventable congenital abnormalities. The purpose is to define cut-point(s) below which folate acid supplementation or fortification is likely to be effective for neural tube defect prevention, and above which folate status is likely to be optimal such that folate acid interventions may not have much effect. Estimates to date appear to only be feasible based on red cell folate, and not serum folate. The new WHO guidance on this question will be released in the near future.

Interactions between anti-malarials and folic acid supplementation during pregnancy

There has been some concern about whether folic acid supplementation during pregnancy interferes with the efficacy of anti-malarial medications, the action of which depends on their anti-folate properties. Alexis Nzila from King Fahd University in Dhahran, Saudi Arabia, provided an update on this question.

In the malaria parasite, cells are rapidly dividing and depend heavily on the availability of folate. The parasites can synthesize folate and also take it up from the blood. Malaria exacerbates folate deficiency, so routine treatment of the disease usually consists of antimalarials, iron and folic acid. There is relatively little evidence that the folic acid in this treatment exacerbates malaria, but on the other hand, since it is given routinely, such evidence has been difficult to obtain.

“Current evidence is that low doses of folic acid (<0.5 mg/day) are unlikely to have an adverse effect [in malaria]“

Current evidence is that low doses of folic acid (<0.5 mg/day) are unlikely to have an adverse effect because given in low amounts the vitamin is virtually all converted to 5-methyltetrahydrofolate, but that high doses (>2.5 mg/day) may exacerbate the disease by providing more unmetabolized folic acid to red blood cells. In pregnancy, when prevention of malaria is particularly important to prevent infant deaths, 5 mg folic acid/day does reduce the efficacy of sulphadoxine/pyrimethamine (SP), which WHO recommends should be given 2–3 times for prevention during pregnancy irrespective of the diagnosis of malaria. A 0.4 mg/d dose does not appear to have this adverse effect on SP efficacy. A daily dose of 5 mg also reduced efficacy of this drug in children, and in Kenya an adverse effect of 5 mg, but not of 2.5 mg, was reported in a population with a wide age range. Folate acid fortification of food is unlikely to interfere with anti-malarials if it increases intake by 0.4 mg/day or less.

2.5 Plenary Session: Recent Trials of Vitamin A Supplementation in Newborns

Coordinator: Lisa Rogers

World Health Organization,
Geneva, Switzerland

Moderator: Rolf Klemm

Johns Hopkins Bloomberg School of Public Health,
Baltimore, MD, USA

Presenters

Sam Newton

Kwame Nkrumah University of Science
and Technology, Ghana

*Trials on the efficacy of neonatal vitamin A
supplementation for improving child survival (NeoVitA):
Ghana, India, Tanzania*

Meshbah Ahmad

International Centre for Diarrheal Disease Research,
Bangladesh (ICDDR,B), Dhaka, Bangladesh

*Mechanistic trials on the impact of neonatal vitamin A
supplementation on immune response*

Lisa Rogers

World Health Organization, Geneva, Switzerland

*Next steps for updating the WHO guideline
on neonatal vitamin A supplementation*

Sofie Aage

Statens Serum Institut, Copenhagen, Denmark

*The effect of neonatal vitamin A supplementation
on the risk of atopy; Long-term follow-up on
a randomized controlled trial in Guinea-Bissau*

Reina Engle-Stone

University of California, Davis, California, USA

*Sensory peripheral nerve function in effect of
short-term, daily supplementation with vitamin A
or beta-carotene on plasma and breast milk
retinol concentration in lactating Filipino women*

The effect neonatal vitamin A supplementation (NVAS) on infant mortality

In settings where vitamin A deficiency is considered a public health problem, the World Health Organization recommends periodic vitamin A supplementation to reduce mortality in infants and young children 6–59 months of age. However, supplementation of younger infants 1–5 months of age, pregnant women and postpartum women has not been shown to reduce early infant mortality. Results of earlier randomized controlled trials (RCTs) on the effect of neonatal vitamin A supplementation (NVAS) for preventing morbidity and mortality had been inconclusive.

In 2009, the WHO received funding from the Bill & Melinda Gates Foundation to coordinate the conduct of three large RCTs on the effect of NVAS on infant mortality and three studies (one animal and two human studies) on the biological mechanisms that could explain the possible effects of NVAS, in an attempt to provide definitive evidence on the use of NVAS in low- and middle-income countries. Lisa Rogers of the World Health Organization (Geneva, Switzerland) provided an introduction to these trials, and the overall aim of this session was to present some of the results of these newly completed trials along with two selected abstracts on related topics.

Trials on the efficacy of neonatal vitamin A supplementation for improving child survival

Samuel Newton of the Kintampo Health Research Centre (Kintampo, Ghana) presented the large RCTs. These were population-based, individually randomized, double blind, placebo-controlled trials conducted in Ghana (n=22,955), India (n=45,000) and Tanzania (n=32,000), and are referred to as the NeoVitA trials.

The trial participants were: at least two hours old; identified at home or facilities on the day of birth or in the next two days; able to feed orally; and likely to stay in the area for at least six months. They were randomized to receive one oral dose of vitamin A (50,000 IU) or placebo immediately after recruitment. Follow-up home visits were undertaken every four weeks when data were collected on deaths, facility use and care seeking.

The primary outcome was post-supplementation mortality to six months of age. Secondary outcomes were post-supplementation mortality to 28 days and 12 months of age; hospi-



An infant in Ethiopia is given a vitamin A capsule as part of a local vitamin A supplementation program.

talizations to six months of age; and potential adverse effects in the three days after supplementation. Supplementing newborns with 50,000 IU of vitamin A within 72 hours was well tolerated. In India there was a 10% reduction in mortality between supplementation and six months of age (95% CI 0.81–1.00) but the range of plausible effects supported by the data range from no effect to a 19% reduction. In Tanzania, NVAS had no beneficial effect on survival post-supplementation to 6 months (or 12 months), RR 1.10 (95% CI: 0.95–1.26; $p=0.19$); and in Ghana, NVAS also had no beneficial effect on survival post-supplementation to 6 months (or 12 months), RR 1.12 (95% CI 0.95–1.33; $p=0.18$). These results do not support universal NVAS.

Mechanistic trials on the impact NVAS on immune response

Shaikh M Ahmad of the International Centre for Diarrheal Disease Research (Dhaka, Bangladesh) presented results of one of the human biological mechanistic studies supported by the WHO. This was a randomized, placebo-controlled intervention trial (ClinicalTrials.gov: NCT01583972) to determine if NVAS affected thymic function and response to T-cell-dependent vaccines given during the neonatal period.

Pregnant women were contacted in their third trimester at a single maternity hospital located in an urban slum area of

Dhaka. Within 48 hours of birth, 306 infants were enrolled and supplemented with either 50,000 IU vitamin A or placebo (stratified by sex and median birth weight) and were then given live attenuated oral polio virus (OPV) and *Bacillus Calmette-Guérin* (BCG) vaccines. Infants also received tetanus toxoid (TT) and hepatitis B virus (HBV) vaccines (as well as other vaccines, including OPV) at 6, 10 and 14 weeks of age. Thymus size was measured by determining the thymic index (TI) using ultrasound. Naïve T-cells and T-cell receptor excision circles (TRECs) were measured in peripheral blood as indices of thymic function. Responses to OPV, BCG, TT and HBV vaccines were assessed by measuring the stimulation index (SI) of peripheral blood T-cells in response to vaccine antigens. Antibody secreting plasma cell responses to OPV, HBV and TT, and the delayed type hypersensitivity skin test response to BCG vaccine, were also evaluated.

Data were analyzed to determine treatment effect with adjustment for sex, birth weight and delivery type using normalized data and the generalized linear models procedure. NVAS decreased TI by 8.0% at 6 weeks ($p=0.056$) as well as naïve T-cell number at 15 weeks ($p=0.098$). However, TREC levels at 6 weeks were increased ($p=0.097$). At 6 weeks, the CD4 T-cell SI for the BCG vaccine and for the polyclonal mitogen *Staphylococcus enterotoxin B* responses were lower in the NVAS group

($p < 0.05$). Significant group differences were not seen at 15 weeks. NVAS improved HBV and TT specific IL-2 and OPV specific IL-5 responses at 15 weeks ($p < 0.05$), while antibody responses to OPV, HBV and TT were not affected. Smaller thymus and lower T-cell SI following NVAS does not suggest benefit. However, changes in cytokine responses do suggest a benefit for some vaccine responses. These data will be useful in evaluating the effect of providing NVAS in regions where vitamin A deficiency is common.

Updating the WHO guideline on NVAS

All six studies supported by the WHO are complete and were published in December 2014. Lisa Rogers explained the process of updating the WHO guideline on NVAS, which will begin later in 2014. Results of the trials presented here, and any other new trials that have become available since the last review of evidence in 2011, will be considered when updating the guideline.

The effect of NVAS on the risk of atopy

Sofie Aage of the Research Center for Vitamins and Vaccines (CVIVA), Statens Serum Institute (Copenhagen, Denmark), and colleagues further examined the effect of NVAS on atopy by conducting long-term follow-up of a previous randomized controlled trial in Guinea-Bissau. In 2002–2004, 4,345 normal birth weight neonates were randomized to NVAS (50,000 IU) or placebo together with their BCG vaccination. In 2013, 1,692 (39%) children now aged 8–10 years who were still living in the study area were visited. A skin prick test was performed and history of allergic symptoms was recorded in 1,478 children found at home. Associations of NVAS and atopy (defined as a skin prick test reaction of ≥ 3 mm) were analyzed using binomial regression – overall and stratified by sex. Of the 1,430 children with a valid skin prick test, 228 were positive (more boys [20%] than girls [12%] $p < 0.001$). NVAS did not increase the overall risk of atopy (RR 1.11 [95% CI=0.87–1.40]). However, NVAS was associated with significantly increased risk among females (1.78 [1.17–2.71]) but not among males (0.86 [0.64–1.15], p -value for interaction between NVAS and sex = 0.005). Furthermore, NVAS was associated with increased risk of wheezing among females (RR 1.78 [1.02–3.09]). Further studies on NVAS and atopy are warranted. These findings might have implications for future policy.

Effect of short-term, daily supplementation with vitamin A or beta-carotene on plasma and breast milk retinol concentration

As breast milk vitamin A (BMVA) may be a useful indicator for evaluating food-based interventions for increasing vitamin A status, Reina Engle-Stone of the University of California (Davis, United States of America) and colleagues assessed the effect of daily supplementation with 600 μ g vitamin A activity as either retinyl palmitate or beta-carotene, or 0 μ g vitamin A activity as corn oil (CO) on BMVA concentration in lactating women ($n = 83$) who were randomly assigned to receive one of the three treatments, 6 days/week for 3 weeks.

Treatments were administered as capsules (containing either 300 μ g or 0 μ g vitamin A activity), 2 times/day, with morning and noon low-vitamin A meals. Plasma and breast milk (as full or casual milk samples) concentrations of vitamin A and beta-carotene were measured before and after the intervention. The initial mean plasma retinol concentration was 1.29 ± 0.41 μ mol/L. The mean change in plasma retinol was greater in the vitamin A group (0.13 μ mol/L) than in the control group (-0.04 μ mol/L), but neither differed from the mean change in the beta-carotene group (0.03 μ mol/L). Initial mean BMVA was ~ 27 nmol/g fat. In full milk samples, mean change in BMVA was greater in the vitamin A group (4.6 nmol/g fat) than in the beta-carotene (0.5 nmol/g fat) and control (-3.6 nmol/g fat) groups. In casual milk samples, mean change in BMVA was greater in the vitamin A (4.8 nmol/g fat) and beta-carotene (4.4 nmol/g fat) groups than in the control group (-2.2 nmol/g fat). The data suggest that BMVA responds within three weeks to small daily doses of vitamin A.



Track 3 Scaling Up Micronutrient Interventions: Bridging the Gaps Between Evidence and Implementation

Introductory Summary

An opportunity for “bridging” conversations

The main goals of this track were:

- a) To show how scaled-up micronutrient interventions can bridge the gaps between evidence and implementation; and
- b) to stimulate “bridging” conversations across the full spectrum of the global nutrition community.

Developed by representatives from the US Centers for Disease Control and Prevention (CDC), the World Bank, UNICEF, the UN World Food Programme (WFP), the US National Institutes of Health (NIH), the International Food Policy Research Institute (IFPRI), Strengthening Partnerships, Results, and In-

novations in Nutrition Globally (SPRING), and the Ministries of Health of Ethiopia and Nepal, this track brought together partners from all sectors of the global nutrition community working in countries to design and implement programs, and created many opportunities for all-important “bridging” conversations. There were a total of 18 sessions that were extremely well attended, with high levels of energy and involvement throughout. Several of these sessions are briefly described below.

Scientific discoveries will only bring benefit in the field if they are delivered via effective programs. To be effective, programs have to be well designed, well implemented, and also

A house-to-house monitoring, conducted by a local Auxillary Nurse Midwife (ANM), helps encourage young lactating mothers, and mothers with infants, to breastfeed at home and to give complementary food to their infants beyond six months of age.





A health-care worker in Bolivia shows a package of prenatal iron-folic acid supplements as part of an education session with women outside a health center.

capable of delivery at scale. A key factor in the scaling-up of nutrition interventions is the use of existing platforms where these may be an appropriate vehicle for delivery. This topic was addressed by Meera Shekar of the World Bank and Marie Ruel of IFPRI providing an overview of the types of platforms, or public health interventions that lend themselves to the delivery of micronutrient interventions. This session analyzed the characteristics of effective platforms and outlined the potential value of a variety of innovations currently taking place in the field of program design and program implementation.

It is essential to monitor micronutrient interventions to improve program performance and make any adjustments that might be needed. The session on disseminating new tools and directions in program monitoring, chaired by Zuguo Mei of CDC, shared lessons learned and views on how to develop and use different monitoring approaches, with special emphasis on assessing coverage and improving the performance of nutrition interventions in the field. This session presented a range of new and increasingly accessible technologies that can be used in innovative ways to improve the quality of data capture.

Howarth Bouis of HarvestPlus and IFPRI led a discussion of the importance of integrating micronutrients into agricultural programs. This session contained a number of case studies illustrating how agricultural development programs can be made more nutrition-sensitive and can serve as effective platforms to deliver nutrition-specific interventions.

Katie Tripp of CDC chaired a session in which five different speakers described their program experiences with issues or problems encountered with program implementation and

scale-up, how these were resolved, lessons learned, and what they would do differently next time when designing and implementing programs.

The crucial topic of cost was also addressed. Shawn Baker of the Bill & Melinda Gates Foundation chaired a session which challenged participants to learn the language of costing in order to obtain essential funding and to ensure that these funds deliver measurable benefits for their target populations.

“Track 3 inspired nutrition professionals to think much more effectively about the design, implementation and monitoring of nutrition interventions”

Track 3 made a large contribution to an excellent conference, inspiring nutrition professionals from around the world to think much more effectively about the design, implementation and monitoring of nutrition interventions, and giving them the language to discuss their work more persuasively with non-nutritionists.

3.1 Platforms for Quality Delivery of Micronutrients to Achieve High Coverage and Use at Scale

Chair: Meera Shekar

World Bank, Africa Region

Co-Chair: Marie Ruel

International Food Policy Research Institute (IFPRI), Washington, DC, USA

Presenters

Marie Ruel

International Food Policy Research Institute (IFPRI), Washington, DC, USA

Agriculture and social protection platforms for delivering and scaling up micronutrient interventions

Meera Shekar

World Bank, Africa Region

Health and early child development (ECD) platforms for delivering and scaling up micronutrient interventions

Lynnette Neufeld

Global Alliance for Improved Nutrition (GAIN), Geneva, Switzerland

Case study: Using research to strengthen the design and delivery of nutrition interventions as part of a conditional cash transfer program in Mexico

Manpreet Chadha

Micronutrient Initiative, India

Case study: Demonstrating effectiveness of delivering Weekly Iron and Folic Acid Supplementation (WIFS) through government systems in Chhattisgarh, India

Vicki MacDonald

Abt Associates, Annandale, VA, USA

Case study: Public-private partnerships approaches for scaling up zinc with ORS

This session aimed to provide an introduction to the broad topic of “platforms” that can be used to deliver micronutrient interventions, to highlight what are the key characteristics of efficient (or promising) platforms, and to provide examples of innovative platforms from different sectors that are currently used in different contexts.

Micronutrient interventions are usually delivered via platforms that exist within the health sector – e.g. child health days and well-baby clinics in health centers. When a mother takes her infant or young child to these venues, the child will receive a series of preventive nutrition and health services such as vaccines, vitamin A supplements, growth monitoring and promotion, and deworming.

The session highlighted that in order to accelerate progress in improving micronutrient nutrition, we need to leverage other platforms as well. These include agriculture platforms (e.g. homestead food production or other agricultural development programs); education and early child development platforms which aim at enhancing young children’s cognitive, motor and social development skills; and social safety net programs such as transfer programs (e.g. conditional or non-conditional transfers of cash, food or vouchers).

The characteristics of effective platforms

Marie Ruel launched the session by defining the characteristics of effective delivery platforms. One important success criterion is high coverage: in order to be effective, a platform needs to deliver to – and reach – a high proportion of the population targeted by the program. This is one reason for leveraging social protection programs: many such programs have been shown to be highly effective at reaching the poor and are often implemented at national scale. Social transfer programs are also well suited for incorporating nutrition goals and nutrition interventions such as behavior change communications or the distribution of supplements such as micronutrient powders or lipid-based nutrient supplements. Similarly, agriculture platforms can be leveraged to incorporate nutrition goals and interventions, and are likely to be effective if well designed and implemented because they too usually target the poorest of the poor, who are also the most likely to have poor nutrition. Targeting women with agriculture and social transfers is another way to ensure



Meera Shekar (World Bank), who stressed throughout the conference the value of developing costed plans for nutrition interventions.

that program benefits (e.g. food, cash, and knowledge) are used wisely and are invested in better nutrition, child feeding and health-seeking behaviors.

“An effective delivery platform is one that achieves high coverage of the population it targets”

As a general rule, platforms will be useful to improve nutrition, and will be worth investing in, if they are working well. This means that they should meet the following key criteria:

- Have an effective targeting mechanism (target poor communities, households, and the nutritionally vulnerable);
- achieve scale, with high coverage and regular contacts with program staff;
- provide a good spectrum of interventions that address the main underlying determinants of nutrition and respond to local needs;
- enjoy high uptake and optimal utilization of the services provided;
- be reliable (offer consistent supply and distribution of services and benefits);
- have been shown to achieve their key goals and impacts (e.g. demonstrated in efficacy and effectiveness studies);
- be sustainable (in terms of resources, beneficiary ownership and political will).

While many opportunities exist for leveraging different platforms to deliver micronutrient interventions, innovation is necessary in terms of the types of platforms and sectors targeted, the mix of nutrition interventions provided, and the groups targeted. Implementation research is also required to test different platforms and assess their suitability for carrying out micronutrient interventions at scale.

Meera Shekar followed with observations on a number of platforms that have been used with success – for example, in the delivery of vitamin A. She remarked that most micronutrient programs need several delivery mechanisms to achieve scale, and that market-based platforms are key to achieving scale, as they can reach the top and the middle of the socio-economic pyramid, thereby conserving public resources for the poor at the base of the pyramid. Micronutrient powders, she pointed out, could particularly benefit from a market-based scale-up ap-



Sylvia, a health field monitor at the Al Amparo health post in El Tumbador, prepares for home visits as part of MI's zinc and ORS co-packaging study in San Marcos, Guatemala.

proach. Meera also stated that schools offer an immediate opportunity to scale up micronutrient delivery.

The overall potential of platforms to help in the delivery of micronutrient interventions is highly dependent on the quality of implementation of the programs they run. The application of implementation science is therefore essential to the overall success of this endeavor.

The importance of implementation science

Marie and Meera's observations were followed by case studies providing concrete examples of some of the concepts they had put forward.

Lynnette Neufeld described a successful example of working with a conditional cash transfer program in Mexico to deliver fortified supplements and nutrition behavior change communications (BCC) to mothers and young children during the first 1,000 days.

Reporting on a program in Chhattisgarh, India, Manpreet Chadha described effective approaches to achieve high rates of coverage and utilization of Weekly Iron Folic Acid (WIFA) supplements among school-going and out-of-school adolescent girls. She observed that the demonstration phase proved that effective multi-department coordination, strong supply chain

management, systemic program reporting and review, and effective Behaviour Change Communication (BCC) result in high rates of coverage and utilization of WIFA supplements. The demonstrated strategies are now being scaled up by the state government, and early experience of scaling up suggests that constant technical and programmatic support should be provided until all components of the program are rolled out.

Finally, Vicki MacDonald described a public-private partnership to deliver zinc supplementation during diarrhea. She emphasized that synergies are realized when public and private sectors work together, and that the public sector has an important leadership, policy and regulatory role to play. The conditions for success in public-private partnerships for diarrhea management are: strong public sector leadership and engagement; access to quality affordable pediatric zinc; improved caregiver knowledge about the role of zinc with oral rehydration salts (ORS) and their correct use; enhanced provider knowledge about zinc as the recommended treatment; and supervision through regulatory agencies.

3.2 Disseminating New Tools and Directions in Program Monitoring

Presenters

Omar Dary

United States Agency for International Development (USAID), Washington, DC, USA

Beyond the tradition: Toward a practical and effective enforcement and monitoring system of fortified flours

Nita Dalmiya

United Nations Children's Fund (UNICEF), New York, NY, USA

Improving effective coverage of micronutrient supplementation: Results from application of the Monitoring Results for Equity System (MoRES) in Bangladesh and Malawi

Mary Serdula | Cholpon Imanalieva

Centers for Disease Control and Prevention (CDC)/UNICEF, Kyrgyzstan

Use of Lot Quality Assurance Sampling (LQAS) to monitor national level coverage of a micronutrient powder/infant and young child nutrition (MNP/IYCN) program in Kyrgyzstan

Rebecca Day Merrill

Centers for Disease Control and Prevention (CDC)
Using GIS in a program setting to understand nutrition intervention coverage in rural Nepal

N Shakira Bandolin

University of Washington, Seattle, WA, USA
Engaging health officials in the Philippines: Application of a bottleneck analysis tool to improve health and nutrition program implementation at the local government level

Celeste Sununtnasuk

International Food Policy Research Institute (IFPRI), Washington, DC, USA

Iron-folic acid distribution and consumption through antenatal care: Identifying barriers across countries

The need for effective programming

Reliable program monitoring is essential in order to ascertain with certainty both the coverage and the effectiveness of nutrition interventions in the field. Besides the necessary funding, capacity allocation and training of personnel, appropriate tools and technology are essential for the monitoring process. Many tools and technologies – some of them, such as mobile phones, smart phones and GPS, relatively recent innovations – are available to assist the process of data capture. However, their potential needs to be understood and communicated if these new possibilities are to deliver their full potential.

This session discussed some of the most recent developments and insights in this area. It drew on the 2008 Innocenti Process initiated by the Micronutrient Forum, which:

- Critically reviewed evidence from real-world programs implemented at scale;
- engaged and gave “center stage” to views of country-level program managers and implementers; and
- built consensus among key stakeholder groups on what programs work, and what needs more work.

Beyond the tradition: Toward a practical and effective enforcement and monitoring system of fortified flours

Objective

Announce an inter-institutional endeavor by CDC/IMMPaCt, FFI, MI, GAIN, USAID, in collaboration from UNICEF and HKI, to gather practical information about the monitoring of food fortification programs.

Methods

A manual aimed to make easier and more efficient monitoring of the production, enforcement, and consumer utilization of fortified flours is being prepared, and will be made available in the near future for field validations and wider use.



Delegates at a packed session in Conference Room 2B.



A woman breastfeeds her infant while a nurse collects a blood sample in Cajamarca, Peru. This family participated in a study on optimal multiple micronutrient powder supplementation schemes.

Results

Being aware that the impact of mass-food fortification programs depends on ensuring the provision of sufficient and good-quality micronutrients to fill dietary gaps to most individuals of affected populations, special efforts should be dedicated to ensure that they have access to, accept, and utilize foods that are fortified according to specifications. Thus, strengthening of monitoring capabilities should be an important goal for any food fortification program. A simple and concise manual in this subject, centered on indicators, might be a good contribution to this topic.

Conclusions

The original concept of food fortification, as presented in the “Guidelines on Food Fortification with Micronutrients” by WHO/FAO, has been further developed to define more clearly the various components of a food monitoring system. The manual will include regulatory monitoring, consumer monitoring, and program-management monitoring. Determination of outcomes for impact monitoring has been reserved for a complementary manual. Specific examples, cases studies, and references are to be included in each chapter. The goal is to help in the consolidation of effective programs whose per-

formance, quality, and dietary and biological impacts can be routinely documented.

Improving effective coverage of micronutrient supplementation: Results from application of the Monitoring Results for Equity System (MoRES) in Bangladesh and Malawi

A UNICEF study, *Narrowing the Gaps to Meet the Goals (2010)*, found that an equity-focused approach to child survival and development is the most practical and cost-effective way of meeting the health Millennium Development Goals for children. The Monitoring Results for Equity Systems (MoRES) was developed to support UNICEF’s equity focus. It helps to ensure that programs are better aligned to address inequities by strengthening government and partners’ capacity to assess deprivations and patterns of inequity, identify key constraints that are impeding effective coverage of interventions, and ensure the requisite program shifts to accelerate results. Progress in addressing the key constraints is then monitored periodically, ensuring the use of more “real-time” information to make course corrections in national and sub-national plans and strategies and to inform policy dialogue. Across all regions, countries are adopting this approach as a way to accelerate progress with equity. We illus-

trate this through examples from two countries – Bangladesh and Malawi – where UNICEF and partners have applied this approach to better understand, address and track constraints to effective coverage of nutrition interventions. In both countries, early experiences in applying MoRES show the usefulness of the approach in ensuring “data for action” to improve programming for the most disadvantaged children.

Using GIS in a program setting to understand nutrition intervention coverage in rural Nepal

Objective

We investigated the association between Euclidean Distance (ED) to multiple micronutrient powder (MNP) intervention services and coverage among 6- to 23-month-olds.

Methods

We used data from a cross-sectional survey of a pilot program implementing free MNP distribution. Female community health volunteers (volunteers) introduced MNPs during volunteer-held community-based Mothers Group Meetings (MGM) and encouraged others to collect MNPs at a government health facility (HF, n = 336). We compared MNP coverage, defined as ever collecting a 60-sachet batch of MNP, by having heard about MNP at an MGM (Chi square test). Additionally, we explored the association between quartiles of ED from caregiver homes to volunteers and HFs and MNP coverage overall and after stratification by having heard about MNPs at an MGM (Fisher’s exact and trend tests).

Results

ED to a volunteer and HF was negatively associated with hearing about MNPs and MNP coverage ($p < 0.01$ for both), respectively. Having heard about MNP at an MGM was positively associated with MNP coverage ($p < 0.01$) and eliminated the association between ED to an HF and coverage ($p = 0.49$).

Conclusions

Attending an MGM mitigated the negative association between distance to getting MNPs and MNP coverage. In this context, MNP coverage may potentially be improved by designing interventions that increase caregiver opportunities for exposure to behavior change strategies, such as community-based group meetings.

Engaging health officials in the Philippines: Application of a bottleneck analysis tool to improve health and nutrition program implementation at the local government level

Background

For children in the Philippines, malnutrition remains a chal-

lenge, especially for the youngest and most vulnerable children. The prevalence of underweight-for-age children has stagnated at 20% between 2003 and 2008 in the setting of low rates of health-promoting practices such as exclusive breastfeeding at only approximately 34%. The UNICEF recognizes that in order to attain the Millennium Development Goal to eradicate extreme poverty and hunger by 2015, equity-focused efforts must be intensified to improve nutrition program implementation at the level of local government units (LGUs). To this end, an innovative systems analysis tool with local government officials in health and nutrition has been implemented that uses existing data on Infant and Young Child Feeding (IYCF) practices and engages local public health workers to identify bottlenecks in service delivery and targeted interventions to improve nutrition programs in their local context.

Methods

Using data at decentralized level, a bottleneck analysis tool was developed and implemented. Following the so-called Tanahashi model, the tool requires the identification of a determinants matrix and subsequent insertion of current data, and uses it to provide context and reveal so-called bottlenecks in the effective implementation of current IYCF programs. The tool helps to assess the delivery of programs to improve IYCF practices for each of the LGUs. Interactive workshops to engage government officials and nutrition experts from each LGU were held in addressing bottlenecks to IYCF program services and interventions. Fifteen LGUs from three provinces in region five and nine were chosen to participate in this initiative. Participants were asked to review the data collected, verify bottlenecks in their respective LGUs, provide insight into the on-the-ground situations in their areas, and identify activities needed to address the bottlenecks and improve IYCF practices in their communities. After the bottleneck analysis was completed for each LGU, officials reviewed data from other LGUs in order to identify common bottlenecks and interventions. Results from each LGU’s bottleneck analysis were compiled and reviewed. Each participant was surveyed to assess the usefulness and potential impact of the workshop activities on subsequent planning and program improvement.

Results

The analysis and subsequent discussions revealed several common bottlenecks to IYCF program implementation across LGUs in the Philippines. For example, multiple LGUs noted a large discrepancy in mothers’ awareness and knowledge of breastfeeding. These localities subsequently proposed interventions to eliminate this bottleneck, such as implementation of culturally appropriate breastfeeding campaigns in their localities or creating targeting educational materials to provide to mothers

with newborns. The respondents rated the usefulness of the workshop to be “4.8” (out of highest score of 5), while 100% of the participants (n = 17) responded that they would recommend using this tool to represent their municipality in discussions with national organizations (i.e. Ministry of Health). Several open-ended responses included “bottleneck analysis contributes to the identification of gaps!”, and “it is an eye-opener.”

Conclusions and lessons learned

The results of this initiative demonstrate the utility of targeted bottleneck analysis at the level of local governments to engage and empower local governments on a decentralized level and stakeholders to assess data and identify interventions in a timely manner for improving key IYCF practices in their communities, leading to data-driven change in some of the most disadvantaged LGUs in the Philippines. By creating a collaborative environment, an open discussion regarding data usage, analysis of available data, and positive program modulation can be achieved. Though the pilot was considered a success, future work in this area will require additional resources to assist local government officials to implement and monitor interventions. This pilot represents the use of this tool to engage local officials and gaining buy-in from LGUs in addressing the needs of their community, and could be adapted in other programmatic contexts and even countries.

Iron-folic acid distribution and consumption through antenatal care: Identifying barriers across countries

Objective

The prevalence of maternal anemia remains unacceptably high in developing countries. At the same time, the percentage of women who consume one or more iron-folic acid (IFA) tablets during pregnancy remains persistently low. This study aims to identify where within antenatal care (ANC) programs pregnant women falter in obtaining and consuming an ideal minimum of 180 IFA tablets.

Methods

Demographic and Health Survey data from 22 countries with high burdens of undernutrition were used to identify four sequential falter points to consuming the minimum of 180 IFA tablets: ANC attendance, IFA receipt or purchase, IFA consumption, and the number of tablets consumed. Women, 15 to 49 years of age, who had a live birth within the previous five years, were included in the analysis.

Results

Across all countries, 83% of all pregnant women had at least one ANC visit, 81% of whom received IFA tablets. Of those receiving IFA tablets, 95% consumed at least one. Overall adherence to daily iron supplementation, however, was extremely low: only 8% consumed 180 or more IFA tablets. There were only two countries in which the percentage of women consuming 180 or more tablets exceeded 30%.

Conclusions

While most women receive and take some IFA tablets, few receive or take enough. This analysis identifies where the ANC distribution of IFA falters in each country and enables policy makers to design and prioritize follow-up activities to more precisely identify barriers, an essential next step to improving IFA distribution through ANC.

3.3 Integrating Micronutrients into Agricultural Programs

Chair: Howarth Bouis

HarvestPlus, Washington, DC, USA, and International Food Policy Research Institute (IFPRI), Washington, DC, USA

Presenters

Lidan Du

The SPRING Project/HKI, Ethiopia
Linking agriculture to micronutrient nutrition
– Early efforts from Feed the Future

Deanna Olney

International Food Policy Research Institute (IFPRI), Washington, DC, USA
Impacts on anemia: Implementing Homestead Food Production and Essential Nutrition Actions in Burkina Faso

Carol Levin

University of Washington, Seattle, WA, USA
Designing, implementing and assessing the costs and benefits of an integrated agriculture and health project to improve nutrition outcomes: The evaluative process for the Mama SASHA project

Making agricultural programs more nutrition-sensitive

This session contained a number of case studies illustrating how agricultural development programs can be made more nutrition-sensitive and serve as effective platforms to deliver nutrition-specific interventions.

The first presentation, *Linking agriculture to micronutrient nutrition*, was a landscape analysis examining how the USAID Feed the Future program (which operates in 19 countries and focuses on value chains) can be adapted to include more nutrition-sensitive approaches. The other two presentations summarized the results of similar homestead production programs, but highlighted different evaluation outcomes. The Burkina Faso study focused on *impact results on anemia* and highlighted not only the positive impacts of the program on anemia, but also how impacts were achieved using results from the program impact pathway analysis. The second study (carried out in Kenya)

described the design, implementation and assessment of the *costs and benefits* of an integrated agriculture and health project. Both studies highlighted the usefulness of process evaluation for identifying bottlenecks in the implementation and delivery of complex, multi-sectoral programs.

Linking agriculture to micronutrient nutrition – Early efforts from Feed the Future

Objective

The goal of the U.S. government's Feed the Future initiative is to sustainably reduce global poverty and hunger by simultaneously promoting inclusive agricultural sector growth and improving women and children's nutritional status. The SPRING Project conducted a landscape analysis of Feed the Future programs in all 19 focus countries to identify the programs' implementation status and operational approaches, and the pathways linking agriculture and nutrition.

Methods

The landscape analysis was conducted primarily via a desk review of over 160 Feed the Future strategy and activity documents. Thirty-five key informant interviews were conducted with the Mission staff and representatives of implementing partners to obtain supplementary information. The analysis was guided by the agriculture-nutrition pathways and principles originally developed by IFPRI and FAO.

Results

A number of programs chose child and/or maternal anemia as a key micronutrient indicator. Some of these countries designed specific micronutrient work, primarily through promotion of bio-fortified crops and/or fortification of cereal flours. Many countries invested in a variety of value chain crops in hopes of increasing the production and consumption of micronutrient-dense foods by women and children as measured through dietary diversity among these same target groups. However, the actual pathways between the production and consumption of these promoted value chain commodities are often not clearly described.

Conclusions

A small but increasing number of Feed the Future activities are explicitly designed to improve micronutrient nutrition of target populations. The potential of food-based approaches adopted



The Ethiopian Public Health Institute was responsible for hosting the Local MNF Steering Committee. Ethiopia has shown a strong commitment to the SUN Movement.

by Feed the Future programs will be better realized when research and implementation come together to enhance nutrition sensitivity in all stages of the food system.

The impacts of an integrated agriculture and nutrition and health behavior change communication program targeted at women in Burkina Faso on children's anemia

Objective

To assess the impact of a two-year integrated agriculture (enhanced-homestead food production [E-HFP]) and nutrition and health behavior change communication (BCC) program on children's (3–12 mo. at baseline) anemia (hemoglobin concentration (Hb) < 11 g/dL) in Burkina Faso.

Methods

A cluster-randomized controlled trial design was used whereby 55 villages were randomly assigned to one of three groups: **1)** Control; **2)** Older Women Leaders (OWL) or; **3)** Health Committee (HC) members. Both OWL and HC groups received the agriculture intervention and BCC but differed by BCC implementer – either OWL or HC members. Impacts on children's Hb and anemia were estimated using difference-in-difference (DID) impact

estimates and considered statistically significant at $p < 0.05$ and marginally significant at $p < 0.10$. Impacts on intermediary outcomes including women's agriculture production, women's knowledge related to the BCC and household and child dietary diversity (DD) were used to demonstrate plausibility.

Results

The E-HFP program improved children's Hb and reduced anemia prevalence. Program impacts were larger among children aged 3–5.9 mo. (DID Hb = 0.74 g/dL, $p = 0.028$; DID anemia = -14%, $p = 0.030$) as compared to children aged 3–12 mo. (DID Hb = 0.51 g/dL, $p = 0.066$). Supporting these findings, we found greater gains in women's agriculture production, knowledge and household and child DD in HC compared to control villages.

Conclusions

Participation in an E-HFP program improved children's Hb and decreased anemia prevalence by increasing women's agriculture production, knowledge and household and child DD. This is the first cluster-randomized controlled trial of an HFP program that documents a statistically significant positive effect on children's Hb and anemia.

Funding

Funding for the study was provided by the United States Agency for International Development, Office of U.S. Foreign Disaster Assistance (USAID/OFDA), the Gender, Agriculture and Assets Project (GAAP), and the CGIAR Research Program on Agriculture for Nutrition and Health (A4NH), led by the International Food Policy Research Institute (IFPRI).

Designing, implementing and assessing the costs and benefits of an integrated agriculture and health project to improve nutrition outcomes: The evaluative process for the Mama SASHA project

Objective

Responding to the call for improved evaluation of agriculture's impact on nutrition, we described the evaluation process to assess effectiveness, acceptability, feasibility and costs of an integrated orange-flesh sweet potato (OFSP) and health service delivery strategy in Western Kenya designed to improve the health of pregnant women and the nutritional status of children up to two years.

Methods

Formative research clarified how to introduce vitamin A rich OFSP to pregnant women through antenatal health visits and community support. We developed an impact pathway to inform project monitoring, conducted a first round of operational research (OR) to refine the project design, plus a second round of OR to assess feasibility and acceptability, and implemented a multi-round household survey and complementary cohort

study to evaluate impact on vitamin A status and health outcomes of pregnant women and their children. For analyzing costs, we used a microcosting approach based on project expense reports and outcomes for 2011–2013, allocating costs by activity and inputs by implementing organization.

Results

Nutrition education and vouchers for OFSP vines are distributed during antenatal care visits, with support provided in the communities and through pregnant mothers' clubs. Baseline results showed that vitamin A deficiency affected approximately 20% of pregnant women and children under 2 years. OR results highlighted that the integrated agriculture and health approach was feasible and acceptable among stakeholders. Over 5,400 women participated in monthly pregnant mother clubs at a cost of \$63 per woman. Of 4,464 women who received vouchers, 3,281 women redeemed vouchers and planted OFSP at a cost of US\$155 per beneficiary. The cost per contact women participating in pregnant women clubs, receiving vouchers, at ANC clinics and redeeming vouchers was US\$27 per contact.

Conclusions

Comprehensive evaluation of integrated agriculture, nutrition and health interventions is feasible, beginning with formative research and evolving with each stage of project implementation, and includes rigorous impact evaluation. Results indicate high acceptability and uptake and a cost per beneficiary that is in the range of published cost estimates for community-based therapeutic feeding programs, supported by community health workers with some referrals to health centers. Together all stages of evaluation will contribute evidence to the potential for scale-up.

Stuart Gillespie (IFPRI) listens to a presentation.



3.4 Resolving Bottlenecks to Implementation and Scale-Up

Presenters

Katie Pereira

JB Consultancy, South Africa

Scaling up micronutrient strategies within countries: Realities and challenges around appropriate labeling and promotion of foods consumed by infants and young children

Giri Raj Subedi

Ministry of Health and Population (MoHP), Nepal
Monitoring and action to address child refusals of micronutrient powders in Nepal

Anna-Marie Ball

HarvestPlus, Uganda

Upscaling biofortified crops in Uganda: Learning our lessons in an integrated implementation approach

Grace Marquis

McGill University, Montreal, QC, Canada

Experiences from the field: Working with multiple sectors towards scale-up of a nutrition-related intervention in Ghana

Kendra Siekmans

Health Bridge, Cincinnati, OH, USA

Revitalizing iron folic acid (IFA) supplementation for pregnant women: Current trends and opportunities based on multi-country formative assessments

The main objective of this session was to tackle the issue of resolving bottlenecks to implementation and scale-up of programs. Five different speakers addressed different topics related to the theme and offered insights into the critical issue of finding solutions to bottlenecks. The session was of particular interest to this conference, entitled Bridging Discovery and Delivery, as one of the critical elements to resolving micronutrient malnutrition is to identify evidenced-based programming and to scale up effective interventions.

Each of the presenters shared program experiences of problems and/or issues encountered with program implementation

or scale-up, describing how these problems were addressed, as well as what would be done differently if they were to be encountered again in another program. The presenters also shared lessons learned and views on sustainability, scaling up of programs, and research gaps.

Scaling up micronutrient strategies within countries

The first presentation of the session was titled *Scaling up micronutrient strategies within countries: Realities and challenges around appropriate labeling and promotion of foods consumed by infants and young children*. Presenter Katie Pereira (JB Consultancy, South Africa) discussed the labeling component of the Helen Keller International's ARCH Project and how this data has contributed to the development of the World Health Organization's Scientific and Technical Advisory Group criteria, which gives guidance on inappropriate promotion of foods for infants and young children.

The results from a cross-sectional study conducted in Nepal, Cambodia, Senegal and Tanzania assessed the labels of commercially produced foods marketed and/or commonly fed to children under the age of 2 years against international guidance and national legislation. The study found that a variety of claims were identified on the labels of commercially produced complementary foods and commercially produced foods for general consumption that are commonly fed to children under the age of 2 years. These included nutrition claims (nutrient content claims and nutrient comparative claims); health claims (nutrient function claims and reduction of disease risk claims); and other claims (non-nutrition claims).

“The ultimate aim of any guidance should be improvements in global child health outcomes”

The presenter emphasized that one of the significant findings from the study is that care should be taken that restrictions on the promotion of appropriate commercially produced complementary foods do not result in unintended negative consequences. Such restrictions include the provision of certain claims. An example would be caregivers selecting other, less appropriate, complementary foods – which often have a



A mother in Bolivia mixes MNP into her child's food as part of an educational demonstration at a health center.

poor nutrient profile, but have fewer claim and promotion restrictions. Their actions could be taken to imply that these are suitable, or even beneficial, for infant and young child feeding. The emphasis from this session is that the ultimate aim of any guidance should be improvements in global child health outcomes.

Monitoring and action to address child refusals of micronutrient powders in Nepal

The subsequent presentation by Giri Raj Subedi, a nutrition specialist from MoHP Nepal, was on *Monitoring and action to address child refusals of micronutrient powders in Nepal*. The results from an internal monitoring system were used to identify a key bottleneck in the MoHP and UNICEF infant and young child feeding (IYCF) and micronutrient powders (MNP) pilot program for children under the age of 2 years. The monitoring data showed that, despite developing a behavior change component to support the intervention package (including IYCF and MNP counseling, messages and instructions on MNP use, among other strategies), there were a number of children refusing food mixed with MNP and caregivers discontinuing use of MNP. The program team took action and designed a small formative study to understand the reason for the rejection of the MNPs. Meeting with households where a child was rejecting the MNPs, they were able to observe MNP food preparation and child feeding. They concluded that there was a need to focus on correct MNP food preparation, active feeding, allowing more time for feeding, and providing preferred foods to children. With this advice to caregivers, the child usually

consumed the food with MNP, and caregivers started giving the child MNP regularly again.

These results from the monitoring system and subsequent formative investigation were used to strengthen and revise the training of the intervention staff (volunteers, health facility staff, and others) so that they could respond effectively to reports of child refusals in the future. The results highlighted the important role of behavior change intervention strategies to support knowledge, skills and motivation of families to correctly prepare and feed children. Without a good monitoring system to which program staff respond in a timely way, problems cannot be identified and subsequently resolved.

“The results highlighted the important role of behavior change strategies”

Upscaling biofortified crops in Uganda

The third presenter, Anna-Marie Ball from HarvestPlus, talked about *Upscaling biofortified crops in Uganda: Learning our lessons in an integrated implementation*. Despite the proven impact of vitamin A-rich orange sweet potatoes on vitamin A status, programs have historically been very small-scale. The presenter showed how a project to scale up delivery of two biofortified crops (orange sweet potato and high-iron beans) increased delivery from about 24,000 farmers to over 225,000 farmers over a five-year period.

Using an integrated agricultural and nutritional approach, HarvestPlus and partners delivered seeds and training to subsistence farmers in 15 districts in Uganda. Extension workers were trained in agronomy (two crops), nutrition (vitamin A and iron), and marketing messages. Farmers had to agree to share seeds with two other farmers in the second season of planting, and compliance was tracked.

“The integration of nutrition and agriculture, combined with the use of community bonds and an appeal to social responsibility, made scale-up possible”

Through this approach, the program was able to reach far more farmers, and the potential impact of the program was more substantial. The integration of nutrition and agriculture,

combined with the use of community bonds and an appeal to social responsibility, made scale-up possible. The methods and techniques used can be adapted for other similar programs.

Working with multiple sectors towards scale-up of a nutrition-related intervention in Ghana

The fourth presentation, by Grace Marquis from McGill University, was on *Experiences from the field: Working with multiple sectors towards scale-up of a nutrition-related intervention in Ghana*. The Enhancing Child Nutrition Through Animal Source Food Management (ENAM) project was a 16-month study to test a multi-sector intervention to increase the use of animal source foods in the diet of 2- to 5-year-old children in rural Ghana. The approach used microcredit loans and group education about entrepreneurship and nutrition, and was designed with the intention to scale up. The speaker discussed the components of the project that contributed both to its success and to its immediate scaling-up. At community level, these were: stimulating income-generating activities; providing access to microcredit loans; training in food processing and storage; training in entrepreneurship and marketing; and training in nutrition education. The extension of continuing education to ministry and NGO staff was also a success factor at regional and country level. Grace Marquis also described the components that were believed to be missing from the project and which could have contributed to even better long-term outcomes.

The presenter emphasized that programs need to have a plan for scaling-up of activities at the proposal stage – and that they should include in the budget the funds to support it. From the beginning of the project, truly active partners are needed who can help seek out opportunities to scale up activities within the permanent institutions. The final point was that to be able to scale up an intervention, it is critical to recognize that it takes time and money to transfer activities to a permanent partner – and that this needs to happen within the timeframe of the project itself.

“To be able to scale up an intervention, it is critical to recognize that it takes time and money to transfer activities to a permanent partner”

Revitalizing iron folic acid (IFA) supplementation for pregnant women

The final presenter, Kendra Siekman (Health Bridge, Cincinnati USA), presented on *Revitalizing iron folic acid (IFA) supplementation for pregnant women: Current trends and opportunities based on multi-country formative assessments*. The focus of this talk was to identify existing barriers and potential enabling opportunities for the revitalization of iron and folic acid (IFA) supplementation to reduce anemia in pregnant women.

Many countries have IFA programs, but access and adherence to programs is often very poor, and there is a great need to understand barriers to IFA programs. Formative research results from eight countries (Afghanistan, Bangladesh, Ethiopia, Indonesia, Kenya, Nepal, Nigeria and Senegal) were analyzed to understand current antenatal care-seeking practices and identify relevant barriers and enablers associated with improved coverage and adherence to prenatal IFA supplementation.

The results showed that, in the countries included in the study, general anemia in pregnancy is a well-known health concern among women, family decision-makers and health-care providers in all countries studied. Widely varying views on when to start IFA supplementation, the dosage and the duration were expressed by women, family members and health-care providers. Overall, improved ANC access and quality is needed to facilitate IFA supplementation. There is potential for community-based delivery and counseling to address concerns with IFA supplement supply and adherence. Renewed investment in IFA programs with strong behavior change designs is urgently needed to achieve reductions in anemia.

Key learnings

There are several common threads addressed by all of these presentations. The first is that there is a critical need to move beyond pilot phases. There exist many effective approaches to improve micronutrient malnutrition, but structures, policies and partnerships need to be created with scale-up in mind from the start. Where possible, integrated approaches should be deliberately used from the outset of a program. What is more, there is a need to create systems that can be scaled up and which will operate well at scale and not simply during the pilot phase.

A crucial element that facilitates scale-up is the design and implementation of well-functioning monitoring systems. Monitoring systems need to be established and used to detect bottlenecks. Formative research methods are also critical to be able to understand why bottlenecks exist and to identify possible solutions. Finally, the involvement of policy makers is critical for program sustainability.

3.5 Developing Costed Scale-Up Plans In-Country: Where and How Does the Micronutrient Agenda Fit In?

Chair: Shawn Baker

Bill & Melinda Gates Foundation,
Seattle, WA, USA

Presenters

Meera Shekar

World Bank, Africa Region
*Costing and financing nutrition-specific
and nutrition-sensitive Interventions:
Approaches and Challenges*

Chris Osa Isokpunwu

SUN focal Point and Head of Nutrition,
Federal Ministry of Health, Nigeria
*Case study #1:
Costing the scale-up of nutrition in Nigeria*

Banji Filani

Federal Ministry of Health, Nigeria
*Case study #2:
Fiscal Space Analyses for Nutrition:
An Example from Nigeria*

Huihui Wang

World Bank, Africa Region
*Case study #3:
Financing nutrition through the health sector:
The case of Ethiopia*

Steve Vosti

University of California, Davis, CA, USA
*Case study #4:
Cost-effectiveness of
zinc supplementation for treatment of diarrhea
in rural Burkina Faso*

The importance of understanding the language of cost calculation

In this session, Meera Shekar provided an overview of various approaches to the process of preparing costed scale-up plans.

This topic had been the focus of the day-long pre-conference workshops organized by the World Bank, which paved the way for diverse presentations of country experiences in developing such plans.

Both this session and the pre-conference workshops generated an overflow crowd. Such a detail might seem extraneous to the reporting requirements of this publication, but it indicates the considerable interest that currently exists within the global nutrition community on the subject of costs. This is for a variety of reasons.

In the first place, nutrition is gaining more prominence in the global development agenda, and this heightened profile is attracting more funding. This progress is greatly welcome, and of course greatly necessary. It presents the global nutrition community with a learning challenge, however. Whereas in the past we had to cope with a climate of austerity, we now have to learn to capitalize on a climate of greater understanding of the importance of investing in nutrition. This means that we have to know how to estimate costs, how to manage them, and how to account for them. Policy makers in particular need to be able to provide clear answers when asked how much programs will cost to **(a)** set up, **(b)** implement and **(c)** monitor and evaluate – and, of course, how much value they will deliver.

The second, and extremely pressing, reason is that we need to know the cost of inaction – that is, we need to be able to calculate the cost of doing nothing (or not enough) and compare this with the cost of taking targeted action driven by up-to-date, evidence-based policies.

Above and beyond this, we need to look beyond the horizon of mere survival and calculate the cost of producing healthy, active and productive populations – as well as being able to calculate the return that such populations will generate for their own economies. We must move from generic advocacy messages to ones that speak the language of cost calculation. Cost is therefore a very hot topic on the global nutrition agenda at present, and will carry weight in circumstances where purely emotional or ethical arguments might fail.



The 2014 Global Conference stimulated impassioned debate about the global nutrition agenda.

“We need to know the cost of doing nothing”

Pre-conference session: Strengthening the “case for nutrition”

The pre-conference session aimed to share the process and early outputs from the work already undertaken by the World Bank, in partnership with the Bill & Melinda Gates Foundation, to support the development of costed plans for scaling up nutrition in Africa.

By combining costing with estimates of impact and cost-effectiveness analysis, this work is helping to strengthen the “case for nutrition”, while also enhancing allocative efficiencies through the identification of the most cost-effective packages of interventions in situations where funding is constrained. This session demonstrated how costed plans can provide policy makers with powerful, evidence-based advocacy tools that demonstrate what kinds of results countries can “buy,” given available resources.

Costing and financing nutrition-specific and nutrition-sensitive Interventions: Approaches and Challenges

The south-to-south knowledge-sharing and country capacity development sessions, entitled *Scaling Up Nutrition – What will it cost at the country level? Developing costed scale-up plans in-countries* were organized by the World Bank during the Micronutrient Forum Global Conference in Addis Ababa, Ethiopia, on Monday June 2nd, with follow-up sessions also held on June 5th.

The sessions were organized to share with participants the process and early outputs of the costing work. Government officials from Nigeria, Zambia, Uganda, and DR Congo presented their costed scale-up plans and discussed their countries’ respective efforts to address high burdens of malnutrition. An official from the Nigerian government’s Saving One Million Lives initiative also spoke to participants about his government’s experience conducting a fiscal space analysis in order to determine available resources for investments in nutrition. The costed plans focus on nutrition-specific interventions, but also provide indicative costs for selected nutrition-sensitive interventions. The sessions were attended by over 150 participants from a wide array of governments, development partners, civil society organizations, and academia.

Each costed plan provided estimates of the costs and benefits of scaling up a package of evidence-based nutrition interventions, which aim to improve nutrition outcomes during the 1,000 day window of opportunity of a child's life from conception to two years of age. These costed plans take into account the current coverage of interventions, the available delivery platforms, and the costs for commodities, monitoring and evaluation, and capacity building. In addition, the plans provide policy makers with several context-specific scale-up scenarios designed to maximize allocative efficiencies in situations where available resources for investments in nutrition are limited. Next, the proposed scale-up scenarios are evaluated based on their cost-effectiveness (in terms of cost per DALYs saved, lives saved, and cases of stunting averted), as well as their potential contribution to future economic productivity. For example, in Nigeria, one proposed scenario requiring a public investment of US\$987 million over five years would yield an internal rate of return (IRR) of 26% and add over US\$1 billion annually to the Nigerian economy over the productive lives of the beneficiaries.

Through its programmatic technical assistance, *Strengthening SUN Analytics and Planning in Africa*, the World Bank is continuing to provide support to African governments with an interest in developing rigorous costed scale-up plans for nutrition. To date, the World Bank has provided support to a total of seven countries, including Nigeria, Togo, DR Congo, Zambia, Uganda, Mali, and Niger, where investments in five year scale-up plans have been found to yield as much as US\$30 in economic returns for every US\$1 invested. Moving forward, the World Bank is planning to expand its support to Kenya and Tanzania, with requests for support pending from the governments of several additional countries.

“Each costed plan provided estimates of the costs and benefits of scaling up a package of evidence-based nutrition interventions”

It is increasingly important to know how to estimate, manage and account for the costs of nutrition interventions.





Track 4 Stakeholders and Sustainability: Elements of an Enabling Environment

Introduction

Klaus Kraemer

Sight and Life, Basel, Switzerland, and,
Johns Hopkins Bloomberg School of Public Health,
Baltimore, MA, USA

The main goals of this track were:

- a) To explore the prerequisites for an enabling environment; and
- b) to discuss how stakeholders across the global nutrition community can work together to create this.

This included two plenary panel discussions covering the critically important enabling factors of *Innovative financing and new business models and Political will and evidence-informed policy*.

During the week, there were parallel session panel discussions covering the topics of *Effective linkages; Defining obligations and taking responsibility for stakeholder actions; Novel approaches to engaging the private sector; Creating and supporting leadership; and How evidence-based policy environments are key to progress*. Each of these facilitated greater discussion on the four factors together with the wrap-up session on *Enabling a world without micronutrient deficiencies* to create a whole and suggest a way forward. The main objective of the track was to encourage delegates to think and act in new ways when considering micronutrient interventions and to provide a global view of what it takes to create supportive, cohesive and sustainable interventions from the perspective of a range of nutrition and non-nutrition stakeholders through discussion and sharing successes and failures.

Conference participants during a plenary session. Regular consumption of water was essential on account of the high altitude of the venue.





A mother in Bolivia feeds her child porridge with MNP – a key intervention to reduce childhood anemia as part of the Bolivian government's Zero Malnutrition program.

The need for a rights approach to nutrition

In philosophical terms, a key precondition of an enabling environment for micronutrient interventions is the recognition that all human beings have a right to food, and specifically to nutrients. Food might fill empty stomachs, but it does not necessarily provide the nutrition needed for a healthy and productive life.

Writing in issue 2/2013 of *Sight and Life*, Martin Bloem, Senior Nutrition Advisor and UNAIDS Global Coordinator for the UN World Food Programme, observed that: “In the human rights documents, nutrition is only considered as a determinant of health, and the right to food only mentions access to ‘nutritious food’, but none of the ‘human rights’ documents recognizes the importance of nutrients in the sense that all required nutrients should be provided in adequate amounts. The particular need of children aged 6–24 months for nutrient-dense foods is very specific, and the fact that, for large segments of the world’s population, these needs are difficult to meet from local foods calls for a discussion of the right to nutrients in order to prevent chronic undernutrition. Nutrition has been mentioned as a component of the ‘right to food’, ‘right to health’ and ‘convention on the rights of the child’, yet the prevention of chronic

undernutrition has not been recognized as a right. In fact, nutrition is sparsely mentioned in the various ‘human rights’ documents. This is due to the fact that nutrition is not regarded as a right in and of itself, but as an element of health or an outcome of lack of access to food.”

“We have to address both food security (quantity) and nutrition security (quality) across the life-course”

In practical terms, the global nutrition community has to address both food security (quantity) and nutrition security (quality) across the life-course. The agriculture-food value chain is just one component of a more extensive system. Food and nutrition security have been separated for many years without a major reduction in the global burden of malnutrition. A systems-thinking approach will be key to achieving food and nutrition

security and increasing resilience, for each element of the food system is interdependent, and each is equally important.

The adoption of a rights-based approach by the global nutrition community will be a key step in strengthening our advocacy work on behalf of those who do not have a voice of their own, and will hopefully lead eventually to the recognition of the right to nutrients as fundamental. But achieving this will involve a great deal of political will – at all levels.

Political will – The foundation for action

The need for political will to enable action can be clearly seen in the approach of the Scaling Up Nutrition (SUN) Movement, which requires high-level commitment for a country to sign up. And yet, as the Department For International Development (DFID) so aptly puts it: “Political will’ is commonly used as a catch-all concept, the meaning of which is so vague that it does little to enrich our understanding of the political and policy processes ... We must begin by giving ‘political will’ a quite specific and narrow meaning. Let us define it as ‘the determination of an individual political actor to do and say things that will produce a desired outcome.’”

“We have everything we need
except political will, but political will
is a renewable resource”

Al Gore

But this is just the start, for political will for its own sake adds little value; it has to serve a purpose. The will has to be entrenched in the types of policies and priorities that governments establish to improve the lives of their people. Typically, global, regional and national policies first need to be in place, as these create the enabling environment, context and priorities into which interventions are then applied. Proving solutions to be effective does not automatically result in the adoption of those interventions. Increasingly, efforts to address social concerns are not only funding direct services, but are also looking further upstream to the conditions and policies that underlie these concerns. Characteristics of a successful policy are that it is, first, technically sound, with evidence-based solutions that are technically practical to implement. The second, and equally important, characteristic is that policies must have the support of, and be acceptable to, all stakeholders. The involvement of stakeholders in policy development is essential in ensuring its acceptability and support when the policy is implemented. Achieving this requires much effort and is often neglected, but it is the foundation for success.

Effective linkages – The need for a systems approach

A systems approach to nutrition may appear to be a complex undertaking and difficult to operationalize, but it has been successfully applied in biology and medicine, and it holds great promise in the light of current innovations in real-time “big data” analyses and mobile technologies.

We should not shy away from the many dimensions of a nutritious food system which is inextricably linked to other sectors such as health, water, sanitation, education, and social protection. Rather, we should see this challenge as an opportunity to develop a common dialogue and to innovate, with novel models and technologies not yet anchored in our systems thinking and new iterations of modeling algorithms. We need a paradigm shift in order to tackle malnutrition in a holistic and sustainable manner that addresses its complexity as a whole and not piece-meal. We need new and different alliances to galvanize action, and we cannot ignore the private sector.

The private sector has a considerable, and yet largely underestimated, ability to reduce malnutrition. However, the private sector’s contribution to making a positive impact on nutrition has not been thoroughly evaluated, and the food industry in particular is still regarded by many more as a problem than as a solution to malnutrition. Recently, development agencies have engaged with private-sector companies to find outcome-driven, solution-oriented approaches to improved nutrition. The SUN Movement calls for further collaboration with the private sector via its SUN Business Network (SBN). This aims to advance opportunities for the private sector to improve access to nutrition services, and therefore accelerate improved nutrition, primarily through public-private partnership (PPP). To date, the private sector has contributed to public health nutrition via product-based partnerships (such as vitamin A capsules or salt iodization), product development partnerships (for example, micronutrient powders), and issues-based partnerships (for example, standards for fortification). But there are many other PPP opportunities to innovate toward better nutrition. It is no longer about whether we should engage with the private sector, but rather about establishing the rules for such an engagement.

“The best way to find out if you can trust
somebody is to trust them”

Ernest Hemingway

Effective linkages will require that we have tough conversations, address the elephants in the room, and are prepared to have a “give and take” attitude. The reality is that we in fact need to move beyond linkages and collaboration to true integra-

tion if we are to address nutrition at scale and sustainably. This also raises the need to clearly define each player's obligation and to ensure that everyone takes responsibility for their own actions. Again, the SUN Movement has captured this concept in one of its four strategic processes, "Bringing people together to work effectively through functioning multi-sector, multi-stakeholder platforms."

Leadership development – A new horizon for nutrition

To scale up nutrition, there is an urgent need in the global health community for both capacity development and leadership development. We need to rethink the concept of "capacity development." For some, capacity development is a useful umbrella term that provides a home for a number of often nebulous "needs." For others, capacity development is about imparting "know-how" (predominantly technical skills) to individuals and institutions. Often people create a checklist of skills that are considered necessary to develop a specific competency, and then the necessary course/training program to develop those skills appears. As delegates complete the course, they are determined to have developed the capacity. But capacity development is, and must be, so much more.

A neglected element of capacity development is leadership development. We need to develop leadership for change. It is transformational leadership where the leader creates successful teams. It is not developing the traditional manager-leader who leads the planning, organizing, directing and controlling of work activities. Rather, it is about the individual who can create an aligned commitment among a diverse group and unlock people's potential so as to improve their performance and productivity toward achieving a united vision. In the words of the writer Lewis Lapham, "Leadership consists not in degrees of technique but in traits of character; it requires moral rather than athletic or intellectual effort."

"Leadership consists not in degrees of technique but in traits of character; it requires moral rather than athletic or intellectual effort"

Developing strong leaders requires a large, sustained financial commitment over time. It involves a fundamental change in the way leadership continues to be viewed in many of the environments where we need to be making a difference. It means creating self-awareness, developing a new orientation, creating self-belief and then walking alongside these new leaders, mentoring and supporting them. Leadership development



Everyone has a role to play in creating an environment that will enable the achievement of the global nutrition agenda.

is not about a two-year grant or a short course. It does not have neat metrics for determining success. Perhaps that is why many avoid it.

Everything that has to be done will require innovative financing and new business models, and we have to be prepared to learn more from our failures than from our successes. We have to think out the box and open new dialogue with new partners. We have to do things differently.

The word enabling means "to make able; give power, means, competence, or ability to; authorize." It is active, not passive. Each of us has a role to play in creating an enabling environment. It is not only something that others must do: an enabling environment must be co-created. **Track 4** of the Micronutrient Forum Global Conference aimed to be the spark to that action from all who are concerned about the interventions necessary to deliver on nutrition (quantity and quality) as a non-negotiable human right.

4.1 Stakeholders and Sustainability: Elements of an Enabling Environment

Summary Report

This summary report is provided by:

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Promoting new ways of thinking and acting

It is now recognized that having proven solutions to address malnutrition and, more specifically, to eradicate micronutrient deficiencies, does not automatically result in the adoption of these interventions. There is a need not only to focus on the evidence (discovery and development) but also to look further upstream to the conditions and policies that underlie the ability to implement (delivery) and then to provide a way to span and provide a passage between the two (bridging).

In “Bridging Discovery and Delivery”, the overall theme of the 2014 Micronutrient Forum, the opportunity was created for a wider discussion of the many elements that create an enabling environment. While nutrition scientists and program implementers are generally comfortable discussing and debating the prevalence, efficacy and effectiveness of interventions and program details and experiences, they have had less exposure to, and are less comfortable with, topics such as financing, leadership, political will and evidence-informed policy. These topics, however, are just as critical for success, especially as countries move towards scaling up nutrition interventions and the post-2015 agenda.

The Micronutrient Forum thus had a specific thematic topic that aimed to provide a global perspective on the stakeholders and associated enabling environment supportive of cohesive and sustainable interventions. The concept was to bring new stakeholders and topics to the discussion of how we sustainably

scale up proven micronutrient interventions, and to promote new ways of thinking and acting.

Taking it literally...

The thematic topic “Stakeholders and Sustainability: Elements of an Enabling Environment” was designed to literally bring together the meaning behind each of the five constituent words:

Sustainability: The endurance of systems and processes.

Stakeholder: Anybody who can affect, or is affected by, an organization, strategy or project.

Elements: Components or constituents of a whole.

Enabling: To supply with the means, knowledge, or opportunity to help people accomplish things they could not do by themselves.

Environment: The conditions and influences that surround or affect something.

Innovative financing – The need to look at new ways to raise money for nutrition, and innovative ways to allocate funds to nutrition

It is vital that the nutrition community should become engaged in issues pertaining to financing if we are to achieve scale-up. It has been estimated that in order to fully implement the 13 proven nutrition interventions globally, some USD 11.8 billion is necessary, yet it is estimated that currently only USD 1 billion is being directed to nutrition (USD 0.5 billion nutrition specific, USD 1.0 nutrition sensitive). There is still a big gap. This is not money that governments, or most agencies, have available, and so finding ways to raise money and to either allocate existing capital or overcome the obstacles we face is essential.

We can no longer neglect this all-important topic, and the two panel discussions at the Forum aimed to stimulate the re-



The exhibit hall during opening reception. Breaks and informal discussions took place here throughout the conference.

alization that if we are interested in addressing micronutrient deficiencies and improving nutrition outcomes, we have to be interested in, and engage with, new financing options.

We need a new skill set and new partners; we need to learn a new language and to start a new dialogue. Although nutrition has been able to convince over 50 countries to sign up to the SUN Movement, we now have to present costed plans and interventions in such a way that they attract funding support and result in programs that deliver impact to ensure ongoing financing.

The saying “one size fits all” is not applicable, and there are various funding options, including hybrid financing, blended funding, catalytic financing and results-based financing. There are even options where donor money can be taken to the capital markets and potentially result in a 6:1 return. For example, one of the challenges faced by many innovative interventions is accessing money upfront before the effectiveness of these interventions can be rigorously proven. In such cases, there is the opportunity to explore social/development impact bonds. These are bonds that seek to improve the efficiency and effectiveness of development programs whereby investors provide external financing for interventions and only receive a return if pre-agreed outcomes are achieved. Funds to remunerate investors come from donors, from the budget of the host country, or from a combination of the two, and are commensurate with the level of success. This approach is intended to encourage the innovations and adaptations needed to deliver successful outcomes. It shifts the focus onto implementation quality and the delivery of successful results.

We need to focus more on results, especially as nutrition is one of the markets that traditional investors will not go into because they perceive it as too risky. Equally, we must focus on the double bottom line – financial return and social return – and must stop always seeing ourselves as “receivers” and develop an appropriate discourse to use as we engage with funding organizations.

The reality is that we need to get more nutrition for the money and to get more money for costed nutrition plans. In so doing, we have to change people’s perspective. Nutrition should not be seen as a welfare issue: investment in nutrition is investment in human capital. The take-home message is that we are very good at communicating with ourselves, but to scale up nutrition we have to know how to engage others and refocus nutrition in order to attract the necessary financing.

“To scale up nutrition, we have to know how to engage others”

Effective linkages – Moving beyond linkages and collaboration to true integration

So much has been, and is, spoken about the need to break down silos. The conversation is usually about how the many individual sectors – which have to be involved so as to address the challenges of malnutrition (in its broadest sense) – function in isolation, with an inward focus and vertical information communication.

Remaining in our silos could lead to nutrition’s biggest missed opportunity. Addressing nutrition problems requires sectoral, multisectoral, intersectoral and trans-sectoral engagement. The “Effective Linkages” panel discussion included representatives from agriculture, civil society and donors, and showed that, although in our heads we have accepted the need for full integration, this is not yet truly reflected in our actions, interventions and programs.

It is important to understand that collaboration cannot be forced: it has to come from mutual agreement, and it takes time and energy to establish the common understanding that has to be the foundation of any effective linkage. The Scaling Up Nutrition (SUN) Movement has gone a long way to help promote effective linkages, but the process needs to be consciously worked at and nurtured.

It was also highlighted that there is a need to find a balance between ensuring community ownership and sustainability of interventions and being driven to show results in order to satisfy funders in a short period of time – the balance between being an experienced realist and an impatient optimist. A tweet during this session summed up much of the discussion, “Economic



Jane Badham, power tweeting for *Sight and Life* to share conference news with the rest of the world in real time.

growth and technical solutions are not enough, we need pro-nutrition actions from different sectors and to create synergies.”

Although it seems that nutrition and agriculture are getting closer, much still needs to be done with other groups such as social protection and education. It was clear that there needs to be more trust, a common understanding, and new ideas to “crowd in” rather than “crowd out” other sectors which could contribute to nutritionally replete, healthy, thriving populations.

“We need to ‘crowd in’, rather than ‘crowd out’ other sectors”

Defining obligations and taking responsibility for stakeholder actions

Any discussion of the need for linkages naturally leads to a discussion of roles and responsibilities of the various stakeholders. A panel that included an ethicist, a human rights and public health expert, the World Food Programme and the Graça Machel Trust tackled this topic.

It was clear that multi-sectoral stakeholder engagement and setting the rules of that engagement has to happen from the very beginning and that it has to reach from the national to the

community level. When it comes to the translation of science into policy, a great deal generally happens at the national level, but it is important that there should be a trickle-down effect to the lower levels of government and the communities where implementation actually happens.

The fact that health and nutrition promotion frequently fails to reflect the latest science shows that there is often a disconnect between policies and their implementation. It is critical to address this, first by ensuring that those involved in implementation are considered as essential to any intervention’s success and are actively included, and second, by engaging civil society. A lesson can be learned from the HIV/AIDS experience, where success was largely driven by civil society demanding treatment and ultimately getting it and then holding stakeholders accountable for their actions. We can use this model and transform nutrition into a rights issue that will carry more power than if we only present the science.

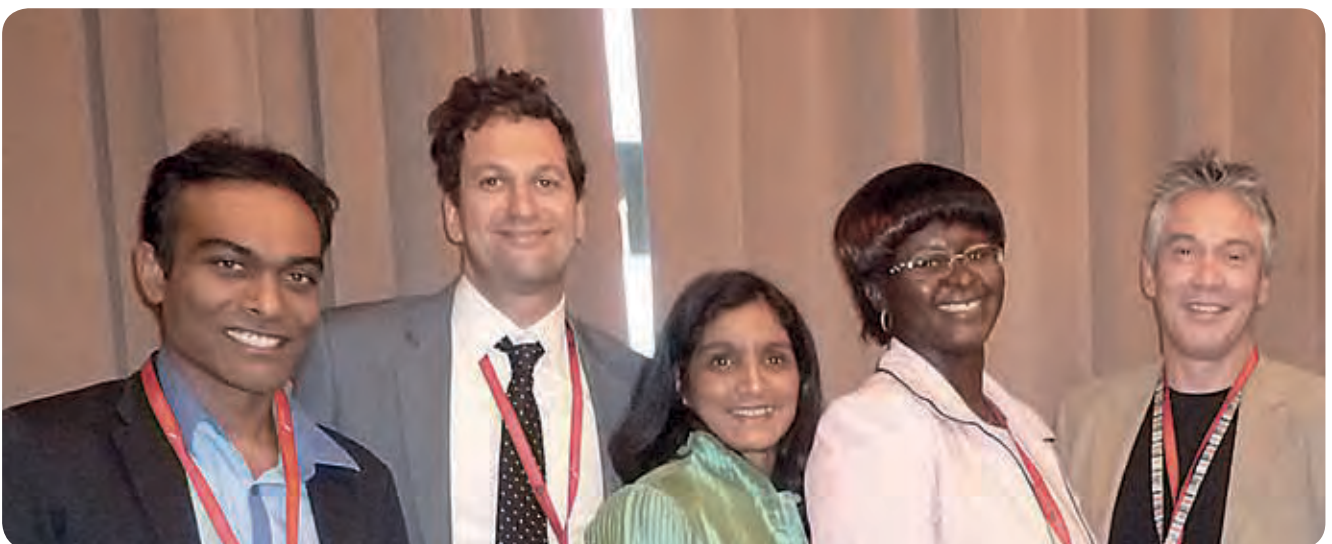
It was suggested that instead of referring to the right to nutrition, we should speak of the right to nutrients, as that is the most critical element of what we need to be addressing. The time has come for the decision-makers and the people to come together. We must learn from everyone if everyone is to benefit, and clearly the private sector has to be at the table and has much to share.



Innovative financing panel (left to right): Caitlin MacLean (Milken Institute), Chris Walker (GAIN – Micronutrient Premix Fund), CJ Jones (Independent Consultant), Joel Spicer (MI), Meera Shekar (World Bank), Niraj Shah (IFC).



Effective linkages panel (left to right): Eleni Asmare (FAOET), Stuart Gillespie (IFPRI), Klaus Kraemer (*Sight and Life*), Mesfin Teklu (WVI), Mag Gaynor (Irish Aid), Omar Dary (USAID).



Defining obligations and taking responsibility for stakeholder actions panel (left to right): Jerome Singh (UKZN), Thiago Luchesi (WVI), Purnima Mennon (IFPRI), Rachel Toku-Appiah (GMT), Martin Bloem (WFP).

This raises the potential for conflict of interest, which remains a hot topic. Two particularly striking comments were the fact that conflict of interest should center not only around the private sector but also around civil society and that the industry and the activists have to engage in a manner that is not counter-productive if we are to address malnutrition in all its forms. This is easier said than done, but unless this stumbling block is addressed, success will be limited.

A clear take-home message was that, while the law defines a minimum standard of what has to be done, ethics sets the standard of what should be done. And if we apply a human rights approach to our obligations, then we must focus on the most vulnerable, take a lifecycle approach, and ensure that we empower people – which includes providing them with valuable nutrition information so that they can make informed choices.

“While the law defines a minimum standard of what has to be done, ethics sets the standard of what should be done”

Engaging the private sector – Not renovation but novelty

In all these conversations, the elephant in the room is always about engaging the private sector. In the panel that addressed this issue, the discussion was lively, and it was stressed that the private sector has a powerful role to play in the food system and that we can neither forget this nor exclude them.

If nutrition is to unlock the potential of business, then we have to address the profit issue, and we need to entice industry to invest in improving nutrition. This might mean that we all have to be challenged and that we must have uncomfortable, even hard and painful, conversations, but ultimately we together have to deliver nutrition solutions and so must leverage the unique skills that each party brings towards a common objective.

Striking – especially when we say we have moved towards scaling up – was the comment that nutrition is one of the only sectors where the private sector has not yet been fully engaged. The example was given that even in environmental discussions, the activist and the private sector meet and discuss with a view to finding solutions. The lack of mutual trust remains the major stumbling block, and clear guidelines for engagement are urgently required.

It is only through an aligned commitment, transparency, collaboration and holding each other accountable that the trust necessary for sustaining linkages can be built. To this end, the private sector should not be viewed by the nutrition community as a homogenous group: suitable and sustainable partnerships



Attendees discuss flour fortification at the food fortification table on the exhibit floor of the conference.

specific to the individual context must be sought and strengthened. The challenge was also put to the private sector that what we need is not renovation but real novelty. We need to see success stories and share our failures so that we can learn and ultimately deliver novel nutrition solutions that both meet public health goals and allow business to operate and succeed.

“We need to see success stories and share our failures so that we can learn”

Creating and supporting leadership: Vital in ensuring cohesive and sustainable scale-up

In order to achieve our goal of improved nutrition for all, we need to think more broadly and realize how important leadership skills (and not just capacity building) are, both at the top level and the community level. Nutrition has to compete for resources, and so to be heard, we have to communicate and convince others of its importance and package nutrition in new ways, using new messages. Unless they take on leadership roles, many nutritionists are wonderfully equipped for a world that no longer exists. Five key thoughts from this panel discussion were:

1. Transformational leadership has a critical role to play in overcoming the natural resistance to change: We need individuals who are prepared to do things differently.



Novel approaches to engaging the private sector panel (left to right): Kesso Van Zutphen (Asian Football Partnership), Matt Freeman (GAIN), Ronnie Pankhurst (DSM South Africa), Inge Kauer (ATNI), Stefan Germann (WVI).



Creating and supporting leadership panel (left to right): Venkatesh Mannar (formerly MI), Anna Lartey (FAO), Noel Zagra (UNICEF), Khor Geok Lin (IMU – Malaysia), Johann Jerling (ANLP), Marc van Ameringen (GAIN), Stefan Germann (WVI).



Political will panel (left to right): Chris Osa Isokpunwu (SUN Nigeria), Anna Taylor (DFID), Martin Bloem (WFP), Joel Spicer (MI), David Pelletier (Cornell University), Marc van Ameringen (GAIN), Banda Ndiaye (Transform Nutrition Champion and MI).

2. You first have to accept that you can be a leader.
The greatest difference will be made when individuals working in nutrition lead from where they stand.
3. Nutrition leaders need to guide and mentor others to take over, otherwise we are creating an ever-widening gap.
4. Teams make programs successful and programs make countries successful, so nutrition needs to make successful teams – and that takes leadership.
5. Nutrition leadership training must lead to change agents being able to take on the complex environment in which we try to implement complex nutrition programs – and that takes commitment.

We can, and must, have nutrition champions who can help us reach our goals, but, ultimately, it is those working directly in the field of nutrition who need to take up the leadership role and must be held accountable for our actions and interventions.

“It is those working directly in the field of nutrition who need to take up the leadership role”

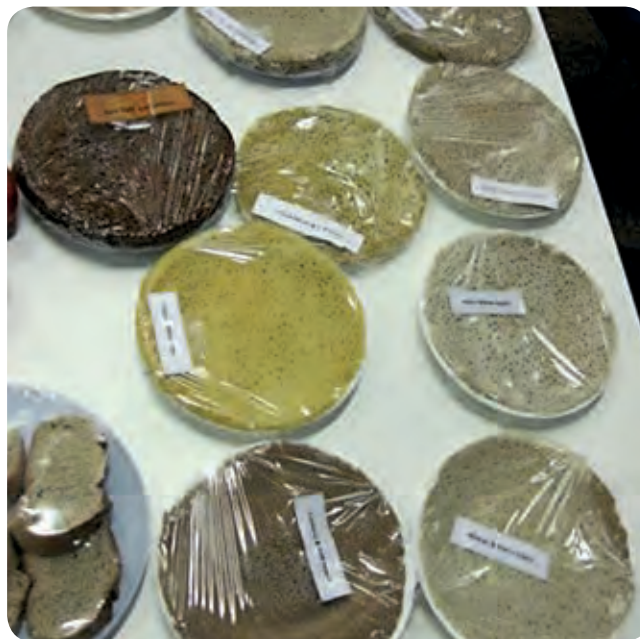
What will it take? Political will, evidence informed policy and implementation science

Nutrition has been placed high on the global agenda, but it is important that we ensure it remains there and is firmly entrenched in the post-2015 development agenda. The Global Nutrition Report, ICN2, and the link to the next Olympics give us the chance to keep the dialogue going, but we as the nutrition community need to determine the narrative and deliver it to the right people, in the right packaging at the right time.

We also need to recognize that sometimes we do not need to take the lead but rather should ensure that we are aligned with other platforms that can assist us in our goal and which might indeed contain the necessary funds! This again points to the need to build new alignments/partnerships and makes a common dialogue critical.

Policy informed by evidence is a critical element, but it must be understood as a milestone in a process and not the end in itself. Currently 97% of child health research is about discovery and efficacy and only 3% is about how to deliver. It is clear that, as we move forward, implementation science must become dominant if nutrition is to continue to take advantage of the window of opportunity before it closes.

The Micronutrient Forum 2014 Global Conference’s closing address was given by Anna Lartey, Director of Nutrition at the FAO and President of the IUNS. It summed up much of what



A display from the Ethiopian Institute of Health booth.

the thematic topic “Stakeholders and Sustainability: Elements of an Enabling Environment” had discussed: “We have a charge. A charge to keep discovering. A charge to scale up delivery. A charge to build bridges between both. We have to make it happen. We cannot continue to condemn 2 billion people because together we did not act.”

“Implementation science must become dominant if a window of opportunity is not to be missed”

Acknowledgments

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The staff of the Micronutrient Forum Secretariat receiving recognition for their hard work.
Left to right: Valerie Friesen, Sara Wuehler, Lucie Bohac and Faben Getachew (all Micronutrient Initiative).

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