SIGHT AND LIFE
Magazine 3/2007 • *Supplement*

Report of the First Meeting of the Micronutrient Forum 16–18 April 2007, Istanbul, Turkey

St. Sophia, Istanbul

Micronutrient Forum. Consequences and control of micronutrient deficiencies
Science, policy, and programs – Defining the issues

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II. About the Micronutrient Forum

The Micronutrient Forum was established in 2006 in response to the growing interest in the role of multiple micronutrients and their interactions. The Micronutrient Forum consolidates and expands upon thirty years of successful leadership by the International Vitamin A Consultative Group (IVACG) and the International Nutritional Anemia Consultative Group (INACG). The Micronutrient Forum aims to serve as a stimulus for policy-relevant science and as the internationally recognized catalyst for moving the global community towards consensus around evidence-based policies and programs that reduce micronutrient deficiencies around the globe. The Micronutrient Forum focuses on micronutrient deficiencies of public health significance, particularly vitamin A, iron, folate, iodine, and zinc.

III. Organizers

The Micronutrient Forum was co-hosted by the Micronutrient Forum Program Committee and the Local Organizing Committee of the Turkish Ministry of Health. These groups include representatives of United Nations technical agencies, multilateral agencies, universities, the private sector, and nongovernmental organizations. The Office of Health, Infectious Disease and Nutrition, Global Health Bureau, U.S. Agency for International Development, and the Turkish Ministry of Health assumed major responsibility for organizing the meeting.

Micronutrient Forum Program Committee

Dr. Alfred Sommer, Johns Hopkins Bloomberg School of Public Health, USA, Micronutrient Forum Program Committee Chair*
Dr. Frances R. Davidson, U.S. Agency for International Development, USA, Micronutrient Forum Secretary*
Dr. Lindsay Allen, U.S. Department of Agriculture, USA*
Ms. Jean Baker, The A2Z Project, USA**
Prof. Maharaj Bhan, Ministry of Science and Technology, India*
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Dr. Michael Zimmermann, Swiss Federal Institute of Technology Zürich, Switzerland

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Ms. Stephanie Carter
Dr. Suzanne S. Harris
Ms. Laurie Lindsay, Consultant
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Ms. Veronica I. Triana

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** Ex-officio member of both the Micronutrient Forum Steering and Program Committees

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V. Exhibits

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United Nations Children's Fund (UNICEF)
U.S. Agency for International Development (USAID) (MAJOR SPONSOR EXHIBIT)
U.S. Centers for Disease Control and Prevention (CDC)
World Health Organization (WHO)

VI. Acknowledgements

The success of the first Micronutrient Forum was due to contributions from many individuals and organizations. The U.S. Agency for International Development, through the A2Z (Micronutrient and Child Blindness) Project cooperative agreement with the Academy of Educational Development, and the Local Organizing Committee of the Turkish Ministry of Health were the primary organizers. The Local Organizing Committee included representatives of United Nations technical agencies, the private sector, and nongovernmental organizations in Turkey. Their hospitality was exceptional and the meeting participants enjoyed opportunities to learn about micronutrient deficiency control programs in Turkey as well as enjoyed the local sights and food.

The A2Z Project gratefully acknowledges major financial contributions from the Bill & Melinda Gates Foundation, SIGHT AND LIFE, United Nations Children's Fund (UNICEF), Unilever Food and Health Research Institute, and the Global Alliance for Improved Nutrition (GAIN). Other supporters included Danone, Kraft, BASF, The Coca-Cola Company, H.J. Heinz Company, Mars. Inc., The Micronutrient Initiative, Monsanto Company and The Procter & Gamble Company. The A2Z Project appreciates SIGHT AND LIFE's support in publishing the meeting report in this supplement and distributing it to all the meeting participants.

The Micronutrient Forum Steering Committee, chaired by Dr. Alfred Sommer, was responsible for organizing the scientific program described in this report. In addition to Dr. Sommer, the following individuals make up the steering committee – Dr. Frances R. Davidson (Micronutrient Forum Secretary), Dr. Lindsay Allen, Ms. Jean Baker, Prof. Marharaj Bhan, Dr. Omar Dary,

Dr. Bruno de Benoist, Dr. Rainer Gross (deceased), Dr. Philip Harvey, Dr. Daniel Kraushaar, Dr. Chewe Luo, Dr. Sean Lynch, Ms. Emily Wainwright, Dr. Emorn Wasantwisut, and Dr. Keith P. West, Jr. The Micronutrient Forum Steering Committee is indebted to Dr. Kenneth Brown, Dr. Serigne Diene, Dr. Gülden Pekcan, and Dr. Michael Zimmerman for their contributions as invited members of the Micronutrient Forum Program Committee.

The Micronutrient Forum extends special appreciation to the meeting rapporteurs, Dr. Christine Clewes, Dr. Marjoleine Dijkhuizen, Prof. David Thurnham, and Dr. Frank Wieringa. These individuals put in many hours of hard work to develop this report covering the meeting presentations, discussion and poster sessions. Additional thanks go to Ms. Amanda Palmer for her contributions as an editor to the report.

Without the many individuals who presented their own scientific and programmatic work in the plenary or poster sessions, the first Micronutrient Forum would not have met its objectives of sharing the latest knowledge regarding science, policy and micronutrient issues to the participants. The Micronutrient Forum Secretariat is also grateful to the chairs of the scientific sessions for their role in guiding the discussions. Finally, the meeting would not have been successful without the dedication of the meeting attendees. The Secretariat hopes that the first Micronutrient Forum provided the micronutrient community with new information and revitalized energy to continue improving and expanding micronutrient deficiency control programs.

VII. Program at a glance

Sunday, 15th April 2007	1500–1830 Registration		1830–2000 GAIN Reception
Monday, 16th April 2007	**Tuesday, 17th April 2007**	**Wednesday, 18th April 2007**	
0800 Registration/Major Sponsors Exhibits Open	0800 Registration/All Exhibits Open	0800 Registration/All Exhibits Open	
0900–1000 **Inauguration**	0830–1000 **National Successes in Micronutrient Programming**	0830–1000 **Dietary Strategies** Biofortification Fortification	
1000–1100 Poster Session and Break	1000–1100 Poster Session and Break	1000–1100 Poster Session and Break	
1100–1130 **Status of Micronutrient Programs in Turkey**	1100–1200 **Tipping Point #1: Zinc and Childhood Mortality**	1100–1140 **Dietary Strategies (continued)** Fortification at Point-of-Use	
1130–1145 **Overview of the Micronutrient Forum**	1200–1230 **Special Session: Cost Analysis as a Tool for Micronutrient Program Planning, Budgeting, Management, and Advocacy**	1140–1230 **Maternal Micronutrient Supplementation**	
1145–1230 **Taking Stock: Physiologic Public Health Implications of Population-Based Deficiencies**	1230–1400 Lunch and Poster Viewing	1230–1430 Lunch and Poster Viewing	
1230–1430 Lunch and Poster Viewing	1400–1510 **Assessment and Evaluation**	1430–1530 **Micronutrients and Infection**	
1430–1530 **Taking Stock (continued)**	1510–1600 Poster Session and Break	1630–1715 **Update on Zinc in the Treatment of Diarrhea**	
1530–1630 Poster Session and Break	1600–1640 **Iodine Deficiency: An Update on Global Progress and Monitoring**	1715–1745 **Concluding Remarks**	
1630–1700 **Taking Stock (continued)**	1640–1740 **Tipping Point #2: Newborn Dosing with High Dose Vitamin A**	1745 End of Micronutrient Forum's formal sessions	
1700 Meeting Adjourns	1700 Meeting Adjourns		
1830 **Welcome Reception**			

VIII. Program

Sunday, 15 April 2007

1830–2000	GAIN Opening Reception

Monday, 16th April 2007

0900	**Inauguration of the Micronutrient Forum** **Moderator: Dr. Alfred Sommer**
0900	Welcome Message from the Chair of the Micronutrient Forum Dr. Alfred Sommer, Dean Emeritus and Professor, Johns Hopkins Bloomberg School of Public Health
0910	Welcome Message from the Ministry of Health of Turkey Prof. Dr. Recep Akdag, Minister of Health of Turkey
0920	Welcome Message from the United Nations Children's Fund Dr. Ian Darnton-Hill, Acting Chief, Nutrition Section, Senior Adviser, Child Survival and Nutrition, UNICEF
0925	Welcome Message from the Food and Agriculture Organization of the United Nations Mr. Brian Thompson, Senior Nutrition Officer
0930	Welcome Message from the World Health Organization Dr. Denise Coitinho, Director, Nutrition for Health and Development
0935	Welcome Message from the United States Government Ms. Deborah Jones, U.S. Consul General, U.S. Consulate in Istanbul
0940	Memorial to Dr. Rainer Gross Dr. Noel Solomons, Scientific Director, Center for Studies of Sensory Impairment Aging and Metabolism
0950	SIGHT AND LIFE Anniversary Acknowledgment Dr. Alfred Sommer, Dean Emeritus and Professor, Johns Hopkins Bloomberg School of Public Health
1000	Poster Session and Break
1100	**Status of Micronutrient Programs in Turkey** Dr. M. Rifat Kose, General Director of Mother and Child Health and Family Planning, Ministry of Health of Turkey
1130	**Overview of the Micronutrient Forum** Dr. Alfred Sommer

1145	**Taking Stock: Physiologic Public Health Implications of Population-Based Deficiencies** Moderator: Dr. Ian Darnton-Hill
1145	Introduction Dr. Bruno de Benoist
1200	Vitamin A Dr. Keith P. West, Jr.
1215	Open Discussion
1230	Lunch
1430	**Taking Stock: Physiologic Public Health Implications of Population-Based Deficiencies (continued)** Moderators: Dr. Bruno de Benoist Dr. Tanju Besler
1430	Iron Dr. Rebecca Stoltzfus
1445	Open Discussion
1450	Zinc Dr. Kenneth Brown
1505	Open Discussion
1510	Iodine Dr. Michael Zimmermann
1525	Open Discussion
1530	Poster Session and Break
1630	**Taking Stock: Physiologic Public Health Implications of Population-Based Deficiencies (continued)**
1630	Multiple Micronutrients Dr. Lindsay Allen
1655	Open Discussion
1700	End of Monday's formal sessions
1830	Welcome Reception

Tuesday, 17th April 2007

0830		**National Successes in Micronutrient Programming** Moderators: Dr. Jose Mora Dr. Gulden Pekcan
0830		Overview Dr. Jose Mora
0840	**T98**	Nigeria's Universal Salt Iodization Program Success Story: The Process and Lessons Learned Dr. Dora Akunyili
0856	**T100**	Nicaragua's Integrated Anemia Control Strategy (IACS) Has Significantly Reduced Anemia in Women and Children Dr. Erick Boy
0906	**T101**	Vitamin A Supplementation for Child Survival in Niger: Maintaining Success in Adversity Dr. Noel Marie Zagre
0914	**T102**	The Challenge of Shifting from Vitamin A Supplementation (VAS) Campaign to Delivering a Package of Key Interventions during "Mother and Child Health Week" Dr. Simon Rakatonirina
0922	**T103**	The Experience of the Nepal Vitamin A Program: A Platform for Scaling-up Community-based Health Interventions Dr. Ram Shrestha
0932		Common Elements of Successful Programs Dr. Phil Harvey
1000		Poster Session and Break
1100		**Tipping point #1: Zinc and Childhood Mortality** Moderators: Dr. Olivier Fontaine Dr. Kadriye Yurdakok
1100	**T104**	Effects of Zinc Supplementation on Mortality in Children 1-48 Months of Age: A Community-based Randomized Placebo-Controlled Trial Dr. Sunil Sazawal
1115	**T105**	Impact of Daily Zinc Supplementation on Preschool Child Mortality in Southern Nepal Dr. James Tielsch
1125		Comments Dr. Juan Rivera
1135		Open Discussion
1200	**T107**	**Special Session: Cost Analysis as a Tool for Micronutrient Program Planning, Budgeting, Management, and Advocacy** Dr. Jack Fiedler

1230		Lunch
1400		**Assessment and Evaluation** Moderator: Dr. Frank Wieringa
1400		Introduction Dr. Frank Wieringa
1405	**T108**	Assessment of Iodine Status Using Dried Blood Spot Thyroglobulin: Development of Reference Material and Establishment of an International Reference Range in Iodine-Sufficient Children Dr. Michael Zimmermann
1415	**T109**	Recommendations for the Assessment of Population Zinc Status: Results of a WHO, UNICEF, IAEA, and IZiNCG Working Group Meeting Dr. Christine Hotz
1425	**T110**	Nicaragua's Integrated System for Monitoring of Nutritional Interventions (SIVIN): An Analysis of the First Three Years of Implementation Dr. Jose Mora
1435	**T111**	Vitamin A and Other Major Micronutrient Deficiencies in China Dr. Xiaoguang Yang
1445	**T117**	Six-monthly Augmented Vitamin A Supplementation from 1 to 6 Years of Age: Block Randomized Trial in One Million Children in Northern India Dr. Shally Awasthi
1455		Open Discussion
1510		Poster Session and Break
1600		**Iodine Deficiency: An Update on Global Progress and Monitoring** Moderators: Dr. Dora Akunyili Dr. Murat Erdogan
1600		New WHO Recommendations for the Prevention and Control of Iodine Deficiency in Pregnant and Lactating Women and in Children Less Than Two Years Old Dr. Bruno de Benoist
1610	**T112**	Global Progress towards Sustained Elimination of Iodine Deficiency: Lessons from Salt Iodization Programs and Monitoring Dr. Nune Mangasaryan
1620	**T113**	Assessment of Household Use of Adequately Iodized Salt in Population Surveys is Best Achieved by a Combination of Testing by Rapid Salt Test Kits and Quantitative Methods Dr. Karen Codling
1630		Open Discussion
1640		**Tipping point #2: Newborn Dosing with High Dose Vitamin A** Moderators: Dr. Shyam Thapa Dr. Yildiz Perk

1640	**T114**	Effect of 50,000 IU Vitamin A Given to Newborns and Infants in Guinea-Bissau, West-Africa Dr. Christine Stabell Benn
1655	**T115**	Efficacy of Newborn Vitamin A Supplementation in Reducing Infant Mortality in Rural Bangladesh: The JiVitA-2 Trial Dr. Rolf Klemm
1710	**T116**	Newborn Vitamin A Dosing: Policy Implications for Southern Asia and Africa Dr. Keith P. West, Jr.
1725		Open Discussion
1740		End of Tuesday's formal sessions

Wednesday, 18th April 2007

0830		**Dietary Strategies** Moderators: Dr. Emorn Wasantwisut Dr. Aziz Eksi
0830		Overview Dr. Emorn Wasantwisut
0845		**Biofortification**
0845	**W112**	Increased Vitamin A Intake and Serum Retinol Status among Young Children in Rural Mozambique Achievable Through Introduction of Orange-fleshed Sweet Potatoes Linked to Nutrition Intervention Programs Based on Group Sessions Dr. Jan Low
0855		**Fortification**
0855	**W113**	Application of NaFeEDTA Fortified Soy Sauce in Controlling Iron Deficiency in China Dr. Junshi Chen
0905		Efficacy and Effectiveness of Iron in Complementary Foods, Rice, Wheat Flour Dr. Richard Hurrell
0915	**W114**	Searching for Indicators for Designing and Assessing Impact of Folic Acid Fortification on Neural Tube Defects Reduction Dr. Omar Dary
0925	**W115**	Opportunities and Challenges for Commercial Food Fortification: A West African Example Dr. France Begin
0935		Open Discussion
1000		Poster Session and Break
1100		**Fortification at Point of Use** Moderators: Mr. Brian Thompson Dr. Gulbin Gokcay

1100	**W116**	Sprinkles for Reducing Micronutrient Deficiencies Among Children in Indonesia, Impact and Large-Scale Program Implementation Dr. Saskia de Pee
1110	**W117**	Micronutrient Sprinkles Reduce Anemia Among Children When Delivered Through an Integrated Maternal and Child Health and Nutrition (MCHN) Program in Rural Haiti Dr. Purnima Menon
1120	**W118**	Efficacy of a Fortified Complementary Food, Sprinkles and a Micronutrient Syrup to Prevent Anemia in Children Under Two Years of Age in Urban Mexico Dr. Lynnette Neufeld
1130		Open Discussion
1140		**Maternal Micronutrient Supplementation** Moderators: Dr. Lindsay Allen Dr. Ferit Saracoglu
1140	**W119**	The Effect of Maternal Multiple Micronutrient Supplementation on Fetal Loss and Infant Death in Indonesia: A Double-Blind Cluster-Randomized Trial Dr. Anuraj Shankar
1150	**W120**	Impact of Postpartum Vitamin A Supplementation on Sexual Acquisition of HIV during the Postpartum Year among Vitamin A Deficient Women in Zimbabwe Dr. Jean Humphrey
1200	**W121**	Effects of Maternal Vitamin A or Beta-Carotene Supplementation on Maternal and Infant Mortality in Rural Bangladesh: The JiVitA-1 Trial Dr. Parul Christian
1210		Consultation on Maternal Micronutrients Dr. Barrie Margetts
1220		Open Discussion
1230		Lunch
1430		**Micronutrients and Infection** Moderators: Dr. Marjoleine Dijkhuizen Dr. Bahattin Tunc
1430		Nutrients and Infection Dr. Charles Stephensen
1445	**W122**	Conclusions of Iron-Malaria workshop Dr. Sean Lynch
1500		Report from Young Investigator Workshop: Defining Research Priorities for Anemia Control in Malarious Areas Dr. Sharon Cox
1515		Open Discussion
1530		Poster Session and Break

1630		**Update on Zinc in the Treatment of Diarrhea** Moderators: Prof. Eng Huot Dr. Songul Yalcin
1630		Results of Effectiveness Study of Zinc in the Treatment of Diarrhea in Pakistan Dr. Zulfiqar Bhutta (presented by Dr. Robert Black)
1640	**W123**	Scaling up Programs Including Zinc in the Treatment of Diarrhea Dr. Robert Black
1655	**W124**	Placebo-controlled, Dose-Response Trial to Assess the Efficacy of Zinc Supplementation, with or without Copper, on Plasma Zinc Concentrations, Morbidity and Growth of Young Ecuadorian Children Ms. Sara Wuehler
1700		Open Discussion
1715		Concluding Remarks Moderator: Dr. Alfred Sommer
1715		Closing Address Dr. Meera Shekar
1745		End of Micronutrient Forum's formal sessions

IX. Report

Consequences and control of micronutrient deficiencies:

Science, policy, and programs – Defining the issues

The first meeting of the Micronutrient Forum opened in Istanbul on April 16, 2007. This was a historic day for the field of micronutrients as this was the first meeting to consider the major micronutrient deficiencies of known public health significance together. The Micronutrient Forum emerged in response to the recognition that micronutrient deficiencies rarely occur in isolation, and to a growing interest in the use of multiple micronutrients in public health programs, particularly vitamin A, iron, folate, iodine, and zinc.

The Micronutrient Forum consolidates and expands upon thirty years of successful leadership by the International Vitamin A Consultative Group (IVACG) and the International Nutritional Anemia Consultative Group (INACG). Over the last decade, knowledge of the interactions among Vitamin A and iron, as well as other micronutrients such as zinc and iodine, became increasingly a focus of both scientific investigation and program design. Hence it was subsequently agreed that all relevant micronutrient issues would be discussed at a single meeting, with contributions from both IVACG and INACG, the International Zinc Consultative Group (IZiNCG), and the International Council for the Control of Iodine Deficiency Disorders (ICCIDD), all of which agreed to contribute to a single program.

Day 1 – 16th April 2007

Inauguration of the Micronutrient Forum

Dr. Alfred Sommer, Professor Dean Emeritus of the Johns Hopkins Bloomberg School of Public Health and Chair of the Micronutrient Forum Steering Committee, opened the meeting by welcoming the delegates from over 60 countries to the beautiful city of Istanbul. He suggested the Micronutrient Forum would provide an opportunity for the delegates to think about all micronutrients in a more effective and efficient way. Dr. Sommer also took this opportunity to thank sponsors from the public and private sectors, the local organizing committee in Turkey, and the Ministry of Health (MoH), Republic of Turkey, which had arranged a special evening visit to the Aya Sofia, the Blue Mosque, and a reception at the Cistern – which all delegates were eagerly anticipating.

Prof. Dr. Necdet Ünüvar, Under-Secretary of the MoH, Republic of Turkey, added his welcome on behalf of the Minister of Health, Prof. Dr. Recep Akdag, and expressed the Ministry's pride in hosting the first meeting of the Micronutrient Forum. Dr. Ünüvar stated that the MoH was aware of the importance of nutrition to health and, as an endocrinologist, he had noted the increase and the importance of scientific research in the field of nutrition around the world. He reminded delegates that the importance of nutrition was recognized as far back as 2,400 BC, with the quotation, "Let nutrients be your doctor and your doctor be nutrition." He concluded his remarks by calling on delegates to "work together for health."

Representatives from the United Nations Children's Fund (UNICEF), the Food and Agriculture Organization of the United Nations (FAO), the World Health Organization (WHO), and the American Consulate in Turkey joined Dr. Sommer and Dr. Ünüvar in welcoming delegates to the first meeting of the Micronutrient Forum. Dr. Ian Darnton-Hill, Acting Chief of Nutrition of UNICEF, remarked that addressing all micronutrients under the umbrella of the Micronutrient Forum reflected current thinking in public health programs. Breaking down the walls between individual micronutrient interventions would help to foster the inclusion of other public health initiatives, such as breastfeeding promotion, deworming, and immunization, providing a complete package of critical interventions needed to attain the Millennium Development Goal (MDG) for child survival.

Dr. Brian Thompson, Director of the Nutrition and Consumer Protection Division of FAO, recounted the significant progress achieved over the last 40–50 years in terms of food supply, nutrition, and health, but underscored that over 100 million people worldwide are still affected by iodine deficiency disorders (IDD), 40 million by VAD, and 2 billion by anemia. He expressed his hope that the Micronutrient Forum

would strengthen linkages between national and international agencies, enabling the global community to achieve the targeted 50% reduction in undernutrition by 2015.

Dr. Denise Coitinho, Director of the Department of Nutrition for Health and Development of WHO, thanked the MoH, the Micronutrient Forum Secretariat, the local organizing committee, the United States Agency for International Development (USAID), UNICEF, SIGHT AND LIFE, the Gates Foundation, and the Global Alliance for Improved Nutrition (GAIN) for their contributions on behalf of the WHO. Dr. Coitinho stressed the need for strong collaboration between all partners to control micronutrient deficiencies, and the importance of strategic communications. She expressed how speaking with one voice could create a winning environment, and promote successful and sustainable development.

Ms. Deborah Jones, (US Consul General of the US Consulate in Istanbul) concluded the introductory remarks, acknowledging the hospitality of the Turkish people on behalf of the US government. She noted that USAID has supported work on the problems of micronutrient deficiencies for over 30 years. She commended the organizers and delegates of the Micronutrient Forum for their efforts in drawing attention to and addressing these problems, and underscored the critical importance of these efforts to maternal and child health.

Tribute to Dr. Rainer Gross (1945–2006), former UNICEF Chief of Nutrition, by Dr. Noel Solomons

After the formal introductions in the inaugural session, Dr. Noel Solomons, of the Center for Studies of Sensory Impairment, Aging and Metabolism (CeSSIAM), asked delegates to observe a moment of silence in memory of Dr. Rainer Gross, who recently passed away. Dr. Gross was an innovative thinker who specialized in a number of areas, including the delivery of micronutrients, and access to education, health care, and economic opportunity. He would not let the world forget about the ongoing 'silent emergency' of undernutrition.

Dr. Gross believed it was important to consider micronutrients deficiencies holistically. At the time of the IVACG meeting in Vietnam in 2001, Dr. Gross was in Peru, organizing a workshop in Lima on MMNs in the lifecycle. He was involved in the International Research on Infant Supplementation (IRIS) trial, which was an attempt to develop the evidence base for policy development in the area of infant multiple micronutrient supplementation. The trial was based on the fact that infant diets in developing countries are often deficient in MMNs rather than in single nutrients, an idea that increasingly came to be recognized during the 1990s. The concept of a "foodlet" – a crushable hybrid between a tablet and food, which is either eaten alone or with other foods – emerged at the Lima meeting. The foodlet contained the recommended daily allowance of 13 micronutrients considered most likely to be inadequate in infant diets, and was successfully tested in Indonesia, Peru, South Africa, and Vietnam. Thus, Dr. Gross was one of the people whose work and vision have contributed to this historic meeting in Istanbul, and it was fitting that his contributions were remembered.

20 years of humanitarian support from SIGHT AND LIFE

The last item in the inaugural session was the presentation of an award, by Dr. Sommer on behalf of the Micronutrient Forum, to SIGHT AND LIFE for its important contributions and partnership in the fight against micronutrient deficiencies. Dr. Klaus Kraemer, Director of SIGHT AND LIFE, accepted a plaque in recognition of 20 years of support by SIGHT AND LIFE to the field of vitamin A and, more recently, all micronutrients. Dr. Kraemer thanked the Micronutrient Forum for the award and all others who had contributed to the success of SIGHT AND LIFE. He called attention to SIGHT AND LIFE's most recent accomplishment: the publication of a new book, *Nutritional Anemia*, a summary of which was distributed at the meeting.

Status of micronutrient programs in Turkey

Dr. Mehmet Rifat Köse, of the MoH, Turkey, provided delegates with an overview of the health and nutrition situation in Turkey, a country with a population of approximately 70 million. Over the past 20 to 30 years, Turkey achieved notable declines in maternal and infant mortality. The maternal mortality ratio (MMR) fell from 208 deaths per 100,000 live births in 1974 to 28.5 per 100,000 live births in 2006. Infant mortality similarly declined from 77.7 in 1988 to 21.7

in 2007. Improvements have also been reported in the area of child nutrition: the proportion of children falling below two standard deviations (SD) decreased from 20.5% in 1983 to 12.2% in 2003 for height-for-age, and from 10.4% in 1983 to 3.9% in 2003 for weight-for-age.

The main goal of the MoH is "to establish healthy nutrition as a way of life through increasing nutritional awareness among the entire community." Exclusive breastfeeding is recognized as a critical first step toward preventing micronutrient deficiencies. Currently, only 21% of Turkish children are exclusively breastfed for the first six months of life. The MoH aims to increase this to 35% by the end of 2008, and to 70% by the end of 2013. A total of 546 Turkish hospitals, accounting for approximately 90% of hospital-based deliveries, have been designated baby-friendly hospitals. Hospitals in only 24 out of 91 provinces are not yet certified. By the end of 2008, the MoH expects that 95% of hospital deliveries will take place in baby-friendly hospitals.

One of the most important nutritional problems in Turkey is iron deficiency anemia (IDA). Although rates vary widely, prevalence reaches approximately 50% in many important population subgroups, including children and women of reproductive age. Turkey employs several strategies to prevent and control iron deficiency (ID). Since 2004, the MoH has promoted free screening and supplementation for infants. Coverage is currently at 73%, with a target of 80% by the end of 2008. Supplements are also available for pregnant women. As is critical for any nutritional intervention, the control of infectious diseases and health education are cornerstones of the MoH strategy. Although certain fortified foods are already available, the universal fortification of flour with iron is expected by the end of 2013.

Although Turkey is a sunny country, vitamin D deficiency and its consequences are a public health concern. Rickets, a clinical sign of severe deficiency commonly found in infants and young children, has been reported in several regions of the country, with prevalence rates ranging from 2% to 19%. Risk factors include inadequate nutrition and lifestyles of pregnant women, failure to meet the increased need of vitamin D for growth, incorrect behaviors and attitudes of mothers to care for their children, and urban air pollution. The Turkish government is addressing these issues by educating pregnant women about calcium and vitamin D deficiencies and providing supplements to infants. As of the end of 2006, nearly two million infants had received free vitamin D supplements. The MoH expects to reach its target coverage of 80% by the end of 2008.

A program to address IDD was started in 1994. Salt iodization was the main thrust of this effort. A logo bearing the slogan "Iodized Salt, Clever Salt" was adopted, in combination with educational activities to inform salt manufacturers and the public about the importance of iodized salt. A law mandating and enforcing the iodization of table salt was passed in 2005. To date, 27 salt producers have been given iodizing machines and potassium iodate to ensure the iodization of all table salt in the country. Monitoring, evaluation and supervision activities are currently carried out by the Ministry of Agriculture and Rural Affairs. According to the most recent data, over 99% of the salt produced in Turkey is iodized, and 78% of the population uses adequately iodized salt. The government hopes to achieve 95% coverage by 2013.

Future plans of the MoH include zinc supplementation, folic acid supplementation, fortification of flour with iron, national health and nutrition surveys, and updating of the Food and Nutrition Action plan. Dr. Köse concluded by saying that solving micronutrient problems requires more than just the MoH – it also requires close integration with the private sector, and he appealed to the audience "to join forces to eliminate micronutrient deficiencies in the world."

Overview of the Micronutrient Forum

Dr. Sommer congratulated the MoH on its accomplishments. He went on to describe the origins of the Micronutrient Forum, recounting how a series of meetings that began with IVACG were later followed by other micronutrient-interest groups, namely INACG and IZiNCG. The overlapping interests of many of the participants quickly became obvious. The Micronutrient Forum would now bring all groups interested in micronutrient deficiencies together to share new, cutting-edge information in the areas of clinical science, policy, and programs, and to suggest integrated solutions. Dr. Sommer noted that, in addition to the main Micronutrient Forum meeting, over 25 satellite meetings were taking place during the week, allowing a fruitful exchange of ideas.

A major focus of the Micronutrient Forum would be to carry out periodic critical reviews of clinical and programmatic knowledge, similar to those summarized in

the Bellagio Brief (1992) and the Annecy Accords (2003) for VAD control. Rigorous reviews would, from time to time, reveal that the accumulation of evidence had reached a "tipping point" and needed to provoke a change in public health policy. The present Micronutrient Forum program would address two such tipping points. The first would consider all of the evidence, to date, regarding newborn dosing with vitamin A, including findings from the most recent trials in Guinea Bissau and Bangladesh. Universal zinc supplementation would be the focus of the second tipping point. The presentations on both of these issues were intended to stimulate conversation among all actors, a first step in motivating changes to public health policy. In the time between this first meeting and the next in 2009, the Micronutrient Forum intends to undertake its next rigorous assessment, this time focusing on programmatic knowledge related to cost and design effectiveness of deficiency control efforts. As with the events planned for the next few days, Dr. Sommer anticipated that discussions on the planned review were likely to be complemented by late-breaking clinical, policy, and program findings and experiences.

Taking stock: Physiological public health implications of population-based deficiencies

The remainder of the day was devoted to keynote speakers whose roles were to update the audience on the state of knowledge related to vitamin A, iron, zinc, and iodine, with the final speaker of the day addressing MMNs.

Integrating biological and epidemiological research in public health nutrition

In recent years, new scientific knowledge has accumulated, allowing us to better define the public health significance of major micronutrient deficiencies, and to design strategies to address them that are better adapted, more effective, and safer. The main sources of information come from epidemiology and physiology, which are complementary and should contribute equally to the development of any deficiency control strategy. In practice, this is not always the case as epidemiological data may indicate a need for public health action even when biological mechanisms are not known. In his presentation, Dr. Bruno de Benoist, of WHO, emphasized the importance of strengthening both the biological and epidemiological research base, and presented a summary of the essential strategic issues outlined in recent WHO Technical Consultations dealing with iron and iodine.

Assessing the iron status of populations (2004)

The participants of the first Technical Consultation reviewed the indicators available to assess iron status in populations and selected the best ones to evaluate the impact of iron interventions on iron status. The performance of the selected indicators was assessed using data from 10 double-blind randomized trials in eight countries where iron was provided as supplements or fortified food.

Hemoglobin is the most widely used indicator, but is not specific. The more specific indicators have limitations and need to be used in combination with others. There is no agreement on thresholds to identify deficiency and assess severity. In addition, serum ferritin behaves like an acute phase protein (APP) and concentrations increase in the presence of inflammation. It was concluded that the performance of the indicators and their interpretation need to be further validated. As there is no consensus on the best indicators for assessing iron status, it is difficult to interpret and compare data across populations. However, the reviewers recommended the use of hemoglobin, the soluble transferrin receptor (sTfR), and serum ferritin to assess the prevalence and severity of ID in populations. Hemoglobin and serum ferritin were recommended for use in impact evaluations.

Future work would be necessary to validate proposed thresholds for serum ferritin and sTfR, and produce international reference material to standardize sTfR assays. The definition and validation of thresholds for all indicators are needed for infants and children aged 6–24 months. The performance of recommended indicators with regard to measuring changes in body iron stores would also need to be more fully assessed. The Technical Consultation participants further recommended a comprehensive review of existing data on APPs that might reveal how best to interpret serum ferritin data during infection. Finally, the group called attention to the need for field-friendly methods to collect and analyze serum ferritin, sTfR, and APP.

Malaria and iron

Recent reports, from a large-scale supplementation trial of iron-folic acid, zinc, or a combination of the

two compared with a placebo have called attention to the potentially dangerous impact of iron, folic acid supplementation in malaria-endemic areas. This trial, conducted on the island of Pemba, Zanzibar (and described in more detail later in the program), reported an increased risk of hospitalization and mortality among infants and children in the iron-folic acid treatment arm. Upon review by the study's Data Safety and Monitoring Board, iron-folic acid supplementation was ceased, and those infants and children reassigned to supplementation with either zinc or placebo.

In response to these findings, WHO convened a Technical Consultation to review the scientific evidence regarding the safety and efficacy of administering iron and folic acid to children under two years of age in malaria-endemic areas. The biological mechanisms for the observed adverse events are not well understood. A primary concern is that folic acid included in micronutrient supplements may have interfered with antifolate antimalarial medications, and participants stressed that folic acid should not be included in iron supplements delivered to children in malarious areas. Questions were also raised regarding the impact of a large oral dose of iron on the immune system, including whether excessive free iron might cause oxidative damage or have a detrimental impact on gut flora. Additional research in this field is needed to understand the interactions between supplemental iron and inflammation, the potential role of co-morbidities in these observed adverse effects, and the risks of iron supplementation in other infections. Furthermore, it is not known whether adverse events are limited to supplementation alone, or whether iron in the form of a fortificant might also be dangerous.

The participants of the Technical Consultation simultaneously emphasized the critical importance of controlling iron deficiency (ID) in children under two years of age. At this time, it was suggested that ID control focuses on a combination of adequate case management of infectious diseases, improving iron stores at birth by delaying cord clamping, and fortification of complementary foods. With regard to supplementation, oral iron therapy should be targeted to children in areas where ID is detected or those who have clinical symptoms of severe anemia. Exceptions to this would be small-for-gestational-age (SGA) and low-birthweight (LBW) infants, who need additional iron to supplement their low stores at the time of birth and therefore should receive therapy regardless of area prevalence or the presence of severe anemia. Further work is needed to develop affordable and field-friendly tools for ID screening of young children.

Control of iodine deficiency in pregnant and lactating women, and children under two years of age

A full discussion on this topic can be found in the report of the presentation by Dr. de Benoist on Day Two.

Vitamin A: Public health implications of deficiency and prevention

Dr. Keith West, of the Johns Hopkins Bloomberg School of Public Health, began his discussion by illustrating the peri-equatorial nature of VAD, a problem that may be considered to be of public health importance in areas where any of the clinical eye signs of deficiency exceed WHO prevalence cutoffs – e.g., where the prevalence of Bitot's spots exceeds 0.5% among young children, or serum retinol concentrations fall below 0.7 µmol/L among more than 15% of the at-risk population. A review published by Dr. West in 2002 estimated that 25% of children under five years of age worldwide are affected by VAD, with the highest prevalence rates and burden concentrated on the Indian subcontinent and in parts of Africa. Surveys conducted since then continue to underscore the magnitude of VAD in young children. Deficiency is also a public health problem among pregnant women worldwide: approximately 18% of women have low serum retinol concentrations (<1.05 µmol/L) during pregnancy, and 5.8% suffer from night blindness, a sign of moderate to severe VAD.

The consequences of VAD are best described using a hierarchical model. At the base of the VAD pyramid is chronic dietary deficiency of vitamin A. Over time, if this deficiency is not addressed, tissue stores become depleted and plasma concentrations of the vitamin decline. Although deficiency is not yet visible, it affects metabolic function and causes systemic alterations to immune function, hematopoiesis, and growth. At the top of the pyramid, deficiency is at its most severe and xerophthalmia becomes clinically apparent. Dr. Sommer and colleagues first called attention to the public health importance of chronic VAD in the 1980s. Based on observational research in Indonesia, they reported a dose-response relationship between the ocular symptoms of xerophthalmia and child mortality. During the next decade, a series of large-scale community trials of vitamin A supplementation (VAS) and fortification confirmed that ensuring adequate vitamin A intake among young children could have a dramatic impact on their survival. The results of several meta-analyses showing a 30% reduction in under-five mortality and considerable advocacy have led to the wide

adoption of VAS as a child survival strategy in more than 70 countries.

The optimal schedule for VAS, particularly during infancy and pregnancy, has not yet been resolved. Supplementation of infants below one month of age with 50,000 international units (IU) and those aged one to six months with 100,000 IU had no effect on mortality in Nepal. A multi-center trial conducted in Ghana, Peru and India also found no effect of supplementation with 25,000 IU at the time of the 6-, 10-, and 14-week Expanded Programme on Immunization (EPI) contacts. A dose of 50,000 IU provided at the time of birth reduced infant mortality by 64% in Indonesia and 23% in South India; however, a similar dosing schedule employed by the Zimbabwe Vitamin A for Mothers and Babies (ZVITAMBO) trial in Zimbabwe had no impact on infant mortality. Among pregnant women, results from Nepal suggest that small weekly doses of vitamin A or β-carotene can decrease pregnancy-related mortality by approximately 40%. Results of the recent JiVitA trials addressing both antenatal and neonatal supplementation in Bangladesh as well as findings of a neonatal dosing trial from Guinea Bissau are discussed in the last session of Day 2.

Lastly, Dr. West discussed the effects of the recent changes to bioconversion factors for the pro-vitamin A carotenoids. For β-carotene, the conversion to retinol, previously calculated to be 6:1, has been changed to 12:1. The ratio of 24:1 is now applied to other pro-vitamin A carotenoids. It should be noted that the conversion of carotenoids also depends on the food matrix in which the carotenoids are consumed. Using the updated conversion factors, the FAO has revised its estimates of vitamin A available in the food supply. By definition, the amount of fruit and vegetable food required to meet the Recommended Dietary Allowance (RDA) has now doubled. Thus, a child aged 1–3 years requiring 300 mg retinol activity equivalent (RAE)/day needs to consume ~90 g of vegetables and fruits to meet the RDA. The revised conversion estimates also improve our understanding of the epidemiology of deficiency in areas previously believed to have adequate food sources of vitamin A.

Dr. West summarized his discussion by underscoring that VAD remains a major public health problem among children and women of reproductive age. Both vitamin A supplementation and fortification have been proven to reduce child mortality. Recent evidence suggests that newborn dosing is very likely to be similarly efficacious in reducing infant mortality, and that low-dose supplementation of pregnant women may reduce mortality related to pregnancy. While improving diets is always a major public health goal, dietary diversification alone is unlikely to sustain adequate vitamin A status. Thus, supplementation is likely to remain the mainstay of VAD prevention and control for the foreseeable future. Dr. West also drew attention to major new initiatives, including the release at this meeting of a UNICEF progress report on VAS, planned revisions to WHO supplementation guidelines, and an upcoming consultation on indicators of vitamin A status.

Taking stock on iron

Dr. Rebecca Stoltzfus, of Cornell University, outlined the importance of ID, which ranks sixth in the disease-control priorities in the developing world. Anemia during pregnancy is strongly linked to maternal and perinatal mortality, and the risk relationship is continuous, not just related to severe anemia. In a recent review by Walker and colleagues published in The Lancet (2007), ID was shown to be one of the four key factors preventing children in developing countries from

Table 1: Primary outcomes for iron-folic acid supplementation in Nepal and Zanzibar trials

Study	Outcome	Placebo rate: Events/ 1,000 child-years	RR (95% CI)
Zanzibar-main	Mortality	15.2	1.15 (0.93 - 1.41)
Zanzibar-main	Hospitalization or mortality	112.5	1.12 (1.02 - 1.23)
Nepal	Mortality	11.7	1.03 (0.78 - 1.37)
Zanzibar-sub-study*	Mortality	11.6*	0.58 (0.19 - 1.72)
Zanzibar-sub-study*	Hospitalization or mortality	85.5	0.75 (0.48 - 1.17)

* Children in the sub-study had more access to medical care and malaria treatment than was available in the overall study

attaining their developmental potential. Likewise, in the Copenhagen Consensus (2006), development economists suggested that benefits from iron intervention ranked highly as a development investment because the correction of ID increases the productivity of workers, both in heavy (aerobic) labor and in light factory work.

The most important question concerning ID control is how to intervene in malaria-endemic areas. **Table 1** shows the increased risk of mortality or hospitalization that occurred in Pemba, Zanzibar, following iron-folic acid supplementation. The increased risk of adverse events reported in the iron-folic acid treatment group of this trial is likely to have a significant impact on iron intervention strategies in regions where malaria is prevalent, and might significantly handicap both program implementation and further research. To date, the main cause of the ill effects has not been determined, although many researchers believe iron is the factor responsible. However, it is unclear whether ID is protective in malarial areas. Drawing on data from the trial's sub-study, Dr. Stoltzfus illustrated that, among children who had poor iron status at baseline, those in the placebo group were twice as likely to be sent to hospital or die compared to those in the iron-folic acid treated control group. However, the children in this sub-study had more access to medical care that may also have influenced their outcome. More research is needed on iron intervention in malaria-endemic areas to identify the cause of the adverse effects and ways of overcoming them.

In the final part of her talk, Dr. Stoltzfus suggested a framework for ID control. Where malaria is endemic and access to treatment is unreliable, the introduction or use of fortified infant foods should be prioritized. Children identified as being iron deficient (for example based on Pemba results, zinc protophorphyrin, or ZPP > 80 mmol/mol hemoglobin) should continue to be treated with iron tablets, syrups, or Sprinkles. To make pregnancy safer and improve neonatal survival, women should continue to receive iron-folic acid supplements, combined with deworming where needed. Furthermore, cord clamping should be delayed by two minutes to ensure maximum transfer of iron to the newborn. Universal supplementation with tablets, syrups, or Sprinkles to young children at high risk of severe malaria should be avoided. However, a question from the floor suggested that, until the measurement of ZPP was feasible and affordable in field settings, or other field-appropriate indicators of iron status can be made available, any public health recommendations on targeted treatment of iron-deficient children may be premature.

Current knowledge of zinc nutrition and gaps in information needed for scaling up zinc intervention programs

Dr. Kenneth Brown, of the University of California at Davis, provided an overview of recent work to identify the best indicators of zinc status (refer to www.izincg.org), and described recent work on the use of zinc supplements or household fortification to promote growth in young children.

A working group convened by WHO, UNICEF, the International Atomic Energy Association (IAEA), and IZiNCG (described more fully in the proceedings from Day 3) concluded that serum zinc concentrations are still the best biochemical indicator of zinc deficiency at the population level. Dietary assessment is also a useful tool to identify the risk of inadequate zinc intake, and the rate of stunting among children under five years of age can be used as a proxy for zinc status.

While serum zinc and stunting may be the best indicators currently available to characterize the zinc status of populations, Dr. Brown noted that a series of efficacy trials involving MMN-fortified foods containing zinc failed to demonstrate any impact on serum zinc or growth in young children. However, there is one exception where an additional 7.8 mg of zinc improved height- and weight-for-age. Point-of-use fortificants containing zinc have also had minimal effect on serum zinc and growth. In contrast, the use of zinc-fortified foods supplying 2.6 to 5 mg zinc/day to schoolchildren all increased serum zinc concentrations. Dr. Brown suggested that the intake of dietary zinc could be improved by enhancing the zinc content of foods, or by stimulating zinc absorption via exclusive breastfeeding, appropriate complementary feeding, use of animal-source foods, food processing to reduce dietary phytate content, and agricultural interventions.

Data regarding zinc supplementation and diarrhea are more consistent than effects on serum zinc. Twelve studies have looked at the effect of zinc supplementation on the duration of acute diarrhea, and analysis of the pooled data suggests that there is ~25% reduction in the duration of diarrhea. WHO and UNICEF have issued a joint statement recommending zinc in the treatment of diarrhea: Twice the age-specific RDA of zinc per day (10–20 mg) for 10–14 days should be distributed with oral rehydration solution (ORS). Progress in the scale-up of this new policy was addressed by Dr. Robert Black on Day 3.

Dr. Brown described an ongoing meta-analysis of zinc supplementation studies that was in progress. Using PubMed and other sources, IZiNCG found 1,622 potential articles, among which 53 were randomized controlled trials (RCTs) including 75 group-wise comparisons. Some preliminary results indicate there is:

– a consistent increase in serum zinc concentration following zinc supplementation (0.60 µmol/L, 95% CI 0.43, 0.76);
– a significant reduction in diarrhea incidence, which is greater in older children (-0.22, 95% CI -0.31, -0.12);
– a positive effect on linear growth, explained by impact among selected populations only; and
– no effect of zinc supplementation on changes in hemoglobin concentration, regardless of whether iron is provided concurrently.

In his summary, Dr. Brown called attention to the need for population-level assessments of zinc status to better understand the epidemiology of deficiency. More information is also needed on the efficacy of dietary interventions to improve the zinc nutrition of preschool children. In the context of the first meeting of the Micronutrient Forum, Dr. Brown welcomed the experiences and lessons learned from interventions in other areas that may be relevant in focusing and scaling-up of zinc interventions.

Taking stock on iodine

Iodine deficiency is the single most important preventable cause of mental retardation worldwide. Dr. Michael Zimmermann, of the Swiss Federal Institute of Technology (ETH), Zürich, reported that despite significant global progress, one third of the world's population is still affected by IDD, including nearly 300 million schoolchildren. Although pockets of severe iodine deficiency probably still exist, Dr. Zimmermann noted that there have been no recent reports of national median urinary iodine (UI) concentrations less than 20 µg/L, suggesting that most of the current iodine deficiency burden is of mild-to-moderate severity.

Three measures – UI, goiter rate, and serum thyrotropin (TSH) – are recommended for the assessment of iodine nutrition in populations, but each has limitations. UI is an indicator of recent iodine intake, but not of thyroid function. The goiter rate is imperfect because thyroid size decreases slowly after iodine repletion, thus the presence of goiters may remain high for several years after improvement of iodine intake. TSH is a sensitive measure of iodine status, but only in the newborn period. Dr. Zimmermann called attention to the report of a recent WHO Technical Consultation on this topic, presented on Day 2

Iodine deficiency during pregnancy and lactation

Iodine requirements are increased by 40–50% during pregnancy and, in areas of iodine deficiency, repeated pregnancies are a major goitrogenic stimulus. WHO has established a recommended intake of 250 µg/day for pregnant and lactating women (an excess intake is > 500 µg/day), and 90 µg/day for children under two years of age (excess intake > 180 µg/day) (WHO 2007).

Table 2 illustrates the use of median UI to categorize the iodine intake in three population groups. Meeting

Table 2: Urinary iodine categorizing iodine intake of pregnant and lactating women, and children under two years of age

Population	Median UI (µg/L)	Category of iodine intake
Pregnant women	< 150	Insufficient
	150 – 249	Adequate
	250 – 499	More than adequate
	≥ 500	Excessive
Lactating women	< 100	Insufficient
	≥ 100	Adequate
Children aged <2 years	< 100	Insufficient
	≥ 100	Adequate

these requirements is critical, as the developing fetus is particularly vulnerable to iodine deficiency. In iodine-sufficient countries, median UI is generally 150 µg/L, whether the dietary source is from universal salt iodization (USI) or other dietary sources. Longitudinal studies, using ultrasound in iodine-sufficient countries, have shown there is no increase in thyroid volume during pregnancy, but in countries with mild-moderate iodine deficiency, thyroid volume increases 15–31% during pregnancy.

Dr. Zimmermann then addressed the issue of iodine supplementation during pregnancy in areas of mild-to-moderate deficiency. Data from approximately 500 mildly to moderately deficient women were identified from RCTs carried out in Europe over the past decade. These studies showed no predictable dose-response to supplements (100–250 µg/d), although doses 150 µg/d may have been more efficacious, based on changes in maternal UI and thyroid volume. There were no reports of aggravated maternal thyroid autoimmunity or postpartum thyroid dysfunction, and only one study reported an increase in infant TSH, indicating the safety of supplements delivered during pregnancy. While supplementation reduced thyroid volume and thyroglobulin concentrations, there was little impact on total or free thyroid hormones, and no information is available on long-term clinical outcomes for the mother or her infant.

Iodine deficiency, child growth and development

Data from cross-sectional studies on iodine intake and child growth are generally positive, with most studies finding modest correlations. In five Asian countries, household access to iodized salt was found to predict increased weight-for-age z-scores (WAZ) and mid-upper arm circumference (MUAC) in infancy. Increases in serum concentrations of insulin growth factor (IGF-1) and other somatic indicators have been illustrated in three more recent studies involving iodine-replete schoolchildren. RCTs in Bolivia, Malaysia, Benin, and Bangladesh have found no clear benefits on cognition after the provision of iodized oil. However, Dr. Zimmermann reported findings from a recent trial that randomized approximately 300 moderately deficient (median UI 50 µg/L) children aged 10–12 years to receive either 400 mg of iodine or a placebo. Children receiving the supplement showed improved performance on four out of seven cognitive and motor tests, with an overall 2–3 point increase in intelligence quotient (IQ).

Salt iodization

Two-thirds of the five billion people living in countries affected by IDD now have access to iodized salt, for a global coverage of approximately 70%. The challenge now is to reach the remaining 30% of households in under-performing countries. Iodized oil or potassium iodide tablets are a useful complement to USI, especially in emergency settings or conflict regions. Iodine excess is occurring more frequently, particularly when USI levels are too high or are poorly monitored. Acute increases in iodine intake increase the risk of iodine-induced hyperthyroidism, mainly in older adults with nodular goiter. However, one study in China reported increased rates of subclinical hypothyroidism and autoimmune thyroiditis even in adults with "slightly" higher iodine intakes (median UI 240 µg/L).

Dr. Zimmermann concluded his talk by stressing the continued importance of salt iodization as the most cost-effective means to ensure adequate iodine nutrition among all population subgroups.

Taking stock: Physiological public health implications of population-based interventions for MMN deficiencies

Dr. Lindsay Allen, of the Western Human Nutrition Research Center, Agricultural Research Service and US Department of Agriculture (ARS/USDA), reported the results of reviews to examine the efficacy of MMNs, delivered as supplements or in fortification programs, for various outcomes in pregnant women and young children.

Child MMN supplementation and fortification

Dr. Allen began her talk by addressing the evidence for an impact on child growth, morbidity, and blood biomarkers. A systematic search revealed 13 studies that compared daily versus weekly supplements, and had both placebo and iron (Fe) controls. Seven delivered the MMNs as supplements or liquids (i.e. a negligible number used cereal), and six used fortified versus unfortified food. In terms of child growth, effect sizes were small (length = 0.25 for supplements, 0.18 for fortified food; and weight = 0.26 for supplements, 0.15 for fortified food) but statistically significant due to the large study population. There was little evidence of larger effects in younger children and it was not clear if stunted children responded more. Only seven studies

considered the effects of MMNs on child morbidity. Two showed a decrease in the prevalence of diarrhea and one an increase; one study showed a decrease in the percentage of children with fever and respiratory infection. There were no data available on child mortality or HIV/AIDS. There was no added benefit of MMNs over iron alone in improving hemoglobin levels; however, there was a 10–40% decrease in anemia with more iron in the supplement and a greater response with higher anemia prevalence. Supplements generally increased serum retinol and zinc concentrations.

Maternal MMN supplementation and pregnancy outcome

In 2006, a Cochrane analysis of nine MMN trials (n=15,378) reported that MMN supplementation significantly reduced LBW (RR 0.83), SGA (RR 0.92) and anemia (RR 0.61), although the effects of MMN supplements were not significantly different from iron-folic acid supplements alone. In addition, the Multiple Micronutrient Supplementation during Pregnancy (MMSDP) 2006 analyses of data from trials using the UNICEF/UNU/WHO UNIMMAP supplement for pregnant and lactating women found the pooled effect from 12 studies using MMN versus iron supplements on birth weight was an increase of 21.2 g (95% CI 7.96, 34.5) and a 7% reduction in intrauterine growth retardation (IUGR). The odds ratio (OR) for a reduction in LBW failed to reach significance (OR = 0.93, 95% CI, 0.85 to 1.01), and there was no overall pooled effect on mortality from eight studies (OR=1.02, 95% CI, 0.83, 1.26). Additional analyses found a highly significant interaction between maternal body mass index (BMI) at baseline and birth weight, with a 24-gram increase in birth weight per unit of BMI. This suggests that adequately nourished women may be better able to respond to increased nutrient intake from MMN supplements.

Supplementing non-breastfed infants and children

WHO guidelines (2005) recommend that non-breastfed infants and children aged 2–24 months should be given fortified foods or micronutrient supplements containing iron. If adequate amounts of animal-source foods are not consumed, fortified foods or supplements should also contain other micronutrients, particularly zinc, calcium and vitamin B12. Unfortunately, Dr. Allen was unable to find any consistent data to support these guidelines. She suggested that future recommendations for fortified infant foods or supplements incorporate the food fortification guidelines published in 2006 by WHO and FAO, which provide for the requirements of 97.5% of individuals for each micronutrient, without exceeding their Tolerable Upper Intake Level (UL).

Dr. Allen concluded her talk by identifying a number of difficulties in increasing the uptake of MMN interventions. Most importantly, there is currently no coordinated, systematic plan linking research, policy, and program delivery in this area. Although data were available from hundreds of studies – many very expensive and demonstrating efficacy – there is no consensus on whether these data can be translated into policy or MMN interventions.

Day 1 Poster Session

Posters from the first day overlapped with topics covered by the speakers; however, they were grouped by themes (child development, health consequences, micronutrient-micronutrient interactions, and science base for policy and surveys) rather than by nutrient. A summary of posters is presented below. For additional information, please refer to individual posters on the Micronutrient Forum website (www.micronutrientforum.org).

Child development

Within this theme, most posters focused on iron nutrition and supplementation (M2–5, M9). The results presented suggest that ID appears to impair not only cognitive and motor development (M2, M4, M5, M9) but also emotional regulation, and social and behavioral adjustment (M2, M4) – even contributing to (severe) long-term behavioral problems in one study that had a long follow-up (M2). On the positive side, the correction of ID seems to improve cognitive, motor, and emotional functioning, especially among children under five years of age. In older schoolchildren in Kenya, however, there was no effect of an iron fortification intervention, but ID may not have been the main cause of anemia in these children, as hemoglobin concentrations were also not much improved (M3). Most studies emphasized the importance of social and emotional interaction, activity level, and the care-giving environment in general as major factors in psychomotor development; these factors are very often difficult to disentangle from the background of poverty and malnutrition that are associated with ID.

The effects on psychomotor development and growth of other single micronutrients and combinations of micronutrients were presented in several other posters (M1, M7, M8, M10, M11) but results were less consistent here. The multiple factors that affect child development are illustrated by the direct and indirect relationships between malaria, anemia, and stunting with developmental indicators in young children in Zanzibar (M9).

Health consequences of micronutrient deficiencies

As micronutrient deficiencies in humans rarely occur alone, nutrition and health consequences can be varied. Two posters on iodine illustrated the interrelationships and functional consequences of the various indicators of thyroid function and iodine status (M12). They further highlighted that iodine nutrition during pregnancy was related not only to iodine excretion of the newborn, but also to birth weight in Turkish women (M13). The interrelationship of vitamin A with immune function was demonstrated in Venezuelan adolescents, who had higher interferon gamma levels when (marginally) vitamin A deficient, implying increased immune activation and/or specific immunomodulatory effects of vitamin A (M14). In seven Turkish women with gestational diabetes mellitus, serum levels of a range of micronutrients related reasonably well to dietary intake (M15). Another study in Turkish pregnant women also highlighted the importance of a healthy balanced diet during pregnancy, showing relationships between maternal hematological and micronutrient status indicators and birth weight (M17). In Mexican women, low vitamin B12 was found to be fairly common; supplementation improved status, but not hematological values. Vitamin B12 deficiency may therefore not be an important cause of anemia in this population (M18), but association with neural tube defects has not been measured. Finally, in North-Indian children, there was no association between a range of hemoglobinopathies and anemia prevalence, indicating that hemoglobinopathies are not a contributing cause of anemia in these children (M19).

Micronutrient-micronutrient interactions

This theme included posters on interactions between specific micronutrients, as well as the effects of interventions with MMNs. The impact of VAS on deficiencies of other nutrients were discussed in two posters. The first reported that VAS reduced the effects of iodine deficiency and the risk of goiter in rats deficient in both iodine and vitamin A (M20). The second poster described how supplementation of vitamin A- and iron-deficient children mobilizes iron from existing body stores to support increased erythropoiesis, an effect likely to be mediated by increased concentrations of circulating erythropoietin (EPO) (M21). An analysis of causative factors of ID and anemia in young women in India showed that inadequate iron content and bioavailability of the diet, together with low dietary intake of other micronutrients, are the primary factors. Parasite infestation was low and not a significant factor (M22). Three studies reported beneficial effects of MMN supplementation during pregnancy compared to folic acid or iron-folic acid supplementation alone (M24, M27, M29). In Indonesian infants, MMN supplementation improved micronutrient status, and minimized age and gender differences in growth faltering, but only when combined with macronutrient supplementation (M27). Finally, two studies showed the beneficial effect of milk fortified with MMNs, including iron and zinc. In Indian schoolchildren, the fortified milk improved growth, iron status, and physical activity, with no evidence of zinc interfering with iron absorption (M26). In Mexican toddlers, after 12 months of Fe-Zn supplementation, the prevalence of zinc deficiency (<650 mg/L) was lower but the concentration of plasma zinc was not significantly different from those receiving milk alone (M28). [The prevalence of inflammation may have contributed to this effect but inflammatory biomarkers were not reported.]

Scientific basis needed for national policy formulation and program commitment

This theme included five posters concerning aspects of vitamin A nutrition (M33–35, M37, M38). Animal models of absorption illustrated the recruitment of several parallel enzyme systems in intestinal esterification of a large dose of vitamin A (M33), and suggested that the current dose recommended for infants at the time of EPI contacts can improve liver stores but may not alleviate deficiency (M38). This latter point was also suggested by research from the Gambia (M37), which showed no advantage on health outcomes or vitamin A status from the IVACG postpartum supplementation schedule (400,000 IU provided in two doses) compared to the WHO standard schedule (200,000 IU). The effects of different doses of vitamin A on morbidity and mortality were also investigated in children in Guinea Bissau, especially in relation to the diphtheria-tetanus-pertussis (DTP) vaccine (M35), although prior work suggesting the benefit of a lower dose for girls was not replicated in the present analysis.

Two posters addressed bioavailability aspects, with a study in Mongolian gerbils showing that both supplements as well as foods provided adequate vitamin A, albeit with different conversion factors (M34), and analysis of crop production and dietary pattern in India showing very low iron intakes and a decline in recent years after considerable improvement over the last decennia. (M42)

UNICEF and WHO summarized the revised recommendations for ID control programs, reiterating the importance of addressing ID and IDA in children with a cautious approach in resource-poor, malaria-endemic settings and a strong recommendation to integrate iron supplementation with other mother-child health interventions (M43). [See also reports by Dr. de Benoist and Dr. Stoltzfus on Day 1, and Dr. Sean Lynch on Day 3.] A systematic review of iron with/without folic acid supplementation during pregnancy showed only a decrease in anemia at the end of pregnancy, with not enough evidence for other beneficial or adverse effects (M44). In Darfur, Sudan, a home-based MMN fortification approach was found to be feasible, reducing the prevalence of anemia in young children, but not in mothers (M40). A report on the salt iodization efforts in Turkey showed that, although legislation is in place, surveillance needs to be improved (M31). In addition, increased consumer awareness and measures against illegal (non-iodized) salt producers are needed. Poster M41 showed it was possible to use existing infrastructure, capacity, and facilities to organize, develop, and implement a large-scale research trial, JiVitA, even in a resource-poor country like Bangladesh (M41). An intriguing poster reported on parental tobacco use as a significant contributing factor to childhood malnutrition as it diverts household funds away from higher quality food items (M46).

Surveys

This theme covered the remainder of the posters for Monday. A series of posters described the iodine status of various populations and countries, and the challenges, constraints and successes of national salt iodization efforts (M48–54). Iodine deficiency was found to be still alarmingly prevalent in some populations, and improved, sustained surveillance of salt iodization programs, and increasing public awareness were common recommendations of the surveys presented.

Surveys in a wide range of populations and countries show that deficiency of vitamin A is still common, often combined with deficiency of other micronutrients, especially in (pregnant) women, infants and children, and indicate the need for micronutrient deficiency control measures, especially in rural areas. (M54–56, M56, M59, M62–64, M83).

Two posters highlighted countries where relief was urgently needed among schoolchildren. In Malawi, both food quantity and quality were inadequate to maintain optimal growth and health. Furthermore, stunting, underweight, anemia, and infectious disease were prevalent (M60). In Aceh, Indonesia, malnutrition, micronutrient deficiencies, anemia, and infection or parasite infestation remained prevalent despite large-scale emergency relief, highlighting the need for long-term health and nutrition intervention programs (M65).

ID and anemia were featured in a large number of posters (M70, M71, M73, M75–78). In Latin America, anemia prevalence in general has declined over the last two decades, and some of the predicting factors have changed in importance (M70). Low socioeconomic status (SES) and educational level, low BMI and stunting, high parity, and diarrheal disease remain important risk factors in women and children, but more research is needed to understand the changes in prevalence and risk patterns.

Providing a global perspective, WHO presented the latest worldwide anemia prevalence estimates per region, with Africa and Asia remaining the highest-risk areas, and stressed the need for future surveys to further explore the factors contributing to anemia in a given population (M71).

The remaining posters covered deficiencies and inadequate intakes for other micronutrients, with three posters reporting on zinc (M80–82) and one on essential trace elements (M85).

Day 2 – 17th April 2007

National successes in micronutrient programming

In his overview of the morning's topics, Dr. Jose Mora, an advisor in international nutrition, noted several critical factors in implementing successful intervention programs for the control of micronutrient deficiencies in Nicaragua. The first of these factors was to correctly describe the problem in terms of its scale: where, why,

and in whom it occurred. Designing an intervention program was then based on the epidemiology of the problem and the resources available for its control. He stressed that program implementation, performance monitoring and evaluation, and education of the public should go hand in hand. The morning's talks illustrated these factors in very different environmental settings.

Integrated approach to anemia control in Nicaragua

Dr. Erik Boy, of the Micronutrient Initiative (MI), introduced Nicaragua's anemia control efforts by highlighting the country's dramatic progress in controlling micronutrient deficiencies. Over the period from 1993 to 2000, and from 2003 to 2005 national prevalence surveys revealed that VAD among under-fives had dropped from 31.3% to 8.8% to 1.8%, and anemia prevalence declined from 33.6% to 22.3% to 11.2% among non-pregnant women. However, little progress was achieved from 1993 to 2003 in reducing anemia among children 12–59 months of age, but it decreased from 29% to 20.1% in 2003 to 2005. Based on these findings, the MoH assigned the highest priority to strengthening its anemia control efforts. The country's Integrated System for Surveillance of Nutritional Interventions (SIVIN), established in 2002 for monitoring and evaluation of this and other nutrition programs, was used to chart the progress of these efforts.

An Integrated Anemia Control Strategy (IACS) was developed by the MoH and initiated in 2004. The IACS draws on a combination of supplementation and food fortification to combat anemia. First, iron and iron-folic acid supplements are targeted to children under five years of age and pregnant women, respectively, with additional deworming of children aged 2–10 years carried out on a semi-annual schedule. The MoH also maintains a semi-annual schedule for VAS of under-fives and high-dose supplementation of women in the postpartum period. In addition to the well-documented success of sugar fortification with vitamin A, Nicaragua has revised its fortification of wheat flour to include 45 mg/kg of ferrous fumarate, for a final iron content of 55 mg/kg after considering the intrinsic iron of the refined wheat flour, as well as B vitamins. Regulatory monitoring of these efforts is carried out by the food industry, and food control authorities, with SIVIN providing a framework for household-level monitoring l since 2002. In addition to these interventions, the IACS has carried out comprehensive training of various cadres to encourage the increased consumption of vitamin A- and iron-rich foods.

National data from a 2005 evaluation suggest a further decline in anemia in all subgroups. Although communities were not randomized to IACS interventions, these declines are associated with increased supplementation coverage rates in the targeted age groups, as well as higher rates of follow-up by community health volunteers – known in Nicaragua as *brigadista* – who ensure adherence to supplementation. Semi-annual distribution of vitamin A supplements to children aged 6–59 months, and anti-helminth medications to those aged 2–10 years during National Health Rallies have ensured high coverage over the evaluation period. Likewise, high coverage and quality of vitamin A-fortified sugar and -fortified wheat flour have been maintained, although the estimated dietary contribution of iron from fortified flour products is barely 6% of the Estimated Average Requirement (EAR).

Dr. Boy concluded his remarks by underlining the need for an integrated approach to anemia control. Nicaragua's success with multiple reinforcing interventions over the past several years can serve as a model for other countries.

Nigeria's USI program success story: Process and lessons learned

Prof. Dora Akunyili, of the National Agency for Food and Drug Administration and Control (NAFDAC), Nigeria, discussed lessons learned during her leadership of Nigeria's efforts to attain USI. First and foremost, Prof. Akunyili emphasized the commitment to USI on the part of both politicians and industry leaders, and the strong partnerships between all those involved. Political commitment was essential to pass the 1993 measure mandating salt iodization, setting iodization standards and enabling an effective monitoring enforcement. Continued government involvement, particularly by NAFDAC, has also been critical in strengthening the confidence of consumers and other stakeholders. A strong partnership between public and private sectors is maintained by the multi-sectoral IDD-USI Taskforce, which collates data from factory, distributor, retail, and household surveys, and meets quarterly to review progress.

The next major lesson derived from Nigeria's experience is the importance of regular monitoring at all levels of production and distribution, as well as identification of weak spots that may be sources of non-iodized salt. The iodization of 98% of all salt consumed in Nigeria is concentrated in large domestic salt companies (five producers and eight factories) producing

640,000 metric tons (MT) per year, making inspection and monitoring easier. The remaining 2% consists of salt smuggled or produced by cottage industries. Through advocacy and severe sanctions, the salt manufacturers now have an umbrella association for effective self-regulation and see the iodization program as part of their social responsibility. NAFDAC has also encouraged the salt industry to establish certified and efficient in-house monitoring systems. Monitoring data are supplemented by annual goiter and UI excretion surveys to monitor the impact of the program.

Finally, achieving USI has required awareness building around the importance of IDD as public health concern. NAFDAC has employed multiple communication channels, including newspapers, TV, radio, public notices, posters, and publications in English and local languages to promote the consumption of iodized salt, which is marketed under a distinctive logo. Campaigns have improved awareness among consumers, manufacturers, government policy makers, and religious and community leaders of the full range of disorders that result from iodine deficiency. NAFDAC has even championed high-profile advocacy by involving the wife of Nigeria's president, the minister of health, leaders in industry and commerce, and traditional rulers.

VAS for child survival in Niger: Maintaining success in adversity

Dr. Noel Marie Zagré, of UNICEF Niger, described the development of Niger's highly successful VAS program. This effort began in 1997 as an extension to the mass National Immunization Days (NIDs) campaign planned by EPI for polio eradication. Supplementation was added to this effort, targeted to children aged 6–59 months. The event was a challenge for the Ministry of Public Health and its development partners, but successfully reached > 90% of children. In 1999, National Micronutrient Days (NMDs) were launched by the President of Niger. NMDs ensured that children received a second annual dose of vitamin A, and targeted supplementation to women in the immediate postpartum period. An additional mass campaign for NMDs was organized in 2002 in 25 health districts since the NIDs only covered 17 out of 42 districts. Between 1999 and 2006, Niger has sustained semi-annual VAS coverage of greater than 80% through combinations of NMDs and NIDs. In addition, since June 2005, the EPI schedule was adapted and materials were produced to ensure VAS to children aged 6–11 months, and the inclusion of deworming in campaigns.

Dr. Zagré concluded by outlining the lessons learned in Niger. As with Nigeria's USI experience, gaining political will and commitment were essential at the outset, as was detailed planning of human, material, and financial resources with local administrative leaders. Attaining high coverage was dependent on scheduling campaign dates to avoid periods of intensive work by women. Program managers also found that promotion of a 'vitamin' was highly salient to mothers and encouraged their participation. The most recent post-campaign evaluation reports >85% coverage with polio vaccine, deworming, and vitamin A, reiterating that success in VAS distribution is possible even in a resource-poor environment.

The challenge of shifting from a VAS campaign to delivering a package of key interventions during Mother and Child Health Week

Dr. Simon Rakatonirina, of the MoH, Madagascar, shared his country's experiences in scaling up its VAS program to reach its three million preschool children. A campaign-style delivery strategy was first adopted by the country in 1998 and, since 2003, the program has consistently achieved semi-annual coverage of >80%.

In June 2006, the MoH and UNICEF decided to build on the success of VAS campaigns by including additional maternal and child health interventions. The country's first Mother and Child Health (MCH) Week was launched in October 2006 as a semi-annual national initiative to reach underserved and hard-to-reach groups with a package of interventions. In addition to VAS for children and women in the immediate postpartum period, MCH Week also includes deworming and catch-up immunizations for children aged 12–59 months, and deworming and a two-month supply of iron-folic acid supplements for pregnant women in their second and third trimesters. Malaria prevention is ensured through the distribution of insecticide-treated nets (ITNs) and Intermittent Preventive Treatment (IPT) for pregnant women. Ancillary activities include counselling on family planning and delivery of contraceptive methods, voluntary HIV screening at established prevention of mother-to-child transmission (PMTCT) sites, and information, education and communication (IEC) on early and exclusive breastfeeding, regular intake of iron-folic acid and maternal nutrition during pregnancy.

The MCH Week was successfully implemented in all 111 districts in the country, and independent assessment indicated 93% of children aged 6–59 months and 94% of newly postpartum mothers were given vitamin A supplements. In addition, 82% of pregnant women were given ITNs, 74% received folic acid, and 54% received deworming tablets. However, the regional health teams found the large number of interventions made it difficult to organize mobile health teams to reach the 40% of the population that resides in outlying areas. Team personnel often did not have the time to provide counselling on family planning and HIV prevention. Stakeholders and peripheral health managers therefore agreed that, for 2007, MCH Week mobile teams would aim to deliver a smaller package of services to persons in outlying areas.

A platform for community-based health interventions

Dr. Ram Shrestha, described Nepal's National Vitamin A Program (NVAP), which was first implemented in 1993 in eight districts and has since been scaled up nationwide. Each district received technical support for one year from the National Training and Advisory Group (NTAG), a Nepali NGO, and financial support from USAID, UNICEF, and later the Australian Agency for International Development (AusAID). Individuals from the health and other sectors at district, Ilaka, and community levels received an orientation on the importance of vitamin A for child survival, and how each sector could support their families so they would receive a vitamin A capsule twice a year. Other program activities include promotion, capsule distribution, and monitoring of capsule coverage.

Expanding the program each year was achieved by establishing a bond between people in the community, the government, NGOs, and donors. Trust was built among the family members and stakeholders in the NVAP program by providing scientific evidence and, later, family experiences of how night-blind children were benefiting from vitamin A capsules. This trust developed into a sense of ownership of the program, which increased attendance at the distribution centers for vitamin A capsules. Family Child Health Volunteers (FCHVs) became respected members of the community, which kept up their motivation. Networks developed in the villages by NVAP have facilitated the scale-up of other community-based programs in Nepal, including deworming, community based-Integrated Management of Childhood Illness (IMCI), and iron-folic acid supplementation to pregnant and lactating mothers. The distribution of anthelmintics started in 1999 and covered all 75 districts by 2004.

Dr. Shrestha commented on the remarkable reductions in under-five mortality in Nepal over the last decades, attributable to multiple factors: improvements in VAS, management of diarrhea, immunization, and the management of acute respiratory infections, especially pneumonia. If this progress continues, it seems likely that Nepal will achieve the MDG target for 2015.

Common elements of successful programs

Dr. Philip Harvey, of the A2Z Project, summarised the morning's talks by highlighting common elements among these successful programs. He suggested that, in any program, four core components must interlink to work properly: the participants, a feeling of ownership, the necessary capacity, and commitment. Motivation and trust are the driving forces that link these components. Partnerships between the donors, industry, field workers, and the public are needed to generate the capacity to deal with problems; without motivation and trust between the groups, efforts will fail. Having established a program, adequate monitoring and supervision are essential for proper supervision and accountability to sponsors, as well as to maintain the enthusiasm of all those involved. While the choice of monitoring and evaluation (M & E) indicators are highly dependent on the program and on the intended use of the data, Dr. Harvey emphasized the urgent need for investment to strengthen program impact evaluation.

Tipping Point 1: Zinc and childhood mortality

In spite of some success with interventions for child survival, approximately 10 million children still die each year from preventable causes. Four studies carried out in Africa and Asia suggest that universal zinc supplementation of under-five children may help to reduce child mortality. Three of these studies were on children selected for being SGA, LBW, or being treated for diarrhea, and hence likely to be zinc deficient. Three studies undertaken in non-selected populations have also reported reductions in morbidity.

Zinc supplementation – Effects on child mortality in an African setting

Dr. Sunil Sazawal, of the Johns Hopkins Bloomberg School of Public Health, gave the first of three talks considering the impact child survival on of universal zinc supplementation. The original trial, referred to earlier in these proceedings, involved the randomization of 53,000 households on the Tanzanian island of Pemba to four treatment groups, using a 2 x 2 factorial design. Groups received either zinc (10 mg), iron-folic acid (12.5 mg/50 µg respectively), a combination of iron-folic acid and zinc, or a placebo, in addition to semi-annual doses of vitamin A as per WHO recommendations. Treatment with iron in the groups that were assigned to it stopped in 2003 due to adverse events (discussed elsewhere in this report), and the children were reallocated to the groups receiving either a placebo or zinc. Field staff visited households on a weekly basis to deliver supplements and to collect information on mortality, compliance, health care consultation, and hospitalizations. Five hospitals were maintained under surveillance by study teams, and all children admitted were assessed for the presence of malaria and/or anemia at the time of admission, during hospitalization, and at discharge.

The primary objective of the present analysis was to evaluate the efficacy of a daily zinc supplement (dispersible tablet) to children aged 1–48 months to reduce mortality in comparison to control group children. The effect of zinc supplementation on mortality showed a significant interaction with both age and gender, rendering overall impact less meaningful. Thus, by subgroup, Dr. Sazawal reported no impact of zinc among infants under 12 months of age. Among children over 12 months of age, there was a significant 18% reduction in mortality and the effect was greater in boys than in girls (**Table 3**). Zinc supplementation was associated with non-significant reductions in mortality due to malaria, infections (including pneumonia and sepsis), and diarrhea, and a significant reduction in infection-related mortality in children over 12 months of age (RR 0.48 (95% CI 0.23, 0.99).

Impact of zinc supplementation on preschool child morbidity and mortality in Nepal

Dr. James Tielsch, of the Johns Hopkins Bloomberg School of Public Health, followed Dr. Sazawal's talk with a description of the study carried out in the Sarlahi district of Southern Nepal, which employed a similar 2 x 2 factorial design. In Nepal, 425 clusters were randomized to each of the four treatment groups (the total sample yielded 66,000 person-years). Field procedures began with a baseline household census of all infants and children aged 1–35 months. Infants born in the study area were enrolled in the study when they reached one month of age and, once enrolled, were followed and dosed until they were 36 months of age. At baseline, the groups were not significantly different on a wide range of baseline characteristics. Ward Distributors visited each household twice a week to give one dose and leave tablets for the other days of the week. As in the Pemba study, the Nepal trial was restructured following the cessation of the iron-treatment arms, with a reassignment of subjects to zinc or placebo.

In Nepal, daily zinc supplementation had a non-significant impact on total mortality, and mortality in infants under and children over 12 months of age (**Table 4**). The impact of gender was the opposite of that described by Dr. Sazawal in the Pemba study, with no mortality reduction in boys, but a close-to-significant reduction in girls. A morbidity sub-study of approxi-

Table 3: Effect of zinc supplementation on mortality overall, by gender and age group

	Zinc	Placebo	RR	95% CI	P
Overall	1.42	1.53	0.93	0.81–1.06	NS
By age					
0–12 m	3.55	3.36	1.06	0.87–1.29	NS
>12m	0.88	1.06	0.82	0.68–1.00	0.045
By gender					
Male	1.23	1.52	0.81	0.66–0.99	0.04
Female	1.62	1.54	1.05	0.87–1.29	NS

Table 4: Meta-analysis of zinc trials in children

Study	RR	95% CI
All preschool ages		
Bangladesh	0.17	0.04–0.75
Nepal	0.92	0.75–1.12
S. Asia combined estimate	0.89	0.73–1.09
Zanzibar	0.93	0.81–1.07
Burkina Faso	0.41	0.15–1.19
Africa combined estimate	0.92	0.80–1.05
Overall combined estimate	0.91	0.82–1.02
Infants <12 months		
Bangladesh	0.35	0.07–1.67
Nepal	1.04	0.83–1.31
S. Asia combined estimate	1.02	0.81–1.27
Zanzibar	1.06	0.87–1.29
Overall combined estimate	1.04	0.90–1.21
Children >12 months		
Nepal	0.80	0.60–1.06
Zanzibar	0.83	0.68–1.00
Overall combined estimate	0.82	0.70–0.96

mately 1,200 children found no differences in episodes/child/year of diarrhea, persistent diarrhea, dysentery, or acute lower respiratory infection in the zinc and placebo groups. Cause-specific analyses suggested that treatment effect on gastroenteritis was focused on the most severe cases and not on routine watery diarrhea or dysentery. A zinc status sub-study 12 months post-supplementation among ~350 children aged 24 months and older found no difference between the mean (SD) concentrations of serum zinc in the placebo 11.08 (2.13) µmol/L [724 (139) mg/L] and treatment 11.63 (2.26) µmol/L [760 (148) mg/L] groups.

Dr. Tielsch concluded by remarking that universal daily zinc supplementation for under-five children was not likely to be a cost-effective child survival strategy as mortality rates are lower in these children and, in light of the Pemba and Nepal studies, evidence for an impact on mortality is weak. However, he emphasized that these findings pertained to universal supplementation and reiterated the proven efficacy of zinc in the treatment of diarrhea. Dr. Tielsch also noted that targeted supplementation of children more than one year of age may be cost-effective, as pooled estimates from the Nepal and Zanzibar studies showed an 18% reduction in infant mortality (**Table 4**).

Comments on the meta-analysis of zinc supplementation and mortality trials in children

Dr. Juan Rivera, of Instituto Nacional de Salud Pública, Mexico, presented the findings of a meta-analysis on universal zinc supplementation. As illustrated in **Table 4**, there was little difference between the two most recent and largest studies from Nepal and Zanzibar. Both reported a non-significant ~8% reduction in mortality. However, four smaller studies carried out in Bangladesh (two studies), Burkina Faso, and India showed a ~50–85% reduction in under-five mortality (**Table 4**).

Various explanations were discussed with regard to the differences between the Pemba and Nepal studies and the earlier, more promising research on zinc supplementation. Neither study design nor baseline mortality appears to have influenced these differences: both of the new studies were well designed, with large sample

sizes. Zanzibar and Pemba both have high mortality rates, and the epidemiology of early childhood morbidity and mortality did not differ widely from earlier study sites. Dr. Rivera further noted that the presence of malaria was unlikely to have influenced these findings, as malaria prevalence was high only in Pemba, while the effect sizes for zinc were quite similar in both sites. Supplements were also similar across all studies. Nutriset tablets used in Pemba and Nepal contained zinc sulfate (ZnSO4), which was also employed in Burkina Faso (tablets) and India (syrup). Both larger and small doses, as well as longer and shorter durations of treatment, were used in other trials, suggesting that supplement formulation, dosage, and schedule cannot explain the observed differences.

Effect sizes were systematically much larger in the four previous trials. It therefore seems unlikely that these differences were due to chance alone. Dr. Rivera pointed out that children in both Pemba and Nepal received vitamin A supplements in line with WHO recommendations. The health benefits of vitamin A may therefore have masked the efficacy of zinc. It is also possible that zinc status may have been better in these two populations. Although stunting rates were high in both Pemba and Nepal, this is not a sensitive indicator of zinc deficiency.

A sub-study in Nepal found that serum zinc concentrations were relatively adequate. In Pemba, the change in serum zinc concentrations over the course of the trial did not differ by treatment group.

Assuming that the differences between studies were due to chance alone, the speaker questioned why protection was conferred only among SGA infants and children over the age of 12 months. He noted that infants generally acquire adequate zinc from their mothers during pregnancy and from breast milk. SGA infants are known to be at higher risk of zinc deficiency. Furthermore, the lack of an effect during infancy may be due to differences in the underlying biological mechanism of zinc's actions. For example, it is possible that zinc supplementation may result in optimal Th1/Th2 cytokine balance only after 12 months of age.

Special session: Cost analysis as a tool for micronutrient program planning, budgeting, management and advocacy

In this talk, Dr. Jack Fiedler, of the A2Z Project, first considered the question, "Why do a cost analysis?" He pointed out that a cost analysis is not an end in itself, but a means to an end. It is an ingredient of a decision-making process. As most costs are concentrated at the most local level, how a program is implemented can be major influence on the total cost. Cost studies are done for a variety of reasons but, in most cases, the need is to have a single figure for budgeting purposes, provide accountability, provide input into developing an implementation plan, and establish a management tool with which to inform policymakers (e.g. about the cost-benefit ratios of different interventions). Cost studies, however, can provide a credible advocacy tool for use within the MoH (district or central level) or for the MoH to use with the Ministry of Finance.

There is a longstanding, general consensus that micronutrient interventions are among the most cost-effective public health interventions. However, the most commonly cited studies were conducted over 25 years ago, when program interventions, health systems, and country conditions were markedly different. Consequently, cost studies are often regarded as having limited relevance to program managers, there are few of them, and their potential is underappreciated. There are enormous variations in the estimated costs of micronutrient interventions, but the literature clearly shows that the costs of supplementation studies are far more expensive than fortification. However, the cost of fortification programs is not meaningful without getting specific information on the composition of the fortificant and the levels of fortification. In addition, the costs of government monitoring and enforcement, social marketing, and the assessment of impact on the recipients should not be overlooked. The true costs of supplementation programs may be difficult to assess when they are embedded within the systems, such as in NIDs, for example. Personnel are "non-traded inputs" and their cost (i.e. wages and salaries) varies enormously by country. However, the true costs of their contribution to the supplementation program may not be assessed if they are part of the regular staff.

Dr. Fiedler then illustrated how to approach a cost analysis and suggested that an "ingredients approach" combined with activity-based costing (ABC) was the

most useful method. This entails calculating costs using a detailed description of the program that would in turn define the program's major activities, and the types and quantities of inputs at each level of the program. It produces what is usually the most systematic, comprehensive, and detailed description of a program's structure, inputs, and implementation. ABC is attractive for two reasons: 1) It provides the opportunity to work with key program staff to define the major activities, and 2) it enables the use of the ingredients approach. The ingredients approach identifies all of the different types and quantities of inputs required to implement the program, starting at the most local level and including each level of the organizational pyramid.

In summary, to maximize the usefulness of cost analysis for improving micronutrient program performance, the preferred approach is to employ economic analysis and the ingredients approach combined with ABC. The ways in which costs are disaggregated become the tools with which program managers are later able to explore how changes in the program would affect costs.

Assessment and evaluation

Dr. Frank Wieringa, of the University Medical Centre (UMC) Nijmegen, opened the afternoon session with the suggestion that future micronutrient trials may have to make greater use of assessment and evaluation prior to intervention. It was previously assumed that non-deficient recipients of a micronutrient supplement would be unaffected by the treatment. However, recent studies of iron and vitamin A supplementation call into question the validity of this assumption. The development of field-friendly methods will assist rapid identification of subjects suitable for supplementation as illustrated in the first presentation of the afternoon.

A dried whole blood spot thyroglobulin assay for use in monitoring iodine deficiency

Dr. Zimmermann described the use of thyroglobulin (Tg) as an indicator of iodine status in school-aged children (see posters T48–51 on the same subject). Current indicators are limited in evaluating the impact of iodized salt – urinary iodine is a sensitive indicator of recent intake, but not thyroid function; goiter is a poor indicator as thyroid size decreases slowly after iodization; and TSH is sensitive only during the neonatal period. An indicator of thyroid status that is sensitive to recent changes in iodine intake is needed.

Tg is a thyroid-specific glycoprotein precursor to thyroid hormone. During deficiency, transcytosis of Tg-containing endosomes results in Tg release into circulation. Serum Tg concentrations are recommended by WHO as a short-term indicator of thyroid function. High concentrations of the protein (> 40 mg/L) indicate poor iodine status and elevated serum Tg concentrations have been reported in iodine-deficient areas with endemic goiter, reflecting TSH hyperstimulation and thyroid hyperplasia. It is a useful indicator for program monitoring as concentrations normalize within a few months of iodine repletion and, therefore, complements the use of UI to measure recent iodine intake, and thyroid volume to assess long-term response. Although Tg is a sensitive marker of thyroid dysfunction, commercially available assays require serum, which is difficult to collect, process, and store in remote areas.

Dr. Zimmermann described the adaptation of a two-stage dissociation-enhanced lanthanide-fluorescent immunoassay (DELFIA) to measure serum TG in blood spots. The minimal detection concentration was 1.42 mg/L and the median coefficient of variation (CV) in controls was 6.3%, although the CV assessed from duplicate samples of greater than and less than 10 mg/L were 16.7% and 13.4%, respectively. There was excellent agreement between concentrations measured in dried blood spots (DBS) with those measured in serum.

To establish an international reference range, DBS-Tg was determined in a sample of 700 children aged 5–14 years. Children were euthyroid, anti-Tg antibody-negative, residing in areas of long-term iodine sufficiency, and represented five major ethnic groups (African, Asian, Arabic, Caucasian, and Hispanic). A reference range of 4–40 µg/L, with a median concentration of 14.5 µg/L, was established. Serum Tg reference material was adapted for DBS using material from the European Community Bureau of Reference (CRM-457). Its stability was tested over a one-year period at –20° C and –50° C, and found to be acceptable. The reference material for DBS-Tg is now available from Dr. Zimmermann's group in Zurich and will soon be available from WHO.

Recommendations for the assessment of population zinc status: Results of a WHO, UNICEF, IAEA and IZiNCG Working Group Meeting

Dr. Christine Hotz, of HarvestPlus, began her talk by remarking that little information is available on the national prevalence of zinc deficiency from direct assessment. A major limiting factor has been the lack of clear guidance and cut-offs for biochemical, dietary, and functional indicators useful at the population level. The joint working group identified three indicators. First, serum zinc was selected as it reflects dietary zinc intake, responds consistently to zinc supplementation, and decreases in response to zinc depletion. Reference data are available for most age and sex groups from the National Health and Nutrition Examination Survey (NHANES), although data are limited for children under three years of age. For population assessment, a risk of deficiency should be considered when the prevalence of serum zinc concentration below the specific cut-offs for age, sex, or time of day is >20%. Dietary zinc intake estimated by quantitative dietary assessment (e.g. 24-hour recall) may also serve as a useful indicator, although it should always be assessed in conjunction with dietary phytate. Reasonable agreement has been reported between the prevalence of inadequate zinc intakes and low serum zinc. A risk of zinc deficiency should be considered when the prevalence of dietary zinc intakes below the EAR is >25%. Finally, meta-analyses indicate that linear growth in stunted populations is responsive to zinc. Although stunting is not a sensitive indicator of zinc deficiency, intervention may be warranted in populations where the prevalence of stunting exceeds 20%. However, it is important to recognize that other nutrient deficiencies and chronic infection can also impair growth, and a MMN supplement may be more appropriate than zinc alone if other zinc-assessment data are contradictory or unavailable.

In summary, all three indicators can be used to identify at-risk populations and determine degree of risk, but the prevalence of low serum zinc concentrations should be used as the primary quantitative indicator. Review papers and guidelines are in the process of being published (Food and Nutrition Bulletin, September 2007).

Nicaragua Integrated System for Monitoring of Nutritional Interventions (SIVIN): A summary of the experience and potential implications for developing countries

SIVIN was first referred to by Dr. Boy in his report on the considerable reduction of anemia prevalence in Nicaragua. In this talk, Dr. Mora expanded on the experience and lessons learned from the first several years of SIVIN's operation.

SIVIN is a management information system that monitors the process and impact of national nutrition programs implemented by the MoH through information collected from various sources, including a national household survey. Operationalized by the MoH in 2003, it is the most important source of policy- and program-relevant information on nutrition programs in Nicaragua. The system has so far produced a significant amount of information on the processes and performance, and outcome and impact of some of the largest nutrition programs being implemented in the country, and on trends of nutrition indicators, all of which have concrete policy and program implications. The system has enjoyed strong MoH political commitment despite its donor-driven inception, and a well-trained technical team operates the system with great dedication and motivation.

SIVIN is designed to collect information on the performance of nutritional programs as well as monitor their effectiveness in the population. However, these objectives made the system somewhat complex. At the national level, the information available for program decisions has not yet been fully utilized, and the prospects of the MoH being able to take full technical and financial responsibility for SIVIN's operation are still unclear. The household survey component does not allow stratification of data by district, limiting its usefulness for decision making at the district level. While local teams currently have the capacity to collect quality M & E data with minimum assistance, their capacity for data analysis is still being developed. Strengthening local capacity for data analysis and report preparation may take longer and require more technical input.

An important issue to resolve is the need to present the M & E results in user-friendly formats. Difficulties

often exist in attributing changes of nutrition indicators to specific programs or interventions, particularly when dealing with problems (such as anemia) that have multiple etiologies or require multi-strategy interventions. SIVIN management should also have a more in-depth understanding of the decision-making process so that the information can be tailored to optimize decisions.

Dr. Boy noted that although SIVIN was developed in response to MoH concerns about the lack of valid data to support nutrition policy and program decisions, significant external technical and financial assistance during early stages may have weakened institutional ownership. However, the presence of well-trained and highly motivated MoH staff responsible for running the system has been a positive outcome. Improvements in the cross-talk between data needs by policy makers and presentation of SIVIN results are expected to promote political sustainability. Despite its relative low cost, financial sustainability with local resources is questionable. The MoH currently covers most of the cost of human resources and physical facilities, and external cooperating agencies pool monetary resources to cover the remaining financial needs. This agreement is likely to continue until 2010.

Vitamin A and other major micronutrient deficiencies in China

Using data from a national survey conducted in 2002, Dr. Yang Xiaoguang, of the Chinese Center for Disease Control and Prevention (China CDC), reported on the prevalence of VAD, anemia, and calcium intakes in the Chinese population. Among children aged 3–12 years, this survey indicated a VAD prevalence (serum retinol <0.70 µmol/L) of 9.2%, with rates higher in rural than urban areas. Approximately 45% of children were marginally deficient (0.7 SR <1.05 µmol/L). VAD was also a problem of public health concern in women of reproductive age and the elderly living in rural areas. Anemia prevalence across all age groups (Hb <110 g/L) was 15.2%. Prevalence was highest in infants and children under two years of age, people over 60 years of age, and women of childbearing age, with 24.2%, 21.5%, and 20.6% of these subgroups affected, respectively. Calcium intakes averaged only 378 mg daily, equivalent to 48% of the recommended dietary intake level. Approximately 10% of this intake is from dairy products. Intakes have changed little since the last time national data were collected in 1992. The findings of this national survey suggest that micronutrient deficiencies are of public health significance in China, especially in rural areas.

Six-monthly VAS from 1 to 6 years of age: A cluster-randomized trial among 1 million children in North India

Dr. Shally Awasthi, of King George's Medical University, reported on an open-labelled, cluster-randomized trial of VAS conducted through the Integrated Child Development Services (ICDS) systems over a five-year period in Uttar Pradesh, India. Residential blocks were randomized to receive either vitamin A capsules (200,000 IU) alone, albendazole (400 mg chewable chocolate-flavoured tablets) alone, both, or nothing. The treatment was given twice a year (in April and October) and on a single day to all children aged 6–60 months within a block. Mortality was quantified by village-to-village riders, followed by two special mop-up rounds in 2001 and 2003, during which house-to-house surveys were conducted in each village to identify deaths that had been missed by earlier data collections. On average, the children received about 10 of their 11 scheduled doses, while the controls received one standard dose of vitamin A.

Over the course of the five-year trial, 25,000 child deaths were recorded. Results showed the probability that a 1-year-old would die before reaching six years of age was 24.9/1,000 in the vitamin A blocks, and 26.0/1,000 in the control blocks (95% CI -0.7, +2.9 per 1000). Dr. Awasthi noted that there were some significant differences between groups following the intervention: Prevalence of Bitot's spots among children aged 1–6 years was 2.2% and 4.3%, severe biochemical VAD (plasma retinol < 0.35 µmol/L) was 11% and 21%, and recent pneumonia was reported in 2.6% and 4.1% of the treatment and control groups, respectively. The prevalence of other diseases was not different between the treatments.

In conclusion, although the under-five mortality remains high in Uttar Pradesh compared with the rest of the country, the results of this intervention suggest that regular VAS would not have a large impact on reducing the remaining mortality. Previous data showed that combining vitamin A with albendazole resulted in increased plasma vitamin A levels and weight gain among children; however, the vitamin A results were not significantly affected by deworming in this trial. Although the findings of this study are not in line with many earlier trials, the size of the study, and the fact that the study closely resembles program implementation conditions, highlight the urgent need

for an analysis of underlying factors which contribute to the success or failure of programs.

Iodine deficiency: An update on global progress and monitoring

Control of iodine deficiency in pregnant and lactating women, and in children under two years of age: Report of a WHO Technical Consultation

Dr. de Benoist shared the outcomes of a WHO Technical Consultation convened to address iodine requirements, indicators of iodine status, and strategies to eliminate IDD among pregnant women, lactating women, and children under two years of age.

Population data are lacking on what constitutes 'sufficient' intake of iodine, particularly for pregnant and lactating women, and children under two years of age from iodine-sufficient populations. Requirements are therefore estimated based on studies of iodine absorption, metabolic needs, and daily losses. The Technical Consultation recommended that iodine requirements for pregnant and lactating women be increased from 200 µg/d to 250 µg/d, but a daily intake of >500 mg is not recommended. Requirements for children under two years of age remain unchanged (90 mg/day) but a lack of data precluded any attempt to suggest requirements for preterm infants.

Median UI concentration is currently the best indicator of the iodine status among adults. UI is a marker of recent dietary intake, but does not provide direct information about thyroid function. During lactation, UI may underestimate iodine intake as iodine is excreted in breast milk. For neonates, serum TSH concentrations may be most useful. Elevated TSH indicates insufficient thyroid hormone and a risk of brain damage. However, assessment protocols have not yet been standardized for this population; therefore, there is a lack of available data to establish a threshold for normal values. Additional information is needed on urinary and breast milk iodine concentrations to inform IDD assessments among pregnant and lactating women, and children under two years of age in populations with sufficient and/or excess intakes.

IDD elimination relies on continued monitoring of household access to and utilization of iodized salt. Where iodized salt coverage is >90% and contains >15 ppm iodine, there is no need for additional iodine intake. If access to iodized salt is <90%, additional iodine is required for pregnant or lactating women (e.g. through iodine supplements), and infants aged 6–24 months (e.g. through complementary foods fortified with iodine or iodine supplements). Infants aged 0–6 months should be protected from IDD by supplementing the mother. Where iodized salt coverage falls below 20% due to a poor or nonexistent program and median UI <20µg/L, iodine intakes are insufficient. Susceptible groups, such as pregnant and lactating women, and children under two years of age, are at high risk of IDD and iodine supplements are critical. However, further work is needed to establish the optimum dose of iodized oil to give to pregnant women and lactating women, and children under two years of age in populations fitting this description.

The Technical Consultation also identified areas for future research. These included further work on the functional and developmental consequences of iodine deficiency and excess, the interactions between iodine and other micronutrients, and the role of iodine nutriture in inflammation. Participants noted that exploration of new pharmaceutical preparations of iodine would also be useful.

Global progress towards sustained elimination of iodine deficiency: Lessons learned from salt iodization programs and their monitoring

Dr. Nune Mangasaryan, UNICEF, described the progress in IDD elimination made since 1993, when WHO and UNICEF recommended USI as a safe, cost-effective, and sustainable strategy to provide sufficient iodine for all individuals. Because of the work that followed, more than 70% of households in developing countries are using iodized salt, and the number of countries with IDD problems has dropped from 100 in 1993 to 50 in 2004. Of those, the vast majority are affected by only mild IDD.

The sustained success of programs to control IDD has been well documented. This is aided in large part by the adoption and enforcement of legislation for iodized salt usage by more than 80 countries. Dr. Mangasaryan remarked that there is far greater improvement in household coverage in countries with legal enforcement. Despite the spread and success of USI, there are significant gaps in QC and QA in some countries, resulting in a significant proportion of the population using inadequately iodized salt. For example, the latest national survey from India reported that 84% of households use iodized salt, but the salt in only two-thirds of

those households was adequately iodized (>15 ppm). For the future, direct reporting of the proportion of households using inadequately iodized salt was recommended. This presentation underscored the issue that aggregated statistics regarding the use of iodized salt may conceal the true level of protection against IDD. Again drawing on the Indian example, since national estimates do not capture the numbers using adequately iodized salt, and the size of the Indian population significantly influences its weight in regional coverage estimates, current USI coverage for South Asia are likely over-estimated.

In early 2006, UNICEF identified 16 countries that were to receive extended support based on the following criteria:

– high numbers of unprotected newborns,
– low level of or slow progress in salt iodization,
– major salt producing/exporting sites, and
– need for special advocacy and technical support to renew national program strategies.

Dr. Mangasaryan concluded that the global coverage estimate of 70–75% would not change unless these remaining populous countries make significant improvements in increasing both coverage and the level of salt iodization. For the rest of the world, further progress is needed to reach the USI goal and sustain it.

Assessing household use of adequately iodized salt: A methodology that combines use of rapid test kits and quantitative assessment

Dr. Karen Codling, of UNICEF Bangkok, noted that global monitoring data on progress in salt iodization are generally collected through national population surveys, most of which depend on rapid test kits to assess the adequacy of iodized salt. Many rapid test kits are available for this purpose. Using one such Thai kit, she illustrated the difficulty in distinguishing between adequately and inadequately iodized salt.

A school-based survey was undertaken in Laos using the field-based rapid test kit. In addition, salt from a sub-sample of students was brought back to the capital city for quantitative testing (by WYD Checker machine, Salt Research Institute, China). A comparison of the rapid test kit classifications with the gold standard laboratory results showed that there were no false positives, and the rapid test kit accurately identified all non-iodized salt. However, there were false negatives: 38.4% of salt that tested negative was actually iodized, though not at adequate levels. Most of the salt testing positive for iodization by the rapid test kit (80.4%) was adequately iodized. These results are comparable to findings from a similar study in Ukraine (78.8%).

Results using rapid test kits are not as accurate as those found in the laboratory and are unable to differentiate between partially and adequately iodized salt. Dr. Codling suggested that the rapid testing protocol for determining coverage with adequately iodized salt should be modified to include quantitative testing of a random sub-sample.

Tipping Point 2: Newborn dosing with high-dose vitamin A

Newborn dosing with vitamin A has been described in three previous studies. Two trials carried out in South Asia reported large reductions in mortality, while a trial among HIV-negative mother-baby pairs in Zimbabwe found no beneficial effect of supplementation on infant mortality. In this session, Dr. Christine Stabell Benn, of Statens Serum Institute, and Dr. Rolf Klemm, of the Johns Hopkins Bloomberg School of Public Health, discussed the conflicting findings of the two most recent newborn dosing trials. Dr. West concluded the day's presentations with a review of the evidence for informing policy with regard to newborn VAS.

Vitamin A with BCG at birth: A randomized, placebo-controlled trial from Guinea-Bissau

The trial conducted in Guinea Bissau randomized 4,345 normal-birth- and adequate-birth-weight infants with no obvious sign of illness to receive 50,000 IU of vitamin A or a placebo at the time of birth. Infants were followed for one year to monitor measles incidence and mortality. Additional morbidity, and anthropometric and biochemical indicators were measured in a sub sample.

Dr. Benn reported that there was no impact of vitamin A on the overall infant mortality ratio (1.08; 95% CI 0.80, 1.45), nor were effects present when deaths were stratified by early versus late infancy. However, there were significant differences between the sexes. Vitamin A supplementation was associated with high-

er mortality in girls (RR 1.36) than boys (RR 0.86), particularly in the latter half of infancy. The incidence of measles and diarrhea were also higher among girls. Supplementation had no impact on infant growth or retinol-binding protein (RBP) concentrations. At six weeks of age, 32% of infants had RBP concentrations <0.7 µmol/L and, at 4 months, the proportion was 16%, regardless of sex.. There was some evidence, in the African data, of increased mortality following DTP vaccination in supplemented infants and girls in particular. While this finding has not been reported in previous trials, Dr. Benn suggested that DTP vaccination coverage in Guinea Bissau is quite high compared to South Asian countries. It should also be noted that VAS had no effect on RBP concentrations, suggesting that vitamin A status may have been satisfactory in these infants.

JiVitA-2: Efficacy of newborn VAS in reducing infant mortality in rural Bangladesh

Findings from the JiVitA-2 trial in Bangladesh were presented by Dr. Klemm. This study recruited 15,948 infants as soon as possible after birth, with random assignment to vitamin A (50,000 IU) or placebo groups. Baseline characteristics of the households and mothers did not differ significantly by treatment group. In this study population, approximately 14% of mothers reported experiencing pregnancy-related night blindness.

Relative to the controls, the risk of death in the supplemented infants was 0.85 (95% CI 0.70, 0.997), and the mortality reduction was similar in both boys and girls. As infants in the JiVitA-2 trial were born to participants of the JiVitA-1 low-dose maternal supplementation trial (presented by Dr. Parul Christian on Day 3), the interaction between maternal and infant treatments was assessed. Dr. Klemm reported that infants whose mothers also received vitamin A during their pregnancy had additional protection (RR 0.76) compared to infant controls, whereas infants from mothers who received control (0.87) or β-carotene treatments (0.92) did not. Dr. Klemm also examined preventable causes of death affected by newborn dosing in the JiVitA trial, and in the previous studies from South India and Indonesia. Supplementation at the time of birth is hypothesized to protect infants by accelerating maturation and functioning of host defences, particularly that of the epithelial barrier. However, while vitamin A may have a common mode of action in all studies, the causes of death did not appear to be linked with the treatment in the different studies, suggesting that environmental or social factors may play an important role in determining impact on mortality.

Dr. Klemm summarized his findings by reiterating that newborn dosing with vitamin A in rural Bangladesh reduced the risk of infant death prior to 24 weeks of age by 15%. This protective effect was evident early in the trial and remained stable over time. Furthermore, protection was conferred regardless of gender, parity, maternal age, birth weight, or maternal supplement group. The JiVitA-2 findings corroborate those from Indonesia and India, adding further evidence to inform policy and action in Southern Asia.

Newborn Vitamin A dosing: Policy implications for Southern Asia and Africa

In the final presentation of Day 2, Dr. West outlined the critical situation a newborn child faces when born in a country where there is VAD. Using human data from India, Ethiopia, and Thailand, he showed how a child might only have a 12-day supply of vitamin A in her liver at birth, and is vitally dependent on breast milk vitamin A to maintain growth and build liver vitamin A stores. An adequate concentration of vitamin A in breast milk at three months is 50 µg/L (0.18 mmol/L), but in many countries like Bangladesh and Nepal, milk vitamin A concentrations of 0.08–0.11 mmol/L have been reported.

The 'vitamin A at birth' trials in Indonesia and South India reduced infant mortality by 64% and 23%, respectively. The trials in South India and Bangladesh involved nearly 30,000 infants, and the combined results suggest that mortality in the first six months was decreased by 20%. In a region where UNICEF estimates infant mortality is 63/1,000 live births, VAS at birth could avert 500,000 infant deaths each year. Thus, Dr. West believed that, in Asia, the evidence for benefit from birth dosing of vitamin A may have reached the 'tipping point' where research can be translated into policy. Dr. West concluded that the size and consistency of the impact of newborn VAS on mortality, coupled with its safety, raises the urgency for a regional, cross-sectoral dialogue aimed at developing policies and program approaches to deliver vitamin A at birth. For example, he suggested that a 50,000 IU vitamin A capsule could be inserted into "safe birthing kits" that could be delivered through

clinics, community health visitors, traditional birth attendants, commercial outlets, or other informal networks. While evidence to support newborn vitamin A dosing seems to have reached a policy tipping point in South Asia, there is still uncertainty about its impact in sub-Saharan Africa. Current data do not allow assessment of the impact of newborn vitamin A dosing in Africa, especially in vitamin A-deficient populations where malaria may be endemic, although a new trial initiated in Ghana will provide more information.

In the discussion, Dr. Benn cautioned that we should perhaps try explaining the negative results obtained in Africa for birth dosing before proceeding too quickly to implement policy in Asia. The factor(s) responsible for the higher mortality in Africa may also emerge in some Asian environments and result in unnecessary child deaths.

Day 2 Poster Session

Approximately one-half of Tuesday's posters were grouped under the theme 'Programs.' Note that food-based programs were presented separately on Wednesday. Other posters covered the themes 'Assessment and Evaluation', 'Communications,' and 'Coverage.'

Programs

In a number of African countries, large-scale integrated micronutrient interventions (ranging from fortification and supplementation, to health and nutrition promotion and education) that incorporated elements of community-ownership, and built on existing nutrition and health infrastructures were shown to be effective in improving a range of nutrition and health indicators in these countries (T19).

Two posters reported on the successful planning of large integrated interventions. In India, a Micronutrient National Investment Plan was developed, primarily to be used as an advocacy tool to strengthen commitment and increase budget allocations for fighting micronutrient deficiencies at the national level. The authors suggested that the Investment Plan would prove useful as a planning tool, and could be used at state level for decision-making (T32). In Pakistan, a National Plan of Action for the Control of Micronutrient Malnutrition was developed primarily as a planning tool to guide the development of national programs (T38).

Twelve posters presented findings from programs to improve vitamin A nutrition, mainly through supplementation, but also using red palm oil. The Global Alliance for Vitamin A (GAVA) recommended revised approach to national VAS coverage and monitoring including the use of an improved coverage indicator based on complete coverage, and improved data quality, more intensive program performance monitoring, increased technical guidance on program implementation and monitoring, and joint work planning between partners to strengthen the use of VAS coverage data for both program management and standardizing global reports (T1), GAVA also reported on progress in advocating for the inclusion of VAD control in Poverty Reduction Strategies (T2). The importance of continuous advocacy and commitment at national and regional levels was described in sustaining the success of the VAS strategy during the 'la Semaine d'Intensification des Activités de Nutrition' (SIAN) child nutrition week in Mali (T3). In Tanzania, cost analyses were used to demonstrate that the supplementation program was a highly cost-effective intervention, and should be regarded as an integral and long-term part of an overall strategy to reduce micronutrient deficiencies (T8).

The advantages of including deworming and/or other locally relevant preventive strategies with VAS were described for the Congo and Senegal. In the Congo, a regional and community-directed approach was built on a highly successful Ivermectin (river blindness) community program (T7). Results from Senegal also show high coverage and acceptability of the combined intervention of vitamin A capsule and mebendazole distribution (T13). The integrated approach will be continued, and an evaluation is planned to measure the impact on anemia reduction.

Several reports were presented of programs designed to address broader nutrition issues that yielded specific benefits for vitamin A. In Mexico, the Oportunidades program combines a diverse set of interventions to support families at risk of micronutrient deficiencies, including the distribution of a fortified complementary food for young children to improve vitamin A and iron status, in particular (T12). In the Philippines, an effective monitoring system, and additional training support for planning and management at local government level improved the coverage of VAS, as well as improved nutritional awareness and indicators in the area (T18). A program from Burkina Faso reported on the potential benefits of local production of red palm oil, both as a food-based strategy for controlling VAD and for income generation (T4).

Pilot programs in VAS for pregnant and lactating women were described in Nepal and Indonesia. Two posters from Nepal described different modes of delivery (take-home treatment vs. clinic-based treatment) targeting pregnant women with night blindness (T9), with home-based treatment being more effective than clinic-based interventions (T10). In Indonesia, an evaluation of postpartum VAS suggests that the low coverage could be improved by engaging non-formal health workers, such as traditional birth attendants and community health volunteers (T11).

Many posters described a diverse range of anemia programs (T15, T21, T22, T23, T25, T26, T27, T28, T30, T33). It is now well recognized that anemia is a complex problem that usually requires effective programs to include.

Several simultaneous interventions to be coordinated, and community support and participation. Examples of such programs include those in Tanzania, which emphasized sanitation, bed-net use, and diet diversity (T15); A wide range of strategies – e.g. participatory drama, community mobilization, village health days, and demonstrations – increased awareness of anemia-related issues, resulted in desirable behaviour change, and reduced anemia prevalence. And in Mali, where malaria control, ID control, and deworming were enhanced, but coverage of the interventions was not high enough to structurally reduce anemia prevalence (T21). A comparison of anemia-control programs for women in Ghana and Malawi showed the importance of programs being context specific, the feasibility of large-scale implementation of both supplementation and dietary diversification interventions, and the importance of community-based administration of such programs (T23).

Evaluation of programs targeting anemia in adolescent girls in India showed that iron supplementation can be effective, efficient, and feasible (T26). A model program in India showed that a community-based anemia-prevention package can reduce the prevalence of anemia, particularly when local health workers are involved (T27). The same program reported an innovative training scheme using a participatory and empowering approach to establish and sustain a network of volunteers and health workers, and create community support. This training was to provide a solid and essential basis for the subsequent up-scaling of the program (T28). In Nepal, a community-based integrated approach focused on awareness, and improved accessibility and acceptance of iron supplementation – including other activities such as training, antenatal care, deworming, and attention to other micronutrients – proved successful, and improved compliance and coverage to levels that were effective (T33).

Seven posters focused on programs using MMNs (T14, T16, T19, T31, T32, T35, T38). In Ethiopia, a school-based program focusing on deworming, VAS, water and sanitation, school gardening, and health education, was effective especially in reducing worm infections and signs of VAD (T14). An innovative but somewhat controversial approach was described from India, where a sweet was used as the vehicle for MMN supplementation ('Nutri-candy,' T16). The candies were highly acceptable among children – an important benefit, especially for iron. It is recognized that instructions on proper dental hygiene should accompany such an intervention.

The application and usefulness of participatory approaches in community-based nutrition programs was reviewed (T39). Several innovative approaches were reported, and these provided insight into key factors that determine the success of participatory approaches in nutrition programs. Examples were presented from Guinea and Uganda (T22, T37).

Assessment and evaluation

A large number of posters were concerned with the assessment of vitamin A status (T44, T45, T47–54, T56, T57). The first two used the modified relative dose response (MRDR) test as an indicator of vitamin A liver stores. In Ghana, vitamin A status, including vitamin A liver reserves, of women improved to a similar extent after postpartum dosing with either 200,000 or 400,000 IU, likely because vitamin A liver stores were only marginally depleted at baseline (T44). In an experimental study using a sow model, 3,4-didehydroretinol was used as a tracer for short-term vitamin A kinetics during lactation (T45). Furthermore, a method using breast milk MRDR values was explored and correlated well with the MRDR using blood samples, making this an interesting alternative method for measuring vitamin A liver stores in lactating women. A study from Iran, where night blindness is a familiar phenomenon, described the use of self-reported night blindness by schoolchildren combined with pupillary threshold screening, as an effective and non-invasive approach to assess vitamin A status (T47). A combination of night blindness assessment and DBS retinol analysis in Burundi revealed a high VAD prevalence among preschool children, but not pregnant women (T48).

Several posters report on technical aspects of vitamin A assessment (T49–52, T54, T57). DBS protocols were described and employed by several groups for analysis of RBP and other commonly used proteins. Few problems were reported in the collection, storage, or transfer of DBS samples (T50, T51), although the combination of extreme heat and humidity may influence recovery. The stability of RBP and α-1-acid glycoprotein (AGP) was uniformly high, with C-reactive protein (CRP) and sTfR more affected by environmental conditions. Agreement between RBP concentrations from DBS, and both serum and plasma was high (T49, T50). Others reported on a simplified sample preparation and analysis method requiring only 25 µL of serum, which showed excellent recovery, accuracy, and precision, and was highly correlated with the results of standard serum sampling (T52). The results of a separate study showed good comparability between capillary and venous blood for the assessment of retinol and RBP (T54).

Iron and zinc status indicators were also addressed by a number of posters (T58–63). Results from an intervention trial in Kenya showed that the interpretation of plasma ferritin concentrations to assess iron status was improved by correcting for APP (T58). A separate analysis suggested that the interpretation of hemoglobin and anemia data can also be enhanced and comparisons facilitated by the use of appropriate cut-offs and adjustment for age, sex, and conditions, such as pregnancy, altitude and smoking (T59). A poster submitted by the working group on zinc status indicators concluded that serum zinc was a useful indicator, and provided guidance on optimal assessments in different circumstances, such as response to dietary zinc restriction and zinc supplementation (T63).

Three posters provided general guidance for field assessment of micronutrient status. A toolkit and accompanying manual have been developed to facilitate the planning and implementation of nutrition surveys (T66). Collection and rapid processing of blood samples is a major challenge in these surveys. As such, one group investigated the effects of delayed sample processing on serum indicators for a range of micronutrients (T64). They found that refrigeration of samples for up to two days had little impact; however, storage at room temperature affected concentrations, often within one day.

Two survey methods to measure dietary diversity and adequacy in South African schoolchildren – the Food Variety Score and the Dietary Diversity Score – were compared, and both were deemed good indicators of the micronutrient adequacy of the diet that also correlated well with child growth (T65).

The other posters addressed various other micronutrients. Posters presenting results on iodine all showed high risk for deficiency in specific vulnerable groups such as pregnant women, formula-fed infants and schoolchildren. (T40–42). In Bangladesh, infant bleeding, suggestive of newborn vitamin K deficiency, was found to be relatively common and associated with high mortality, especially in the neonatal period (T67). However, there was no association between reported infantile bleeding and maternal vitamin K levels, either at the end of pregnancy or at three months postpartum. Further research is needed to establish the etiology and risk of infantile bleeding in Southeast Asia.

Communications

A report from Nepal on a campaign to promote the use of adequately iodized salt showed that promotion alone is not enough; actual consumption needs to be followed up and targeted for additional interventions if necessary (T68). Furthermore, the campaign demonstrated the crucial role of local community involvement, ownership, and mobilization. In Afghanistan, children were targeted for health and nutrition education, and results showed that boys and girls were reached equally, irrespective of school attendance (T69). Furthermore, health and nutrition knowledge and practices improved markedly, which was directly noticeable in hygiene practices. That children can affect adult practices was evident from the marked increase in households using iodized salt.

Coverage

With the exception of a poster describing low household coverage of iodized salt in Ukraine (T74), the posters in this section reported on VAS programs. The usefulness of collecting coverage data through post-VAS coverage assessments was reviewed in both Africa and Asia, and thought to be worth the investments required in terms of benefits to advocacy and program management (T75). An illustration of the above finding is provided by an analysis of coverage data in West and Central Africa (T79). The surveys showed that coverage was often less that estimated from tally sheet, and could assist in identifying key constraints affecting coverage. Many of the programs described included vitamin A as one component of an 'integrated child health package.' Such packages make efficient use of available resources, and improve participation and access (T76).

Examples of coverage estimates made through a variety of methods and put in a range of purposes were reported from African and Asian countries. In Senegal, vitamin A coverage was assessed, and found to be both high and in accordance with the estimated coverage, even with only limited resources available (T80). Combining vitamin A with other child survival interventions, such as deworming, proved successful, well accepted, and very relevant in view of the high prevalence of anemia. Descriptions of coverage data in Niger (T83), Cameroon (T84), the Democratic Republic of the Congo (T85), Nigeria (T86), and Zimbabwe (T87) were presented, and the uses of these data in the context of each program described.

Similarly, coverage data were reported for VAS programs in Asia, and their uses described. In India, sustained advocacy efforts resulted in increased interest by the central as well as the state government in VAS and the biannual approach (T88). Coverage increased markedly, and this was confirmed by several validation surveys. Also in India, the barriers to high coverage were analyzed and important program needs identified. These included:

– providing advocacy at all levels on the importance of high coverage;
– addressing supply gaps and other distribution problems with the vitamin A syrup;
– lack of guidelines and monitoring;
– strengthening collaboration and communication among the different partners in the program; and
– The inaccuracy of certain target population sizes, which resulted in unreliable coverage estimates (T90).

In Bangladesh, coverage data from the Helen Keller International (HKI) nutrition surveillance system were analyzed to identify groups of children that were not reached by the vitamin A program (T91). The results led to recommendations to focus efforts on poorer households in remote areas, and to increase the awareness and involvement of health providers as well as community leaders. Similar posters from Cambodia (T92) and Indonesia (T93) reported that the focus for increasing coverage should be squarely on the disadvantaged. VAS coverage of high-risk and sick children was markedly improved in the Philippines through strengthening the IMCI strategy to deliver vitamin A (T94, 95). Promotion of VAS through the country's Early Child Development and School Health and Nutrition Education programs may also have contributed to good coverage (T96). Similar successful experiences were reported from Guatemala (T78).

Day 3 – 18th April 2007

Overview of Dietary strategies

Dr. Emorn Wasantwisut, of Mahidol University, opened Day 3 with some comments on dietary strategies designed to control micronutrient deficiencies. Diverse efforts, ranging from home gardening initiatives to biofortification, may help to alleviate co-existing micronutrient deficiencies with limited risk of antagonistic interactions. Furthermore, dietary strategies are likely to be more culturally acceptable, sustainable, and economically feasible than supplementation since they empower communities to help themselves. She emphasized the necessity for adequate monitoring and evaluation to demonstrate nutritional impact and, to provide a basis for improving programs, motivating staff, and advocating their larger-scale implementation.

Biofortification

Increased vitamin A intake and serum retinol status among young children in rural Mozambique achievable through introduction of orange-fleshed sweet potatoes

Although dietary strategies are considered more sustainable than supplementation, the first speaker of the morning, Dr. Jan Low, of the International Potato Center, noted that few studies have had an adequate design or sufficient resources to demonstrate an impact on micronutrient status. However, over the last four years, she and her colleagues on the "Towards Sustainable Nutrition Improvement" project have been studying the effectiveness of orange-fleshed sweet potatoes in combating VAD in three drought-prone districts of Zambézia province in central Mozambique. Sweet potatoes are widely consumed in Africa. Research on the β-carotene content of several varieties common in Africa has yielded a range of values from adequate to excellent bioavailability (100 to 1,600 µg RAE/100 g, respectively). Prior work has shown that color and taste appeal to young children . Furthermore, sweet potato is a classic food security crop because of its flexible planting and harvesting times, and its resilience in harsh conditions. It is also generally considered a woman's crop in Africa.

The two-year study involved 53 villages and had three components: agriculture, nutrition, and marketing. The main agricultural outcome was to increase the supply of β-carotene and energy by introducing orange-fleshed sweet potato. The selection of treatment and control villages was based on size and access to services, with treatment villages further randomly assigned to receive low- or high-intensity nutrition information using group sessions and home visits. Nine surveys carried out over two agricultural cycles showed that vitamin A intakes were almost eight times higher among intervention than control children (426 µg vs. 56 µg RAE). Children under one year of age tended to eat sweet potato when their caregivers ate it, or an average of 300 g/day, two to three times a week, comprising 90% of vitamin A intake on days eaten and 35% of total vitamin A intake over the survey period. VAD prevalence (retinol < 0.7 mmol/L) fell from 60% to 35% among the treatment villages, and was accompanied by a significant increase in plasma retinol concentration (by 0.1 mmol/L) in apparently healthy children (CRP <5 mg/L). In addition, a 24-hour recall suggested that the median intake of energy, protein, and many micronutrients was significantly higher in the intervention compared with the control villages. For the future, it is hoped that agricultural output will increase income for the mothers from the sale of surplus sweet potatoes over time.

In conclusion, Dr. Low believes that orange-fleshed sweet potato eaten by young children as part of an integrated agriculture-nutrition strategy can have an impact on vitamin A status. Group sessions positively increased vitamin A intake and serum retinol concentrations of young children, but improvements in other components of diet quality may necessitate some kind of one-to-one contact between change agents and caregivers. The remaining challenge is to scale-up the approach in Zambézia under the HarvestPlus biofortification initiative.

Fortification

Application of NaFeEDTA-fortified soy sauce in the control of ID in China

Dr. Junshi Chen, of the China CDC, shared experiences from China in employing a food fortification strategy toward the control of ID and anemia. The project, which provides sodium iron ethylenediaminetetraacetate (NaFeEDTA)-fortified soy sauce to 50 million people, was supported by GAIN and aimed to reduce anemia by 30% over five years. It has also received strong support from provincial health authorities, and was listed in the 11th Five-Year Plan of the China CDC.

Development and testing of the food-grade fortified product has been ongoing for 10 years. Initial research focused on the most efficient compound and led to the selection of NaFeEDTA over ferrous sulfate due to the two-fold absorption of iron from the former compound. A randomized, controlled effectiveness trial of the fortified soy sauce (26.7 mg Fe/100 mL) carried out in the early phase of the project reported a 70% reduction in anemia prevalence, an improvement in iron status in all population groups, and an improvement in the growth of pre-school children after one year of the intervention.

For the GAIN project, 19 out of 69 producers were initially invited to produce the fortified soy sauce containing 23–27 mg Fe/100 mL. That number has now climbed to 110 manufacturers that produce a variety of products for the market, with an annual output of 90,000 MT. Approximately 50 million people in seven provinces, including 33 million at-risk persons, now have access to the fortified product. Anemia prevalence in the at-risk population of seven provinces in Phase I of the project has been reduced by 30%, and 80% of this population are aware of the health benefits of the fortified sauce. This achievement has been attributed to the development of a variety of product grades and packages to encourage purchase by persons in all social strata, wide-scale publicity and education, and effective quality control procedures that included the removal of non-conforming products from the market. Government support for the project was also critical.

While rigid QC has given the iron-fortified sauce a good reputation and the expanded program is beginning to show an impact on IDA, Dr. Chen remarked that coverage with the iron-fortified sauce is still low. Further education and social marketing will be crucial to achieve nationwide penetration of the market, and to effectively control IDA in China.

Efficacy and effectiveness of iron in complementary foods, rice and wheat flour

WHO/FAO jointly released comprehensive guidelines on food fortification in 2006. The presentation by Dr. Richard Hurrell, Swiss Federal Institute of Technology (ETH), Zürich, reviewed the portion of those guidelines pertaining to the use of iron in fortifying complementary foods, rice, and wheat flour.

National fortification programs are advised to provide all the iron lacking in the diet in one or two food vehicles. The principle iron compounds recommended by WHO/FAO are presented in **Table 5**. Dr. Hurrell stressed that there are critical differences in iron fortification versus fortification with other micronutrients. For most nutrients, fortificant levels are determined based on the EAR of the target population. However, a full probability approach, detailed in the WHO/FAO guidelines, is needed for iron to ensure sufficient intakes for all individuals in the targeted population. Although no true effectiveness studies have been published, Dr. Hurrell described a number of efficacy studies in infants and children where the expected benefits from iron were obtained, to a large extent, when these guidelines were followed. He provided the examples of South Africa and Oman, where IDA persists as a public health program even after the large-scale introduction of iron fortification. These two countries add 35 ppm and 30 ppm as electrolytic iron to flour, respectively, based on an EAR approach, whereas the fortification level should be more than doubled (e.g. 60–90 ppm) for effective ID and IDA control (**Table 5**). Dr. Hurrell reiterated the importance of following the WHO/FAO guidelines for food fortification.

Lessons learned from folic acid interventions as applicable to food fortification

Dr. Omar Dary, of the A2Z Project, discussed folate deficiency, which has been linked to the occurrence of neural tube defects (NTDs) in infants, cardiovascular disease (CVD), and megaloblastic anemia. Folic acid supplements have been shown to reduce the prevalence of NTDs, reduce blood homocysteine concentrations, and cure anemia, but optimal levels of fortificant for use in food vehicles have not yet been established. Foods are more efficient vehicles for folic acid than capsules as there is a limit to the amount of folic acid that the body can absorb at one time. Furthermore, other nutrients are necessary for efficient functioning of serum folate activity, such as riboflavin, pyridoxine, and vitamin B12. Dr. Dary argued that the amount added should reflect the folate intake in the specific population; thus, populations with a high intake of folate would need less added to the food vehicle. He suggested that the aim should be to raise serum folate concentrations to 25 nmol/L when NTD prevalence is around 6–10 per 10,000. Based on serum folate concentrations in Costa Rica, the USA, and Chile, and their responses to the three folate fortification programs, Dr. Dary calculated the additional supplementary folic acid needed to raise plasma folate concentrations to 25 nmol/L in the three countries. From the evidence he presented, the amount of fortificant needed in the US was 166 mg/day where the estimated dietary intake of folate is 303 mg/day, while the extra amount needed in Costa Rica, which has a much higher dietary folate intake (518 mg/day) than the US, was 40 mg/day. In Chile, the estimated intake was 240 mg/day, and the additional folic acid required was 203 mg/day.

In summary, Dr. Dary believed good knowledge existed from both epidemiological studies and biochemical research to justify using blood folate levels to make rational decisions on minimum efficacious levels for folic acid fortification.

Opportunities and challenges for commercial food fortification – A West African example

Dr. France Begin, of the Micronutrient Initiative, outlined the enormous need in African countries for micronutrient-fortified foods. In 34 Sub-Saharan African (SSA) countries, at least 50% of children under five years of age suffer from IDA; only 21 coun-

Table 5: Suggested iron compounds for complementary foods, rice and wheat flour (WHO 2006)

Food vehicle	Iron compound
Cereal-based complementary foods	Ferrous sulfate, encapsulated ferrous sulfate, ferrous fumarate, electrolytic Fe (2x amount)#, all with ascorbic acid at ≥2:1 molar ratio to Fe
Rice	Ferric pyrophosphate (2x amount)
Low extraction wheat flour, degermed maize flour	Dry ferrous sulfate, ferrous fumarate, electrolytic Fe (2x amount), encapsulated ferrous sulfate or fumarate
High extraction wheat flour, maize flour	NaFeEDTA, ferrous fumarate (2x amount), encapsulated ferrous sulfate or fumarate (2x amount)

Two times the iron fortification level used in the community (see below)

tries reached at least 70% of children aged 6–59 months with semi-annual VAS in the most recent reporting year; and, each year, 3.5 million children in this area of the world are born mentally impaired due to iodine deficiency. While there has been some progress in the identification of potential food vehicles, the establishment of national fortification alliances, and government planning, only three countries in the region (Ivory Coast, Nigeria, and South Africa) have established mandatory fortification programs.

The main obstacles to food fortification in SSA were described by Dr. Begin. First, finance was an issue, as industry needs incentives, assistance with start-up costs, lower taxes on imports, and money to invest in necessary equipment and other capital costs. Education to promote consumer demand for fortified foods and to discourage non-fortified foods was also lacking. Finally, fortification requires partnerships to coordinate activities and create the right environment for success. She indicated, however, that there were emerging institutions, such as the African International Food Organization, and partnerships between industrial groups, NGOs, and the private and public sectors that were interested in promoting fortification on the continent. She suggested that these partnerships should be encouraged, since all the basic foodstuffs consumed in Africa are produced in Africa. While commercial fortification does not reach everyone, increasing urbanization is improving the accessibility of commercially processed foods, and these gains may enhance future potential to reach the most at-risk populations. Currently, 388 million people in sub-Saharan Africa potentially have access to commercially-produced foods.

Dr. Begin called for increased efforts to encourage action on the part of governments and industries, including seed financing to industry, the promotion of public-private partnerships to assist in the development and marketing of fortified products, and the establishment of an effective M & E system.

Fortification at point-of-use

Sprinkles for reducing micronutrient deficiencies among children in Indonesia: Impact and large-scale program implementation

Dr. Saskia de Pee, of HKI and the World Food Programme (WFP), discussed the role of "point of use" fortification to control micronutrient deficiencies in young children, drawing on two feasibility studies carried out in Indonesia.

Approximately 60% of Indonesian children are anemic. While scientific trials have demonstrated the efficacy of micronutrient Sprinkles in reducing anemia, the translation of those findings into programmatic success will depend largely on the acceptability and uptake of this product by mothers. Dr. de Pee reported the results of a pilot intervention designed to assess whether mothers could be persuaded to purchase Sprinkles at cost. The at-cost distribution model was piloted by four local NGOs in the slums of Semarang and Solo, Indonesia, using different distribution systems (health posts, NGO programs, and small stores). An evaluation eight months into this pilot revealed that 90% of mothers were aware of the product, but only 60% had purchased Sprinkles for their children. Those who purchased the product bought it more than once, indicating an interest in the product. Nevertheless, almost none of the children had received the stipulated 90 sachets.

A second study assessed the impact on anemia and morbidity following free distribution of Vitalita Sprinkles to internally displaced persons (IDP) following the December 2004 Indian Ocean tsunami and May 2006 Yogyakarta earthquake. By December 2006, more than 35 million sachets had been distributed in Indonesia to over 370,000 children. This study showed a 25% reduction in anemia prevalence among IDP children who had received Sprinkles. There was no relationship between the number of Vitalita sachets received and either diarrhea or anemia prevalence among children aged 6–59 months after controlling for confounding factors. The data indicated that acceptability of the product was generally good. However, it was not consumed by all children. Dr. de Pee suggested that restrictions on its use – i.e. that Sprinkles cannot be used on hot foods or in liquids – and a lack of understanding regarding the need for and benefit of the product may account for this.

Although Vitalita Sprinkles can reduce anemia and ID, the acceptability of the product was inadequate even when freely distributed. To overcome this issue, Dr. de Pee proposed the need for improved behavioral change communication and subsidies for very low-income households to overcome cost limitations in the future.

Feasibility and effectiveness of distributing micronutrient Sprinkles to children aged 9–24 months in the context of a food-assisted integrated maternal and child health and nutrition (MCHN) program in rural Haiti

Past research illustrates that fortified wheat-soy-blend and local foods alone cannot meet the iron and zinc needs of young infants in rural Haiti. In her presentation, Dr. Purnima Menon, of Cornell University, described the feasibility of incorporating Sprinkles into a food-assistance MCH program in this population.

A supply of 60 sachets of Sprinkles was provided to mothers of infants and young children aged 9–24 months in the context of small group education sessions. Evaluation of the acceptability of the Sprinkles intervention by mothers was assessed by observation, interviews, and focus group discussions, which were supplemented by focus groups to gather staff perceptions on the integration of this intervention into other program tasks. Over the course of the two months between baseline and the first follow-up, anemia prevalence decreased by more than half among targeted children (54% to 24%, P<0.05), whereas there was a non-significant increase in anemia among children receiving only food assistance. Changes in hemoglobin were larger for younger children (aged <18 months at baseline) and for children who were anemic (Hb <100 g/L) at baseline. The Sprinkles intervention prevented the recurrence of anemia for seven months. Dr. Menon suggested that these highly positive results were due to the program's excellent venues for educating mothers about the importance and proper use of Sprinkles.

Efficacy of a fortified complementary food, Sprinkles, and a micronutrient syrup to prevent anemia in children under two years of age in urban Mexico: A randomized controlled trial within the *Oportunidades* conditional cash transfer program

The use of Sprinkles was also described by Dr. Lynette Neufeld, of Instituto Nacional de Salud Pública, Mexico, in the context of Mexico's *Oportunidades* program, a government intervention that aims to promote health, nutrition, and education among urban Mexicans. *Oportunidades* provides fortified foods to infants aged 6–23 months and older children (aged 2–4 years) who are underweight. The iron-fortified foods provided by the program have had little impact on anemia, partly because mothers share the food among all the children in the family.

Dr. Neufeld reported on a supervised comparative study of the fortified food, Sprinkles, and a micronutrient syrup with a similar composition to Sprinkles given to infants aged 4–12 months, and continued through 24 months. After four months of treatment, Sprinkles and the syrup were more efficacious than the fortified food (Hb 5 g/L higher, P<0.01). At 10 months, however, the comparative results were similar – all treatments increased hemoglobin by ~10 g/L with no clear differences. There was no control group but the magnitude of change was unlikely in this population without supplementation. Dr. Neufeld reported that, under the controlled conditions of the study, the consumption of the complete dose was more common among the Sprinkles group than among the other groups. Final recommendations to the program were still awaiting other outcomes.

Maternal micronutrient – supplementation

The effect of maternal MMN supplementation on fetal loss and infant death in Indonesia: A double blind cluster randomized trial – Supplementation with Multiple Micronutrients Intervention Trial (SUMMIT)

Dr. Anuraj Shankar, presented the first paper on behalf of the SUMMIT Study Group, which described a double-blind, cluster-randomized intervention with MMN or iron-folic acid alone among 31,290 pregnant women in Lombok, Indonesia. The main objective was to compare the two supplements on infant and maternal deaths in this population, where the infant mortality rate in 2001 was estimated at 106 per 1,000 live births, and the MMR was 537 per 100,000 live births. Women received supplements monthly from enrolment through to 12 weeks postpartum. Enrollment began in July 2001 and ended in April 2004. Researchers found that MMN supplementation reduced early infant mortality – i.e. in the first 90 days, by 18%. In the 50% of women who consumed 85% of their supplements, there were 22% fewer infant deaths (RR 0.78, 95% CI 0.64–0.95). There were no differences in maternal deaths between the groups. The speaker concluded that the effects on infants may be greater with increasing age and the benefits were obtained in a programmatic setting indicating the feasibility of utilizing the health services to administer the program.

Impact of postpartum VAS on sexual acquisition of HIV among vitamin A-deficient women in Zimbabwe

Dr. Jean Humphrey, of the Johns Hopkins Bloomberg School of Public Health, presented results from the ZVITAMBO trial, which assessed the impact of postpartum VAS on HIV acquisition overall and according to baseline plasma retinol levels (< 0.7 or > 0.7 mmol/L). VAD in animal models has been shown to cause cornification and reduced epithelial integrity of vaginal epithelium, which are early and consistent signs of deficiency and respond quickly to VAS. These changes may make young women more vulnerable to HIV infection.

Mother-baby pairs (n=14,011) were enrolled within 96 hours of delivery, and the 9,562 HIV-negative mothers were randomized to receive 400,000 IU vitamin A or placebo. Women were tested for HIV at baseline and mothers who tested negative were tested at subsequent blood draws.

Overall, VAS had no effect on the incidence of HIV infection (HR 1.09, 95% CI 0.85, 1.38). However, susceptibility to HIV infection was significantly higher among women who were deficient at baseline (adjusted HR 1.98; 95% CI 1.39, 2.80), compared to those with adequate vitamin A status. Vitamin A supplementation among the 676 deficient women showed a tendency toward protection (HR 0.64), but this finding was not statistically significant (95% CI 0.33, 1.23; p=0.18). Incident infections were also higher in women with low hemoglobin concentrations. VAD at baseline coexisted with anemia, thinness, and poverty; therefore, poor malnourished women were at greatest risk of acquiring HIV. Vitamin A-deficient women were not more likely to report a new sexual partner, yet having a new partner was a much stronger risk factor for incident HIV among vitamin A-deficient than vitamin A-replete women.

In conclusion, low plasma retinol and hemoglobin concentrations were associated with a higher risk of incident HIV infection but vitamin A supplementation did not influence the rate of infection.

Effects of vitamin A and β-carotene supplementation on maternal and infant mortality in rural Bangladesh: JiVitA-1

Dr. Parul Christian, of the Johns Hopkins Bloomberg School of Public Health, gave details on the JiVitA-1 trial in north-eastern Bangladesh, which assessed the efficacy of weekly supplementation with either vitamin A (7 mg RE) or β-carotene (42 mg) from the first trimester until 12 weeks postpartum.

Almost 60,000 pregnant women were enrolled over the course of the five-year study period. Randomization resulted in highly comparable treatment groups. Mean adherence to supplementation across the three groups was 95%, with 80% of supplements given directly by staff. Although a prior trial of low-dose vitamin A and β-carotene supplementation had detected a 40% reduction in all-cause pregnancy-related mortality (PRM), no mortality impact was observed in either the vitamin A (RR 1.15) or the β-carotene groups (RR 1.21). Likewise, there was no impact of maternal treatment on neonatal (to 12 weeks of age) or infant mortality. A comparison of the two studies suggests that pregnancy-related mortality in Bangladesh was one third that in Nepal, and that the prevalence of early gestational VAD was 20% of the prevalence rate observed in Nepal. Likewise, diet and services are poorer in Nepal than in Bangladesh. Dr. Christian concluded that the large-scale implementation of low-dose maternal supplementation should only be considered where VAD and pregnancy-related mortality rates are both high.

Meta-analysis of the effects of MMNs in pregnant women

The last presenter in this session, Dr. Barrie Margetts, of the University of Southampton, gave details on the current status of a meta-analysis comparing the effects of MMN with iron-folic acid supplements on mother and infant nutritional status and pregnancy outcomes among mothers assumed to be HIV-negative. The analysis is still incomplete, but results so far suggest that: (1) MMN supplementation improves the nutritional status of mother and baby over iron-folic acid supplementation alone; (2) the effects of the MMN supplement are greater in better-nourished mothers; and (3) post-28-day infant mortality is lower among mother-infant pairs randomized to receive MMN versus iron-folic acid supplements. The speaker concluded by proposing that micronutrient interventions would be more beneficial if targeted to women before they become pregnant, in addition to taking action to maintain adequate nutritional status throughout pregnancy.

Table 6: Serum retinol data from Bangladesh classified by CRP concentration

Serum retinol (µmol/L)	Serum CRP, mg/L (n)					
	<1 (132)	1 to <2 (142)	2 to <5 (185)	5 to 10 (80)	≥10 (38)	P
Mean	0·93[a]	0·89[a]	0·81[b]	0·77[b]	0·62[c]	<0·001
% "Decrease"	0	4	13	17	33	
< 0·70 (%)	16	24	36	39	74	<0.001
0·70 – 1·05 (%)	54	53	47	50	21	
≥ 1·05 (%)	30	23	17	11	5	

[a-c] Unalike superscripts significantly different

Solution 1: Correction based on MLR for serum CRP (mg/L) levels

1 to < 2 add 0·04 µmol/L to serum retinol concentration
2 to < 5 add 0.12 µmol/L to serum retinol concentration
5 to < 10 add 0.16 µmol/L to serum retinol concentration
10 add 0.32 µmol/L to serum retinol concentration

Micronutrients and infection

Nutrition and immune function – The acute phase response and assessment of nutritional status

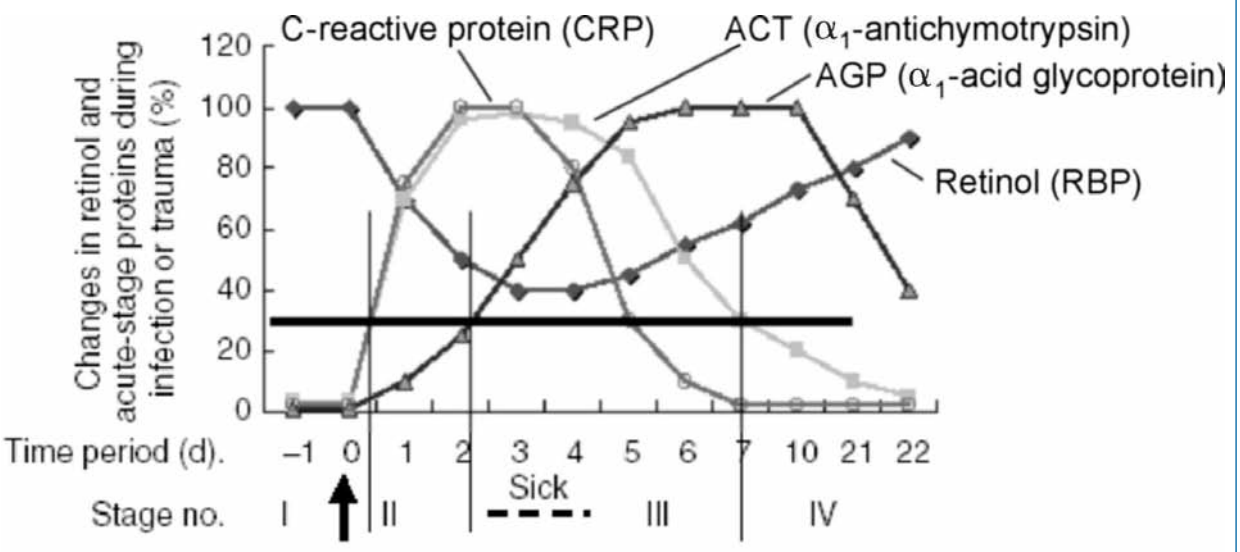
Dr. Charles Stephensen, of the Western Human Nutrition Research Center, ARS/USDA, addressed the subject of nutrition and inflammation. Inflammation is the body's normal reaction to injury, a major part of which is the acute phase response (APR). The APR is a coordinated physiological response to infection or injury that clears pathogens and repairs tissue damage, and nutrient metabolism is redirected to support these functions. The APR is a "nuisance" to nutritionists because during the APR, serum concentrations of iron, zinc, vitamin A (retinol and carotenoids), and several other nutrients decrease while ferritin increases. The changes in nutritional biomarkers persist even during convalescence, so prevalence data from apparently healthy people may be inaccurate if results influenced by inflammation are not removed or corrected. Three solutions are currently being discussed: (1) using an acute phase protein such as CRP to identify individuals with inflammation, and to stratify results by inflammation status; (2) adjusting nutrient concentration based on the difference in concentration of those with and without a raised CRP; and (3) using multiple APPs to adjust for the phase of infection severity.

Table 6 shows an application of solutions 1 and 2 to data from a cross-sectional study of 577 healthy children aged 3–7 years in a poor Dhaka community. In the lowest category of CRP concentration (< 1 mg/L) (the healthiest children), mean serum retinol was 0.93 µmol/L and was progressively lower as the CRP concentration of the sub-sample increased. The table shows the percentage of subjects below the usual cut-off value for VAD, < 0.7 µmol/L. The overall prevalence of deficiency in the whole population was 31%, a value inflated by the high prevalence of inflammation. Multiple linear regression was used to characterize the impact of different concentrations of CRP on serum retinol, and a correction factor used to re-calculate the prevalence of deficiency.

The third method of correction was reported by Dr. David Thurnham and colleagues from their meta-analysis of community data from South America, Africa, and Asia. Data were used to derive correction factors based on idealized distributions of various APPs, shown in **Figure 1**. The measurement of two proteins could be used to infer the stage of infection and calculated correction factors, as previously described.

Dr. Stephensen concluded that workers should report data in those with and without an APR. However, when the prevalence of APR is high, adjustment of the data is needed. He also called attention to an important assumption in Methods 2 and 3 – namely that the prevalence of nutritional deficiency would be the same in those with and without inflammation (i.e. that nutritional deficiency does not increase or decrease inflammation). If there is an increased APR in deficient subjects, correction would underestimate the prevalence

Figure 1: Solution 3 – correction based on stage of infection using multiple APP*



of deficiency, and the converse would over-estimate the prevalence. Further work is needed to resolve these issues.

Group	Stage of inflammation	Raised APP*	Retinol decrease
I	Healthy	None	None
II	Incubating or pre-clinical	CRP only	13 %
III	Early convalescence	CRP & AGP	24 %
IV	Late convalescence	AGP only	11 %

Conclusions of the WHO consultation on prevention and control of ID in infants and young children in malaria-endemic areas

Dr. Sean Lynch, of Eastern Virginia Medical School, described the conclusions of a consultation arranged by WHO and UNICEF in June 2006 to discuss the higher infant mortality that occurred following the iron-folic acid intervention in the malaria-endemic island of Pemba, Zanzibar. Two trials took place at the same time – one in Nepal, where malaria prevalence is low, and one in Pemba, where malaria transmission is intense, perennially stable, and mainly from Plasmodium falciparum. For other details on these trials, see the reports of the presentations by Dr. Sazawal and Dr. Tielsch (in the Tuesday morning session).

As discussed, iron-folic acid treatment in Zanzibar – but not Nepal – was associated with a 12% (95% CI 1.02, 1.23, p = 0.02) higher risk in the likelihood of hospital treatment or death than those receiving no iron. Sub-study analyses further revealed that children with good iron status (ZPP < 80 and hemoglobin >100 g/L) experienced more severe morbidity, while those who were deficient in iron or hemoglobin had a lower risk of severe morbidity (RR 0.62 for iron; 0.59 for hemoglobin, respectively). Members of the consultation were in general agreement about the importance of adequate iron nutrition in infancy and that, for unknown reasons, iron–folic acid supplementation in malaria-endemic regions was associated with a significantly increased risk of severe morbidity. Thus, it was concluded that the indiscriminate use of iron supplements in such regions should be discontinued, and alternative measures used to improve iron status (see the report of the presentation by Dr. Stoltzfus on Day 1).

It was concluded that strategies to prevent and treat ID should be integrated with malaria control programs, and supplemental iron should only be given to iron-deficient children. In addition, supplemental folic acid was not recommended because folate deficiency is not widespread in young children, and folic acid may render antifolate antimalarial drug therapy less efficacious.

Report from the Young Investigator Workshop: Defining research priorities for the prevention of anemia in malaria-endemic countries

In the last presentation for this session, Dr. Sharon Cox, of the London School of Hygiene & Tropical Medicine, reported on a pre-conference meeting of young investigators, which included representatives with a wide range of backgrounds from 15 countries.

The central theme of the meeting was to discuss the adverse effects of iron on infant mortality in Pemba, in terms of biological mechanisms, ethical implications, the role of the RCT, future research on MMN interventions, and the safety of other iron delivery strategies. Of particular interest to the participants was the formation of an "anemia consortium" to share expertise and protocols for large-scale multi-country studies. This suggestion originated from concerns regarding the lack of standard cut-offs and methods for assessing key exposures and outcomes, like iron status and malarial incidence, and the difficulties of making meaningful comparisons between studies due to differences in study protocols. Other suggestions included further investigation of effect modification in these large datasets, and the identification of biomarkers that might assist in the interpretation of study results. Discussions extended beyond the topics of iron and malaria to include the nature of academic scientific research and the current research environment.

Update on zinc in the treatment of diarrhea

Effectiveness of zinc for the management of diarrhea in rural Pakistan: Pakistan Zinc Effectiveness Trial

The first paper in this session, presented by Dr. Robert Black, of the Johns Hopkins Bloomberg School of Public Health, on behalf of Dr. Bhutta, of Aga Khan University, described an effectiveness study carried out in Pakistan to address the use of zinc in the case management of diarrhea. Sixteen clusters of 859 villages were randomized to control or treatment groups. In the treatment villages, Zincol dispersible tablets were provided free of charge by government health care facilities, or at cost in pharmacies when treatment was sought for diarrhea. The treatment of diarrhea in control villages was based on standard case management protocol. Surveillance on the use of zinc in diarrhea management was conducted every three months and (1) considered the current use among children with diarrhea in the last 24 hours, and (2) recent use among children with a diarrheal episode during the previous two weeks. Additional follow-up was conducted by the study team of every fifth child who currently had diarrhea. The intervention group showed an increased trend in the use of ORS and zinc, and a reduction in the use of antibiotics and anti-diarrheals.

Based on these preliminary data, Dr. Black concluded that it is possible to introduce zinc into the health systems, at scale, for the treatment of diarrhea. A social marketing scheme for the use of zinc, and public sector training led to a significant uptake of zinc and alterations in prescribing patterns by both public and private health care providers. As expected from the efficacy trials, the use of zinc in the intervention clusters was accompanied by a significant reduction in diarrhea incidence, and reduced rates of hospitalization.

Accelerating the scale-up of zinc for diarrhea management around the world

Dr. Black went on to describe progress in accelerating the adoption of zinc for diarrhea management around the world. This work has been driven by the Zinc Task Force, a collaborative working group established in September 2005 by UNICEF, WHO, the Johns Hopkins Bloomberg School of Public Health, and USAID, with support from the Bill and Melinda Gates Foundation.

The Zinc Task Force is intended to support advocacy, assist in planning and start-up activities in countries, and continue operations research, and monitoring and evaluation of early programs. Since its inception, the group has identified the steps needed for successful country adoption of zinc for diarrhea management, and has organized five regional advocacy workshops in Southeast Asia to inform policy makers of the rationale for using zinc. Various educational tools have also now been produced. A major obstacle to the widespread provision of zinc was that, prior to 2006, there was no manufacturer of a zinc dispersible tablet or syrup that met WHO pre-qualification standards. Several manufacturers now meet the Good Manufacturing Practice qualification for UNICEF procurement. At present, more than 20 countries have

adopted zinc as part of their diarrhea management policy, and more than 15 have placed orders for initial zinc supplies.

Dose-response trial to assess the impact of zinc supplementation, with or without copper in young Ecuadorian children

Finally, Ms. Sara Wuehler, of the University of California at Davis, described a dose-response trial to assess the impact of zinc with and without copper among 631 young Ecuadorian children. Children aged between 12 and 30 months, with an initial length-for-age Z-score of <-1.3 and an altitude-adjusted hemoglobin of >105 g/L, were recruited. Children were stratified by age and sex to receive placebo; 3 mg, 7 mg, or 10 mg ZnSO4; or 10 mg ZnSO4 plus 0.5 mg copper sulfate (CuSO4) for six months. Morbidity data were collected 3–5 times a week by field workers who also observed supplement taking

This trial revealed 21–42% fewer cases of diarrhea in children who received any dose of zinc, compared with the placebo. Growth rates were not affected and there were no adverse effects of 10 mg zinc on zinc or copper status, or lipoprotein concentrations. Ms. Wuehler concluded that plasma zinc concentrations increased in relation to zinc dosage. Supplemental zinc at 3 mg/day was sufficient to reduce the incidence of diarrhea. She added that further research is needed in other populations to confirm whether this dose-response relationship varies by population. Current recommendations for the safe upper level of zinc may also need to be re-evaluated.

Concluding remarks

In her concluding remarks, Dr. Meera Shekar, of the World Bank, highlighted the main themes of the meeting in terms of the four major nutrients discussed:

1. VAS programs have achieved considerable success in reaching children under five years of age. This momentum needs to be sustained and extended to all countries. Newborn dosing has also reached a tipping point, at least in South Asia, where programmers and policy makers are now poised to start discussions on the scale-up of this intervention. Maternal dosing may also be considered in areas with a high burden of VAD, and higher pregnancy-related mortality. Promising evidence was also presented for the first time on the scale-up and effectiveness of a biofortification initiative involving orange-fleshed sweet potato.

2. Iodine programs are well established; however, it is concerning that progress in achieving USI may be stagnating at around 70% global coverage. More efforts are needed to reinvigorate USI, to extend coverage to the remaining 30%, and to improve the regulatory monitoring necessary to ensure adequate fortificant levels in all salt. It is also time for those in the research community to improve the knowledge and technology needed in an era with mild-to-moderate deficiency, and potential concerns of iodine excess.

3. Much of the discussion in the meeting was focused on the concerns of iron supplementation to young children in malaria-endemic areas. Programmatic approaches to protect these children from the consequences of ID and IDA must begin before birth, addressing deficiency in the mother and scaling up the recommendation for delayed cord clamping. The scale up of fortified foods in line with WHO/FAO recommendations is also needed.

4. Translation of clinical research on zinc in the treatment of diarrhea is already well into policy and program translation, with data emerging to attest to the effectiveness of this intervention in the field. The continued commitment of the international community will be necessary to oversee this transition. The second Tipping Point of this meeting unfortunately suggests that earlier evidence on the child survival benefits of universal zinc supplementation may be less promising. Scale up of this intervention for children 1–5 years will depend on further evidence of the invention's cost effectiveness.

Dr. Shekar concluded her summary by encouraging participants to view their work in the broader development context. This first meeting of the Micronutrient Forum provided an excellent opportunity to build consensus on policy and programs. It is now time for this community to present a united front on evidence-based actions, such as newborn vitamin A dosing in South Asia or zinc treatment for diarrhea, to apply the same rigorous review to programmatic knowledge and to focus on micronutrient deficiency control at the large scale.

Day 3 Poster Session

Wednesday's posters addressed the following five themes: 'Dietary diversification,' 'Biofortification,' 'Food fortification,' 'Fortification at point-of-use,' and 'Micronutrients and infection.'

Dietary diversification

Several posters focused on breastfeeding and the adequacy of milk to meet the needs of infants (W1, W2, W27). A study from Spain showed that breast milk has higher iodine content than most formula preparations, especially those for premature babies, suggesting that non-breastfed infants may be at risk of deficiency (W1). Historical data from Northern Congo indicated a close correlation between urinary and breast milk iodine concentrations, in support of the notion that mammary iodine transport is based on facilitated diffusion rather that active transport (W2). An assessment in Turkish women using both biochemical and dietary indicators showed that vitamin A status is adequate to meet the needs of breastfeeding infants (W9). In Turkey, an ambitious, integrated, nationwide program was launched to specifically address IDA in infants and young children via the promotion of breastfeeding, in line with international recommendations and targeted supplementation (W17).

A poster from the Philippines illustrated that iron absorption from brown rice, which has a higher iron content than white rice, is inhibited by fiber, phytic acid, and tannic acid, resulting in iron absorption similar to that of white rice (W19). In another study from the same country, iron absorption data from a carefully controlled dietary intervention were used to compare predicted values using six commonly used equations, of which only two (Hallberg and Bhargara) produced values in line with observations (W20). A study in India measured in vivo iron absorption from a rice meal in iron-deficient and non-iron-deficient young women, showing that iron absorption is reduced by 60–70% by consumption of tea with the meal, and increased 2–3 fold by the addition of vitamin A (W24). Finally, predicted iron absorption from an in vitro model was compared with actual iron absorption from maize and different varieties of beans (W21); correlations were high only for maize, but not for the beans, indicating that the model needs further refinement to more accurately reflect human absorption.

In Pakistan, red palm oil was used to fortify a traditional cooking fat product, and consumer acceptability, stability, and effect on the vitamin A status of household members were found to be very good (W6). In Ghana, an assessment of postpartum women showed that a daily portion of indigenous green leafy vegetable could significantly improve vitamin A liver stores assessed using MRDR (W10). Bangladesh's integrated Homestead Food Production (HFP) program improved vitamin A intake and anemia prevalence in mothers and children to a greater extent than in a control group, suggesting that the approach is a feasible strategy to improve micronutrient intake in poor households (W15). Results from the HFP program compiled from several countries in Asia show a modest impact on anemia prevalence, especially among non-pregnant women (W18). A study in Indonesia used an innovative approach to help nutrition planners identify optimal food-based strategies, and to determine whether these need to be combined with other strategies to ensure recommended dietary intakes (W22).

Another study from India evaluated the nutrient contribution of mandatory hot school meals, and recommended the inclusion of micronutrient supplements, fruits, and milk to ensure adequate intakes (W26). In the Philippines, analysis of dietary intake and micronutrient status of schoolchildren showed inadequate intakes of energy, protein as well as micronutrients.

Biofortification

A series of posters reported on scientific and programmatic developments in biofortification (W28-W34). Three posters addressed scientific progress. The first demonstrated the high bioavailability of β-carotene from Golden Rice using intrinsically labelled stable-isotopes, noting that this crop is one of the most bioavailable plant sources of vitamin A (W29). The Golden Rice Project also reported on the progress of making available agronomically-attractive, productive, and GMO-deregulated varieties to subsistence rice farmers in developing countries free of charge and limitations, and via public, national rice institutions (W31). Extreme precautionary regulations for GMO products were identified as a bottleneck in the use of Golden Rice, even though preliminary studies have shown good potential impact and effectiveness. In another study, a model legume, Lotus Japonicus, was used to identify genetic markers that could be used to effectively and quickly assess high micronutrient traits during selective breeding (W34). In the area of program development and advocacy, a model was developed to assess the potential impact and cost-effectiveness of biofortified staple foods in addressing micronutrient malnutrition in India (W30). The analysis showed that biofortification could be a cost-effective, efficient, and economically viable intervention that may complement the existing mix of strategies to control micronutrient malnutrition. The Vitamin A Partnership for Africa Program reported on the progress in promoting, distributing, and extending the impact of new varieties of orange-fleshed sweet pota-

to with very high β-carotene content in 10 sub-Saharan African countries (W28). In Colombia, beans with high iron and zinc content, and high quality protein were developed using existing crop diversity (W33). Adaptation and farmer acceptance of the new varieties was successful, and preliminary assessment of bioavailability and nutritional impact are promising.

Food fortification

Thirty-four posters reported on food fortification, with 8 posters covering progress in IDD control though salt iodization (W36-39, W41-42, W76, W77). The IDD control program in Turkey reported good progress since 1994 (W36). Both compliance and iodine status of the population have shown improvement. Progress in Pakistan has been hindered by the scale of producers, the majority of whom operate on a small scale, with only 4 % operating at industrial-scale production (W37). Other identified constraints were the lack of training, the supply of potassium iodate, and costs. In India, a recent survey showed that the coverage of adequately-iodized salt had increased to 57% (W39). In the same country, the iodine status of pregnant women was assessed in relation to household use of iodized salt. The results indicated that the use of iodized salt correlated well with sufficient iodine status in schoolchildren, but not as well with sufficient iodine status in pregnant women (W38). This indicates a different dietary pattern in pregnant women and shows that, in order to eliminate iodine deficiency, not only should iodized salt be used, but it is also necessary to find other ways to meet the needs of pregnant women. It was found in the Philippines (W41) that the use of iodized salt does not have negative effects on processed foods. In India, a double-fortified salt, delivering iron as well as iodine, was evaluated for stability and nutritional impact (W42). The stability of the iron and iodine as well as the impact on hemoglobin and iodine excretion was found to be good. The consumer availability of non-iodized salt from the many small-scale salt farms in Indonesia is a continuing problem (W76). Hand-spray iodization was assessed for stability and safety, and could be a feasible strategy to ensure iodization at small-scale, low-tech salt production sites. The coverage of iodized salt in Darfur, Sudan, is reported to have significantly improved after efforts to strengthen the national program; this was done through the development of national policies with supportive legislation, adequate quality control and monitoring, the cooperation of the salt-producing sector, and increased political will for the actual implementation of the national program (W77).

Progress in vitamin A food fortification was reported by a much smaller number of countries. In Bolivia, the development of a mandatory vitamin A fortification program for vegetable oil was reported, and results so far are satisfactory (W44). In order to sustain the success of the program, effective evaluation and monitoring needs to be implemented and visible public sector interventions to enforce standards are needed. The effectiveness of national interventions to control VAD in Guatemala was assessed using health systems data on the impact of sugar fortification and VAS on the prevalence of xerophthalmia (W45). Results show that the national VAD control program is successful, as xerophthalmia prevalence has been greatly reduced. In Morocco and Cote d'Ivoire, vitamin A content was well-retained in fortified cooking oil during traditional uses. This validated the decision to use this vehicle in each country (W46, W47). Significant contributions to vitamin A intake can be expected from the fortified cooking oil for women, but less so in young children because dietary intake of foods prepared with cooking oil is much lower.

Several posters reported on advances in fortificant technology for iron. Evaluation of the solubility, bioavailability, and safety of ferric phosphate nanoparticles showed that this novel technology produces iron compounds that are comparable to iron sulfate in solubility and bioavailability in rats (W50). The bioavailability of elemental iron in commercial products was assessed using different methods, and results show that the estimated bioavailability differs significantly between different commercial iron powders, depending primarily on the production method. Only in a few of them was bioavailability high enough to expect an impact on iron status (W51). A study from Brazil demonstrated the efficacy of supplying iron-fortified drinking water to preschool children (W52). Dosing of FeNaEDTA among young children aged 6–24 months was also assessed in relation to maximum safe levels of EDTA intake (W55). Dosing at a desired level for iron would exceed current safety limits for EDTA intake by a factor of two or more.

In infants in Vietnam, flour fortified with MMNs and amylase used as complementary food improved hemoglobin, serum ferritin, zinc, and retinol levels. However, micronutrient deficiencies were still prevalent, and complementary interventions need to be considered (W56). In Mexico, a food supplement for toddlers fortified with iron gluconate proved more effective in improving iron status and growth than a similar supplement containing ferrous sulfate as a fortificant (W57). The duration and frequency of consumption of

the food supplement determined the total effect on iron status in the individual toddlers. In Cambodia, iron-fortified fish sauce to deliver 10 mg iron – from either ferrous sulfate and citric acid, or NaFeEDTA – proved effective in reducing ID and anemia (W59). Two types of iron-fortified rice were compared in a dietary intervention among anemic schoolchildren in the Philippines (W60), and iron supplementation and iron fortification among severely malnourished children in Senegal were reported (W61). In Vietnam, weekly iron supplementation was compared to the consumption of MMN-fortified biscuits among schoolchildren (W62). Although both interventions improved iron status, only the biscuits reduced the prevalence of anemia, showing that other micronutrients, and perhaps additional energy intake in addition to iron, were needed to improve anemia in these children. Finally, acidification of maize was shown to improve bioavailability and solubility of iron, without affecting organoleptic qualities very much. (W67)

Results from a wide range of studies investigating a variety of vehicles and iron fortificants were presented. These included fortified rice in Mexico (W64), fortified soy sauce in Indonesia (W66), and fortified brown bread in South Africa (W68). In Oman, national mandatory flour fortification with iron and folic acid was started in 1997. A national survey showed that, since then, iron status in women is positively related to flour consumption, and that the incidence of neural tube defects has declined (W70). In Tanzania, small-scale fortification of maize at local mills or at home was effective in reducing the prevalence of anemia in women, but not in children, perhaps because of the high incidence of malaria in children (W71). Another small scale-fortification pilot project to fortify maize at local mills in Nepal showed that such an approach is feasible using appropriate technology, and well accepted by both millers and consumers (W73). Two posters described the process of introducing flour fortification in Pakistan (W72, W75). A tool that models the costs and potential contributions to nutrient intake of mass-fortified foods with different premixes was presented (W75); this "calculator tool" is formatted as an Excel spreadsheet, where information on the nutritional goals, intake estimates, costs, usual consumption estimates, expected nutritional impact, and desired fortification levels are systematically compiled and processed, and lead to estimates of minimum and maximum fortification levels, and premix formulations.

A study in Peru that compared zinc-fortified porridge to an aqueous zinc supplement (in combination with other micronutrients) showed no effect on growth or morbidity during infancy, compared to a control group receiving MMNs without zinc (W63). Zinc status and functional outcomes need to be studied in other populations to extend knowledge in this field.

Fortification at point-of-use

This theme grouped posters reporting on a variety of different approaches that can be referred to as point-of-use or "home fortification." Progress in home fortification of complementary foods, with powdered vitamins and minerals for infants in the form of a MMN product called Sprinkles, was reported (W79). The product has been successfully developed and its efficacy established now in many different countries. The products are centrally produced, and strategies were presented for marketing and distribution. Posters on the effectiveness of the approach were submitted from Pakistan and Afghanistan (W80). In Mali, home fortification proved feasible and acceptable (W81). In India, a trial among infants and young children showed better compliance with fortified complementary food than with these powders, possibly because the latter may have affected the color and taste of the food (W82). Furthermore, fortified weaning food had the larger impact on growth. Therefore, the authors conclude that fortified weaning food seems the most feasible approach to prevent iron and zinc deficiency in preschool children.

Micronutrients and infection

Antenatal supplementation with β-carotene or vitamin A in Bangladesh reduced oxidative stress during the third trimester, although further analysis is needed to assess the precise effect and functional implications (W83). A study in HIV-positive adults in Kenya showed that inflammation, as indicated by various APP, depressed β-carotene concentrations, and response to supplementation remained lower than in subjects without inflammation (W84). In Ghana, VAS provided to very young infants with the three pentavalent diphteria-polio-tetanus-Heamophilus influenza Type B-Hepatitis B vaccines appeared to enhance antibody response to the HepB, although sero-conversion to the HepB component was very high without additional VAS (W86). A trial in Burkina Faso showed that daily zinc supplementation combined with semi-annual VAS was associated with lower malaria and fever attack risk in preschool children, compared to VAS alone (W90).

Several posters addressed iron status and supplementation in the context of HIV. A long-term follow-up of

HIV positive patients in West Africa showed that iron status elevation predicted clinical tuberculosis and mortality, independent of other HIV-related conditions, such as immuno-suppression and other infections (W95). In Tanzania, when iron status and anemia were assessed postpartum in HIV-infected women, around half were anemic and, of these, 50% were iron deficient (W97). However, there was no direct association between iron status and disease progression or negative outcomes. Two posters on HIV-positive women in the postpartum period in Zimbabwe showed an association between serum ferritin and both increased viral load and maternal mortality, but not with MTCT (W98, W99). In this population, AGP was found to reliably reflect the influence of the APR on iron status indicators, although the original findings could not be explained by adjusting for AGP. In the United States, daily MMN supplementation with iron was found to be effective in improving iron status and reducing anemia, and did not increase Hepatitis C or HIV viral activity, nor affect liver enzymes (W100).

Additional analyses from the iron-folic acid-zinc supplementation trial in Pemba, Tanzania, suggested that folic acid in the supplements did not inhibit sulphadoxine therapy, nor did it increase hospitalization rates significantly (W101). In Brazil, iron, copper, and zinc nutritional status was assessed in children with symptomatic *Helicobacter pylori* infection, and compared with non-infected children (W103). Interestingly, and in contrast to earlier findings (mainly from wealthier countries), iron-deficiency anemia was not associated with *H. pylori* infection; neither were copper nor zinc status in this population. Hepcidin, an important regulator in iron metabolism and an indicator of hypoxia, was found to be especially associated with parasitemia and markers of inflammation in Ghana, although not with anemia and hemoglobin concentration (W94). Surveys pre- and post-malaria season in the Gambia showed that, with adequate treatment, hemoglobin concentrations in the population do not decrease over the malarial season (W96), although this association was modified by the Hp22 genotype.

In India, the severity of the acute phase reaction was assessed in young children hospitalized for severe pneumonia; zinc supplementation was shown to significantly increase the duration of hospitalization among children with severe acute phase response (W104). Among children in Bangladesh, serum zinc was assessed and related to acute phase reaction, common infections, nutritional status, and parental socio-economic variables in order to identify predictors of serum zinc concentration and populations at risk of zinc deficiency (W105). The prevalence of zinc deficiency was high, and the most important predictors of low serum zinc concentrations were found to be raised CRP levels, T. trichiura infection, and stunting. In Turkey, hair zinc concentrations were assessed in young children and found to be higher in children with malnutrition and/or infection, possibly explained by poor hair growth due to protein energy malnutrition and/or infection (W106).

In Malawi, a daily MMN supplement at around RDA levels, but not containing iron, was effective in reducing anemia in non-HIV-infected pulmonary tuberculosis patients when given in addition to standard tuberculosis (TB) treatment (W109). However, in pulmonary TB patients with concomitant HIV infection receiving standard TB treatment without antiretroviral therapy, the supplement did not improve nutritional status. Further research is needed to assess the effectiveness of micronutrient supplementation in patients who are also receiving antiretroviral therapy. [Ed. NB: The effect on anemia may have been due to the release of endogenous iron trapped until the infection was removed.] In the same trial, the impact of daily MMN supplementation on the mortality of HIV-infected adults with pulmonary TB was assessed (W110). The patients received standard TB treatment but no antiretroviral therapy, and there was no impact of the supplementation on survival in these patients. Again, further research is needed to assess the impact of antiretroviral therapy on nutritional status and survival in these patients, and whether supplementation at RDA levels is sufficient among HIV patients.

X. Acronyms and abbreviations

ABC	Activity-based costing
ACT	α_1-antichymotrypsin
AGP	α_1-acid glycoprotein
APP	Acute phase protein
APR	Acute phase response
ARS	Agricultural Research Service
AusAID	Australian Agency for International Development
BMI	Body Mass Index
CCDC	Chinese Center for Disease Control and Prevention
CeSSIAM	Center for Studies of Sensory Impairment, Aging and Metabolism
CI	Confidence Interval
CRM-457	European Community Bureau of Reference
CRP	C-reactive protein
CuSO4	Copper sulfate
CV	Coefficient of variation
CVD	Cardiovascular disease
DBS	Dried blood spot
DELFIA	Dissociation-Enhanced Lanthanide-Fluorescent Immunoassay
DTP	Diphtheria-tetanus-pertussis (vaccine)
EAR	Estimated Average Requirement
EPI	Expanded Programme on Immunization
EPO	Erythropoietin
ETH	Swiss Federal Institute of Technology, Zürich
FAO	Food and Agriculture Organization of the United Nations
FCHV	Family Child Health Volunteer
GAIN	Global Alliance for Improved Nutrition
GMO	Genetically Modified Organism
HFP	Homestead Food Production
HIV/AIDS	Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome
HKI	Helen Keller International
IACS	Integrated Anemia Control Strategy
IAEA	International Atomic Energy Association
ICCIDD	International Council for the Control of Iodine Deficiency Disorders
ICDS	Integrated Child Development Services
ID	Iron Deficiency
IDA	Iron Deficiency Anemia
IDD	Iodine Deficiency Disorders
IDP	Internally Displaced Persons
IEC	Information, Education, and Communication
IGF-1	Insulin-like Growth Factor
IMCI	Integrated Management of Childhood Illness
IMR	Infant Mortality Rate
INACG	International Nutritional Anemia Consultative Group

IPT	Intermittent Preventive Treatment
IQ	Intelligence Quotient
IRIS	International Research on Infant Supplementation
ITNs	Insecticide-treated nets
IU	International Units
IUGR	Intrauterine Growth Retardation
IVACG	International Vitamin A Consultative Group
IZiNCG	International Zinc Consultative Group
LBW	Low Birth Weight
M & E	Monitoring and Evaluation
MCH	Mother and Child Health
MCHN	Maternal and Child Health and Nutrition
MDGs	Millennium Development Goals
MI	The Micronutrient Initiative
MMN	Multiple micronutrient or multi-micronutrient
MMR	Maternal Mortality Ratio
MMSDP	Multiple Micronutrient Supplementation During Pregnancy
MoH	Ministry of Health
MRDR	Modified Relative Dose Response
MT	Metric tons
MUAC	Mid-Upper Arm Circumference
NAFDAC	National Agency for Food and Drug Administration and Control, Nigeria
NaFeEDTA	Sodium Iron Ethylenediaminetetraacetate
NGO	Non-governmental organization
NHANES	National Health and Nutrition Examination Surveys
NIDs	National Immunization Days
NMDs	National Micronutrient Days
NTAG	National Training and Advisory Group, Nepal
NTDs	Neural tube defects
NVAP	National Vitamin A Program, Nepal
OR	Odds ratio
ORS	Oral Rehydration Solution
PMTCT	Prevention of Mother-To-Child Transmission
QA	Quality Assurance
QC	Quality Control
RAE	Retinol Activity Equivalents
RBP	Retinol-Binding Protein
RCTs	Randomized Controlled Trials
RDA	Recommended Dietary Allowance
RE	Retinol Equivalents
SD	Standard Deviations
SES	Socioeconomic status
SGA	Small for Gestational Age
SIAN	La Semaine d'Intensification des Activités de Nutrition, Mali
SIVIN	Integrated System for Surveillance of Nutritional Interventions, Nicaragua
sTfR	Soluble Transferrin Receptor

SUMMIT	Supplementation with Multiple Micronutrients Intervention Trial, Indonesia
Tg	Thyroglobulin
TSH	Thyroid-Stimulating Hormone, or Thyrotropin
UI	Urinary iodine
UL	Tolerable Upper Intake Level
UMC	University Medical Centre, Nijmegen, the Netherlands
UNICEF	United Nations Children's Fund
USAID	United States Agency for International Development
USDA	United States Department of Agriculture
USI	Universal Salt Iodization
VAD	Vitamin A Deficiency
VAS	Vitamin A Supplementation
WAZ	Weight-for-Age Z-Scores
WFP	World Food Programme
WHO	World Health Organization
$ZnSO_4$	Zinc Sulfate
ZPP	Zinc Protophorphyrin
ZVITAMBO	Zimbabwe Vitamin A for Mothers and Babies Project

Colophon

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