Micronutrient Forum 5th Global Conference

CONNECTED 2020

sightandlife | Special Report

Micronutrient FORUM

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Micronutrient Forum 5th Global Conference **CONNECTED 2020**

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The Micronutrient Forum CONNECTED conference took place from 9 to 13 November 2020 at the end of an unprecedented year dominated by the COVID-19 pandemic. Since the conference had originally been scheduled to take place in Bangkok as an in-person event in March 2020, the Micronutrient Forum team was obliged to reconfigure its delivery for a virtual space. We worked diligently to keep the full program promised for the Bangkok event intact, appropriately naming it Micronutrient Forum (MNF) CONNECTED.

Equitable and inclusive

While the decision to deliver a virtual conference was driven by COVID-19, there were some real benefits as a result of that decision. The presence of a record number of 3,600 participants, mostly from low- and middle-income countries, made the conference more equitable, allowing for more inclusive participation and discussions. The online platform also facilitated the participation of a greater number of high-level speakers than might have been possible at a traditional conference, and also more extensive knowledge-sharing online and through social media. There are lessons to be learned here and replicated for the future.

> **"The program included 23 live plenary sessions, 38 on-demand sessions, over 350 posters in the gallery, and 35 sponsored sessions"**

In addition, realizing the importance of an event that would allow participants to connect, engage, learn and network in a year during which the pandemic saw all in-person conferences canceled, the organizers were keen to select a technology that would allow for plenty of engagement opportunities and networking.

Engagement and knowledge sharing

During the sessions, participants were able to ask questions and generate ideas through chat sessions, reach out to presenters, and engage in conversations and discussions happening on social media across all time zones. The 'CONNECT with the Experts' sessions, and the 'Learning Centers' for smaller groups in the weeks around the live week, were opportunities for participants to discuss, engage and expand their knowledge of specific nutrition topics. In addition to all of this, cooking demonstrations by chefs from the Chefs' Manifesto and an online dance competition, #DanceForNutrition, were offered as fun activities for participants during the breaks, and were greatly appreciated.

The Micronutrient Forum and *Sight and Life* have worked together to capture the rich content of the CONNECTED conference in this Special Report. In addition, all the recorded sessions of the conference will remain available for participants for one year after the live conference week itself, at: rebrand.ly/MNF2020.

> **"The MNF CONNECTED conference turned out to be a week of hope at the end of a challenging year"**

Encouraging increased collaboration

In summary, the Micronutrient Forum CONNECTED conference turned out to be a week of hope at the end of a challenging year. Hope that the world may move in the direction of more international collaboration, which is a prerequisite for tackling the global challenges identified during the conference. Hope that we can nourish the world with nutrient-rich foods so that everyone can thrive and reach their full potential. And hope that this conference, which has brought together experts from around the world, working in different disciplines (agriculture, food systems, nutrition, climate, health and economics) and different sectors (academia, private sector, civil society, the UN and governments), will mark a new future for nutrition. A future of nutrition post-COVID-19, in which we will continue to embrace new and necessary forms of collaboration connecting the food systems, health, agriculture, economic and nutrition communities. And a future in which we will make sure that the current disabling environment is turned into an enabling environment for nutrition and will lead to more and bigger investments in nutrition by all stakeholders.

Our thanks to so many

A heartfelt thank-you is due to everyone who contributed to making MNF CONNECTED a milestone event in a year that confronted us all with such challenges.

We would like to express our gratitude to our sponsors for their continued trust and support: the Bill & Melinda Gates Foundation, HarvestPlus, USAID, Kirk Humanitarian, *Sight and Life*, DSM, the International Rice Research Institute and so many others whose support made this conference possible.

Delivering the impressive content of MNF CONNECTED would not have been possible, however, without the dedication and passion of our speakers and the trust of the Forum's leadership: the Micronutrient Forum Board and the Micronutrient Forum Scientific Advisory Committee. Particular thanks go to Maria Elena Jefferds, Chair of the Program Committee; Emorn Udomkesmalee, Chair of the Local Organizing Committee; and Howarth Bouis, Chair of the Micronutrient Forum Board. We would also like to thank the Micronutrient Forum team – Aynsley Morris, Jennifer Buter, Marti van Liere, Nola Martin, and Reed Atkin – for their tireless endeavors behind the scenes, as well as the rapporteurs whose work you will read in this Special Report: Jaime Marquis, Martin N Mwangi, Rebecca Olson, Tsitsi Chimhashu, Chiara Ferraboschi and Kris Woltering.

Last but by no means least, a big thank-you goes to each and every one of our 3,600+ conference delegates: your presence, engagement and feedback made this conference a success whose energy will take us forward as we confront the challenges and opportunities of 2021.

A full thank-you with detailed acknowledgements is available at: www.youtube.com/watch?v=3Kre6OpZrno

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Key takeaways

MNF CONNECTED provided us with five key takeaways:

1. **We have to understand the problem and collect more data on micronutrient intake and status**, on the monitoring and evaluation of programs, and on the costs and cost-effectiveness of interventions.

2. **We have to listen and learn from programs and voices on the ground** in order to replicate what solutions worked and avoid those that did not work. We also have to identify opportunities to overcome challenges.

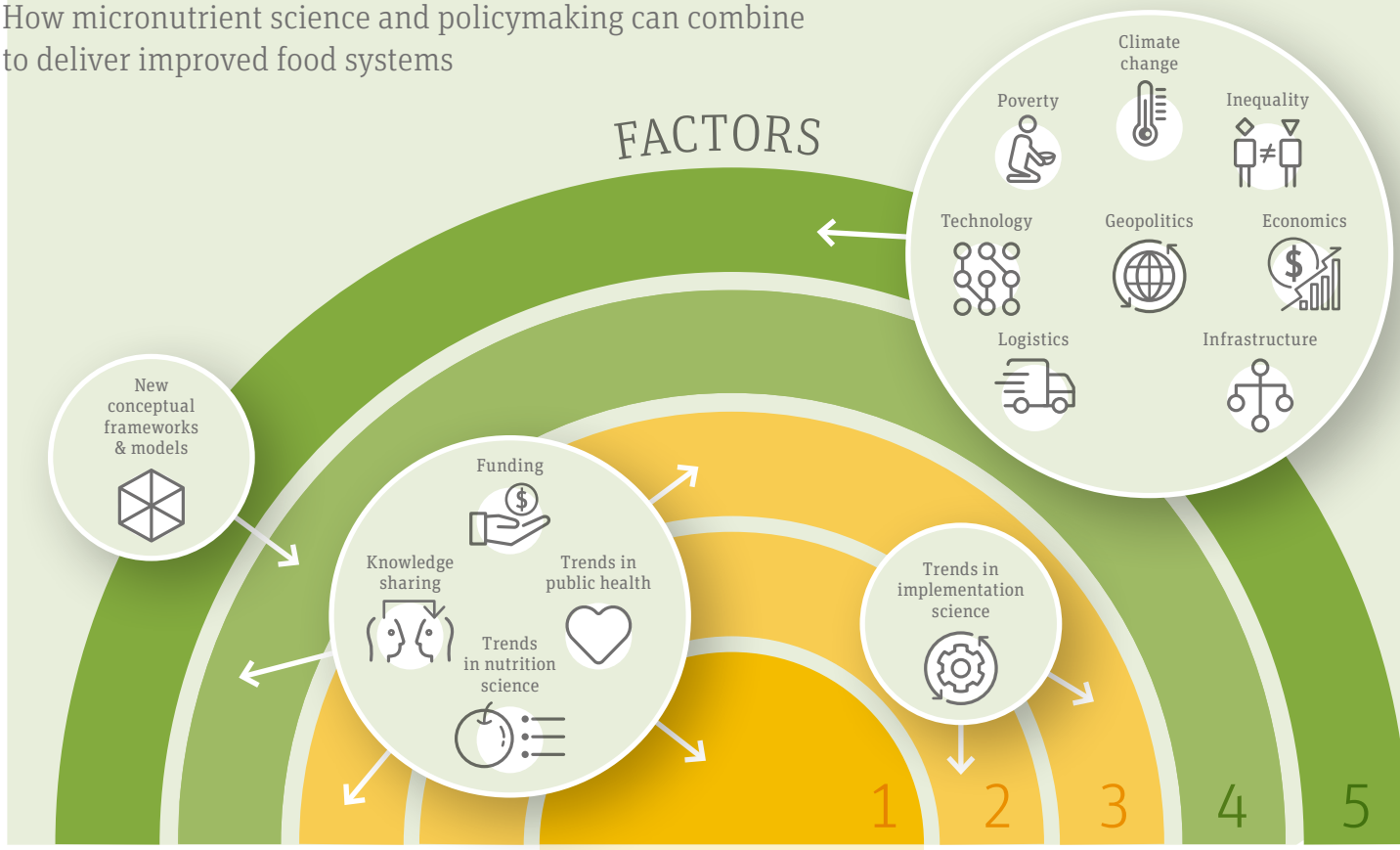
3. **Context and consumers matter!** Whether it relates to harmonizing Nutrient Reference Values, calculating the cost-effectiveness of programs, delivering iron interventions to young children, or providing practical recommendations to scale up effective programs such as large-scale food fortification or maternal multiple micronutrient supplementation (MMS), it is essential always to consider the context and the consumer.

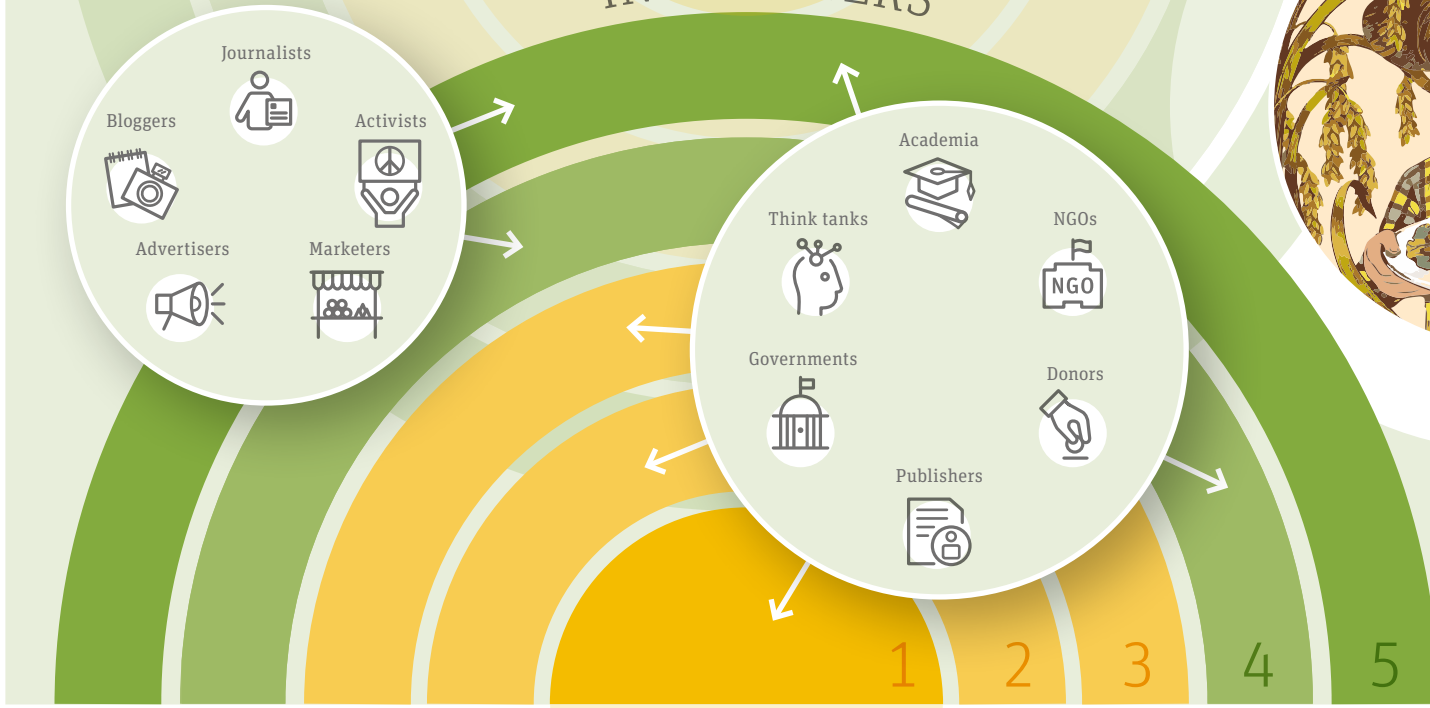
4. There are no magic bullets in nutrition or micronutrient nutrition. **We need to prepare nutrition champions and to convince policymakers that integrated, multiple-intervention and multisectoral programs are needed.** When it comes to micronutrient malnutrition, there is a space and time for a palette of solutions discussed during the week: supplementation, promotion of healthy diets, fortification, biofortification, and agricultural solutions.

5. **We need to continue to strengthen our collaboration with other sectors:** the COVID-19 crisis and its consequences for all diet and nutritional outcomes are clear. We need to work with climate change experts, agronomists and behavioral scientists to address the impacts of how we grow and consume our food on the environment and on malnutrition, and vice versa. We need to work with the private sector to make nutritious foods more available and accessible to everyone. And we need to work with economists and the designers of social protection programs to make sure that these include nutrition, consumer and women's rights groups. All these working relationships are essential if we are to successfully tackle the complex challenges ahead of us.

From the Lab to the Plate

How micronutrient science and policymaking can combine to deliver improved food systems





Nutritionists act as advisers and influencers in combination with other actors.

TRACK 1
Micronutrient Biology & Status Assessment

TRACK 2
Efficacy & Safety of Micronutrient Interventions

TRACK 3
Program Effectiveness

TRACK 4
Designing an Enabling Environment for Micronutrients

TRACK 5
Food Systems

INFLUENTIAL PUBLICATIONS & EVENTS

Major reports

Scientific books

Recent research findings

Classic research findings

Scientific conferences & symposia

General media

1 2 3 4 5

TRACKS

ACTORS

Governments

NGOs

Nutrition leadership

Public health professionals

Economists

Climate scientists

Social scientists

Smallholders

Farmers

Big agriculture

Food producers

Food distributors

Donors

Banks

Food service providers

Social philosophers

Implementation scientists

Public health professionals

Nutrition scientists

Public health professionals

1 2 3 4 5

TRACKS

Nutritionists have executive capability, delivering data, information, insights, models and recommendations.

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TRACK

1

Micronutrient Biology and Status Assessment

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

Introduction

The main objective of this track was to provide an overview and update on micronutrient nutrition and status assessment.

Topics included

- Benchmarks, methods and metrics for improving food systems and micronutrient delivery;
- Innovations and updates in the assessment of micronutrient status;
- Epidemiology and global prevalence of micronutrient deficiencies;
- Absorption, metabolism and interaction of micronutrients;
- Innovative technologies for micronutrient delivery;
- Effects of genetics, infection/inflammation and other environmental exposures on micronutrient deficiencies; and
- Micronutrients and the double burden of noncommunicable diseases.

This track prioritized topics related to new evidence, as well as existing questions that still remain to be answered. One of the common themes continues to be how to best address data gaps within micronutrient status assessment and prevalence estimates. Bridging this data gap, by means of standardized deficiency definitions, harmonized measurement methodologies and strengthened lab capacity, will lead to greater success in reducing micronutrient deficiencies through targeted and safe interventions. To do this, a multicomponent approach is recommended through the Micronutrient Data Generation Initiative.

"One of the common themes continues to be how best to address data gaps"

Folate and vitamin B_{12} emerged as priorities to build global capacity in measuring status, through a dedicated session. This session provided an overview of the biochemical basics of folate and vitamin B_{12}, and their interactions. It emphasized the need to measure folate and vitamin B_{12} in conjunction when using the information for the planning of cohort and population-based interventions. This will allow folic acid supplementation to be safe and targeted to those most in need.

Further, another session highlighted innovative micronutrient assessment methods that are field-friendly, safe and accurate. The session provided meaningful updates on several practical assay methods and calculation approaches to deal with missing values, along with an update from the BRINDA (Biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia) project on inflammation adjustment approaches. The use of population-based kinetic modeling to assess micronutrient status was discussed, as was the use of electronic data collection during surveys. Lastly, the use of dried plasma spots to measure nutritional and inflammatory markers, the use of dried serum spots to determine total body vitamin A stores and a noninvasive approach for iron deficiency diagnosis were presented.

"A key session in this track focused on the global burden of iron deficiency anemia"

A key session in this track focused on the global burden of iron deficiency anemia and the role of nutrition interventions. This session presented novel research on the efficacy and safety of iron supplementation in sub-Saharan Africa and southeastern Asia. Treatment in the context of thalassemia and hemoglobinopathies was discussed, as was the lack of evidence for the impact of iron interventions on developmental or functional outcomes in children. A key takeaway from the session was that controlling the incidence of malaria allows for iron to be absorbed and iron deficiency to be reduced – hence, a multidisciplinary intervention approach is required.

Inflammation was another key topic that received attention throughout the track. The impact of iron deficiency on inflammation, immune response and vaccine efficacy was explored in depth. The role of iron regulation (both iron deficiency and over-

load) in innate and adaptive immunity was discussed, as was the predictive power of iron deficiency anemia to poor diphtheria and pneumococcus vaccine responses in children. Novel research was presented on the promise of delivering iron supplements at the time of routine pediatric vaccination.

Finally, maternal nutrition and micronutrient status during pregnancy were discussed as key desired health outcomes throughout the lifespan. Recent guidance from WHO recommends multiple micronutrient supplementation (MMS) during pregnancy in the context of rigorous research. Recommendations for specific age subgroups are lacking. Findings from a meta-analysis indicate that pregnant adolescent women benefit most from MMS, in terms of small for gestational age (SGA). Furthermore, this session presented data on the effect of maternal obesity during pregnancy on maternal iron status, stating the importance of reducing pre-pregnancy body mass index (BMI).

Overall, **Track 1** made significant contributions to the Micronutrient Forum 5th Global Conference: CONNECTED by inspiring nutrition professionals to think deeply about the solutions to data and intervention gaps, in addition to the roles that micronutrient biology and status assessment play in designing evidence-based, life-changing nutritional programming.

Global state of micronutrients: Estimates, uncertainties and addressing data gaps

Accurate estimates of micronutrient status and prevalence of micronutrient deficiencies are essential to the success of nutritional programming, policy and continued monitoring and evaluation. Understanding the prevalence of micronutrient deficiencies, as well as subgroups of highest vulnerability, enables interventions to address deficiencies in a safe and cost-effective way.

> **"Understanding the prevalence of micronutrient deficiencies enables interventions to address deficiencies in a safe and cost-effective way"**

This session provided an overview of the current state of micronutrient status estimates and their burden. Different methodologies used to estimate prevalence for the Global Burden of Disease reports, and their challenges, were presented. Areas of continued need in terms of enhancing status estimates and burdens of deficiency included standardization of deficiency definitions, harmonization of measurement methodologies and filling the gap of population-based deficiency data. Building laboratory capacity at the regional level in low- and middle-income countries (LMICs) will contribute to harmonized data collection and analysis methods. The session concluded with the introduction of the Micronutrient Data Generation Initiative, a multicomponent approach designed to bridge the current data gap and provide more accurate estimates. The objective of the initiative is to ensure the availability of adequate data, informing evidence-based policies and programming and better targeting populations with micronutrient deficiencies with appropriate and effective interventions.

WHO estimates of global and regional anemia and micronutrient status

Accurate and timely data is essential to the achievement of the Sustainable Development Goals and universal healthcare coverage, monitoring the global health situation and assessing health trends. WHO maintains the Vitamin and Mineral Nutrition Information System (VMNIS), a tool to collect and summarize population-based data. VMNIS also plays a vital role in tracking progress and evaluating the impact of intervention strategies Lisa Rogers, from the Department of Nutrition and Food Safety at WHO, presented on estimates and trends of micronutrient status. She also provided insight into how such values are calculated and the key factors to consider moving forward to improve data quality.

Anemia prevalence estimates have evolved over time as more insights have emerged regarding the determinants of anemia. The Bayesian hierarchical mixture model is used to estimate country prevalence of anemia each year. The model is informed by data from each country by year. The database is currently restricted to data on women of reproductive age (WRA) and children aged 6–59 months. However, WHO is exploring the possibility of including data on adolescent girls and additional covariates, such as malaria incidence and dietary factors.

Similarly, WHO uses the Bayesian hierarchical probit model to estimate trends in vitamin A deficiency for children aged 6–59 months. Serum retinol is the biomarker used, and covariates, such as mean weight-for-age and national income, are included in the model. Estimates suggest that deficiency prevalence has trended downwards since 1991. Nevertheless, deficiency remains highest in southeastern Asia and sub-Saharan Africa, though there is limited data in these regions.

> **"It is important that harmonization across assays used should be achieved, which requires development of global guidance"**

Global folate status of WRA is only available for 39 countries. Large differences exist between folate assays used worldwide. WHO has attempted to account for such differences and to adjust cutoffs for better comparison across data sources; however, results remain difficult to interpret. To overcome these differences, WHO encourages the use of microbiological assay (MBA) in assessing folate status. Building laboratory capacity at the regional level will ensure that folate insufficiency and deficiency are accounted for when assessing global trends and programming needs.

Moving forward, it is important that harmonization across assays used should be achieved, which requires development of global guidance and continued collection of data in populations. Researchers should also keep in mind that differences may exist between population subgroups, which may be overlooked in national surveys. Enhanced in-depth assessments of the methods used within national surveys will improve the quality of prevalence estimates.

IHME (Institute for Health Metrics and Evaluation) methods to develop estimates of global burden of disease attributable to micronutrient deficiency

Several challenges persist in estimating the disease burden of nutritional risks. Challenges include limited data availability, limited data accessibility and limited data consistency. Consensus in terms of how to best define and measure nutritional risks is also lacking. Ashkan Afshin from the University of Washington presented how the Global Burden of Disease (GBD) study aims to overcome challenges in quantification of the effects of micronutrient deficiencies.

GBD currently has estimates for iodine, iron, vitamin A and zinc deficiencies. Quantification of the effects of micronutrient deficiencies begins with defining the deficiency. Definitions used for GBD are based on where the most data exist for each micronutrient deficiency; however, errors and inconsistencies persist because of the lack of standardization of measurement methodology among available data. Existing data, including a multitude of covariates, are then inputed to estimate the prevalence of a micronutrient deficiency. From there, the deficiency prevalence is paired with effect size to then establish the population-attributable fraction. The population-attributable fraction is an estimate of the mortality related to a specific micronutrient deficiency. This fraction is then multiplied by the disease-specific burden, such as disability-adjusted life years (DALYs) associated with the deficiency, to calculate the attributable disease burden.

Estimating the burden of micronutrient deficiencies remains an iterative process. To best achieve accurate estimates, the process requires continuous updating from new data sources and new data-processing methods. New insights will enable the GBD to continue as a key provider of information necessary for performing meaningful micronutrient interventions.

The challenges of estimating the micronutrient prevalences and related global burden of disease with IHME's GBD estimates as a case study

Sonja Y Hess, Institute for Global Nutrition at UC Davis, built on Afshin's presentation to further discuss the challenges of estimating micronutrient deficiencies prevalences and the global burden of disease. Afshin discussed the risk factor approach, but a second approach – the causal attribution approach – is also used by the GBD study. The risk factor approach, which estimates attributable deaths and DALYs, is primarily used for iron, zinc and vitamin A deficiencies, whereas the causal attribution approach, which estimates years lived with disability (YLD), is primarily used for dietary iron, iodine and vitamin A deficiencies.

This information plays a vital role in enabling evidence-based, safe, effective and sustainable intervention programming. It also ensures that the impacts of such interventions are monitored and held accountable. GBD relies on reliable biomarkers, nationally representative surveys, access to such data, adequate evidence linking the micronutrient to health outcomes and transparent documentation. One persistent challenge is defining micronutrient deficiencies. Definitions of micronutrient deficiencies used by nutritionists tend to differ from those used by the GBD. Bridging the gaps between the various definitions will help to generate missing data and improve estimations.

> **"Bridging the gaps between the various definitions of micronutrient deficiencies will help to generate missing data and improve estimations"**

Future needs and challenges for generating better data on micronutrient status

Kenneth Brown from UC Davis and member of the Global Conference Committee, introduced the Micronutrient Data Generation Initiative, which is hosted by the Micronutrient Forum, as a solution to increase the availability and utilization of reliable data globally.

Several different sources of information related to micronutrients currently exist, yet only nutritional biomarkers can be used to define the prevalence of micronutrient deficiencies. Brown cited the example of how data from a vitamin A intervention program in Guatemala was used to drive national policy and programming decisions, mainly for sugar fortification. Using population data enabled Guatemala to focus on those areas most at risk, which served as a cost-effective move. As a result, the prevalence of vitamin A deficiency has decreased from 25 percent in 1965 to less than 2 percent in 2017.

Unfortunately, data on micronutrient biomarkers in national surveys worldwide remain limited and outdated. In key informant interviews, the financial burden of including micronutrient biomarkers was the most cited barrier to including data on biomarkers. Other barriers cited included knowledge, laboratory and contextual restraints. Enablers included political support, advocacy from locals, availability of technical experts and existing micronutrient programming.

"The collection of data based on micronutrient biomarkers will allow for more evidence-based policies and programming to be implemented"

The collection of data based on micronutrient biomarkers will allow for more evidence-based policies and programming to be implemented. To achieve this, the Micronutrient Data Generation Initiative recommends a multicomponent approach. Nutrient selection will be based on estimated high prevalence of deficiency, as well as the severity of implications associated with deficiency. Components of the strategy include advocacy and information dissemination, technical and financial support, regional resource laboratories, open-access data repositories and periodic analyses. Though the costs of this initiative remain a barrier, optimized micronutrient programs will ultimately result in higher effective coverage at lower total costs. As Brown stated, "The time has come to focus on the remaining sets of activities that are needed to close the data gap and to leverage the necessary financial resources and professional support to do so."

Folate and vitamin B_{12}: Update on biomarkers, status and interactions

Folic acid fortification is associated with a decrease in neural tube defects. Mandatory folic acid fortification policies were first introduced in the USA, and are now established in over 80 countries of the world. However, folic acid fortification remains to be instituted in many countries where the risk for neural tube defects is high. Additionally, low vitamin B_{12} status is highly prevalent across both developed and developing countries, among all age groups. This is particularly a concern in areas where animal-source food consumption is low. Concerns also remain surrounding the role that a high intake of folic acid plays on the diagnosis of vitamin B_{12} deficiency. These concerns include elevated levels of homocysteine, increased risks of anemia, and cognitive dysfunction in older adults. For these reasons, folate and vitamin B_{12} are included in the series of Biomarkers of Nutrition and Development (BOND) reports.

This session provided an overview of the biochemical basics of folate and vitamin B_{12}, as well as their interactions, and the consequences of their deficiencies. The session also reviewed folate and vitamin B_{12} as they are related to planning cohort and population-based interventions and evaluations. Finally, the presenters reviewed the need to increase global capacity to measure biomarkers of folate and vitamin B_{12} in a cost-efficient way.

"Folic acid fortification remains to be instituted in many countries where the risk for neural tube defects is high"

Folate and vitamin B_{12} biomarkers and functions: Biology and mechanisms of interaction

Folate and vitamin B_{12} are essential for *de novo* DNA synthesis, specifically for the production of red blood cells. The clinical manifestations of folate and vitamin B_{12} deficiency are similar because of the mechanistic interaction between the two vitamins. For this reason, deficiency of either vitamin leads to impairments of DNA synthesis and anemia. Folic acid therapy in vitamin B_{12} deficiency will treat the anemia component of vitamin B_{12} deficiency, but it will not treat the methylation component, which is associated with neuropathy and cognitive dysfunction.

Currently, the only biochemical parameter of folate deficiency is serum total folate. However, in nutritional and population studies, plasma total homocysteine (tHcy) is widely used to identify folate deficiency. Serum total vitamin B_{12}, serum holotranscobalamin (holoTC), serum methylmalonic acid and tHcy are used as biomarkers of vitamin B_{12} status; however, each biomarker has its own benefits and drawbacks.

In practice, the combined deficiency of folate and vitamin B_{12} can present a confusing clinical case. To determine the overall status, it is important to measure biomarkers for both folate and vitamin B_{12} to ensure proper diagnosis of deficiencies.

"It is important to measure biomarkers for both folate and vitamin B_{12} to ensure proper diagnosis of deficiencies"

The importance of considering folate-vitamin B_{12} biology and interactions for planning interventions and evaluations

Questions of how to assess folate and vitamin B_{12} status, when to intervene and how best to deliver interventions remain. Reliable and accurate evaluation of status is needed to accurately estimate the prevalence of deficiency and to develop suitable strategies. To evaluate interventions, it is important to monitor the impact and safety of the intervention using the same indicators employed to establish baseline data. No single blood biomarker provides sufficient information to diagnose deficiencies; therefore, both folate and vitamin B_{12} status should be measured during evaluation.

Folate and vitamin B_{12} biomarkers are useful, and predictive values improve when employed in conjunction. Assessment methods exist, but several disadvantages remain. New directions for measuring vitamin B_{12} status include measuring vitamin B_{12} concentration in breast milk to assess maternal status and the risk of infant inadequacy. Additionally, the use of omics may improve the understanding of the dual deficiency and imbalance of folate and vitamin B_{12}. The combined vitamin B_{12} indicator (cB_{12}) is used to detect increased risk of cognitive impairment in elderly populations and to detect adverse interactions between folate and vitamin B_{12}.

> **"New directions for measuring vitamin B_{12} status include measuring vitamin B_{12} concentration in breast milk"**

Experimental evidence to establish the causal effect between elevated folic acid intake and the modification of vitamin B_{12} deficiency remains lacking. Moreover, the development of practical and efficient evaluation methods remains a need to best assess status in populations.

> **"A regional approach is the most relevant and efficient way to achieve lab capacity"**

Laboratory capacity building to improve folate assessment on a global scale

A great need to improve folate laboratory capacity remains. Microbiologic assay (MBA) provides a practical provides a practical choice for low-resource laboratories, as it is simple and inexpensive. To improve lab-to-lab variability, a common critical reagent, such as a microorganism and calibrator, is needed. A regional approach is the most relevant and efficient way to achieve lab capacity. Personnel, facilities and supplies are needed to maintain efficiency. A network of labs in-country also helps with strategic support.

An important component of capacity building includes learning tools and training aids on how to conduct high-quality MBA measurements, as well as performance verification programs. The Centers for Disease Control and Prevention (CDC) has released a freely available step-by-step folate MBA training video. Ready-to-use assay kits have also been developed for epidemiological use to facilitate in-country setup and to harmonize lab results.

Potential barriers to the success of laboratory capacity building are mainly logistical in nature. These include staff retention, lack of access to supplies, insufficient funds, lack of fee collection mechanisms, processing and shipping issues, and the limited availability of assay kits. Strategic support from international partners is required to address each of these barriers.

Innovations and updates in micronutrient assessment

Timely and accurate data is needed to ensure effective programming. However, assessment of micronutrient status remains difficult to carry out in low-resource settings where laboratory infrastructure is typically lacking. The need for nutritional biomarkers adjusted to factors such as infection and inflammation also persists. Field-friendly, safe and accurate assessment methods must be developed to enhance programs that address micronutrient deficiencies.

> **"If we are serious in our efforts to improve nutritional status, we must make micronutrient assessment a priority"**

This session reviewed recent advances in specimen collection and laboratory assessment that make determining micronutrient status more reliable, easier, practical and affordable. The session began with a call to action from Omar Dary, Health and Nutrition Science Specialist at USAID, in which he stated, "If we are serious in our efforts to improve nutritional status, we must make micronutrient assessment a priority." Presenters then discussed their approaches for improving micronutrient assessment, each of which has great promise for enhancing assessment, specifically in low-resource settings. Vitamin A and iron were the main micronutrients discussed; however, each presenter discussed how improvements could be expanded to other micronutrients, such as calcium and vitamin D.

Novel methods and practical approaches for measuring and interpreting blood-based micronutrients in the epidemiologic context

The enhancement of data collection and quality requires practical approaches for measuring and interpreting micronutrient biomarkers. Christine Pfeiffer, from the Division of Laboratory Sciences at CDC, presented on practical methods for micronutrient status measurements. In terms of lab measurement, several practical assay approaches are already in use. The benefits of the Quansys Q-Plex™ micronutrient array are well known. A minimal sample volume is needed: one sample preparation generates multiple results, and the process is overall relatively simple. Additionally, the assay has recently been redeveloped for improvements specifically in soluble transferrin receptor (sTfR), α-1-acid glycoprotein (AGP) and retinol-binding protein (RBP). Rapid vitamin A assay performance is also practical because of its strong precision and low imprecision. MBA, used for folate and vitamin B_{12} measurements, is available in low-income countries as it is low in cost.

Data interpretation components also need to be considered. Currently, the measurement of red blood cell folate status is both time- and resource-intensive, as the calculation requires three measurements. Mechanisms to address what to do when there are missing measurements have been researched. Pfeiffer presented novel calculation approaches for use in the case of missing value(s). If the serum folate measurement is missing, the calculation can either factor in the assumption that the value is 0 or impute the median serum folate (S-FOL) value from the population. If the hematocrit value is missing, the two approaches are to impute the population median value or to estimate the value from hemoglobin and mean corpuscular hemoglobin (MCH). If both values are missing, the best approach is to predict S-FOL from a random sample and to estimate the hematocrit value.

> **"Access to external method verification programs continues to pose a challenge to data quality in LMICs"**

Access to external method verification programs continues to pose a challenge to data quality in LMICs. To combat this, the CDC offers a micronutrient performance verification program. This provides participants with documentation of proficiency, and the data can be used to adjust the cutoff and/or survey data. The CDC has also developed laboratory quality assurance materials to monitor long-term assay performance.

Inflammation adjustment approaches to improve micronutrient status assessment: BRINDA updates

Appropriate analysis following the obtainment of biomarker data is required to ensure an understanding of micronutrient measurements. The presentation by Parminder S Suchdev, a member of the BRINDA project team at Emory University, opened with a timely quote from Lord Kelvin: "If you cannot measure it, you cannot improve it."

A cycle of association between nutrition and inflammation exists. Inflammation can act as a confounding factor on nutrition biomarkers. As a result, incorrect diagnoses may occur and/or an underestimation or overestimation of micronutrient deficiency prevalence in a population may occur. In turn, this can interfere with assessment of the impact of nutritional interventions.

Suchdev presented on the BRINDA project, a multipartner project that sought to improve nutrition programs by refining micronutrient status estimation approaches. The research focused on WRA and preschool children. Results indicate that one out of two children from the collected surveys had some inflammation – a key finding with large implications for deficiency prevalence estimations. For example, as inflammation increases, levels of the acute phase protein ferritin increase; thus, iron deficiency prevalence would be underestimated. This linear association appears to be true in children for C-reactive protein (CRP) and AGP values.

The BRINDA regression correction approach estimates what ferritin levels would be if inflammation is resolved. For specific uses, the macros of the BRINDA regression correction model are also available for download for application to other data. Overall, if inflammation is ignored, the prevalence of iron deficiency would be underestimated, while the prevalence of vitamin A deficiency would be overestimated. The magnitude of the effect varies by region. This holds significant relevance for interventions, especially in terms of monitoring and evaluating impact over time.

The question then is: should all nutrition biomarkers be adjusted for inflammation? Suchdev stated that the answer is no. The BRINDA approach is limited to cases in which a clear biological rationale for a relationship between nutrient biomarker and inflammation appears to be present, paired with a linear relationship between the nutrient biomarker and AGP and CRP. For cases of pregnant women, more data is needed to make conclusive recommendations.

> **"If you cannot measure it, you cannot improve it"**

Use of population-based kinetic modeling to assess population micronutrient status

Kinetic modeling is useful for assessing micronutrient status across a continuum. For example, it can be used alongside the two current methods employed to measure vitamin A status, retinol

isotope dilution (RID) and model-based compartmental analysis, in both individuals and populations.

Jennifer Ford of the University of North Carolina explained how kinetic modeling can be used to provide a more accurate calculation of total body stores (TBS). Currently, two methods are used to estimate vitamin A TBS–retinol isotope dilution (RID) and model-based compartmental analysis, or a combination of the two.

RID is a method that requires an oral tracer dose of vitamin A to be administered to the individual in order to measure retinol plasma specific activity (SAp). The measured variable (SAp) is then used as a coefficient in the calculation of TBS via the RID equation. One drawback of the RID equation is that the other two coefficients in the equation, FDstores, the fraction of the dose absorbed and found in the body at the time of sampling, and SAratio, the specific activity in plasma over specific activity in stores at the same time, rely on assumed values derived from animal and human studies. Such assumed values may not hold true for all populations.

Kinetic modeling, specifically model-based compartmental analysis, addresses this drawback by estimating more accurate, population-specific values for FDstores and SAratio to quantify TBS. Model-based compartmental analysis for studying vitamin A includes the administration of a stable isotope of vitamin A orally, followed by continued monitoring of vitamin A intake and collection of blood samples. Then analysis of plasma samples is completed, and the data is modeled via software and a compartmental model. Differential equations and weighted nonlinear regression analysis are used to estimate kinetic parameters and TBS.

Relevant to improving the RID equation, the model can be simulated to determine more population-specific FDstores and SAratio coefficients. Modeling of vitamin A status in three countries – Bangladesh, the Philippines and Guatemala – found significant differences in RID coefficients between the three countries.

Population-based modeling approaches have significant relevance, as they enable micronutrient status to be more confidently assessed in children. The use of kinetic modeling seems to allow for more accurate and efficient micronutrient assessments in populations and individuals. This is highly relevant when determining the prevalence of vitamin A deficiency and high vitamin A stores, as well as when measuring the success of vitamin A intervention studies. Additionally, the kinetic modeling method is not limited to vitamin A and can be used for any micronutrient in which an exchange between plasma and body pools occurs.

> **"The use of kinetic modeling seems to allow for more accurate and efficient micronutrient assessments in populations and individuals"**

Use of electronic data collection for micronutrient survey

The Myanmar Micronutrient and Food Consumption Survey (MMFCS) is the first comprehensive nationwide micronutrient survey in Myanmar. Electronic data collection was utilized through the use of the CommCare application.

Min Kyaw Htet, Researcher at the University of Indonesia, reported that the application allowed for logic-controlled and user-friendly collection of data. For example, the app automatically generates a list of relevant tests to be measured based on the target group into which the individual falls. The data can be entered offline and automatically uploads once connection is restored. Another benefit is that the data are instantly available, which allows for easy data cleaning and rapid feedback. This further enables reports to be released quicker, which allows for immediate use of the data collected. The successful use of electronic data collection by the MMFCS offers great promise for future surveys and dietary collection, both national and multicountry.

> **"The successful use of electronic data collection by the MMFCS offers great promise for future surveys and dietary collection"**

Measurement of nutritional and inflammatory markers in ViveBio dry plasma spots

Neal Craft, Chief Scientific Officer of Craft Nutrition Consulting, presented on research that used dry plasma spots (DPS) to examine the transferability of the analysis of nutrient biomarkers to Quansys Q-Plex methodology in three independent labs.

There appears to be greater stability of the nutritional biomarkers at lower temperatures. Spearman correlation between liquid plasma and DPS with the Quansys Q-Plex assay indicated highly correlated data across nutritional biomarkers – ferritin, AGP, thyroglobulin (Tg), sTfR, CRP, histidine-rich protein 2 (HRP2) and retinol binding protein 4 (RBP4). However, the apparent recovery of biomarkers from DPS appeared low, indicating that the estimate of volume in DPS may be less than previously assumed. There is a potential need to revise estimates of blood volume in DPS pads. Within the three independent labs, there was high comparability for CRP, RBP4, Tg and ferritin. Therefore, it is suggested that DPS is a plausible option for the analysis of nutrient biomarkers.

> **"DPS is a plausible option for the analysis of nutrient biomarkers"**

Determination of total body vitamin A stores from a dried serum spot

The RID method remains the best quantitative estimate of vitamin A TBS. However, the maintenance of cold chain until sample analysis is a persistent challenge for population-based vitamin A status assessments. The use of dried blood spots (DBS) would minimize the logistical demands and associated costs of frozen serum maintenance. Georg Lietz from Newcastle University, presented on research that evaluated the feasibility of using DBS in Filipino children.

Lietz reported several benefits of using DBS over serum. Shipment of DBS did not require dry ice, as DBS can be shipped at room temperature. Additionally, the extraction is fast and simple. When three spots were used, all samples met the limit of quantitation. This translates to the ability to quantify TBS of vitamin A from 120 microliters of serum from the three DBS.

Retinol-specific activity from DBS was also highly correlated to retinol-specific activity from liquid plasma. Additionally, the intra-individual difference to compare methods using Bland–Altman analysis was under 5 percent. Therefore, the DBS is a suitable substitute for liquid plasma when assessing vitamin A status in infants and young children. This brings great promise to the field of population-based vitamin A status assessments.

> **"The DBS is a suitable substitute for liquid plasma when assessing vitamin A status in infants and young children"**

Portable non-invasive screening device for iron deficiency diagnosis

Proper screening for iron deficiency used to be difficult to conduct in resource-limited settings, as it required both laboratory capacity and trained personnel. The TibayMeter is a method that overcomes several historical obstacles. Christian Homann, founder and CEO of FerroSens GmbH, presented on the potential of the TibayMeter in screening for iron deficiency. The measurement is noninvasive, portable and cost-efficient.

This method does not require blood samples to be taken; rather, it is an optical measurement of zinc protoporphyrin (ZnPP) on the lower lip. Six clinical studies have evaluated the accuracy of the TibayMeter and found very good correlation with reference blood samples. The TibayMeter is also more stable against infection and inflammation compared with ferritin. This method has other great benefits, as it is portable and fast, producing results in less than one minute. Because it is an optical measurement, there is no need for a laboratory, transportation or specialized personnel. This is ideal for remote areas, where point-of-need application is utilized and laboratory infrastructure is lacking. Overall, the TibayMeter could greatly reduce the burden of iron deficiency screening and enable large screening programs, such as targeted interventions like iron supplementation.

> **"The TibayMeter could greatly reduce the burden of iron deficiency screening and enable large screening programs"**

Reducing the global burden of anemia: What's the role of nutrition?

Making evidence-based policy decisions related to anemia requires a clear understanding of the effects of iron supplementation, both on iron stores and on health outcomes. Questions remain surrounding the impact of iron intervention programs, as well as the best mode of delivery. Two known approaches, home fortification and iron supplementation, are currently used to address iron deficiency anemia. Multiple micronutrient powders are also increasingly used as a way to deliver iron to young children. However, concerns linger regarding iron interventions, including the fact that they increase infection rates in low-income settings. The lack of clear evidence indicating cognitive development and growth benefits from iron interventions is another concern.

This session provided an overview of the burden of anemia and review of interventions to further alleviate the global burden. Key takeaways included:

- Data suggest no harm from universal iron interventions.
- Universal iron interventions effectively reduce the prevalence of iron deficiency anemia. However, there is no evidence that universal iron interventions result in a clinical, functional outcome. Benefits may occur at the individual level, but there is no benefit at the population level.
- Treatment of malaria must be considered when addressing iron deficiency and anemia. By controlling malaria infection and spread, it is possible that the burden of such deficiencies may be reduced.
- In areas with significant prevalence of thalassemia, programming for iron supplementation must consider the impact this syndrome has on anemia.
- In the case of anemia, one size does not fit all. All potential mechanisms of iron deficiency and anemia must be considered before defining the appropriate intervention.

> "In the case of anemia, one size does not fit all. All potential mechanisms of iron deficiency and anemia must be considered."

The biology of anemia and an overview of the hemoglobinopathies

Data suggest that several different pathologies play a role in causing anemia. A common cause of inherited anemia in endemic regions, such as Thailand, is thalassemia and other hemoglobinopathies.

Vip Viprakasit, a doctor and professor of thalassemia, reported on new, unpublished cohort data from Thailand that shows a high prevalence of thalassemia disease among pediatric hemolytic anemia patients. The majority of thalassemia and hemoglobinopathies in Thailand are largely due to mutations or deletions involving the coding sequences of globin genes. Thalassemia can result in a reduction in the synthesis of alpha or beta chains of hemoglobin. Globally, this inherited disorder is widely spread, but concentrated in sub-Saharan Africa and southeastern Asia. Nearly half of the people living in Thailand have the thalassemia gene.

> "Thalassemia is widely spread, but concentrated in sub-Saharan Africa and southeastern Asia"

Clinical severity varies from asymptomatic to life-threatening. Clinical presentation of thalassemia syndrome can include anemia, jaundice, growth retardation, bone fractures and overt infection. Iron overload may also occur as a result of blood transfusions in response to anemia. The high prevalence of thalassemia and hemoglobinopathies in endemic regions, paired with the clinical significance of the syndrome, calls for the consistent evaluation of such cases. Furthermore, concerns remain that universal iron supplementation may cause iron overload in thalassemia patients and carriers; however, Viprakasit reported no harm in providing universal iron supplementation, as iron deficiency anemia persists in the majority of individuals.

Nutrition-sensitive and nutrition-specific interventions for controlling anemia: What can we hope to achieve?

The question remains as to the developmental or functional benefits that children experience following iron supplement interventions and the subsequent reduction of iron deficiency anemia. Sant-Rayn Pasricha, Division Head at the Walter and Eliza Hall Institute of Medical Research, presented on Benefits and Risks of Iron InterventionS in Children (BRISC), a phase-three efficacy trial conducted in Bangladesh. This trial recruited infants aged 8 months ± 2 weeks and assigned them to one of three arms – micronutrient powder (MNP) + dummy, iron + dummy, or double dummy.

At baseline, the prevalence of anemia was severe. Within the placebo group, the prevalence of anemia was higher at follow-up versus baseline, which indicates that the prevalence of anemia increases over time within this population. Changes were similar among the MNP and iron intervention arms. Within both intervention groups, children had increased iron stores, and there was a decrease in the prevalence of anemia.

However, the MNP and iron interventions had no effects on child development, language, motor development, weight-for-age or length-for-age. There was also no effect on child behavior or temperament. This was true even if the child had a previous deficiency. There were also no differences in adverse outcomes or number of clinic visits between the intervention and placebo groups.

> "The time is coming when we will need to redefine what we understand by the syndrome of anemia"

The results indicate that iron interventions did not have an effect on developmental or functional outcomes. As Pasricha stated, "The time is coming when we will need to redefine what we understand by the syndrome of anemia." Anemia may be the endpoint of a broad range of symptoms; data indicate the possibility of other factors influencing a child's developmental or functional development. These factors include, but are not limited to, maternal nutrition before and during pregnancy, the burden of malaria and inflammation.

The genetic interactions between iron metabolism, the red blood cell and malaria

Malaria may be an essential part of the strategy needed to address the global burden of anemia, specifically in sub-Saharan Africa. Malaria transmission is persistent and widespread, and it is estimated that at any time, one in four children in sub-Saharan Africa has malaria parasitemia.[1] Sarah Atkinson from the University of Oxford and the KEMRI-Wellcome Trust Research Programme, reported on evidence that strategies to prevent malaria, as well as other infections, should be an integral part of programs to reduce iron deficiency.

Atkinson's presented research used a genetic proxy – sickle cell trait HbAS that works through the malaria exposure – to evaluate impact on iron deficiency. The main advantages of using a

genetic proxy include the fact that it is less susceptible to confounders and reverses causality. Results indicate that inflammation and malaria significantly increase hepcidin levels, resulting in impaired iron absorption. This translates to the theory that malaria is causing iron deficiency through a hepcidin-mediated block in iron absorption. Therefore, controlling the incidence of malaria allows for iron to be absorbed and iron deficiency to be better controlled.

> **"If the incidence of malaria were halved, iron deficiency would decrease by 49 percent"**

Atkinson predicts that if the incidence of malaria were halved, iron deficiency would decrease by 49 percent. These findings have staggering implications for anemia and iron deficiency interventions in Africa. She recommends that anemia reduction interventions should take a multidisciplinary approach, reducing malaria, to enable iron to be absorbed.

Anemia, micronutrient and inflammation status of young adolescents in rural Bangladesh: The JiVitA-1 birth cohort

It is well known that the adolescent years serve as a critical period of growth and development. During the adolescent period, about 50 percent of adult weight and 50 percent of adult height occurs. In Bangladesh, while the rates of stunting are declining, the lack of dietary diversity, along with obesity, among adolescent girls remains a concern. Efforts to improve nutritional status among adolescents are needed to ensure proper growth during this life stage.

Kerry Schulze, Center for Human Nutrition, Johns Hopkins Bloomberg School of Public Health, presented research conducted at the JiVitA field site in northwest Bangladesh. The work sought to characterize anemia and micronutrient status in young adolescents (9–13 years of age), by exploring status determinants such as sex, age, inflammation, diet, season and activity patterns.

Vitamin D deficiency was the most prevalent deficiency, and the only one with significant differences between boys and girls. The deficiency was significantly higher in girls compared with boys, as boys in the area are more likely to play outdoors. Seasonal variation also occurred within vitamin D deficiency, with higher rates of deficiency during the rainy season.

Iodine may be in more demand because of pubertal growth patterns, as evidenced by age-specific patterns of elevated Tg levels. Sex and age differences were found among iodine deficiency. In girls, Tg levels decreased with each increase in age year, which suggests that the demand for iodine decreases with the decline in linear growth velocity. Moreover, higher Tg levels in boys were associated with lower anthropometric measures. These findings suggest that poorer iodine status was associated with poorer growth.

> **"Findings confirm the need for a multifaceted response to micronutrient deficiencies"**

Despite a lack of iron deficiency, anemia occurred in approximately 10 percent of the population. The prevalence of anemia within the sample was likely due to unexplained factors outside of the diet. Persistent inflammation was also common, yet inflammation was not a strong determinant of anemia or iron status within the population. Findings confirm the need for a multifaceted response to micronutrient deficiencies.

Effects of iron deficiency on immune status and vaccine response

New links have emerged between nutrition, dietary intake and the immune system. The connection between iron and vaccine response is highly relevant, especially given the COVID-19 pandemic. Evidence indicates that children in LMICs have suboptimal adaptive immune responses.[2] Persistent iron deficiency is hypothesized to play a role. Hepcidin regulates iron homeostasis by blocking dietary uptake and iron recycling out of macrophages. Chronically raised hepcidin and inflammation contributes to reduced levels of iron in circulation and reduced iron absorption. In The Gambia, researchers found high levels of hepcidin in over 50 percent of children, which was predictive of blocking iron absorption.[3] However, the consequences of low iron availability on adaptive immunity have yet to be clearly established.

This session highlighted recent research on iron deficiency and its impact on innate and adaptive immunity. Further, the session reviewed the potential impact of iron supplementation during vaccination on immune response and infection severity. To maximize the potential of vaccination campaigns, nutrition, specifically iron, must be considered.

> **"To maximize the potential of vaccination campaigns, nutrition, specifically iron, must be considered"**

Iron powers adaptive immune responses to immunizations and influenza virus

Serum iron deficiency persists among children living in LMICs. The impact of iron deficiency on adaptive immunity remains relatively unknown. In mice, serum iron deficiency results in a practically nonexistent antigen-specific immune response and inhibits the primary response to immunization. There is a reduced quality of immune response within the mice. It is theorized that this result does not depend on immunization route.

Further, it has been observed that serum iron deficiency has a lasting impact. The deficiency results in a reduced number of memory T cells and a reduced magnitude of recall response. This is true for both pre- and post-secondary immunization. Improvement in vaccine-specific antibodies occurs after iron supplementation in iron-deficient piglets. This indicates that high hepcidin levels suppress adaptive immunity in animals.

Serum iron deficiency also compromises viral control and results in significantly higher levels of viral RNA. In the lungs, higher inflammation levels are associated with serum iron deficiency during influenza infection. Serum iron deficiency is also associated with greater weight loss during infection, whereas patients with normal serum iron experienced weight regain.

> **"Serum iron deficiency, and increased concentrations of hepcidin, can inhibit immunization and influenza virus response"**

In humans, individuals with high hepcidin levels and low iron stores displayed weak antibody responses to Rubella, *Haemophilus influenzae* and *Streptococcus pneumoniae* when compared with healthy controls. This confirms that serum iron deficiency, and increased concentrations of hepcidin, can inhibit immunization and influenza virus response. Moreover, targeting hepcidin to manipulate serum iron levels may provide potential to control adaptive immunity.

These findings hold significant relevance in LMICs, as individuals in LMICs have high rates of chronic inflammatory disorders

TABLE 1.1: Logistic regression analysis of factors associated with diphtheria seronegativity at 18 months

Diphtheria		
Seronegative at 18 months: R^2 = 0.322		
	Odds ratio	**95% CI**
Sex	1.5	0.534, 3.969
Birthweight	1.0	0.996, 1.000
Anti-diphtheria IgG in cord blood	1.0	0.283, 3.419
Anti-diphtheria IgG at age 10 weeks	0.002	0.000, 0.097 (*P* = 0.0027)
Weight-for-age z-score (mean at 10 to 24 weeks)	1.4	0.798, 2.369
Serum transferrin receptor at 24 weeks	**1.2**	**1.011, 1.315 (*P* = 0.0439)**
α-1-glycoprotein at 24 weeks	2.2	0.983, 5.127
Retinol binding protein at age 24 weeks	4.2	0.432, 39.888
Analyzed using logistic regression analysis		

TABLE 1.2: Linear and logistic regression analysis of factors associated with pneumococcus seronegativity at 18 months

Pneumococcus serotype 19		
Seronegative at 18 months: R^2 = 0.146		
	Odds ratio	**95% CI**
Sex	1.9	0.754, 4.878
Birthweight	1.0	0.999, 1.001
Anti-pneumococcus 19 in cord blood	1.1	0.974, 1.296
Anti-pneumococcus 19 at age 10 weeks	0.6	0.279, 1.153
Height-for-age z-score (mean at 10 to 24 weeks)	0.9	0.633, 1.346
Serum transferrin receptor at 24 weeks	**1.2**	**1.013, 1.342 (*P* = 0.0327)**
α-1-glycoprotein at 24 weeks	0.8	0.362, 1.737
Retinol binding protein at age 24 weeks	0.2	0.024, 1.781
Analyzed using linear and logistic regression analysis		

and/or iron deficiency anemia. These findings also hold relevance for potential responses to the COVID-19 vaccination, as research indicates that severely affected COVID-19 patients have lower serum iron levels.

Iron deficiency anemia in Kenyan infants at time of vaccination predicts poor response to diphtheria and pneumococcus vaccines

Infections persist as major causes of child morbidity and mortality worldwide, as vaccines do not reach their maximum potential. Disparities exist between LMICs and high-income countries in terms of infection mortality and vaccine efficacy. For example, seroprotection after vaccination varies across regions and is lowest in low-income countries. Such disparities must be addressed to ensure vaccines can obtain their full potential and lower the burden of deaths of children under the age of five.

Potential explanations for why vaccines do not work as well in LMICs include many factors, from concurrent inflammation to malnutrition. This is a major concern in sub-Saharan Africa, where 46 percent of pregnant women have iron deficiency anemia. Maternal iron deficiency anemia is predicted to be associated with low iron stores in infants at birth – which, when paired with frequent infections, can result in iron store depletion within an infant's first 2 months of life. Vaccinations typically occur at 6 and 14 weeks of age – by which time infant iron stores may already be depleted.

A 2-year prospective birth cohort study in Kenyan infants reviewed the timeline of iron deficiency anemia, as well as its impact on vaccine titers and seroprotection. At 10 weeks of age, approximately 50 percent of infants had anemia. By 6 months of age, 93 percent of infants had anemia, which was mostly moderate to severe. Inflammation, probably due to infection, was also prevalent throughout the infant growth period.

Results indicate that primary vaccine responses against diphtheria and pneumococcus are high, yet secondary vaccine responses vary. At 18 months, the strongest risk factor for seronegativity against diphtheria was iron-deficient erythropoiesis, as displayed in **Tables 1.1** and **1.2**. Further, results reveal that anemic infants in the study population had over two times the risk of being unprotected against diphtheria and pneumococcus at 18 months.

> **"Better understanding of the relationship between iron deficiency and vaccine responses can increase the efficacy of vaccines"**

Responses to the diphtheria and pneumococcus vaccines may be impaired by anemia and iron deficiency at the time of vaccination. Better understanding of the relationship between iron deficiency and vaccine responses, paired with future findings, can inform policies and programs to increase the efficacy of vaccines.

The role of iron in innate and adaptive immunity

Both iron deficiency and iron overload appear to affect susceptibility to, and outcomes of, infection. This has great impact on the needs of interventions, policies and programming.

Regulation of the iron concentration in plasma occurs via the hormone hepcidin. In the presence of hepcidin, ferroportin cannot export iron to blood plasma. Iron gets trapped and iron concentration in blood plasma decreases. This process protects against excess iron in plasma.

This mechanism of increased hepcidin production fails during iron overload. Iron exportation becomes dysregulated. Transferrin can no longer bind iron, resulting in toxic iron levels. In the presence of iron overload disorders, virulence is increased by the presence of non-transferrin-bound iron in the plasma. The increased virulence is specific to Gram-negative extracellular infections. The severity of virulence due to bacterial growth depends on the amount of transferrin in the plasma. This can result in increased mortality.

Iron is required for T- and B-cell clonal expansion; therefore, iron deficiency may also play a role in adaptive immunity impairment. In normal individuals, transferrin is taken up by cells to meet these iron requirements. However, in iron-deficient patients the uptake of transferrin is poor. While iron appears to be sufficient at baseline in iron-deficient patients, it does not appear to be sufficient during rapid proliferation. Further, iron deficiency can result in lower IgG, lower memory B cells, and defects in T- and B-cell proliferation. This can also impact vaccination.

> **"Both iron deficiency and iron overload appear to affect susceptibility to, and outcomes of, infection"**

Effect of iron and prebiotic supplementation at time of vaccination on short- and long-term immune responses to measles vaccine in Kenyan infants

In rural Kenya, anemia prevalence at infancy is approximately 70 percent at the time of routine vaccination. Limited data exists that links anemia, iron deficiency and vaccine response. More specifically, limited data explores the impact of iron supplementation on vaccine response during pediatric vaccinations.

A randomized controlled trial conducted in Kenya sought to determine the effects of iron supplementation at the time of first measles vaccination. Iron supplementation at the time of first vaccination improved infants' iron status and resulted in higher levels of anti-measles serum IgG, stronger IgG avidity and greater seroconversion. Compared with the infants that received iron supplementation, infants that received no iron at the time of measles vaccination had approximately a three times higher risk of seronegativity at 11.5 months.

These results indicate that iron supplementation at the time of measles vaccination can contribute to a stronger immune response. These findings should be considered when developing vaccination programs, as iron supplementation in early infancy may help to increase the efficacy of vaccinations.

Multiple micronutrient supplements improve birth outcomes for pregnant adolescents: Evidence from an individual participant data meta-analysis

Pregnant adolescents in LMICs account for 7.3 million births per year. Alarmingly, complications of pregnancy are the leading cause of death among adolescent girls in LMICs. The burden of malnutrition in LMICs is high and disproportionately affects women and children. Pregnant adolescents tend to have a poorer nutrition profile and have heightened vulnerability because of their growth needs and the needs of the fetus. Pregnant adolescents have a higher risk of adverse pregnancy outcomes and maternal death because of these vulnerabilities.

> **"Iron supplementation at the time of measles vaccination can contribute to a stronger immune response"**

Iron and folic acid (IFA) supplementation continues to be recommended by WHO for pregnant women.[4] Recent guidance from WHO recommends MMS that include IFA in the context of rigorous research.[4] However, no guidance or specific research exists for pregnant adolescent women.

The individual participant data (IPD) meta-analysis sought to address this gap. As displayed in **Table 1.3**, the review found a significant reduction in the odds of low birth weight (LBW) and preterm births among pregnant adolescent women who received MMS ver-

TABLE 1.3: Outcomes of interest and effect modification by age from one- and two-stage individual participant data (IPD)

Outcome		One-stage IPD			Two-stage IPD		
		N (trials)	Odds ratio (95% CI)	Test for interaction	*N* (trials)	Odds ratio (95% CI)	Test for interaction
Low birth weight	All women	13	0.87 (0.80–0.95)		13	0.86 (0.79–0.92)	
(< 2,500 g)	< 20 years		0.87 (0.77–0.97)	*P* = 0.89		0.81 (0.74–0.88)	*P* = 0.65
	≥ 20 years		0.87 (0.80–0.95)			0.88 (0.79–0.99)	
Preterm birth	All women	13	0.89 (0.83–0.95)		13	0.87 (0.83–0.92)	
(< 37 weeks)	< 20 years		0.88 (0.80–0.98)	*P* = 0.87		0.86 (0.79–0.95)	*P* = 0.67
	≥ 20 years		0.89 (0.83–0.96)			0.88 (0.82–0.95)	
Small for	All women	13	0.95 (0.87–1.03)		13	0.94 (0.87–1.01)	
gestational age	< 20 years		0.90 (0.81–1.00)	*P* = 0.18		0.86 (0.79–0.94)	*P* = 0.05
(< 10th centile)	≥ 20 years		0.96 (0.88–1.04)			0.97 (0.88–1.07)	
Stillbirth	All women	13	0.96 (0.88–1.05)		13	0.98 (0.86–1.13)	
(≥ 28 weeks gestation)	< 20 years		1.07 (0.90–1.25)	*P* = 0.15		1.12 (0.82–1.51)	*P* = 0.20
	≥ 20 years		0.92 (0.83–1.03)			0.95 (0.80–1.12)	
Neonatal mortality	All women	10	1.02 (0.93–1.13)		10	1.03 (0.93–1.14)	
(≤ 28 days)	< 20 years		0.98 (0.84–1.16)	*P* = 0.54		0.99 (0.84–1.16)	*P* = 0.83
	≥ 20 years		1.05 (0.93–1.19)			1.08 (0.88–1.31)	
Perinatal mortality	All women	11	0.99 (0.92–1.06)		11	1.04 (0.92–1.18)	
(≥ 28 weeks gestation	< 20 years		1.04 (0.92–1.18)	*P* = 0.32		1.07 (0.91–1.25)	*P* = 0.28
up to ≤ 7 days)	≥ 20 years		0.96 (0.88–1.05)			1.00 (0.84–1.20)	
Maternal anemia	All women	8	1.05 (0.95–1.18)		8	1.06 (0.95–1.19)	
(3rd trimester	< 20 years		1.07 (0.86–1.33)	*P* = 0.94		1.06 (0.86–1.31)	*P* = 0.85
Hb < 110 g/L)	≥ 20 years		1.06 (0.94–1.18)			1.08 (0.91–1.27)	

sus IFA. Within the adolescent age group, there is a greater reduction in the risk of delivering a baby that is SGA. This indicates that women of younger age appear to benefit most from MMS in terms of SGA. There are no other substantial differences between age groups related to the impact of MMS. Additionally, the meta-analysis found no improvement or harm due to MMS on stillbirth, neonatal mortality, perinatal mortality or maternal anemia. For each of these, there were no differing effects between age subgroups of women.

Findings indicate that pregnant women of all ages would benefit more from MMS as compared with IFA supplementation. It is recommended that policies and programs to scale up MMS supplementation for pregnant women are supported.

The double burden of obesity and iron deficiency: Effect of maternal obesity during pregnancy on maternal iron status

Epidemiological data indicates that obesity is associated with reduced iron status. Explanations for the association include increased blood volume in obese individuals, greater adiposity resulting in lower fractional iron absorption, and higher levels of hepcidin, resulting in lower systemic iron availability. Hepcidin, the main iron regulatory protein, is higher in obesity and associated with inflammation. Higher hepcidin levels impact transportation, which results in lower iron availability.

The higher concentrations of hepcidin associated with obesity are a concern for pregnant women, as iron requirements increase tenfold during pregnancy. Maternal hepcidin regulates the amount of iron transferred to the placenta. In healthy pregnancies, there is a decrease in hepcidin levels. This decrease allows for an increased supply of iron to be transferred to the fetus.

The Pregnancy Iron Absorption Normal Weight Overweight/Obese (PIANO) study was conducted in Switzerland, Mexico and Thailand. The prospective case-control study explored if pre-pregnancy obesity affects the transfer of iron to the fetus, and if so, how the placenta compensates for low maternal iron status.

Compared with the normal weight group, body iron stores were decreased at greater levels in overweight and obese women. This decrease was about 30 percent compared with the normal weight group. Results also indicate that overweight and obese pregnant women have higher rates of inflammation; however, this does not result in higher hepcidin levels among the overweight and obese group. It is predicted that the lower iron status offsets the effects of inflammation. Within the normal weight group, iron absorption was upregulated at a much higher rate during the third trimester. Iron absorption was twice as high in the normal weight group as compared with the overweight and obese group.

Results indicate that decreased maternal iron absorption and iron stores have an impact on infant iron stores. Women's pre-pregnancy BMI predicts lower body iron stores in the first 6 months of infancy. Infants born to overweight or obese mothers had body iron stores that were 15 percent lower than those of infants born to normal weight mothers. Infants born to overweight or obese mothers also had higher TfR levels. Higher TfR levels indicate greater levels of iron-deficient erythropoiesis. These findings allow for the assumption that pregnancy BMI and inflammation are predictors of the level of circulating iron transferred from the mother to the fetus during pregnancy. Higher maternal BMI and levels of inflammation, measured through CRP, are associated with reduced maternal–fetal iron transfer.

Findings indicate a need to address maternal overweight and obesity status. Lower iron stores are a risk factor for reduced physical and mental development; therefore, reducing pre-pregnancy obesity is an important consideration.

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Micronutrient FORUM

About Us

The Micronutrient Forum serves as a global catalyst and convener for sharing expertise, insights and experience relevant to micronutrients in all aspects of health promotion and disease prevention, with special emphasis on the integration with relevant sectors.

Vision

A world where all people have access to all essential micronutrients at levels needed to promote health and prevent disease.

Mission

To be a global leader bridging scientific knowledge with policy and programs across multiple sectors, by providing support for capacity development and continuous dialogue for action, to ensure the full integration of nutrition, and in particular the importance of micronutrient adequacy, in health promotion and disease prevention throughout the life cycle.

The Micronutrient Forum works through:

Advocacy
Facilitating coordinated action among diverse stakeholders.

Consultations
Bringing together global experts on key topics to synthesize existing knowledge into actionable insight.

Convenings
Creating a multi-sectoral exchange of information and necessary conversations.

TRACK

2

Efficacy and Safety of Micronutrient Interventions

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Takeaway points

- To obtain a 'high' level of evidence as rated by WHO, the nutrition and health community should aim to conduct high-quality, context-specific randomized controlled trials, systematic reviews and meta-analyses, including individual participant data meta-analyses.
- Proven interventions that work at scale, such as intravenous iron, should be prioritized by all stakeholders.
- Oral iron should be given when dealing with mild, uncomplicated iron deficiency in the absence of active bleeding. It can also be provided during the first trimester of pregnancy or during the second trimester of pregnancy when hemoglobin (Hb) › 10.0 g/dL.
- Contextual factors, including political will, should always be considered when designing nutritional interventions to avoid unintended consequences.
- Climate effects should be considered when designing nutritional interventions.
- The positive or negative micronutrient effects on the brain are based on timing, dose and exposure duration; the best time to intervene is during the first 1,000 days of life.
- There are new, more practicable, methods of assessing childhood development in low-resource settings. These include brain imaging.
- Vitamin A is an essential nutrient, a mediator of infectious mortality and prophylactic against blindness. However, chronic ingestion of excessive vitamin A may reduce bone mineralization and predispose the individual to fractures. There is consequently a need to balance the benefits and risks of overlapping vitamin A interventions such as supplementation and food fortification.
- Neglected B vitamins (thiamine, riboflavin, niacin and pyridoxine) must be studied to determine/develop: (1) standardized biomarker assays, cutoffs and methodological harmonization; (2) nationally representative assessments of dietary intake and status; and (3) identification of localities in need of intervention, fortification and supplementation.
- Fortified rice appears to be beneficial in reducing the prevalence of anemia and zinc deficiency.
- Rice fortification programs can be combined with nutrition-specific and nutrition-sensitive public health interventions – such as water, sanitation and hygiene (WASH), deworming, iron and folic acid (IFA) supplementation – to amplify child health outcomes.
- Multiple-micronutrient-fortified salts could be an effective way to eradicate micronutrient deficiencies at the population level.
- There is no evidence to recommend a change in the policy of immediate iron supplementation post-malaria treatment in children with moderate anemia living in malaria-endemic areas.
- Lower doses of zinc given daily for 14 days were non-inferior to the standard dose of zinc in terms of diarrhea and the mean number of stools in children with acute diarrhea.
- Stable isotope techniques are increasingly being used in nutrition and health research to study the bioavailability of nutrients.

Introduction

An estimated 250 million children globally are not fulfilling their developmental potential. SDG 4.2 targets that, by the year 2030, all boys and girls will have access to quality early childhood development, care and pre-primary education to be ready for primary education.

Micronutrient deficiencies affect all age groups, but young children and women of reproductive age are most at risk. Worldwide, iron, vitamin A and iodine deficiencies are the three most common micronutrient deficiencies. Zinc and vitamin D deficiencies are also of emerging concern. The important role of the neglected B vitamins in human health necessitates a re-focus on these nutrients. This report summarizes most of the proceedings of *Track 2: Efficacy and safety of micronutrient interventions*.

Existential evidence: Quality of evidence for nutrition policies

Though systematic reviews and meta-analysis of high-quality randomized controlled trials (RCTs) of appropriate quality and de-

sign remain the gold standard of information for policy guidance, many systematic reviews and meta-analyses do not sufficiently adjust for context, trial size and quality. Greater weight must be given to scale and effectiveness trials in assessing benefits and real-life evidence using mixed methods. To facilitate data verification and quality checks, open access to meta-analyses should become the norm, even outside of individual participant data (IPD) meta-analyses.

"RCTs can play a role in building scientific knowledge, and useful predictions, but they can only do so as part of a cumulative program, combining with other methods, including conceptual and theoretical development to discover not 'what works', but 'why things work'!"

Sir Angus Deaton
(Nobel Laureate for Economic Sciences, 2015)

The WHO guideline development is based on the best evidence available, preferably systematic reviews and meta-analyses. The hierarchy of evidence is used, with expert opinions at the bottom and RCTs and systematic reviews at the top. WHO then grades the levels of evidence into high, moderate, low or very low. For some nutrition topics/questions, there are more systematic reviews than there are trials on the topic. There is a saturation of systematic reviews compared with RCTs.

Systematic reviews are not the only way to bring knowledge. When drugs or vaccines are past drug trial phase 3, if successful, they go into approval, e.g., by the US Food and Drug Administration. There is no need to wait for systematic reviews. This means that there are different paradigms for assessing evidence. The question then is: how should we go about generating nutrition and health knowledge – should we rely on systematic reviews and meta-analyses? Yet again, if we have an important question, e.g., the safety and efficacy of parenteral iron in pregnancy, should we move directly to RCTs, which might cost millions of dollars, but which might also lead us to the answer?

The hierarchy of evidence starting from top to bottom has not changed:

1. Meta-analyses including IPD meta-analyses
2. Multicenter RCTs and cluster RCTs
3. RCTs
4. Prospective cohort studies
5. Case-control studies
6. Cross-sectional cohort studies
7. Descriptive or case series
8. Case reports

Different types of meta-analyses, including IPD, can be used depending on the context of the research question.

The use of RCTs and systematic reviews has grown exponentially. From 2013 to 2020/21, the nutrition field has added over 3,500 systematic reviews, making the synthesis of data very difficult for researchers and policymakers. Systematic reviews are just too easy to do compared with designing and implementing expensive and complicated RCTs such as multicenter/multicountry RCTs. For micronutrients, there are approximately 10 more systematic reviews than there are studies every year. Thus, people are adding all manner of studies to the systematic reviews, raising concerns about the quality of the papers added. Issues identified include:

- Massive duplication versus replication;
- Pooling of contextually different studies;
- Issues with studies, e.g., poorly conducted trials, poorly sized/powered and designed trials;
- Data veracity given replicability – use of summary data versus quality data checks; and
- Mixing efficacy and effectiveness studies.

A Cochrane review demonstrated that deworming had no effect on growth. This led to considerable debate. Bhutta and colleagues, Centre for Global Child Health, The Hospital for Sick Children, undertook to evaluate the studies on this topic more critically. They found that, on average, the effects of mass deworming on child nutritional status and cognition are small at the population level (moderate certainty). Deworming may have small effects on weight but not on height or Hb levels (very low certainty evidence) for children with moderate-intensity infections. The effects of deworming are uncertain in children with heavy-intensity infections. Larger studies with better confidence intervals (CI) are warranted.

Benefits versus risks of parenteral iron in pregnancy as a public health intervention

There is no doubt that intravenous (IV) iron is superior to oral iron in treating iron deficiency in every population. However, IV iron is a complicated and more expensive therapy to deliver. It usually takes the form of iron encapsulated in a carbohydrate shell. The stability of the shell has improved and changed over time. The key advantage of IV iron is that 1,000–1,500 mg can be administered in a 15-minute infusion. This dose lasts for a long time and is safe. The team delivering IV iron to patients need to be aware of the possible adverse events, even if these are extremely rare. Hypophosphatemia needs to be investigated

if ferric carboxymaltose (FCM) is going to become a frontline drug. Infection and safety, especially in malaria-endemic countries, need to be established.

The use of parenteral iron is not new; rather, the method of use has evolved. Sydenham first used oral iron in 1687 to treat 'green sickness' by adding iron filings to cold wine. Blaud renamed green sickness 'chlorosis' in 1832, and was the first to use ferrous sulfate. During the American Civil War, iron was used to treat war wounds. Today, iron deficiency is the most common micronutrient deficiency globally, affecting > 35 percent of the world's population and > 50 percent of gravidas. It is 100 times more prevalent than cancer, yet more than 300 years later oral iron – which is often ineffective and usually poorly tolerated – is the frontline intervention.

Maternal iron deficiency potentially affects fetal, neonatal and childhood brain growth and development, with adverse effects on myelination, neurotransmitters and brain programming.[1] Children born to iron-deficient mothers demonstrate lower cognitive function, memory and motor development up to 19 years of age.[2] Iron deficiency anemia (IDA) in pregnancy is associated with an increased risk of adverse perinatal outcomes, including preterm birth, low birth weight and small-for-gestational-age infants.[3] Fetal iron status is reduced when maternal ferritin is < 15 µg/L.[4]

Iron deficiency is common in neonates, even after iron supplementation in pregnancy.[5] Unfortunately, babies are rarely screened for iron deficiency at birth. The critical period for iron in neonatal brain development is 2 months before delivery up to 1 month after birth. If interventions are not appropriate, detrimental effects are seen up to the age of 19 years.[6] Infants at risk of neonatal iron deficiency include those from:

- Iron-deficient mothers or those previously treated for IDA;
- Mothers who are underweight or obese, or who have diabetes;
- Vegetarian mothers;
- Multiparas;
- Mothers who have inflammatory bowel disease;
- Mothers who have HIV or are smokers;
- Mothers who have an inter-partum interval of < 6 months; and
- Mothers who have a history of abnormal uterine bleeding.

Oral iron should be given when dealing with mild, uncomplicated iron deficiency without active bleeding. It can also be provided during the first trimester of pregnancy when IV iron is not recommended, or during the second trimester of pregnancy when Hb concentration > 10.0 g/dL. The absorption of oral iron is hindered by diet and disease. Adverse events (constipation, metallic taste, nausea, gastric cramping, tenacious stool) occur in more than 70 percent of oral iron patients. In Nigeria, compliance with oral iron supplementation guidelines is low; up to 20 percent of pregnant women do not comply, probably because of the aforementioned adverse effects.

Alternate-day dosing seems to result in better total oral iron absorption compared with daily iron dosing. One iron tablet taken every other day is less toxic and more effective. Large doses of iron trigger an acute hepcidin surge, which might make a case for alternate-day dosing. There are WHO guidelines on intermittent oral iron supplementation in pregnancy.

IV iron formulations can be administered in a single total-dose infusion, obviating multiple visits, decreasing infusion reactions and increasing adherence. Examples of IV iron include FCM, iron isomaltoside (Europe only) and ferumoxytol. IV iron should be given in the case of:

- Patients who are intolerant of, or unresponsive to, oral iron;
- Abnormal uterine bleeding;
- Inflammatory bowel disease;
- Angiodysplasia;
- Iron-restricted erythropoiesis; and
- Comorbid 'inflammatory' condition.

It should also not be given:

- During the second trimester of pregnancy, if Hb concentration < 10.0 g/dL;
- During the third trimester of pregnancy; and
- After bariatric surgery.

IV iron is probably safer than most physicians believe and should be moved forward in the treatment paradigm. However, in low- and middle-income countries (LMICs), there may be challenges. For example, in Nigeria, identified challenges include: the availability of personnel to administer IV iron, especially in rural areas; lack of appropriate diagnostic tools; the possibility of worsening of malaria and infections; acceptability levels among physicians and pregnant mothers; cost-effectiveness; and lack of evidence that IV iron affects clinical outcomes. Proposed solutions include: training, especially of nurses in the primary healthcare setting to give IV iron; preventive treatment of malaria; screening for infections beforehand; community advocacy; research on the cost-effectiveness of IV iron; and publication of evidence of IV iron on clinical outcomes. The IVON trial in Nigeria, which is currently being implemented, will use an effectiveness–implementation design to study the use of iron isomaltoside to overcome the challenges listed above. The REVAMP trials in Malawi are also being implemented, and will document the cost-effectiveness of IV iron as an intervention.

The best timing for IV iron as a nutrition intervention is early on in the second trimester. However, IV iron can also be used as a rescue intervention in the third trimester, just before delivery of the baby. In IV iron, infusion reactions (1–3 percent) such as pressure in the chest, arthralgia or myalgia, headache and/or flushing may occur. Severe hypersensitivity (< 1:250,000) may

also occur. Intramuscular iron should not be given to patients, as better IV iron formulations have been developed that are safer and less painful.

Healthcare financing in the context of intravenous iron

Policymakers need data on the cost and cost-effectiveness of IV iron formulations in order to be able to make policies for the adoption and use of parenteral iron. The local supply of drugs, including quality assurance procedures to be able to assure safe, effective, quality and cost-effective medicines to the population, is essential. Information and research will be necessary to make IV iron a routine drug during pregnancy. The health workforce and their ability to deliver IV iron will also be a significant consideration for policymakers. Besides, diagnosis of anemia, which is currently carried out using point-of-care devices such as HemoCue, is problematic because of frequent stock-outs of Hb cuvettes and the breakdown of devices. Thus, if IV iron is to be based on Hb diagnostics, the programmatic implication of such a policy will need to be reviewed. For a country to adopt the national use of IV iron, operational guidelines will need to be drafted, a rollout plan made across all health facilities and a decision taken about which level of the health system the IV iron will be introduced. Further, trained human resources, especially frontline nurses, will be needed.

The importance of 'context' when planning nutrition interventions and how to avoid unintended consequences

It is essential to precede any nutrition/micronutrient intervention program with an assessment of the needs and a thoughtful analysis of the feasibility and local sustainability of the interventions. Efficacy trials do not guarantee that programs will be effective; to improve effectiveness, a program must take into account the following factors: environment, the biological need of the population, compliance, adherence to the intervention and programmatic sustainability. The nutrition community has forgotten the 1990 UNICEF Triple-A approach for program design and implementation, which emphasized characterizing the problems (prevalence, magnitude, severity), identifying the causes, and analyzing the acceptance, feasibility and programmatic viability of the potential interventions.

> **"Planning without acting is day-dreaming but acting without planning is a nightmare"**
>
> *(Chinese proverb)*

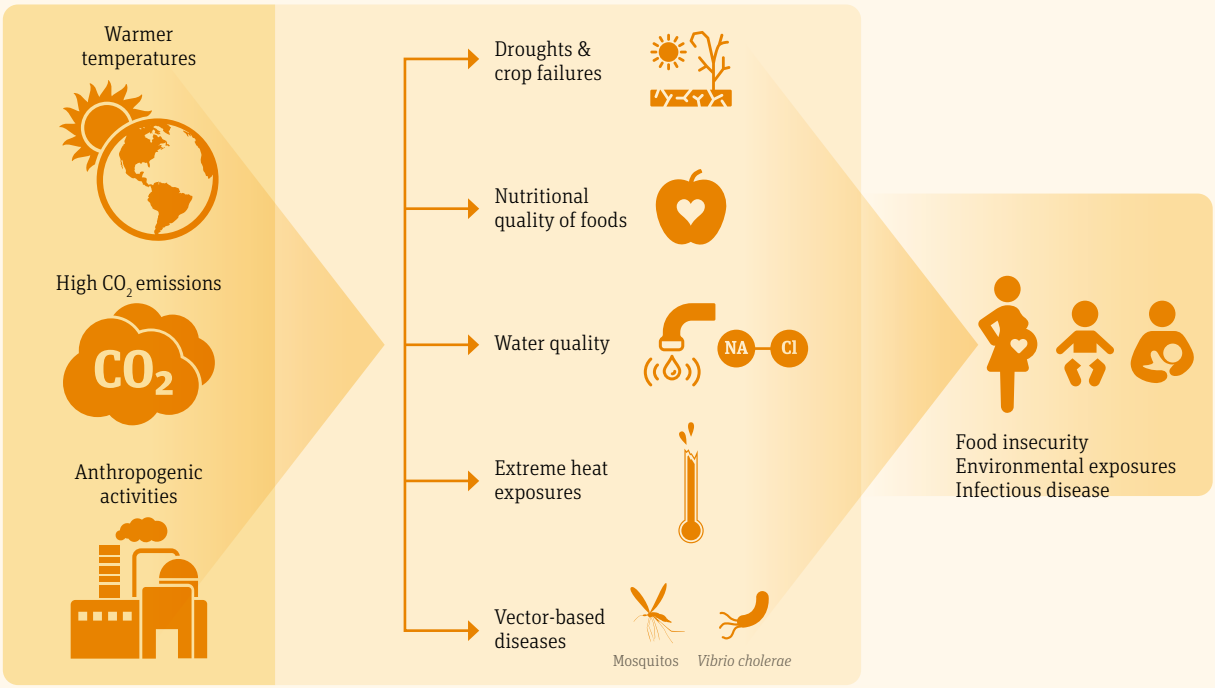
Contextual factors, including political will, should always be considered when designing nutritional interventions so as to avoid unintended consequences. We have to think: 'In my context, what is driving the problem, and what do I need to do to overcome this problem?' For example, what is driving neonatal mortality in various places within different contexts? The nutrition community needs to think about the internal and external factors that influence the contexts in which they act, and they must adapt nutrition interventions accordingly. We must first try to understand the context before providing solutions; let's forget the activism and move to the actions. Whether we are talking about infant and young child feeding (IYCF) or another such program, we must collect data and share it throughout the continuum of research to understand the context. The context is important, and if we ignore it and pursue the nutrition plan, we are bound to fail.

The SHINE (Sanitation, Hygiene, Infant Nutrition Efficacy Trial) project, which was conducted in rural Zimbabwe, was a 2 × 2 cluster-randomized trial that assessed the impact of WASH and IYCF interventions on enteric infections. The study assessed interventions to promote exclusive breastfeeding from birth to 6 months and improve complementary feeding. The research team encountered a perceived problem: mothers cited the open fontanel as the reason for feeding their babies from the first month of life, and thus abandoning exclusive breastfeeding. To mitigate against the perception that the open fontanel is a problem for babies, messages needed to be targeted to the context in rural Zimbabwe.

The SHINE project tested the independent and combined effects of improved WASH and improved complementary feeding on child stunting. Exclusive breastfeeding from birth to 6 months was promoted as a blanket intervention across all arms, primarily because of the high prevalence of HIV. The study explored why exclusive breastfeeding rates are low, yet any breastfeeding is the norm in Zimbabwe (89 percent are still breastfeeding at 12 months, but only 23 percent of babies < 6 months were exclusively breastfed). Formative research conducted among 295 mothers with babies < 6 months showed that all of the mothers introduced non-breast milk food before 6 months of age, and 68 percent began giving non-breast milk foods in the first month of life. During the first 2 months of life, non-breast milk foods were given to treat three perceived problems: *nhova* (fontanel), *ruzoka* (colic) and crying. Common foods given included cooking oil, water and traditional medicines. After the second month of life, mothers believed that breast milk was no longer sufficient to meet their babies' dietary demands. They therefore introduced other foods, especially porridge.

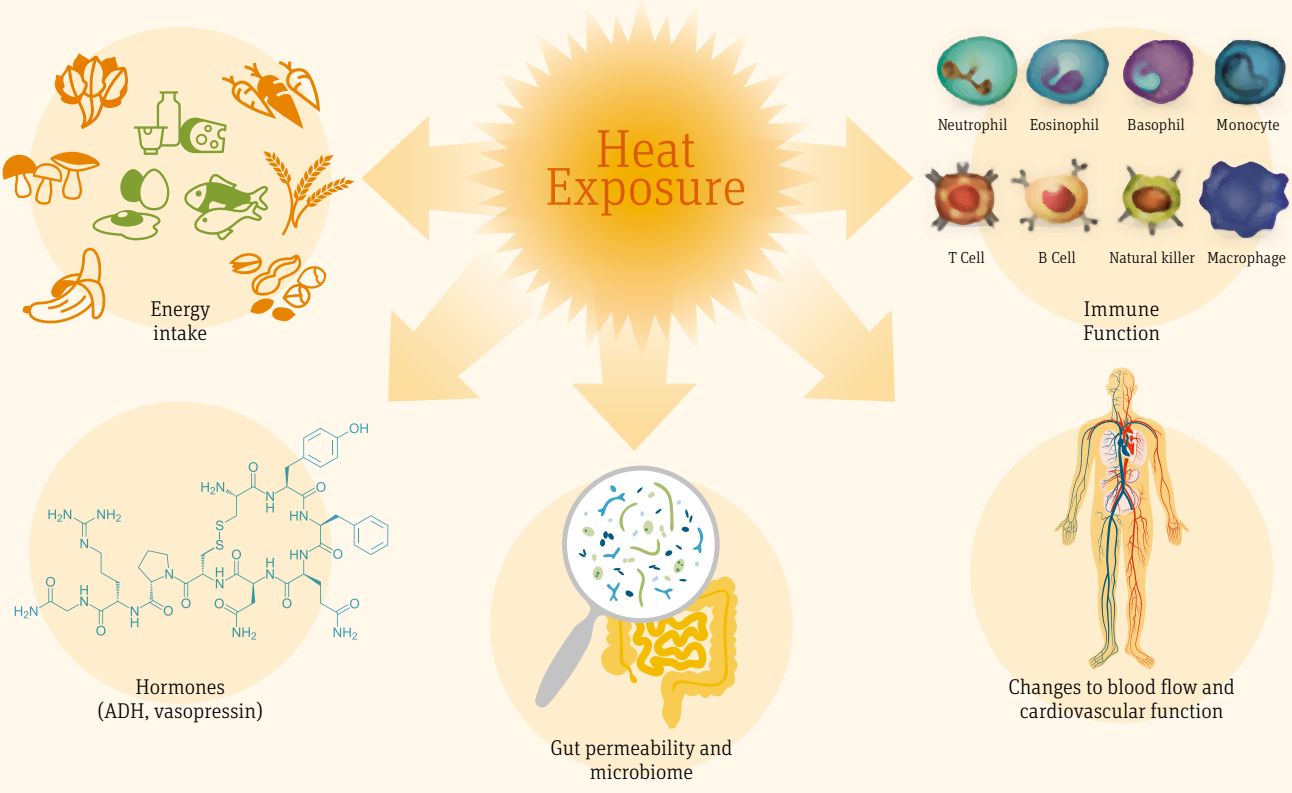
> **"Obese children are still at risk of thiamine deficiency due to a high intake of energy-dense foods"**

FIGURE 2.1: Impacts of climate on health



Generously provided (with permission) by Kartik Shankar, Section of Nutrition, University of Colorado School of Medicine

FIGURE 2.2: How excess heat affects health outcomes



Generously provided (with permission) by Kartik Shankar, Section of Nutrition, University of Colorado School of Medicine

The importance of understanding the dual-burden context that exists in populations was explained via a thiamine and obesity trial in Thai children. This was a cross-sectional study of 124 obese children aged 7–15 years, with exogenous obesity based on the WHO criteria (weight-for-height > median +3 SD). The children were physically examined, and dietary intake data were analyzed. Biochemical assays to determine thiamine deficiency were carried out. Researchers found that obese children are still at risk of thiamine deficiency due to a high intake of energy-dense foods. Screening for thiamine deficiency and early recognition of symptoms should be recommended, especially because thiamine deficiency is initially asymptomatic. Thiamine supplementation was recommended as an adjunct to therapeutic lifestyle modification in the treatment of obesity.

Should climate effects be considered in nutritional interventions?

The year 2020 was estimated to be among the hottest years since climate recording started. The world's five warmest years have all occurred since 2015, and nine of the 10 warmest years during the 140 years of climate recording have occurred since 2005. Heat-related mortality, estimated at ~12,000 premature deaths in the USA,[7] is the leading cause of weather-related mortality (**Figure 2.1**).

Warmer global temperatures, high CO_2 emissions and anthropogenic activities lead to droughts and crop failures, the altered nutritional quality of foods, altered water quality, extreme heat and vector-borne diseases such as malaria and cholera. The overall result is food insecurity. A systematic review of 28 studies globally[7] found that heat exposure was correlated with a greater incidence of preterm birth (15 out of 17 studies). Six out of seven studies found significant negative associations of ambient temperature increase and birth weight at delivery. Ambient heat stress has significant negative effects on intrauterine growth. In resource-limited settings, exposure to high ambient temperature during the first trimester decreases linear growth *in utero*. Improved maternal nutritional status provides resilience against heat-induced growth restriction. Nutrition indicators are impacted by the high temperatures, possibly due to food insecurity pathways (**Figure 2.2**).

Micronutrient-responsive pathways to early childhood cognitive development

The brain grows rapidly during the first 1,000 days of life. It is highly metabolically active and accounts for 60 percent of total body oxygen consumption. At this stage, it is vulnerable to damage but more amenable to repair. According to Kretchmer and colleagues (1996), the positive or negative micronutrient effects on the brain are based on timing, dose and exposure duration.[8] This is because the brain is not a homologous organ but consists of different regions, e.g., cortex, hippocampus, striatum and cerebellum.

Nutrition is a major environmental factor in DOHaD (Developmental Origins of Adult [mental] Health and Disease). Altered nutrient status during fetal and neonatal life can affect organ structure and function, but the cost to society is mainly from the long-term effects. For example, intrauterine growth restriction increases adult cardiovascular risk by 25 percent and reduces IQ.[9,10] Eradicating iron, zinc and iodine deficiencies would increase the world's IQ by 10 points![11]

Zinc deficiency leads to decreased embryonic/fetal brain DNA, RNA and protein content, and decreased brain growth factor insulin-like growth factor 1, gene expression. Fetuses of zinc-deficient mothers demonstrate decreased movement, heart rate variability and altered autonomic nervous system stability. Postnatally, fetal zinc deficiency causes decreased preferential-looking behavior. Iodine deficiency causes the greatest effects during the first 12 weeks of pregnancy. The head is reduced in size, and irreversible global mental deficits occur. In childhood, lack of iodine in the diet leads to reduced verbal IQ and decreased reaction time (motor effect), probably due to delayed myelination or reduced synaptogenesis. Early-life iron deficiency results in neurodevelopmental alterations that persist despite iron repletion. In the first trimester, maternal iron deficiency may lead to an increased risk of autism.[12] In the second trimester, maternal iron deficiency may lead to schizophrenia,[13] while in the third trimester and early postnatal period, iron deficiency may lead to increased risk of depression/anxiety and cognitive dysfunction.[14] Two mechanisms account for the long-term loss of synaptic plasticity: residual structural deficits (critical period hypothesis) and epigenetic modification of chromatin.

Methods of assessing childhood development in low-resource settings: The Brain Imaging for Global Health (BRIGHT) Project as a pacesetter

It is said that one in every three preschool-age children living in LMICs is failing to meet basic milestones in either their cognitive or their socio-emotional development. Currently, there are few objective methods to assess cognitive development, especially in low-resource settings. Brain imaging provides an objective assessment used from birth to identify atypical brain function before behavioral signs are evident. It informs on the mechanisms of disrupted function and enables cross-cultural comparison. Functional near-infrared spectroscopy (fNIRS) uses low levels of near-infrared light to map oxygen distribution in the brain as a brain function marker. It is noninvasive, safe, ideal for use in infants from birth, portable and low-cost.

The BRIGHT Project is a collaborative, longitudinal, multimethod study that follows infants in the UK and The Gambia from birth through to 24 months of age. BRIGHT aims to establish infants' brain function growth curves, and to study the effects that malnutrition and other environmental insults, including living in a low-resource setting, have on infant neurocognitive development. The BRIGHT Project is developing brain function-for-age

curves using novel biomarkers of neurocognitive development from birth in Gambian and UK infants but also using other methods such as behavioral assessments, anthropometrical measures or questionnaires, and neuroimaging techniques such as fNIRS and electroencephalography (EEG).

"One in every three preschool-age children living in LMICs is failing to meet basic milestones in either their cognitive or their socio-emotional development"

Benefits and risks of vitamin A interventions

Vitamin A is an essential nutrient, a mediator of infectious mortality and prophylactic against blindness. Vitamin A reduces mortality in complicated measles, prevents bronchopulmonary dysplasia in very low birth weight babies and even acts as a dermatological agent; high doses are effective against common facial acne. However, chronic ingestion of excessive vitamin A may reduce bone mineralization and predispose people to fractures. Vitamin A may also lead to manifestations of chronic hypervitaminosis A. Acute ingestion of toxic amounts of vitamin A induces potentially fatal cerebral and hepatic consequences.

Low-quality, plant-based diets with minimal diversity have predisposed people to endemic hypovitaminosis A. The availability of synthetic vitamin A sources allowed for interventions to complement the dietary content of the vitamin. Hypovitaminosis A is worse than hypervitaminosis A in terms of mortality and morbidity; thus, we must always look to balance the pendulum between benefits and risks. The main strategies adopted by countries to increase the vitamin A status of populations include:

- Fortification of wheat flour and maize flour;
- Use of micronutrient powders (MNPs);
- Supplementation with vitamin A capsules; and
- Fortification of products such as vegetable oil, margarine and sugar.

Inadequate intake of vitamin A can lead to xerophthalmia and a decreased resistance to infections, while excessive intake of vitamin A, e.g., from a combination of supplementation and food fortification, can lead to increased risk of liver cirrhosis and an increase in the risk of osteoporosis.

The retinol isotope dilution technique is used to assess total body vitamin A pool size. It provides an estimate of mean vitamin A pool size for groups of subjects in a target community, detects changes in vitamin A pool size in response to supplementation and can be used to estimate the impact of vitamin A interventions. There is concern that the retinol isotope dilution test underestimates the total body stores during hypervitaminosis A. A degree of concern for baseline vitamin A status exists: it is assumed that 80 percent of retinol is stored in the liver. Hypervitaminosis A is defined as ≥ 1 µmol/g liver stores. In a study of children in Zambia, 2.3 percent of the children had liver vitamin A reserves of > 3 µmol/g, and may have been at risk of hypervitaminosis.

"Vitamin A deficiency is not acceptable, but we need to mitigate toxicity"

Currently, there are overlapping programs all aimed at delivering vitamin A, especially to children under 5 years. High-dose supplements are administered at least every 6 months, yet maize meal and wheat flour fortification with vitamin A is on the rise. This would seem to suggest the scaling back of interventions, but evaluation is key before any interventions can be scaled back. The Global Alliance for Vitamin A (GAVA) has formulated criteria to consider before scaling back any interventions. Data are needed based on quantitative biomarkers, such as the modified relative dose response. Vitamin A deficiency is not acceptable, but we need to mitigate toxicity. Countrywide survey data will be required before scaling back high-dose vitamin A supplements. Most concerning is the preformed vitamin A's impact on growth and bone health.

The Global Vitamin A Safety Assessment (GloVitAS) Project: What level of retinol storage is safe?

According to the GloVitAS Project, many countries have overlapping vitamin A interventions: 43 countries have at least two interventions, and 27 countries have at least three interventions. Burundi, Kenya, Malawi, Nigeria, Rwanda and Uganda have six overlapping vitamin A interventions. GloVitAS aims to assess whether vitamin A intakes above the tolerable upper intake level (UL) are related to exposure to multiple vitamin A intervention programs, and whether this is associated with high total liver vitamin A concentrations and with biochemical indicators that could be used as biomarkers of excess vitamin A. The team found that exposure to multiple vitamin A supplementation and fortification programs can expose children to intakes above the UL, which is associated with liver vitamin A concentrations above the current biomarkers of nutrition for development (BOND) cutoff of 1 µmol/g liver stores. However, no adverse clinical effects were detected in children with liver concentrations as high as 8 µmol/g liver. This led the GloVitAS team to conclude that the BOND cutoff point of > 1 µmol/g liver stores is too low. GloVitAS supports the 'high' status category of 3–10 µmol/g liver stores, although the

toxicity cutoff of 10 µmol/g liver stores needs further investigation. Programs designed to eradicate vitamin A deficiency should include assessment of vitamin A excess if exposure to multiple sources of vitamin A is apparent.

The impact of interventions during pregnancy and lactation on micronutrients in human milk

Poor maternal micronutrient intake and status reduces micronutrients in milk. Maternal supplementation could increase the concentration of micronutrients in milk. However, there are numerous challenges, such as large numbers of micronutrients, how to analyze micronutrients in the milk matrix, the decision on when to supplement, uncertainties about the method or timing of milk collection, and changes throughout lactation. Various factors could affect how milk nutrients respond to maternal supplements. These include the characteristics of the nutrient, the dose, antiretrovirals, frequency of intake of the micronutrient during the day, maternal status at baseline, and when supplementation starts and ends, i.e., early or late pregnancy, duration of lactation, or the stage of pregnancy or lactation. Concentrations of at least 12 micronutrients are affected by maternal micronutrient status and/or diet. Breast milk micronutrient status is directly proportional to the quality of the diet.

The Women First (WF) trial was conducted in four countries/sites, namely Guatemala, India, Pakistan and The Democratic Republic of the Congo. The WF trial studied the impact of supplementation before conception or during pregnancy on micronutrients in breast milk. Specifically, the WF trial was designed to study the effects of maternal supplementation, site and maternal body mass index (BMI) on B-vitamin milk composition at 14 days postpartum. The intervention was a lipid-based nutrient supplement (LNS) in which one group of women received LNS from the preconception period onwards, the second group received LNS from 12 weeks' gestation onwards and the control group did not receive any LNS. All interventions ended at birth, and the milk concentrations of B vitamins were assessed at 14 days postpartum. Milk B-vitamin concentrations at 14 days postpartum were generally not different between groups, but varied substantially among sites and were positively associated with maternal BMI. It was found that in these low-resource settings with high rates of maternal undernutrition, a substantial risk of inadequate intakes of B vitamins exists, and the functional impact of this deficiency is unclear.

A substudy of the JiVitA-3 Trial was set up to study the micronutrient content of human milk and estimated the micronutrient intakes of 3-month-old infants in rural Bangladesh. The parent project (JiVitA-3) was conducted in northwestern Bangladesh, where infants are born and remain small and illness-prone despite prevalent breastfeeding. The JiVitA-3 was conducted between 2008 and 2012. In this project, multiple micronutrients reduced stillbirth (11 percent), preterm (15 percent) and low birth weight (12 percent), and increased birth weight by 54 g. Work was also done to characterize the micronutrient content of human milk from samples collected from JiVitA-3 mothers at 3 months postpartum. The researchers wanted to estimate the ability of human milk to meet intake recommendations and explore determinants of milk nutrient content. For vitamin A, milk values increased ~18 percent with multiple micronutrient supplementation (MMS), thus doubling the estimate of the percentage of the infants meeting the Adequate Intake (AI) (from ~10 percent to 20 percent). Vitamin E was one of the most prevalent deficiencies in mothers. After MMS, α-tocopherol increased ~17 percent, while γ-tocopherol decreased ~15 percent. There was a strong positive association with maternal vitamin E status. Vitamin B_{12} values increased ~23 percent with MMS, yet < 1 percent of children would have met AI values. The low levels of vitamin B_{12} were consistent with vitamin B_{12} deficiency being prevalent among mothers.

Vitamin D and calcium in pregnancy

The role of vitamin D in musculoskeletal health is well established.[15] Severe vitamin D deficiency (25(OH)D < 12.5 nmol/L) in early childhood leads to vitamin D deficiency rickets. It may also lead to impaired bone mineralization and long-bone growth, general muscle weakness, and pain.[16] Vitamin D deficiency in pregnancy is prevalent worldwide,[17] and neonatal vitamin D status is dependent on maternal vitamin D status.[18] At a minimum, vitamin D deficiency during pregnancy should be prevented to ensure adequate development of the fetal skeleton.[19] There is inconsistent evidence for prenatal vitamin D supplementation having an effect on childhood bone mineral content/density. Also, evidence for an association between maternal vitamin D status and childhood muscle strength is lacking. Prevention of maternal vitamin D deficiency avoids neonatal deficiency, but the effects on health outcomes are less clear.

High calcium intake may mask the effects of vitamin D. The effect of calcium in humans goes beyond bone health. For example, calcium reduces: blood pressure by 1.43 mmHg (95% CI, −2.15 to −0.72), body weight by 0.43 kg (95% CI, −0.68 to −0.17), and LDL cholesterol by 0.12 mmol/L (95% CI, −0.22 to −0.02). Calcium also reduces the risk of colon adenomas (RR 0.89, 95% CI, 0.82 to 0.96). WHO's recommendations for the prevention and treatment of pre-eclampsia and eclampsia state that in areas where dietary calcium intake is low, calcium supplementation during pregnancy (at doses of 1.5–2.0 g elemental calcium/day) is recommended for the prevention of pre-eclampsia in all women, but especially those at risk of developing pre-eclampsia. WHO also states that fortification of staple foods with calcium may be an important public health intervention strategy. Further, dietary counseling of women considering pregnancy should include the promotion of intake of calcium-rich foods such as dairy products.

"Three and a half billion people are at risk of calcium deficiency"

Three and a half billion people are at risk of calcium deficiency. The highest population at risk of deficiency is in Africa (80 percent), followed by Asia (57 percent). Strategies to improve calcium intake include promoting the consumption of calcium-rich foods, the use of supplements and food fortification. Food vehicles that could be fortified with calcium include flour and water. Many countries already have regulations for flour fortification, and for some, e.g., the UK, mandatory calcium-fortified flour has existed since 1943. Water might also be a strategic fortification vehicle, especially because it is universally consumed, recommended as part of a healthy diet, calorie-free (thus will not fuel the global obesity epidemic) and consumed daily. Moreover, water intake is spread out during the day, which improves calcium absorption.

Nutritional rickets is a disorder of children that is characterized by a failure or delay in endochondral calcification of the growth plates of long bones. The greatest burden of disease worldwide is probably in Africa, the Middle East and Asia (reported prevalence: 10–70 percent). However, prevalence estimates are lower in population surveys combined with confirmation by physician examination or X-rays (e.g., Gambian children aged 0.5–18 years: 3.3 percent). There are three types of nutritional rickets:

- **Calciopenic:** low plasma calcium leads to elevated plasma parathyroid hormone (PTH) concentration, which leads to internalization of phosphate transporters in the kidneys, thereby resulting in decreased renal phosphate reabsorption.
- **Phosphopenic:** elevated fibroblast growth factor-23 (FGF23) or renal disorders lead to decreased renal phosphate reabsorption.
- **Inhibited mineralization:** caused by aluminum toxicity and excessive fluoride ingestion.

FGF23 is a phosphate-regulating hormone, and its deficiency leads to decreased plasma phosphate concentrations. From observational studies, pregnancy is associated with iron deficiency and decreased bone mineral density, leading to the question of whether iron deficiency predisposes to rickets. In a secondary analysis of data and samples from a Kenyan study, Braithwaite and colleagues, from Cambridge University's MRC Human Nutrition and Bone Research Group, studied the effect of antenatal iron supplementation on FGF23 and bone metabolism in Kenyan women and their offspring. The researchers hypothesized that maternal iron deficiency leads to perturbations in FGF23 regulation that may be implicated in the pathogenesis of hypophosphatemia-driven rickets in the offspring. They therefore sought to measure the effect of antenatal iron supplementation on circulating concentrations of FGF23 at birth in pregnant Kenyan women and their offspring. Similarly, they measured intervention effects on other markers of phosphate and bone metabolism (including vitamin D) and kidney function, and explored to what extent the response of these markers to intervention depended on initial iron status. The researchers concluded that antenatal iron supplementation might provide health benefits to pregnant women and their offspring beyond increasing iron status, but whether iron supplementation reduces present and future infant risk of rickets remains unclear.

Neglected B vitamins

B vitamins include thiamine (B_1), riboflavin (B_2), niacin (B_3), pantothenic acid (B_5), pyridoxine (B_6), biotin (B_7), folate (B_9) and cobalamin (B_{12}). Of these, thiamine, riboflavin, niacin and pyridoxine are neglected.

Thiamine has various functions, including energy production (ATP), DNA/RNA synthesis, NADPH synthesis and nerve function. Biomarkers of thiamine status include:

- Thiamine diphosphate (ThDP): a direct biomarker of thiamine status found in whole blood or erythrocytes. No universally agreed upon cutoff thresholds exist, but 70–180 nmol/L for whole blood and > 150 nmol/L for erythrocytes are used.
- Erythrocyte transketolase activity (ETKA): the ETKA assay is used for the functional assessment of thiamine status. ETKA is measured before and after the addition of exogenous ThDP and is expressed as an ETKA coefficient (ETKAC). The ETKAC cutoffs for thiamine deficiency are: < 1.15 (low risk), 1.15–1.25 (moderate risk) and > 1.25 (high risk).

Thiamine deficiency may lead to infant mortality, or any of the four forms of beriberi:

- Dry beriberi: severe muscle wasting, leg cramps, tenderness, and decreased feeling in feet and toes (peripheral neuropathy).
- Wet beriberi: swelling (edema) of arms and legs, enlargement of heart, breathing problems and possible heart failure.
- Infantile beriberi: seen in babies that are breastfed by thiamine-deficient mothers. Can lead to heart failure.
- Cerebral beriberi (Wernicke-Korsakoff syndrome): often caused by alcoholism (low vitamin B_1 intake plus impaired absorption). Causes involuntary movement and paralysis of the eye, poor muscle coordination, confusion and short-term memory loss.

However, thiamine deficiency may also lead to impaired child neurocognitive development. For example, in Israel, delayed language development and motor and cognitive deficits were observed during long-term follow-ups of children who demonstrated overt signs of thiamine deficiency.[20]

FIGURE 2.3: Global occurence of thiamine deficiency

Generously provided (with permission) by Taryn Smith, Institute for Global Nutrition, University of California Davis

Globally, conditions associated with thiamine deficiency include: monotonous diets low in animal-source foods (meats, fish, milk), polished rice or cassava as primary energy sources, foods containing thiamine antagonists (betel nuts, tea leaves), foods containing thiaminases (raw fish, African silkworm larvae), drought, conflict and displacement. Endemic deficiency can be seen in Cambodia, Laos, Myanmar and Kashmir.

WHO has published guidelines for the treatment and prevention of thiamine deficiency. There is insufficient data on the optimal mode of administration, dose and duration of treatment for thiamine deficiency. Thus, thiamine deficiency cases are often suspected rather than confirmed, and a final diagnosis is often based on a positive response to thiamine administration. This varies depending on clinical presentation, population and the underlying risk factors.

A study in Cambodian mothers concluded that longer-term maternal supplementation might be needed to correct thiamine deficiency in breastfed infants. Thiamine supplementation of thiamine-deficient mothers rapidly increased maternal thiamine and breast milk thiamine concentrations but not the thiamine concentrations of the breastfed infants.[21]

The optimal dose, duration and timing of thiamine supplementation in the perinatal period are unclear. Larger doses of thiamine go largely unabsorbed. The challenges of understanding thiamine deficiency include: poor understanding of the global burden of thiamine deficiency, highly variable clinical presentations, symptoms that overlap with other conditions (e.g., viral infection, pneumonia, sepsis and meningitis), misdiagnosis, and missed treatment opportunities leading to fatal and sometimes irreversible consequences, and uncertain interpretation of biomarkers[22] (**Figure 2.3**).

Riboflavin is a water-soluble vitamin first identified from milk whey in 1879. It is a precursor for coenzymes such as flavin adenine dinucleotide (FAD) and flavin mononucleotide (FMN). Riboflavin is a much-neglected vitamin that has important health impacts, and its deficiency is not restricted to LMICs. Deficiencies have been seen in Canada, Ireland and other countries. Riboflavin plays a role in energy (ATP) production and in the synthesis or activation of vitamin A, folate, niacin, vitamin B_6 and vitamin K. It also functions in neurotransmitter metabolism. Deficiency in riboflavin leads to ariboflavinosis. Riboflavin reduces blood pressure in individuals with a genetic predisposition to high blood pressure. Genome-wide association studies (GWAS) have identified genetic variants that appear to contribute modestly to blood pressure variability. The MTHFR gene is among eight genetic loci linked to the variation in blood pressure in GWAS.[23,24] The common

C677T polymorphism in MTHFR (affecting 10 percent of people worldwide) predisposes to increased blood pressure throughout adulthood and in pregnancy, and also a higher risk of developing hypertension, including hypertension in pregnancy. Riboflavin has a novel role in people who have the variant TT genotype in MTHFR in maintaining healthier blood pressure in pregnancy and adulthood, and in treating hypertension independently of current antihypertensive therapy. Ongoing and future research priorities include studies of blood pressure in pregnancy.

The biomarker status of riboflavin is rarely measured, but deficient/low status may be a more widespread problem than generally perceived. Globally, riboflavin deficiency conditions include monotonous diets low in animal-source foods (meats, eggs, milk) and gastrointestinal infections. Countries with reported deficiency include Côte d'Ivoire, Cambodia (urban and rural), Canada (Vancouver area), Kenya and Zambia.

Niacin has many functions, including energy (ATP) production and metabolism of many compounds such as fatty acids, cholesterol, steroid hormones, DNA, vitamin C and folate. Niacin lowers LDL and raises HDL cholesterol. Deficiency in niacin causes pellagra and the famous 'four Ds', i.e., dermatitis, diarrhea, dementia and death. Globally, conditions associated with niacin deficiency include monotonous, maize-based diets, drought, conflict and displacement. Malawi and Angola have reported niacin deficiency.

Pyridoxine deficiency is of higher prevalence among people over the age of 60 living in high- and middle-income countries. The main functions of pyridoxine include: synthesis of non-essential amino acids (transaminases); synthesis of neurotransmitters such as serotonin and dopamine (decarboxylase); heme synthesis (first step); one-carbon metabolism (e.g., serine-glycine interconversion and homocysteine catabolism); and lipid and carbohydrate metabolism. Deficiency in pyridoxine leads to microcytic anemia due to inhibited heme synthesis, convulsions/EEG abnormalities, and the accumulation of toxic products of tryptophan metabolism, hyperhomocysteinemia, and inflammatory disease. Conditions associated with pyridoxine deficiency include low dietary intake and inflammatory diseases. Countries/regions with reported pyridoxine deficiency include the USA, South Korea, Zambia, Egypt, Indonesia and Uganda.

"There are still some research needs concerning neglected B vitamins"

In general, there are still some research needs concerning neglected B vitamins:

- Standardization of biomarker assays, cutoffs and methodological harmonization.
- Nationally representative assessments of dietary intake and status.
- Identification of localities in need of intervention, fortification and supplementation.

Nutrient-specific research needs include:

- Assessment of the role of thiamine in preventing/treating heart failure.
- Assessment of the efficacy of riboflavin supplementation in lowering blood pressure and reducing the risk of hypertension in individuals with the MTHFR 677 TT polymorphic variant.
- Assessment of the benefits, if any, of vitamin B_6 supplementation in inflammatory conditions.

New evidence on the efficacy of food fortification and biofortification

Effectiveness of rice fortification with iron and zinc in Bangladesh

Fortification of staple foods such as rice is a proven and effective way to ensure consumers at risk of vitamin and mineral deficiencies have access to vital nutrients. Globally, the use of fortified rice has improved the intake of micronutrients and reduced micronutrient deficiencies in several countries. Iron-enriched rice fed to anemic schoolchildren in the Philippines reduced anemia by 38 percent.[25]

An endline survey in Bangladesh found a statistically significant reduction of 4.8 percent in anemia in the iron and zinc fortified rice (FFR) group area, whereas anemia increased by 6.4 percent in the non-FFR group. Zinc deficiency decreased in the FFR group in the endline survey by 6 percent. Women in the fortified rice group experienced significantly fewer diarrhea episodes and less fever during the 2 weeks compared with the non-fortified rice group. Fortified rice appears to be beneficial in reducing the prevalence of anemia and zinc deficiency.

"Multiple-micronutrient-fortified salts could be an effective way to eradicate micronutrient deficiencies at the population level"

Alleviating micronutrient deficiencies through a multiple-micronutrient-fortified salt in children in South India

To combat multiple micronutrient deficiencies, a community-based randomized controlled trial was conducted in Kariapatti,

Virudhunagar District, Tamil Nadu, South India. In one arm of the trial, participants received fortified salt enriched with multiple micronutrients. The second arm received nutrition education, while the third arm, the control group, received no intervention. Periodic deworming was done in all three arms.

Hb increased only in the micronutrient group; it decreased in the other two groups. A reduction in the prevalence of anemia, IDA and iron deficiency was only seen in the micronutrient group, and not in the nutrition education group or in the control group. There was a significant reduction in transferrin receptor after intervention only in the micronutrient group, showing a reduction in iron deficiency, whereas in the education group and in the control group, there was a significant increase in transferrin receptor, showing an increase in iron deficiency post-intervention. Body iron stores increased only in the micronutrient group. A significant improvement in the serum retinol status was also seen in the micronutrient group, compared with no significant changes in status in the other two groups. Multiple-micronutrient-fortified salt improved iron and vitamin A status, whereas no improvement was seen in the nutrition education group. Multiple-micronutrient-fortified salts could be an effective way to eradicate micronutrient deficiencies at the population level. One of the main deterrents to adopting multiple-micronutrient-fortified salts is lack of knowledge about them, especially among government policymakers.

The impact of rice fortified with seven micronutrients fed through an Indian school meal program on hemoglobin and anemia prevalence among children aged 6–12 years

Rice is an ideal fortification vehicle in India because, in terms of consumption, it is the staple food for 70 percent of the Indian population, and it meets 31 percent of the population's energy intake. Rice is also well accepted, and fortified rice can be stored in the same way as normal rice with minimal loss of nutrients (18–24 months shelf life). The extrusion technology required to fortify rice is simple, cost-effective and well established in India. Twenty research and field studies conducted in various places globally demonstrate the efficacy, effectiveness, acceptability and safety of fortified rice. Peer-review research has shown that fortified rice can lead to an increase in levels of blood Hb, serum ferritin, zinc, plasma vitamin A and vitamin B_{12}, and thiamine, and that it can also decrease the prevalence of anemia and iron deficiency.

Six hundred and sixty-six local schools in Ahmedabad (Ahmedabad District, Gujarat: 200 schools) and Gandhinagar (Gandhinagar District, Gujarat: 466 schools) received fortified rice. One kilogram of fortified rice contained 20 mg iron (ferric pyrophosphate), 1,300 µg folic acid, 10 µg vitamin B_{12}, 1,500 µg retinol equivalents, 3.5 mg thiamine, 42 mg niacin and 5 mg vitamin B_6. The intervention group exhibited a 0.4 g/dL improvement in Hb concentration over the control sample. The Hb concentration improved by 0.24 g/dL in the intervention group and decreased by 0.15 g/dL in the control group. The prevalence of anemia declined by 10.1 percent within the intervention group and increased by 4.3 percent within the control group. India's midday meal program has a wide reach, serving 95.2 million children in 1.1 million schools across the country between 2017 and 2018. The Government of India has approved fortified rice in school meals and in the Integrated Child Development Services (ICDS) program. Rice fortification programs can be combined with nutrition-specific and nutrition-sensitive public health interventions (e.g., WASH, deworming, IFA supplementation) to amplify child health outcomes.

Iron bioavailability from iron-biofortified, orange-fleshed sweet potato: A stable isotope study in Malawian women

Stable isotopes have been used in nutrition research to generate new evidence on the (bio-)efficacy of food fortification and biofortification. For example, in Malawi, iron bioavailability from iron-biofortified, orange-fleshed sweet potato (OFSP) was studied using stable isotopes of iron (^{54}Fe, ^{56}Fe, ^{57}Fe and ^{58}Fe). The International Atomic Energy Agency (IAEA) has outlined the use of nuclear applications in nutrition as shown in **Figure 2.4**.

The main cause of iron deficiency and IDA in LMICs is the insufficient intake of bioavailable iron from monotonous plant-based diets. The prevalence of iron deficiency and IDA in Malawian women is 15.1 percent and 21.0 percent, respectively.[26] Sweet potato is a primary staple crop in Malawi (> 80 kg/capita/year consumed). The OFSP food matrix is favorable for iron absorption. It is high in ascorbic acid and β-carotene, yet low in phytic acid. The researchers designed a study aimed at estimating iron absorption by Malawian women of reproductive age after consuming two test meals: the control OFSP (Irene variety; Fe: 6.3 µg/g FW), and the iron-biofortified OFSP (MUSG2505-2 variety; Fe: 10.7 µg/g FW).

Fractional iron absorption (FIA) of ~6 percent for both OFSP test meals was within the 5–10 percent range expected for plant-based diets (WHO, 2004) despite low phytic acid content and low infection levels in the population throughout the study period. The high polyphenol content in both OFSP varieties was the main inhibiting factor to iron absorption.

OFSP has the potential to become a food vehicle for iron biofortification, and could be used to deliver iron to communities that need it. First, however, it must become part of the food basket of the target communities. Other OFSP-based food products that are low in the antinutrient factors, including polyphenols, could also provide avenues for delivering the iron in OFSP to populations. This study's findings will go very well with the current African strategy to scale up vitamin A and iron in sweet potatoes. Soil conditions will need to be factored in, especially because calcium can hinder the absorption of iron in the human body.

Focus on four hot trials

RCT of oral iron for treatment of post-malaria anemia in Malawian children comparing the immediate versus delayed administration

Malaria is a common morbidity in children under 5 years, with one attack per child per year in Malawi. Clinical practice is to provide iron at the end of the malaria treatment, but this period is characterized by low iron absorption due to inflammation, which lasts about 2 weeks. Iron may be sequestered and made available again after infection. Is it better to delay giving iron so that it is given when inflammation has ended?

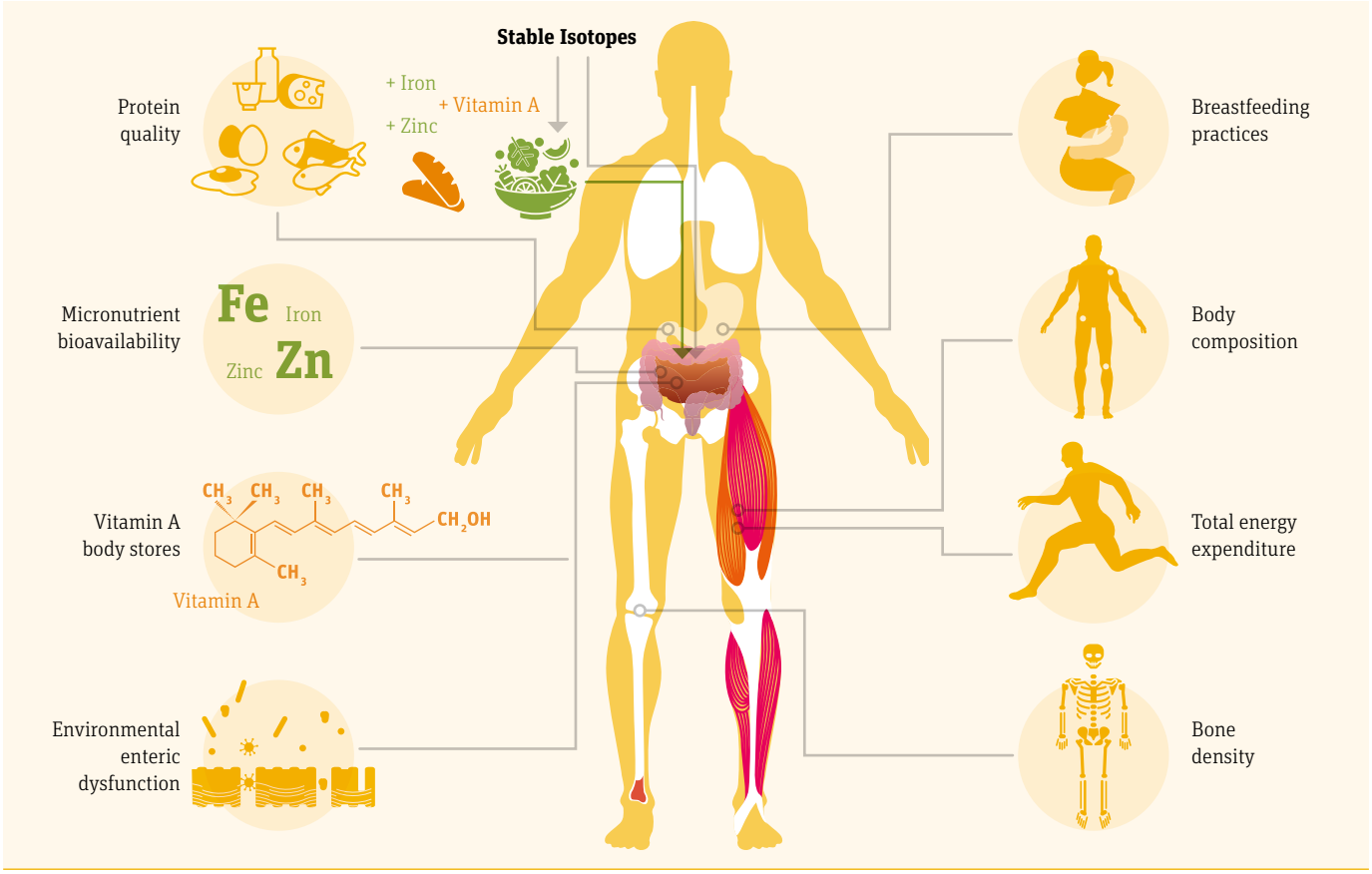
In a three-arm, double-blind, placebo-controlled trial, children were given iron syrup (3 mg/kg BW/day) for 2 months. Children were randomized into three groups: immediate iron group (given syrup immediately after malaria treatment), delayed iron group and no iron group. There was no statistical difference in the Hb levels of the immediate and delayed iron groups, even after adjusting for sex, malaria or previous admission. There were also no statistically significant differences in morbidity in terms of sick visits, malaria or hospital admission. No difference was seen in the rate of iron absorption between the immediate and delayed iron groups; thus, there is no evidence to recommend a change in the policy of immediate iron supplementation post-malaria treatment in children with moderate anemia living in malaria-endemic areas.

Effects of daily preventive zinc, daily multiple micronutrient powder or therapeutic zinc supplementation for diarrhea on health and nutritional status of Laotian children

The study was designed to determine the optimal method for delivering zinc to young children, both for preventing zinc deficiency and for the treatment of diarrhea. A randomized, masked, community-based trial was conducted in Khammouane Province, Central Laos PDR. Children (n = 3,433) aged 6–23 months were included, and were randomized to one of four groups: therapeutic zinc supplementation (20 mg zinc for 10 days during diarrhea), daily preventive zinc supplementation (7 mg zinc daily), daily preventive MNP (10 mg zinc, 6 mg iron and 13 other micronutrients) and placebo-control (powder sachet). The study duration was 9 months, and the reported adherence to daily preventive supplementation was very high (~91 percent), and attrition was ~13 percent.

There was no difference in Hb concentrations between groups, but there was a significant increase in plasma zinc in the preventive zinc and the MNP groups. Plasma ferritin was increased significantly in the MNP group. MNPs increased plasma folate concentrations, zinc and ferritin. Preventive zinc supplementation had no impact on growth or overall diarrhea incidence and

FIGURE 2.4: International Atomic Energy Agency's (IAEA) support of nuclear applications in nutrition



duration. Therapeutic zinc supplementation for the treatment of diarrhea reduced the risk of diarrhea among older children (>18 months); thus, therapeutic zinc supplementation should be provided as part of diarrhea management. The benefits of MNPs seem to outweigh the potential risks, thus MNPs should be provided to young children at risk of micronutrient deficiencies, along with appropriate diarrhea management.

A randomized controlled trial in Malawi on the effect of feeding children eggs on early child development in the Mazira project

The egg is a highly nutrient-dense complementary food. For breastfed infants aged 7–12 months, eggs provide > 50 percent of nutrients. The egg white is rich in protein and selenium, while the egg yolk is rich in protein, choline, riboflavin and selenium, among other nutrients. The Mazira project was an individually randomized controlled trial with two groups (n = 331 children per group): the egg group (one egg per day for 6 months for the child, plus seven extra eggs per week for the family); and the control group (usual diet with delayed intervention food basket after 6 months). The study enrolled children aged 6–9 months. Overall, the provision of one egg per day for 6 months during the early complementary feeding period did not affect child development in the study area in rural Malawi, and this was consistent with the lack of effects on linear growth and stunting. However, these findings were in contrast with those of the Lulun trial in Ecuador, which found that eggs had a positive effect on child growth. It is possible that the potential impact of the Malawian study may have been limited by the diet being rich in animal-source foods, especially fish, and a low prevalence of stunting at baseline.

Lower-dose zinc for childhood diarrhea: A randomized, multicenter trial

The study was conducted among children aged 6–59 months in India and Tanzania (n = 4,500) with acute diarrhea, and compared two lower doses of zinc (5 mg and 10 mg) with the recommended dose (20 mg) to assess whether lower doses of zinc are at least as effective as the standard dose of zinc in terms of burden of illness. The study also evaluated the improved effectiveness (as evidenced by a reduction in the risk of vomiting during the 30 minutes after receipt of the supplement) of the lower doses of zinc compared with the standard dose.

It was found that lower doses of zinc given daily for 14 days were non-inferior to the standard dose of zinc in terms of diarrhea and the mean number of stools in children with acute diarrhea. Both the 5 mg and 10 mg doses were superior to the 20 mg dose with respect to vomiting. Based on these results, it may be useful to explore changing zinc supplementation guidelines.

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TRACK

3

Program Effectiveness

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Introduction

The major objective of this track was: Bridging the gap between evidence and implementation to optimize the scale-up of micronutrient interventions. This track brought together experts from the global nutrition community to share their views and experiences of designing, delivering and monitoring nutrition programs. The track's 15 sessions, several of which are described below, reflected the complexity of micronutrient deficiencies and made an important contribution to the conference.

"This track brought together experts from the global nutrition community to share their views and experiences of designing, delivering and monitoring nutrition programs"

A few common themes that emerged in this track include the following:

Filling gaps in micronutrient status and dietary data

It is essential to monitor the nutrient status of populations to develop and implement appropriate interventions and improve existing program performance. Building a bridge between **Track 1** and **Track 3**, an important point made by presenters was the necessity of collecting and analyzing data on micronutrient status and program coverage, as well as understanding the context-specific drivers of micronutrient deficiencies. Several sessions were focused on sharing country efforts in collecting and analyzing dietary data and using it to inform policy and programming decisions, highlighting the need to collect more data on micronutrient status, nutrient and dietary intakes and on program impact in addressing nutrient deficiencies.

The need to learn from delivery experiences

Implementation bottlenecks and barriers often reduce the effectiveness and impact of nutritional interventions, and learning from experiences in program implementation is critical to improving performance and impact. During the session entitled 'Why didn't this work? Program effectiveness post-mortem,' speakers described their experiences of issues or problems encountered during program implementation and scale-up, how these were resolved and what they would do differently next time. Investments in implementation research are also essential to understand what drives improvements in the coverage, quality and equity of nutrition interventions.

Costs matter

The crucial topics of the cost and cost-effectiveness of nutrition interventions were addressed in several sessions that highlighted the importance of assessing costs both before and during program implementation so that appropriate investment decisions can be made. During the plenary session 'Cost analysis is essential before considering scaling up micronutrient interventions,' panelists examined different platforms and models for estimating the costs of nutrition interventions and considering how to ensure that funds deliver measurable benefits for their target populations.

Dietary patterns, nutrient intakes and food safety

Current issues for improving iodine nutrition

Iodine deficiency is considered one of the world's most prevalent, yet easily preventable, nutrient deficiencies. Despite the progress of iodized salt programs in many areas of the world, over a third of the global population remains iodine-deficient. Good iodine status during pregnancy is particularly important, as requirements for iodine sharply increase at this time, but it is commonly inadequate in pregnant women. This session presented new evidence on the measures of iodine intake during pregnancy, discussing a new tool to assess the inclusion of iodized salt in processed foods and its potential use for salt reduction efforts, the changing landscape for salt iodization programs, and emerging innovations that can help ensure sustainable achievement of optimal iodine nutrition.

TABLE 3.1: Potentially modifiable factors associated with anemia

	Children	Adolescent boys	Adolescent girls	Nonpregnant women of reproductive age
Nutrition				
Iron	↓	↑	↓	↓
	(ferritin)	(soluble transferrin receptor)	(ferritin)	(ferritin)
Vitamin A (retinol-binding protein)	↓	↓	↓	↓
Flesh-, organ- or blood-based foods		↓		
Micronutrient powders	↓	–	–	–
Infection				
Recent fever	↑			
Recent cough				↓
C-reactive protein	↑			
Water, sanitation and hygiene				
Open defecation		↑		
Dirt/earth floor				↑
Hormonal contraceptive use	–	–	–	↓

↓ and ↑ indicate that the characteristic was associated with anemia in multivariable models
– indicates that the characteristic was not measured

"Iodine deficiency is considered one of the world's most prevalent, yet easily preventable, nutrient deficiencies"

Global progress achieved through universal salt iodization

Today, most (88 percent) of the world uses iodized salt, which has resulted in immense progress over the past three decades in reducing iodine deficiency as measured by goiter rates and median urinary iodine concentrations (MUIC). In 1993, 113 countries were iodine-deficient (with high goiter rates and low MUIC); by 2017, only 19 countries were iodine-deficient (with low goiter rates and sufficient MUIC). These developments have occurred in the context of an increasing number of countries mandating the fortification of salt by law. However, progress is threatened by emerging issues, including dietary changes, salt reduction policies, the use of salt as a vehicle for other micronutrients and difficulties achieving universal salt iodization in countries experiencing conflicts.

Iodine status during pregnancy

Despite the recognition that iodine deficiencies are common during pregnancy, the WHO criteria defining adequate iodine intake in pregnant women based on MUIC are poorly defined. Maria Andersson from the University Children's Hospital Zurich proposed a new measure of median iodine status during pregnancy based on dried blood spot thyroglobulin (DBS-Tg) – a biomarker of population iodine status. In a study[1] to test this new measure, her research team found that DBS-Tg is a sensitive biomarker of iodine status in pregnant women and is therefore useful for detecting iodine deficiency and should be considered when revising UIC thresholds for pregnant women.

Exploring the potential of scaling up double-fortified salt

Meena Jadhav, an independent consultant in global health and nutrition, presented results from a pilot project for scaling up double-fortified salt (DFS) through integration with the public distribution system (PDS), a federal food security program in Uttar Pradesh, finding that the PDS provided a readily available and expansive platform for DFS distribution and that it supported accelerated scale-up. Nevertheless, while bundling DFS with other subsidized commodities increased the purchase of DFS, it did not guarantee consistent use. On the demand side, the main challenges to optimal scale-up were lack of consumer awareness, consumer preference concerning the physical appearance of salt and discoloration of some food items, while supply-side challenges were inadequate state government resources for subsidizing DFS and lack of financial incentives to PDS shopkeepers for additional work.[2]

Filling gaps in micronutrient data: Use of modeling tools and dietary data for program decisions

Correlates of anemia in national micronutrient surveys and population-based surveys, and policy implications

Anemia is a widespread global public health problem that is responsible for approximately 8.8 percent of the world's years lived with disability, with the burden concentrated in low- and middle-income countries (LMICs).[3] In children, anemia is associ-

ated with poor growth and impaired cognitive and motor development, while among adolescents and women, it is associated with poor linear growth, delayed menstruation and sexual development, impaired cognitive performance and poor reproductive outcomes. During this session, presenters shared findings from national and population-based micronutrient surveys in Nepal, India and Malawi.

> **"Anemia is a widespread global public health problem that is responsible for approximately 8.8 percent of the world's years lived with disability"**

Country experiences in collecting and analyzing anemia data

Nicole Ford from the Centers for Disease Control and Prevention (CDC) shared findings from three studies[4,5] to evaluate factors associated with anemia among children aged 6–59 months, adolescents and nonpregnant women of reproductive age in Nepal, using nationally representative samples. The study found that approximately 18.6 percent of children, 20.6 percent of adolescent girls, 20.2 percent of women and 10.9 percent of adolescent boys were anemic. Among children, common non-modifiable factors include age, ethnicity and glucose-6-phosphate dehydrogenase (G6PD) deficiency, and modifiable factors include a recent fever, consumption of micronutrient powders (MNPs) and inflammation. For adolescent girls, non-modifiable factors include age, ethnicity and ecological zone, while the modifiable factors include iron levels and inflammation. For nonpregnant women, non-modifiable factors include G6PD deficiency, hemoglobinopathies and ecological zone, while modifiable factors include recent cough, residing in a house with a dirt floor, inflammation and contraceptive use. Given these findings, it is clear that understanding context-specific drivers is crucial to developing effective, evidence-based public health programming for anemia control (**Table 3.1**).

Leila M Larson from the University of South Carolina shared estimates of anemia in nonpregnant women aged 18–49 years and children aged 6–59 months, the correlates of anemia and how the correlates are interconnected in Uttar Pradesh, India. The study found that in children, iron, folate and hemoglobin levels were all important predictors of anemia, while iron, folate and vitamin B_{12} on hemoglobin were important predictors of anemia in women. There was significant association with C-reactive protein through hepcidin in both populations.

Anne Michal Williams from the Division of Nutrition at the CDC shared findings from a study conducted in Malawi to understand what is associated with anemia. The study considered severity (moderate or severe anemia, compared with mild and no anemia), and found that anemia prevalence indicated a moderate public health problem for women and children in Malawi based on WHO classification (› 20 percent prevalence). Moderate or severe anemia prevalence was 13.1 percent in children 6–59 months old and 7–8 percent in women and children 5–14 years old. In addition, iron deficiency and malaria were consistently correlated with anemia, and improving the zinc status of women may also improve anemia status.

Collecting and using dietary data for policy and program decision-making

Diet is consistently ranked at the top of risk factors in the global burden of disease. However, food intake or dietary data remains fragmented and incomplete, particularly in LMICs, and no robust monitoring system exists for tracking diet quality metrics. During this session, presenters discussed how to maximize the value of dietary data for policy and strategic decisions while considering limitations and lessons learned.

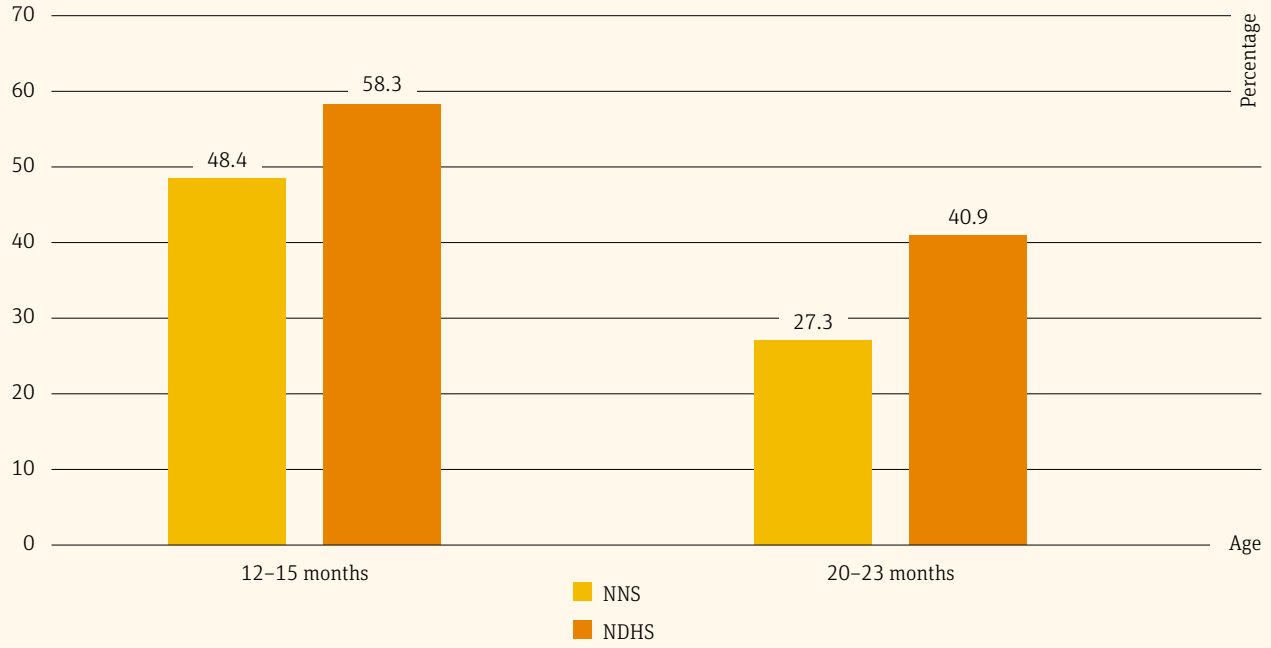
Rebecca Heidkamp from Johns Hopkins University's Bloomberg School of Public Health provided a summary of the direct and indirect approaches across sectors that can be used to improve dietary intakes in LMICs, and the range of diet-related indicators – both simple and complex – that can measure nutrient intakes and quantify consumption. Simple indicators are generally qualitative, such as dietary diversity scores, while complex indicators are quantitative and are related to the intake of specific nutrients. They often require intensive and expensive data collection methods.

Collecting dietary data in LMICs: Opportunities and challenges

Building upon the discussion of simple versus complex dietary indicators, Cecilia Acuin from the International Rice Research Institute provided an overview of why dietary surveys are important, and why measurements matter when conducting them. Population-level dietary surveys in LMICs are critical to: assess and monitor the dietary situation of the population; determine the adequacy and safety of the food supply; determine the effects of dietary patterns on nutrient intake and health status; identify needs for changes in national food policies or regulations; and assess changes in dietary patterns and their effects on nutrient intake. However, while in an ideal world the methods of a dietary survey would determine resource needs, the reality in LMICs is that resources generally drive decisions regarding methods.

> **"Population-level dietary surveys in LMICs are critical to: assess and monitor the dietary situation of the population"**

FIGURE 3.1: Continued breastfeeding at 1 and 2 years – Philippines 2013, National Nutrition Survey (NNS) versus National Demographic and Health Survey (NDHS)



The Philippines is remarkable in that it has conducted National Nutrition Surveys (NNS) every 5 years since 1978. These surveys have become the official source of nutrition data; and the Philippines has additionally conducted Demographic and Health Surveys (DHS) every 5 years since 1993. In 2013, both the DHS and NNS were conducted, which allowed for comparison of infant and young child feeding (IYCF) indicators (**Figure 3.1**). Substantial differences were found, however. These were primarily due to the way questions were framed – while the DHS starts with the assumption of breastfeeding, the NNS does not. This example highlights that measurements do matter: simple indicators (used in DHS) are often used to assess program performance and identify problems at the population or program level because of efficiency and low cost, while more complex indicators (used in NNS) provide more detail and opportunities for rearranging and re-evaluating the data for other purposes. The most important trade-offs between the two types of indicator are resources and the time and manpower needed to collect and process the requisite data.

In Ethiopia, efforts to develop food-based dietary guidelines (FBDGs) reached a milestone in June 2018, when a national workshop was held. Tesfaye Hailu Bekele from Wageningen University shared the methodology for developing the Ethiopian FBDGs and also for creating and evaluating a Healthy Eating Index and scoring tool used to monitor the adherence of the population to FBDGs. The study found that in Ethiopia vitamin A, zinc, calcium and folate intakes are inadequate, the prevalence of iron deficiency is 9–18 percent and only 8–12 percent of women of reproductive age have adequate iron intake. In addition, the study identified dietary gaps including low dietary diversity among different populations, low fruit and vegetable consumption, low animal-source food consumption, and inadequate intake of vitamin A, zinc and macronutrients, as well as significant regional variations. In response, the Ethiopian FBDGs were designed not only to improve diet quality and support the transition to healthier diets, but also to enable the government and food system actors to make healthy diets affordable, accessible and acceptable.

In Sri Lanka, the prevalence of noncommunicable diseases (NCDs) is high: they are estimated to account for 75 percent of total deaths.[6] In 2019, the Ministry of Health adopted a salt reduction strategy. Renuka Jayatissa shared the results of a study aimed at estimating the contribution of industrially processed foods to dietary salt and iodine intakes. The study found that iodine status in all populations and the levels of iodine in salt were adequate, but that average salt intake was high at about 10.5 grams nationally (compared with the WHO recommended level of 5 grams). In the context of salt reduction initiatives, a reduction of iodine intake from salt is likely, but iodine content can be revised to ensure that adequate intakes are sustained. Further studies and monitoring are needed, however.

Identifying indicators that reflect healthy diet patterns at the population level

To solve some of the challenges and gaps surrounding the measurement of diet and nutrient intake, the Global Diet Quality Project was initiated to monitor global diet quality and generate the

data and tools for routine, valid and comparable diet data collection across countries. In addition, the Diet Quality Questionnaire (DQ-Q) was developed to capture consumption information for 29 food groups, along with a suite of indicators that reflect global dietary recommendations (validated in the USA and Brazil). Dietary diversity scores are readily available from the data, including the minimum dietary diversity for women of reproductive age (MDD-W).[7–9] By 2022, the first Diet Quality dataset across 40 countries will be available, and the DQ-Q is being adapted for more than 90 countries, with support from the US Agency for International Development (USAID) and The Rockefeller Foundation, as well as the European Union and BMZ through GIZ's Capacity for Nutrition.

Nutrition information systems: Meeting the needs of program decision makers

A nutrition information system is a system that allows for continuous collection and interpretation of nutrition-related data to enable timely decision-making by governments and their development partners on policy and program development. This session provided a global overview of the decisions and data needs of program-level decision makers, and showcased examples of country-level efforts to collect and use data across platforms for planning and management.

> **"This session provided a global overview of the decisions and data needs of program-level decision makers"**

Nutrition as key to achieving gender equality

Good nutrition and gender equality are mutually reinforcing, as improving nutrition supports the achievement of gender equality, and vice versa. As a key nutrition-sensitive intervention, the empowerment of women and girls can help reduce and prevent malnutrition in LMICs, but to date no measurement frameworks exist to assess nutrition and empowerment. Nutrition International (NI) has developed simple and practical tools to generate timely and quality data using gender equality indicators for nutrition program delivery and performance. It has also built a data system in collaboration with the University of Toronto and Campbell Collaboration – the Nutrition Intervention Monitoring System (NIMS). The aims of this toolkit are to standardize survey data collection, assure quality and timely data reporting, and integrate gender- and nutrition-related data into the NIMS. To refine the tool, a formative review of the first round of NIMS survey protocols was conducted to assess needs and gaps in sampling, sample size and survey design, which resulted in a streamlined and standardized NIMS toolkit. The next steps in this project include analyzing the gender-related data, conducting an internal evaluation of the survey procedures and updating the toolkit based on the findings.

Nutrition behavior change using new tools and approaches

The Suaahara II program in Nepal, funded by USAID, is a 5-year (2016–2021) multisectoral nutrition program that aims to improve the nutritional status of more than 1.5 million women and children under 2 years of age. A cluster-randomized control trial conducted in Kanchanpur evaluated the effectiveness of using SMS messaging, layered into a large-scale behavior change program, to improve egg consumption and dietary diversity among children 12–23 months of age. It found that SMS message sharing among family and community members was common practice – a promising result to bring about nutrition behavior change – and that this practice should be encouraged, as family decisions are taken collectively, particularly in rural settings.

Real-time monitoring in vitamin A campaigns

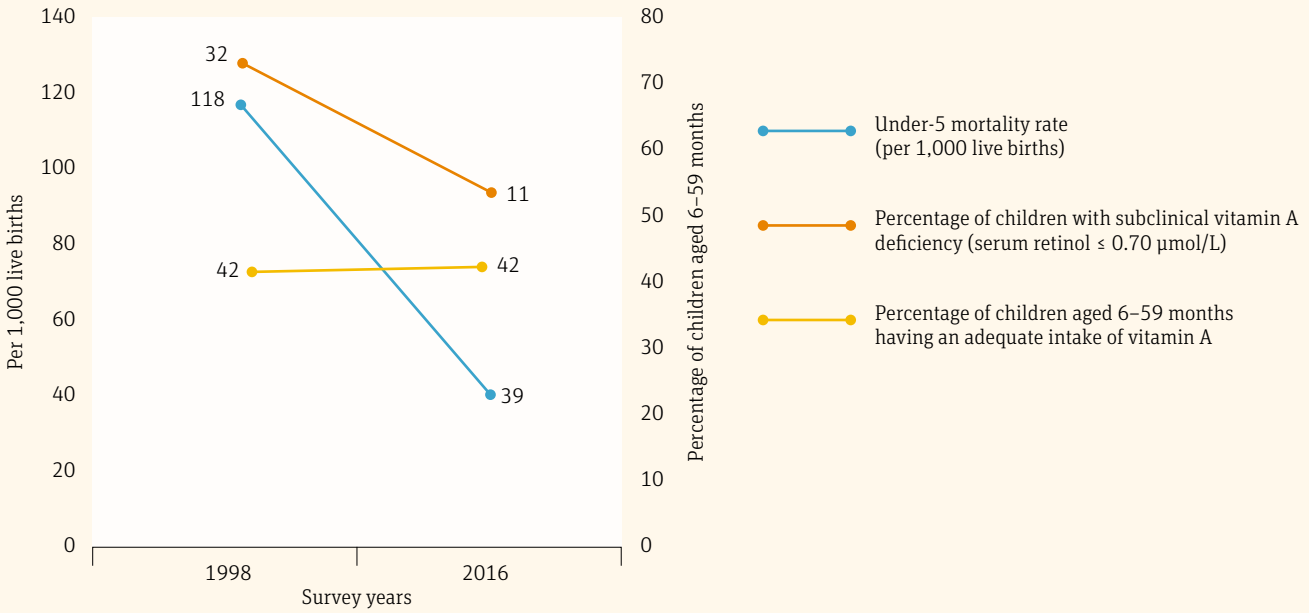
In 2019, with support from UNICEF, real-time monitoring and reporting (RTMR) was initiated in Bangladesh to enhance the efficiency and effectiveness of vitamin A distribution and enable health workers using smartphones to report data. While vitamin A was distributed during child health days, because of COVID-19 in October 2020 the government organized the national vitamin A plus campaign over a 12-day period and used RTMR to track the operation and monitor performance on a daily basis. Overall, the approach provided positive results: 99 percent of the distribution centers were open during the campaign; quality indicators were above 90 percent; 96 percent of the sites provided nutrition counseling; nearly all of the sites followed health and safety protocols; and only 7 percent of the centers had any shortages of capsules. The results of the campaign using RTMR allowed 21.5 million to be reached with vitamin A (94 percent of the 23 million target).

Frameworks and tools for successful program design and implementation

Deciding what to implement where and when to improve micronutrient nutrition

Hidden hunger, or a chronic lack of essential vitamins and minerals, is widespread in LMICs; and deficiencies in one or more micronutrients compromise the physical and cognitive capacity of millions of people. The objective of this session was to understand where we are with respect to tools and approaches to make informed decisions about overlapping strategies, and to use illustrative country examples that highlight successes and challenges in improving micronutrient malnutrition.

FIGURE 3.2: Nepal has not met all three criteria to scale back the preschool vitamin A capsule distribution program



"Deficiencies in one or more micronutrients compromise the physical and cognitive capacity of millions of people"

Tools to advance food fortification globally

Today, over 100 countries have mandatory food fortification programs, but information on whether and how well these programs are working to reduce micronutrient malnutrition remains limited. In 2013, the Global Alliance for Improved Nutrition developed the Fortification Assessment Coverage Toolkit (FACT) and conducted assessments of the application of FACT surveys or modules in Nigeria, Pakistan and Tanzania. Across all three countries, household coverage results were found to be actionable and drive programmatic and policy decisions. For example, in Nigeria in 2017, FACT results revealed universal coverage of fortifiable bouillon cubes in Ebonyi and Sokoto States (> 99 percent), and these findings were used to advocate for bouillon as a fortification vehicle, which led to efforts now being scaled up across West Africa. In Pakistan in 2017, FACT revealed that a large proportion of the population (40–68 percent) consumed flour that is milled at small-scale *chakki* mills that are not currently included in the fortification program. This resulted in a feasibility assessment of *chakki* mill fortification to determine if the scope of the program should be expanded.

"Since 2013, FACT surveys or modules have been deployed in 18 countries to assess fortification program coverage ... results were found to be actionable, answer pertinent questions, and drive programmatic and policy decisions"

Biofortification is the process by which food crops are grown to improve their nutritional value. In 2013, HarvestPlus developed the Biofortification Priority Index (BPI) to ensure efforts to develop and deliver biofortified crops were as targeted, cost-effective and impactful as possible. Using recent national-level data on eating and growing patterns, as well as micronutrient deficiency rates, the BPI ranks 128 countries in Africa, Asia and Latin America and the Caribbean (LAC) according to their potential for biofortification for eight different crop–micronutrient combinations. The result is a clear prioritization of where biofortified crop interventions are most suitable. BPI subnational maps have also been developed for seven large countries (available at: bpi.harvestplus.org).

Improving micronutrient malnutrition in LMICs

In Nepal, the vitamin A deficiency prevention and control program started in 1993, and since then female community health

volunteers (FCHVs) have been distributing vitamin A capsules to children aged 6–59 months biannually. Recently, the Government of Nepal considered scaling back the program and conducted a study using public health data, biomarkers and dietary intake data to arrive at a decision. The study found that vitamin A deficiency remains a moderate public health problem in Nepal, as more than 50 percent of children aged 6–59 months do not have access to a diet rich in vitamin A. While under-5 mortality and the percentage of children with vitamin A deficiency have decreased in the past two decades, the low proportion of children aged 6–59 months with an adequate intake of vitamin A is stagnant. Based on this evidence, Nepal has taken the decision to continue the preschool vitamin A program, as the three criteria for scaling it back have not been met (**Figure 3.2**).

In Rwanda, micronutrient deficiencies are high in women and children, but the extent of the burden and the suitability of current strategies to address the deficiencies are unclear. Dr Joanne E Arsenault from Intake – Center for Dietary Assessment at FHI Solutions presented findings of work aimed at estimating the prevalence of micronutrient deficiencies and strategies to address them. It found that there are few studies for each nutrient and no large national survey data studies in Rwanda, and that there is a lack of quality data for schoolchildren, adolescent boys, men and older adults, and for certain micronutrients (zinc, B vitamins, vitamin D, etc.). Using data from the most recent DHS (2014–2015), the analysis found a high prevalence of anemia among: older infants and young children aged 0–23 months (53 percent), children aged 24–59 months (29 percent) and children under 5 (34 percent); adolescent girls (19 percent) and boys (29 percent); and adult men (20 percent) and women (19 percent). More complete and up-to-date data and appropriate strategies to address micronutrient deficiencies for all populations are needed. The presentation concluded with recommendations for improving data availability and programming, which included: encouraging interest in nutrition by government and partners; conducting assessments of the coverage, utilization and effectiveness of interventions being implemented; and collecting national quantitative dietary information (**Tables 3.2** and **3.3**).

Marrying sound design, implementation and technology to strengthen behavior change: What can we do to improve design, implementation and effectiveness?

This session highlighted innovations to strengthen the design and effectiveness of behavior change communication (BCC) strategies.

TABLE 3.2: Results on the number of studies and prevalence of micronutrient deficiencies in Rwanda

Problem	Population group	Number of studies	Prevalence of deficiency (Rating of burden)	Rating of quality
Iron	Children < 5 years	3	6% (Low)	Moderate
			17% (Moderate)	Moderate
			56%, 88% (High)	Low
	Adult women	1	5% (Low)	Moderate
Vitamin A	Children ≤ 6 years	2	3% (None)	Moderate
			6% (Low)	Low
	Adult women	1	3% (None)	Moderate
Folate	Adult men and women	1	0 (None)	Low
Vitamin B_{12}	Adult men and women	1	10% (Low)	Low
Iodine	Children 5–19 years	1	– (None)	Low
	Households	1	– = zero (0)	Moderate

TABLE 3.3: Results on the number of studies and prevalence of anemia in Rwanda

Population group	Prevalence (Rating of burden)	Rating of quality
Children < 0–23 months	53% (Severe)	High
Children 24–59 months	29% (Moderate)	High
Children < 5 years	34% (Moderate)	Moderate
Adolescent girls	19% (Mild)	High
Adolescent boys	29% (Moderate)	Moderate
Adult men	20% (Mild)	Moderate
Adult women	19% (Mild)	High

> **"Just telling people what to do is not enough to achieve sustainable behavior change"**

Social behavior change communication platforms to improve nutrition outcomes in LMICs

The Suaahara II project in Nepal aims to improve the health and nutritional status of pregnant and lactating women and children. Pooja Pandey Rana from Helen Keller International (HKI) presented findings from an evaluation of the relationship between degree of exposure to social behavior change communications (SBCCs) and maternal and child dietary diversity. It found that the SBCC platforms that mothers were most exposed to were community events, followed by radio programs and then interpersonal communication (IPC) from community health workers. There was also an increasing trend in the degree of exposure, measured as the number of contacts over time: around 75 percent of mothers in the sample were exposed to at least one platform, while less than a quarter were exposed to all three. The degree of exposure for men in the household was low. A positive significant association was found between the number of SBCC platforms to which a mother was exposed and their child's dietary diversity, with exposure to all three platforms having the strongest association. There was also a positive association between the number of SBCC platforms to which a mother was exposed and her own dietary diversity; again, exposure to all three platforms had the strongest association. The findings provide evidence that prioritizing a few behaviors is important, as is exposure to multiple platforms, which helps to reinforce messages and increase behavior change. Targeted efforts are needed to improve nutrition knowledge among male household heads, and multipronged SBCC nutrition intervention practices are critical to change nutrition practices.

SBCC interventions delivered through IPC and/or mobile phone-based health (mHealth) interventions show considerable promise to address child malnutrition. However, while IPC is often costly and difficult to implement, mHealth is low-cost, can reach inaccessible areas and allows for high-frequency contact. Rolf Klemm from HKI presented findings from a study that assessed the effectiveness of two existing Government of Tanzania interventions – IPC (*Mkoba wa Siku 1,000*) and mNutrition SMS text messaging module (*Wazazi Nipendeni*) – separately and in combination, on maternal, infant and young child nutrition behaviors in two districts in Tanzania (Newala and Tandahibma). The study found significant improvement in maternal knowledge for all topics (breastfeeding, child feeding, micronutrient, hygiene) across the SMS, IPC and SMS+IPC groups compared with the control group, and improvement was higher in the IPC and SMS+IPC groups. With respect to impact on dietary behaviors, the study found that the percentage of women reaching minimum dietary threshold increased significantly in the IPC and SMS+IPC groups, and not in the SMS group alone; however, only 40–50 percent of women met the threshold. With respect to children's diets, the study found significant improvement in the percentage reaching dietary diversity (+10 percent) and minimum adequate diet (doubled) in the IPC and SMS+IPC groups. These findings demonstrate that while costly and time-consuming, IPC strategies significantly improved maternal and young child diets, and combining IPC and SMS appeared to improve diets slightly more.

Mexico suffers from the triple burden of malnutrition with simultaneously high rates of stunting (14.2 percent), obesity (6.8 percent) and micronutrient deficiencies in children under 5. The Integrated Strategy for Attention to Nutrition (EsIAN in Spanish) is a national strategy within Mexico's conditional cash transfer program (PROSPERA) that is designed to improve the health and nutritional status of its beneficiaries. Dr Anabelle Bonvecchio from the National Institute of Public Health in Mexico shared findings from a review and formative research that used an SMS strategy for the prevention of undernutrition, micronutrient deficiencies and childhood obesity in two states in Mexico.[10] Results revealed that several barriers and issues limit program coverage, utilization and acceptance, including misconceptions about pregnancy and infant feeding, nonalignment of practices with international recommendations, and lack of knowledge about nutrition and related topics. These results were used to identify priority behaviors and elaborate key messages for mothers/caregivers and providers so as to develop a BCC strategy.

Designing a training strategy to prevent childhood malnutrition in Mexico

In Mexico, nurses and doctors are a credible and reliable source of IYCF counseling, but often have little nutrition training or are ill-equipped to assess nutritional status and provide effective nutrition counseling. A 2016–2017 evaluation was conducted in three states in Mexico (Chihuahua, Oaxaca and Veracruz) to assess the influence of a semi-virtual training on providers' knowledge and abilities, and on outcomes in terms of general nutrition knowledge and abilities and also those specific to breastfeeding. It found significant improvements in healthcare knowledge between baseline and post-training. The effects were greatest for physicians, followed by registered nurses and then nurse technicians. The effects were greater for the breastfeeding questionnaire than for the general questionnaire, and breastfeeding scores were significant for all types of providers. Lessons from this experience include: (1) improving health workers' capacities is fundamental to improve nutrition, and findings confirm that at baseline the providers lacked the general knowledge to provide services to mothers living in poverty; (2) improving workers'

capacities is expensive and difficult to implement, so carefully designed, evidence-based, online and semi-virtual trainings are good because of quality control and follow-up; and (3) while health workers' general knowledge significantly improved, other areas might require hands-on training.[11]

Experiences from implementation science

Why didn't this work? Program effectiveness post-mortem

During this session, presenters described program effectiveness studies of MNPs, lipid-based nutrient supplements (LNS) and corn soy blend (CSB) interventions with high program fidelity and performance, yet no effect on micronutrient status indicators. Presenters and panelists discussed potential reasons for these findings, focusing on evaluation design, biology and program implementation considerations.

Country experiences in combatting undernutrition using nutrition supplements

Guatemala has the highest prevalence of stunting in the LAC region and the sixth highest prevalence in the world, with 47 percent of children under 5 years of age affected.[12] Results from an evaluation of the *PROCOMIDA* program examined the absolute impact on reducing anemia compared with a control group, as well as the differential impacts of the size of the family food ration and the type of micronutrient-fortified individual ration. It found that while anemia prevalence decreased among mothers and children in all groups, this may have been due to government initiatives to address anemia and not the *PROCOMIDA* program itself. In addition, among mothers in the full group, the prevalence of anemia decreased initially, but had increased by 24 months, which could be due to the high phytate levels of the beans provided in the family ration plus the CSB. The impact of LNS was positive among children at 12 months, but it was no longer significant at 24 months. Overall, these results highlight the fact that micronutrient-fortified products delivered with or without a family ration did not have consistent impacts on reducing anemia. When designing similar programs, context-specific factors and more comprehensive data on other initiatives should be considered.

Another study[13] that evaluated the impact of an integrated IYCF–MNP intervention on anemia and micronutrient status among children aged 12–23 months in Eastern Uganda found that despite high program fidelity the intervention was associated with reduced hemoglobin concentrations but no change in anemia, iron status (ferritin) or vitamin A status. Contextual factors, such as cooking with soda ash, might explain the lack of effectiveness, as it can affect the physical properties of micronutrients and absorption.

Effective nutrition interventions to improve adolescent nutrition

Adolescence is a critical period for nutrition, with rapid physical and emotional changes. During this session, presenters described the forthcoming Lancet Series on adolescent nutrition, results of a recent systematic review, and process and impact evaluations of adolescent nutrition interventions, including their effectiveness and lessons learned.

How food environments influence adolescents' food and beverage choices

Food environments are the collective physical, economic, policy and sociocultural surroundings, opportunities and conditions that influence people's food and beverage choices and nutritional status. Findings from a systematic review[14] that assessed published evidence on the effects of food environment interventions on anthropometric (body mass index and weight status) outcomes in school-age children (5–9 years) and adolescents (10–19 years) in LMICs yielded limited evidence to support a beneficial effect of food environment interventions on BMI and weight status outcomes. Given that gaps and challenges in food environments persist, especially in the context of COVID-19, the authors recommend that future work should identify key components of the food environment that may be amenable to modification by well-designed and feasible interventions, which must then be rigorously tested.

> **"Future work should identify key components of the food environment that may be amenable to modification"**

Iron and folic acid supplementation in adolescent girls

Anemia is a moderate public health problem among adolescent girls in Ghana, with 26 percent of the population affected. While proven interventions such as school-based iron and folic acid (IFA) supplementation exist to reduce anemia, they have a limited scope and reach. The Girls' Iron-Folic acid Tablet Supplementation (GIFTS) Program is an integrated health and nutrition education program providing intermittent weekly IFA supplementation that is designed to reach adolescent girls (10–19 years) simultaneously via school and local health center delivery platforms. Results from a study[15] to assess the barriers to, and facilitators of, the fidelity of a school-based IFA supplementation program in the Northern and Volta regions of Ghana found that 90 percent of adolescent girls had ever consumed IFA tablets, whereas 56 percent had consumed at least 1 IFA per week, indicating that average intake adherence was equivalent to about half

of the available tablets. Among the ever-consumers, 88 percent of the girls liked the tablet, and 27 percent reported undesirable changes (primarily heavy menstrual flow). These results demonstrated that school-level factors were barriers to adherence (attendance at school, educators' training, etc.) – representing 75 percent of the variance in IFA consumption over the school year. Modifications such as expanded training, formalizing IFA distributions, awareness-raising and additional support to high schools may improve adherence, as may spreading the responsibility for IFA distribution to other teachers, streamlining monitoring to reduce the burden at the school level and strengthening health education.

Maternal nutrition programs: Innovative program delivery models to improve micronutrient status with case studies from African and Asian countries

Maternal malnutrition is a key determinant of poor pregnancy outcomes. It increases not only the risk of maternal morbidity and mortality, but also the risk of giving birth to infants who are low birth weight (LBW) due to small-for-gestational-age (SGA) or premature birth. This session examined the status of maternal nutrition policies and programs, and highlighted innovative case studies to deliver maternal nutrition programs.

Innovative program delivery models to improve maternal nutrition in LMICs

NI has significant experience of scaling up the coverage of IFA supplementation globally. Between 2010 and 2015, NI successfully scaled up the coverage of IFA supplementation in South Asian and African countries, reaching more than 2 million women across eight countries. This was achieved by using a comprehensive approach focused on building the enabling environment, and intense technical, financial and operational support. NI drew on these experiences to construct a program logic model – the NI Program Pathway – for IFA supplementation that shows the comprehensive and integrated pathways to increase coverage. In addition, NI has developed a suite of tools that support planning, budgeting and financing, and delivery, including the NI MMS Cost-Benefit Tool; guidance on quality nutrition counseling in antenatal care (poster); the NIMS to monitor coverage and adherence of maternal supplementation; and the Outcome Modeling for Nutrition Impact (OMNI) tool.

"Investing in maternal nutrition is important not just for health outcomes but also for gender equality and women's empowerment"

The *Projet intégré de nutrition dans les régions de Kolda et de Kédougou (PINKK)* in Senegal is a 5-year project funded by the Government of Canada that links healthcare, agriculture and business with the aim of improving nutrition and food security for women and children. Between 2015 and 2019, three evaluations were conducted to assess the impact of the project on desired outcomes. The results indicate that: anemia in women of reproductive age decreased by 16 percentage points (pp); anemia in pregnant women decreased by 7 pp; IFA coverage among pregnant women increased by 10 pp; access to growth monitoring and promotion services increased by 22 pp for children aged 0–23 months; access to screening services for acute malnutrition improved by 19 pp among children aged 6–59 months; and vitamin A supplementation (VAS) increased by 15 pp among children aged 6–59 months. In addition, knowledge of good nutrition practices and knowledge of good hygiene practices among women of reproductive age both improved in most departments. Household food insecurity also decreased significantly, while access to credit/financial loans among women, multisectoral integration and local nutrition integration into development plans, and gender equality and empowerment increased. Challenges remain in the delivery of services, especially in the context of COVID-19, but Balla Moussa Diedhiou underscored the importance of high-level political commitment, integration of several strategies, program target-setting and the use of nutrition as a means of entry to discussions at the household level, as well as scaling up the *PINKK* model and transitioning it to the Government of Senegal.

Innovative program or delivery models, including multisectoral interventions

Cost-effectiveness and cost-benefit of delivering nutrition and health interventions to improve nutrition

The importance of understanding the cost and cost-effectiveness of nutrition interventions cannot be understated. Cost-effectiveness analysis supports priority setting by defining areas of action where the greatest health and nutrition gains can be achieved with the available resources; however, evidence on the cost-effectiveness of nutrition interventions is still limited. During this session, presenters described new tools for assessing cost-effectiveness along with results from nutrition-specific and nutrition-sensitive cost-effectiveness studies, and discussed whether and how to compare apples to oranges in the context of the cost-effectiveness of interventions for anemia control.

"The importance of understanding the cost and cost-effectiveness of nutrition interventions cannot be understated"

Cost-effectiveness analyses on increasing IFA coverage and adherence

A cost-effectiveness analysis of an intervention focused on frontline health workers using IPC to improve IFA adherence in Bangladesh found that the intervention was able to increase the proportion of women who take IFA supplements for at least 90 days during pregnancy from 36 percent to 84 percent. In addition, the impact extended to other health outcomes, such as increased coverage of antenatal care during pregnancy, and increased capacity of health workers to raise awareness and change behaviors at the community level. The cost-effectiveness results were also robust, finding not only that capacity among frontline healthcare workers increased as a result of trainings, but also that the reported IFA supplement consumption and adherence rates were also highly cost-effective.

A cluster-randomized design of the *Tubaramure* program in Burundi that assessed the impact of food-assisted maternal and child health and nutrition programs on linear growth found that hemoglobin decreased and anemia increased for mothers markedly from baseline to follow-up, but *Tubaramure* had a significant beneficial effect on both children (6.1 pp) and mothers who had given birth in the previous 3 months (34.9 pp). The program also had significant impacts on dietary diversity, the consumption of iron-rich foods and morbidity, among other factors, as well as providing a cost-effective programmatic model for certain treatment groups.

"Vitamin A supplementation is a key public health intervention. If you reach 80 percent of children twice a year in countries with high vitamin A deficiency prevalence, you can reduce mortality by up to 24 percent."

In the past decades, rapid progress has been made in eliminating vitamin A deficiencies, but new delivery mechanisms are needed to sustain progress. For example, many VAS programs are combined with polio immunization campaigns. As these campaigns are being phased out, new models are needed to sustain progress and reach the remaining children. A 2019 HKI study aimed to evaluate the costs (overall and per child reached) of three different approaches to VAS: a mixed approach in Kenya, a door-to-door approach in Burkina Faso, and a routine approach in Mozambique. It found that the coverage of VAS varied significantly, from 40 percent to 81 percent, between countries, and that coverage was significantly higher in countries where HKI provided support, although still with significant variation among the three countries. VAS coverage was highest among children aged 36–59 months, who were reached by all three platforms. The highest coverage was achieved in Burkina Faso with the door-to-door approach, but other countries with limited funding are unable to fund such a platform. In terms of cost-effectiveness, the costs varied significantly between US$1.77 and US$11.12 (it should be US$2–3), even excluding opportunity costs. As VAS distribution platforms change, it is essential to understand the cost and effectiveness of platforms, and also to develop a more standardized approach and tools for cost-effectiveness studies.

Plenary session: Cost analysis is essential before considering scaling up micronutrient interventions

The plenary session on cost analysis highlighted the need for, and value of, cost analyses undertaken both before investing in micronutrient intervention programs and after program choices have been made.

Stephen Vosti, from the Department of Agricultural and Resource Economics – UC Davis, provided an overview of the importance of cost analyses, sharing findings from Cameroon and Uganda, where the Micronutrient Intervention Modeling (MINIMOD) tool was applied to estimate the costs of different interventions and platforms. In Cameroon, the model was used to predict the impacts and costs of alternative vitamin A intervention programs on vitamin A dietary adequacy and deaths averted among young children.[16] In Uganda, the model was used to test the cost-effectiveness of different platforms for distributing MNPs – community and facility based – and found that when scaling up MNP programs, a community platform delivery is more cost-effective. Omar Dary from USAID then reviewed evidence on the cost-effectiveness of food fortification, noting that while food fortification is beneficial because it takes advantage of existing products and delivery platforms, when compared with MNPs the inputs are very costly, whereas manufacturing, social marketing and delivery costs are low. Thus, food fortification is cost-effective, but only if: (1) fortified foods are produced by formal and centralized factories, (2) increments in the cost due to fortification are incorporated into the price of the product, and (3) reliable, efficient and low-cost enforcement systems ensure a level 'playing field' for manufacturers.

Keith Lividini from HarvestPlus/International Food Policy Research Institute shared preliminary results from a study on the importance of zinc supplementation in reducing NCDs and NCD disability-adjusted life years (DALYs). He reported that zinc has the potential to address the double burden of malnutrition in many countries and achieve cost-effectiveness, but that more data on impact and cost are needed.

Finally, JV Meenakshi from the Delhi School of Economics highlighted common conclusions from the presentations, including: (1) micronutrient deficiencies are widespread and a multi-

plicity of interventions are needed to address them; (2) the most efficacious interventions are not necessarily the most cost-effective; and (3) modeling exercises are a good way to examine the trade-offs and context-specific priorities for investments.

Experiences and lessons learned from country programs

Innovations in reaching children with biannual vitamin A supplementation: Maximizing morbidity and mortality impact in the absence of campaigns

VAS for children under 5 years of age has been a cornerstone of global child survival programs for decades. Periodic, high-dose VAS is a proven, low-cost intervention that significantly reduces mortality in children.[17] This session focused on exploring lessons learned in reaching children with VAS where they are, optimizing existing platforms within the health system and discussing ways to prioritize reach for maximum morbidity and mortality impact.

Banda Ndiaye from NI highlighted the fact that VAS coverage rates have dropped in recent years. In sub-Saharan Africa (SSA), the number of countries with VAS programs changed from a low of five countries in 2000 to a high of 27 in 2009, and dropped to 10 in 2016. Many SSA countries have started planning the transition of VAS delivery from campaigns to the routine primary healthcare contacts. In Kenya, Ethiopia and Senegal, VAS coverage rates dropped once countries reached scale, and in all three settings, VAS coverage dropped in children aged 12–59 months as a result of the increased availability and use of routine healthcare platforms, and the availability of providers, among other factors.

> **"The economic crisis that has followed the COVID-19 pandemic has turned into a food crisis on the ground"**

Andreas Hasman from UNICEF HQ highlighted how COVID-19 halted the delivery of VAS campaigns with effect from March 2020. Data shows significant disruptions to routine services, particularly of immunization in Asia and Latin America, but less so in SSA. UNICEF estimates that during the first half of 2020, 200 million children missed out on VAS.[18] In the latter half of 2020, VAS programs were reinitiated, and countries such as India were able to bring coverage rates up (V-shaped recovery), although they still fall short of pre-COVID-19 levels. Furthermore, donors were already showing the desire to move away from supporting the delivery of VAS as a single program to a more integrated model of delivery, so additional work is needed in this area.

To explore the transition from campaigns to integrated system delivery, HKI undertook four case studies to distill best practices. They found that platforms matter: while there has been success in delivering VAS with the polio platform, a lot of platforms exist and need to be identified and adequately resourced, whereas combined integration with campaigns is a disincentive to full integration. Furthermore, while in-country partner support can help achieve high coverage rates, it can also reduce real commitment and integration by the countries. Service delivery needs to be flexible and simple, accountability clear and centralized, and performance targets and indicators specific and achievable.

Integrated infant and young child feeding and micronutrient powder programs: Challenges, lessons learned and opportunities

During this session, presenters provided an update on the global status of MNP programs and the challenges, lessons learned and opportunities of integrated IYCF–MNP programs. They also presented recent programmatic effectiveness and evaluation findings.

Challenges and opportunities for integration of infant and young child feeding into other platforms

To frame this session, Aashima Garg from UNICEF provided an overview of the status of MNP programs globally. In 2019, 58 countries had programs on home fortification using MNPs, down from 61 in 2018. Data on the reach of home fortification with MNPs were reported for 46 countries: a total of about 16 million children were reached (up from 15.1 million in 2018, and almost double the 8.1 million in 2015). With regard to the prioritization of MNP programs within government policies, strategies and plans, in 2019, 60 countries had a government policy, strategy or plan of action on MNPs (up from 55 countries in 2018), but only 30 countries allocated government funding for MNP programs. The COVID-19 pandemic significantly disrupted MNP service delivery, with an estimated 12.7 million children reached with MNPs (meaning that 3 million children missed out on MNPs in 2020).

Theogene Dusingizimana from Massey University, New Zealand and University of Rwanda, Musanze, provided an example of subnational MNP delivery. In Rwanda, 37 percent of children under 5 years of age are affected by anemia, with those aged 6–8 months and 9–11 months being most affected (DHS). Rwanda is one of the first countries to successfully scale up home fortification with MNPs subnationally. A study to determine the factors influencing access to, and use of, MNPs in rural Rwanda found that despite good program coverage, barriers persist to achieving scale and impact. These include distribution issues, misinformation and understanding among mothers/caregivers on the benefits and use of MNPs, and the incompatibility of current IYCF practices and MNP usage. Additional support and focus in the form of improved MNP supply chains, nutrition education and complementary programs are needed to improve program reach, as is additional research.

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TRACK 4

Designing an Enabling Environment for Micronutrients

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Introduction

Presenters and panelists in **Track 4** were in agreement that, in order to create an enabling environment for micronutrients and inform policy, a less fragmented nutrition community that speaks with a unified voice, together with a multisectoral approach that includes the private sector, is essential. In addition, there is power in scientific research informing policy, but a strong evidence base from countries must be built to justify interventions. Furthermore, lessons from the COVID-19 pandemic should be an example to the nutrition community that they have to keep nutrition on the agenda and not let it fall as a global priority.

> **"The COVID-19 pandemic should be an example to the nutrition community that they have to keep nutrition on the agenda"**

How to keep micronutrients as a priority with shifting global, national and donor priorities?

With changing priorities due to development challenges, such as climate change, refugees, wars, terrorism and epidemics, interest in micronutrient nutrition may be reduced. In this plenary session chaired by Eileen Kennedy, Tufts University, panelists discussed ways in which micronutrients can be kept on the agendas of policymakers, donors and implementers.

Kelly Brownell, Duke University, suggested scientists need to convince not only themselves but also the outside world. He proposed the use of new models in combination with traditional programmatic science models. One example is the Strategic Science Research Model.[1] This model begins by identifying change agents and developing a scientific agenda based on information gaps that are helpful for change agents to fill; finally, the information gaps that have been gathered are communicated to the change agents. Implementing a model such as the Strategic Science Research Model is possible together with producing best quality science, and publishing in reputable peer-reviewed journals. Brownell used three case studies (calories on restaurant menu labeling, soda taxes and children's food marketing) to illustrate how strategic, simple, quality and straightforward research can influence, inform and sometimes change policy and legislation.

Joel Spicer, Nutrition International, highlighted how the COVID-19 pandemic is a health crisis that has set up an economic environment and perfect conditions for an accelerated malnutrition crisis. He highlighted the possibility of losing a decade of progress in less than a year, and that of not meeting Sustainable Development Goal (SDG) 2: Zero Hunger. Spicer recommended that a significant emergency action is required now and over the medium term to prevent massive damage, particularly to children, adolescents and women. He added that, at a time when doubling down on nutrition has never been more important, nutrition has never been more at risk of waning as a global priority. This he attributed to the contraction of the fiscal space from donor and governments because of the damage caused by COVID-19.

Ali Winoto Subandoro, World Bank, highlighted the importance of micronutrients in the Investment Case, and emphasized that this is a country-led process. To ensure micronutrient interventions are being prioritized, financed and monitored, there is a need for updated country-specific information on costing, available resources and cost-effectiveness. Subandoro highlighted that it is important to source finances from local resources through fiscal policies and other innovative financing instruments. For micronutrient interventions to be monitored, accountability for results must be present. In conclusion, he remarked: "What gets measured will get done."

Katharina Lichtner, Family Larsson-Rosenquist Foundation, discussed how knowledge that is being generated is not creating an impact. Spicer agreed and pointed out that the evidence base that has been built for critical interventions is still not getting to the vulnerable. Lichtner emphasized that the 'how' should not be left out when speaking about the 'what' and 'why' in policy discussions. She added that understanding how to operationalize policies is important. Lichtner emphasized that understanding micronutrient interventions' capital requirements will enable the nutrition community to build business cases for interventions. To ensure healthy babies and mothers, she recommended the nutrition community includes breastfeeding and complementary feeding, and thinks from an operational perspective about how to deliver programs without wasting human capital.

> **"We need to align as donors in strategy and implementation because there is no single bullet for nutrition"**

Andreas Blüthner, Bill & Melinda Gates Foundation, highlighted that there has been enormous progress in supplementation, biofortification and scaling up of large-scale fortification. However, lessons should be taken from oil and flour fortification, and how social safety schemes can transform nutrition. Blüthner mentioned that more work in dietary diversification is still needed, and pointed out that the donor community should also be unified. In Blüthner's own words: "We need to align as donors in strategy and implementation because there is no single bullet for nutrition; in complementarity lies the beauty of a holistic strategy that is sustainable and impactful." He noted that 10 years ago the nutrition community was even more fragmented, but progress has been made since then.

Gerda Verburg, Scaling Up Nutrition (SUN), emphasized the need for the nutrition community to have the correct knowledge and experience for making social and economic cases. She highlighted the need to understand the distinction between nutrition and food security. Verburg suggested that there is a need for convergence and coherence with all other initiatives and actions to fight and prevent malnutrition. She also suggested that the nutrition community should put themselves in the shoes of the policymakers and advisors, ensure the audience is part of the conversation and encourage ownership of the programs. Furthermore, she emphasized that we should sit at the table and be ready to support thinking and conversations about how to get food systems right.

To prevent the 'nutrition voice' from fading and also that of funding and investment, panelists proposed several recommendations:

- Spicer suggested we concentrate on what works and build our tools and evidence base. He proposed we should focus on prioritizing low-cost, high-impact evidence-based interventions that save lives and build resilience. He emphasized that we need to recognize the difference between things that are ready to scale now and those that will be ready in five or 10 years' time. He suggested we look at how to bring primary healthcare, social protection and food systems together for nutrition. Lichtner agreed with this point, and mentioned that breastfeeding should remain a priority and multiple micronutrient supplementation (MMS) should be integrated into the 1,000-day approach.
- In this session, all panelists were in agreement that there is a need to move from evidence to action, and to connect nutrition science with policy.
- Panelists agreed on the need for the nutrition community to speak with one voice; as Spicer noted, the messaging and approach of the nutrition community is sprawling, lacking prioritization and focus. This fragmentation may lead to confusion at the country level about how and what to prioritize on when resources are scarce – a sentiment that was echoed by Verburg.
- Lichtner agreed with Subandoro that there is a need for the nutrition community to build a good business case and financing model.
- Spicer suggested that we should take a 'no missed opportunities' approach by looking at other platforms into which we can integrate nutrition, such as social safety net programs, education investments and contact points with people who have the potential to advance nutrition.
- The need to have bridging organizations that disseminate research for policy and action was mentioned by Lichtner. Blüthner agreed and commented that platforms and institutions that disseminate research towards concrete policy and subsequent action, such as SUN and the Micronutrient Forum, are needed.
- The need to engage with and involve the private sector was addressed. Panelists agreed that the nutrition community should not be hostile towards the private sector and food manufacturers. The key, according to Brownell, is to empower the consumer so that he or she can make the right healthy diet choices. This approach will lead to the reformulation of products to deliver healthier options. All of the panelists agreed that nonengagement with the private sector is not the solution. Blüthner recommended that more emphasis should be placed on creating an interface between scientific research and the private sector, as this will help to inform policy. He reminded the panelists of the positive role that industry has played in the past, citing the examples of salt iodization and flour fortification. According to Blüthner, the key is to change the perspectives of the private sector. He recommends helping the private sector to see the opportunity in empowering populations, and also reminding them of the beauty that adequate nutrition can unfold. Brownell made the important observation that: "Industry will not move unless they have too."

Supporting country-led policy decisions to implement multiple micronutrient supplementation during antenatal care

This session chaired by Gilles Bergeron, New York Academy of Sciences, provided an overview of evidence available as to why countries should implement and adopt MMS in national programs

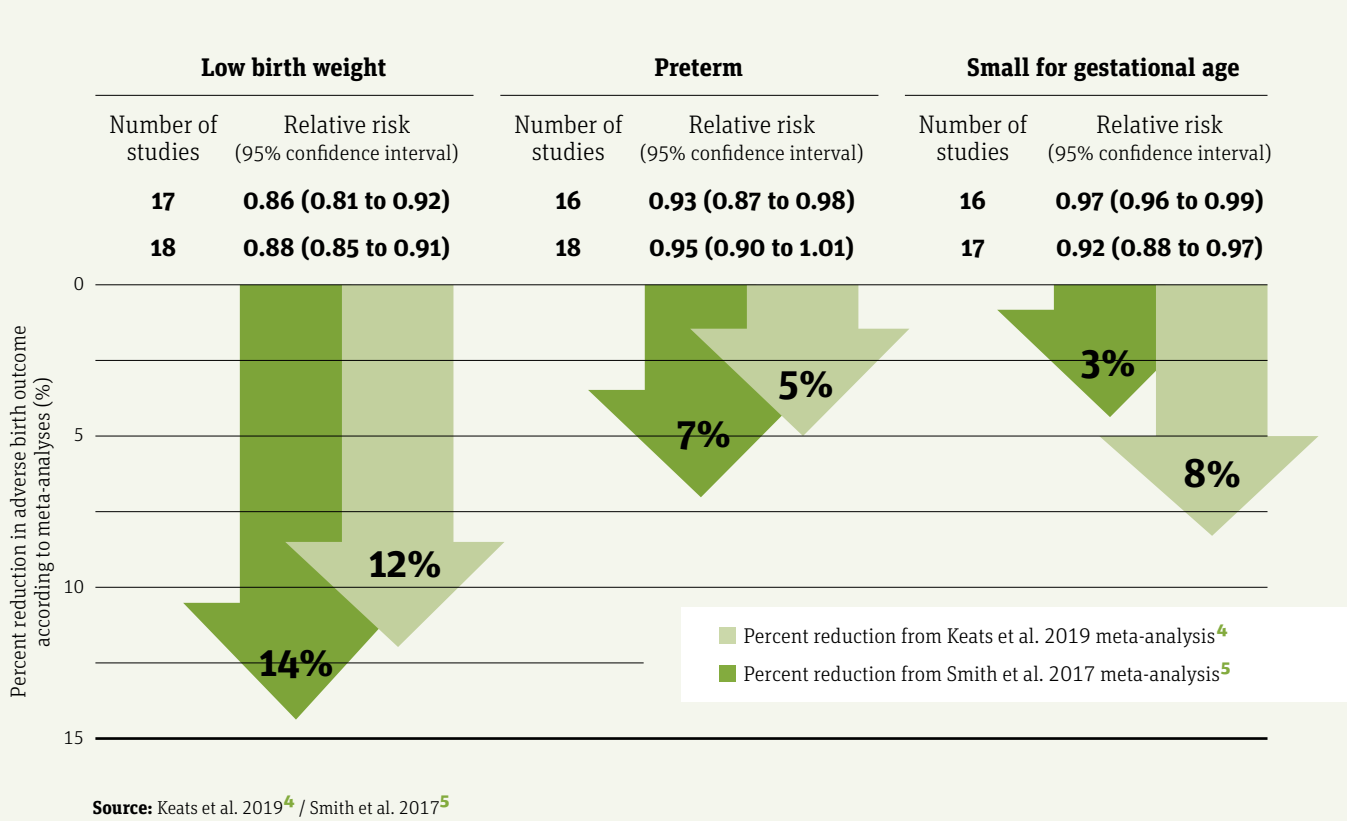
rather than iron and folic acid (IFA) as standard in antenatal care (ANC) programs.

Emily Smith, George Washington University, gave a brief background on evidence to support the use of MMS. Decades of research have revealed that inadequate maternal nutrition is a driver of adverse birth outcomes such as small for gestational age (SGA), stunting, preterm birth, and infant morbidity and mortality. In 2015, 14.6 percent of births globally were low birth weight (LBW), totalling 20.5 million, and mainly occurred in sub-Saharan Africa and Southeast Asia. During the past three decades, child mortality has been reduced by 58 percent, and while this progress has been astounding, Smith suggested it is not fast enough. From 2000 to 2015, the annual rate of reduction was just over 1.23 percent. She recommended that this rate needs to triple in some areas to meet global goals by 2030. Furthermore, she noted that the causes and timing of child mortality are changing. This is a huge public health problem because, as she said, we have so few tools in our toolbox to address the causes of death.[2] Solid evidence has been put forward to show the benefits of MMS use over IFA supplements during pregnancy. Babies of women who receive MMS during pregnancy have a lower risk of LBW and SGA compared with those of women receiving IFA supplements. To acknowledge the new evidence, the World Health Organization (WHO) revised the 2016 ANC guidelines in August 2020.[3] WHO recommend that countries aiming to adopt MMS and not IFA should do so within certain parameters. The updated 2020 WHO ANC guidelines were informed by two systematic reviews that included 17 randomized trials conducted in low- and middle-income countries (LMICs)[4,5] (**Figure 4.1**). Smith showed that everyone benefits from the use of MMS,[5] especially undernourished women. Furthermore, Smith showed that MMS reduces the risk of mortality for female infants during the first year of life, and that there was an overall reduction in neonatal mortality for the general population.

Reina Engle-Stone, University of California, Davis, presented the economic rationales for the adoption of MMS over IFA. The costs of MMS tablets relative to IFA tablets have been calculated in an analysis from Bangladesh, India, Pakistan and Burkina Faso.[6–8] Cost-effectiveness analyses conducted for WHO state that the switch from IFA to MMS can cost US$3–47 per disability-adjusted life year (DALY) averted, or up to US$113.[9] Engle-Stone added that the abovementioned cost analyses do not account for population change over time, gradual transition from IFA to MMS, and differences in tablet distribution, consumption and adherence. She stated that the tablet cost depends on how the tablets are purchased and distributed. Using models that account for program transitions and tablet distribution patterns, the cost for MMS in Bangladesh and Burkina Faso was US$3–15 per DALY averted or US$6–105, respectively.[8]

The WHO guideline recommends that when a country is adopting the MMS program, implementation research is important to

FIGURE 4.1: Meta-analyses summarizing data from high-quality randomized trials and showing the benefits of multiple micronutrient supplementation (MMS)



Source: Keats et al. 2019[4] / Smith et al. 2017[5]

ensure acceptability, feasibility, equity and cost-effectiveness. Megan Bourassa, New York Academy of Sciences, presented on lessons learnt from countries implementing MMS. The dramatic impact of COVID-19 on the quality of diets and access to ANC services during pregnancy was acknowledged. Bourassa pointed out that MMS can be used to respond to the pandemic, especially in contexts of high nutritional deficiencies and disruptions to food distribution. Bourassa emphasized that an enabling environment to support implementation research must be created through advocacy of the use of MMS and the creation of MMS policies that everyone is supportive of and understands. She also highlighted the importance of improving coverage and adherence to maximize the cost-effectiveness of MMS. In conclusion, Bourassa emphasized that: "In settings where dietary quality is poor, micronutrient deficiencies are common and anemia and low birth weight are significant public health problems, daily MMS with iron and folic acid can contribute to improved micronutrient intakes in pregnancy, prevent maternal anemia, and reduce adverse pregnancy outcomes, including low birth weight."[10]

"Daily MMS with iron and folic acid can contribute to improved micronutrient intakes in pregnancy"

Thereafter, Nita Dalmiya, United Nations Children's Fund (UNICEF), presented lessons learnt from IMPROVING: Improving Maternal and Pregnancy Outcomes through Vital Interventions for Nutrition and Growth. The objective of this initiative is to establish proof of concept in Burkina Faso, Tanzania, Madagascar and Bangladesh for MMS introduction. Results from these four countries will later inform the national scale-up and expansion of MMS introduction in other countries. These lessons were:

- Introducing MMS requires global and national planning and coordination. Dalmiya presented how UNICEF collaborated with the Supply Division, Nutrition International, *Sight and Life* and the Global MMS Technical Advisory Group to introduce MMS into these four countries.
- Country-level planning and coordination are important for the successful introduction of MMS. Dalmiya stated that countries in IMPROVING benefited from clear messaging that MMS is low-cost (US$0.02 per tablet), good value for money and equitable. This approach was instrumental in securing government buy-in based on the message that MMS is a social equalizer that offers all women the same standard of care during pregnancy, which resonated with policymakers.
- Introducing MMS needs clear context-specific advocacy.
- MMS planning and implementation should be designed for scale-up. In IMPROVING countries, MMS is embedded in ongoing ANC programs and not as stand-alone programs.
- MMS is part of a systems-strengthening approach and should be planned for as such.
- The supply chain should be at the country level to ensure uninterrupted supplies of quality MMS. Dalmiya highlighted that a clear understanding of political and policy context is important to inform advocacy and the introduction of MMS into countries.

Lwin Mar Hlaing, National Nutrition Centre, Department of Public Health, Ministry of Health and Sports, presented on the successful reduction in Myanmar of the prevalence of iron deficiency anemia in pregnant women from 71 percent in 2003 to 56 percent in 2016. As the Myanmar Government target for anemia prevalence is 35.5 percent by 2025, anemia is still a public health concern. With the support of UNICEF, Myanmar shifted from IFA to MMS use in 2016. This is because of a possible coexistence of multiple micronutrient deficiencies (MNDs) in women and the benefits of MMS over IFA. During MMS implementation, the Myanmar Government faced challenges that included: shortfalls in MMS supplies, limited government budget, domestic production that could not fulfill demand at the initial stage, the use of different MMS specifications by suppliers, data gaps on MMS adherence, and the ability to supply MMS only to pregnant women. The Myanmar Ministry of Health has now received commitment and support from the government to proceed with MMS, and will receive MMS donations from Kirk Humanitarian until 2023.

Tackling under-5 mortality: Nutrition as a priority for investment

This session was chaired by Scott Dowell, Bill & Melinda Gates Foundation. It aimed to address malnutrition as a cause of childhood mortality. Dowell remarked how surprisingly hard it is to understand the causes of child mortality as they are often grouped into large categories such as neonatal or perinatal mortality, or into syndromes such as pneumonia or diarrhea mortality. These are usually not the specific causes that allow interventions to prevent death. Neural tube defects are a good example of a specific cause of child mortality that is preventable.

Dianna M Blau, Centers for Disease Control and Prevention, Child Health and Mortality Prevention Surveillance (CHAMPS), gave an overview of child mortality and methods used to determine cause of death. She presented how under-5 mortality rates have decreased by almost 60 percent since 1990. The SDG 3 target is to end the preventable deaths of newborns and children under the age of 5 years by 2030. Blau noted that most countries have met the goal to reduce under-5 deaths to at least 25 per 1,000 live births. Despite this global progress in reducing child mortality, 5.2 million children died in 2019 (~14,000 under-5 deaths per day),

and more than half of these deaths occurred in sub-Saharan Africa. Currently, death certificate, clinical records, verbal autopsy, complete diagnostic autopsy (CDA) and minimally invasive tissue sampling (MITS) are the methods used to estimate cause of death. The importance, strengths and weaknesses for each of these methods were presented. Blau pointed out that there are inconsistencies between countries in the accuracy and details provided on death certificates and the quality of information collected.[11] There is also a lack of correlation between clinical and pathological data.[12] Furthermore, she highlighted that current verbal autopsy forms for children include only two questions about nutrition status. She emphasized that diagnostic autopsy is the gold standard for cause of death determination but that in LMICs cultural and religious reasons, scarcity of pathologists, histologists and related consumables, and limited laboratory capacity limit its use. MITS is an alternative to CDA because of its acceptability and feasibility. An example of a surveillance program that uses MITS is the CHAMPS program.

Jay Berkley and Moses Ngar, from KEMRI/Wellcome Trust Research Programme, presented on the Childhood Acute Illness and Nutrition Network, or CHAIN Network.[13] The CHAIN cohort included children (aged 2–23 months) from Bangladesh, Burkina Faso, Kenya, Malawi, Pakistan and Uganda, who were admitted into hospital with acute illness. The study showed that regardless of nutrition status, the risk of death in children was high during the first 30 days of admission. When compared with non-wasted children, severely wasted *kwashiorkor* (SWK) children were six times more likely to die after all adjustments. Abnormal discharge, HIV exposure, signs of illness severity at admission, high signs of illness at discharge and medium to high underlying conditions were associated with a high risk of post-discharge mortality. In this study population, hospital admission duration was not associated with discharge characteristics, and presenters recommended that longer hospital stays are not necessary. Discharge signs were associated with post-discharge mortality, and this discovery may lead to the development of biomarkers that can help to prioritize children that need follow-up. The point of discharge in terms of mortality was equally as important as the point of admission in terms of assessment and planning. Caregiver characteristics were directly associated with post-discharge mortality, suggesting that improvement of the mothers' characteristics may directly reduce mortality. The presenters also highlighted the use of mid-upper arm circumference (MUAC) as a good measure of all underlying factors and household factors.

"Malnutrition is considered to be the cause of 50 percent of all child mortality"

Malnutrition is considered to be the cause of 50 percent of all child mortality.[14] However, there are gaps in the determination of malnutrition. Parminder Suchdev, Emory University, presented preliminary results from the CHAMPS network to address these gaps.

Gap one: How to best measure malnutrition. In 2019, anthropometric data quality gaps, such as rounding, digit preference and high standard deviations, were found in the data of 783 children that had undergone the MITS examination. A lack of standard equipment and training on its use as well as difficulties in conducting anthropometry postmortem due to rigor mortis were the reasons cited for this. To improve postmortem anthropometry, a pilot study was conducted in Kenya, which showed that anthropometric data quality, precision and accuracy could be improved by training and the use of standard equipment. Furthermore, standard anthropometry is possible in a postmortem setting. However, Suchdev highlighted that further adjustment of 3D-imaging technology is needed.

Gap two: Assignment of cause of death. From extracted postmortem anthropometric data, it was found that among children aged 0–59 months wasting appeared to be a contributor to child mortality. However, more guidance is needed to standardize when malnutrition should be included as a cause of death.

Gap three: Accounting for malnutrition in all its forms. A pilot study to assess vitamin A liver samples and the role of vitamin A deficiency in child mortality is still to be conducted. Suchdev introduced the MITS Surveillance Alliance Undernutrition Committee, whose goal is to develop guidelines for the systematic integration of undernutrition into the casual chain of events leading to child death.

Michael Dibley, University of Sydney, presented results from the Shonjibon study, Bangladesh. The aim of this study was to determine whether the use of antenatal IFA supplements improved neonatal survival. The primary hypothesis was that daily 60 mg iron/400 µg folic acid supplements starting during the first trimester of pregnancy and continuing for at least 180 days would reduce neonatal mortality by 25 percent (from 33 to 24.8 per 1,000 live births) compared with the usual IFA supplementation program. Compared with the control group, the community-based, cluster-randomized controlled trial approach revealed that no side effects were experienced in the intervention group. Unbeknown to the Shonjibon study group, the groundwater in Bangladesh contains highly bioavailable iron. This discovery posed a problem because, in groundwater areas with high levels of iron, women who consume 2–3 liters of water daily can have an iron intake of 60 mg. Although the group did not stratify randomization by groundwater iron, they measured groundwater iron levels

and planned subgroup analyses. In their study population, 20 percent of households had no iron in their groundwater. In the intervention group, rates of early neonatal mortality and neonatal and infant deaths were slightly lower, and there was no difference between the perinatal deaths and stillbirth outcomes. Dibley reported that, in rural Bangladesh, daily antenatal IFA supplements with 60 mg iron starting during the first trimester of pregnancy reduced neonatal mortality by 13 percent compared with usual antenatal programs. There was a larger protective effect on perinatal mortality outcomes, including neonatal mortality, among women from households with no groundwater iron. Finally, he concluded that to maximize reductions in neonatal mortality in pregnant women in settings where iron deficiency anemia and neonatal mortality are high, there is a need for 60 mg of iron in nutrient supplements.

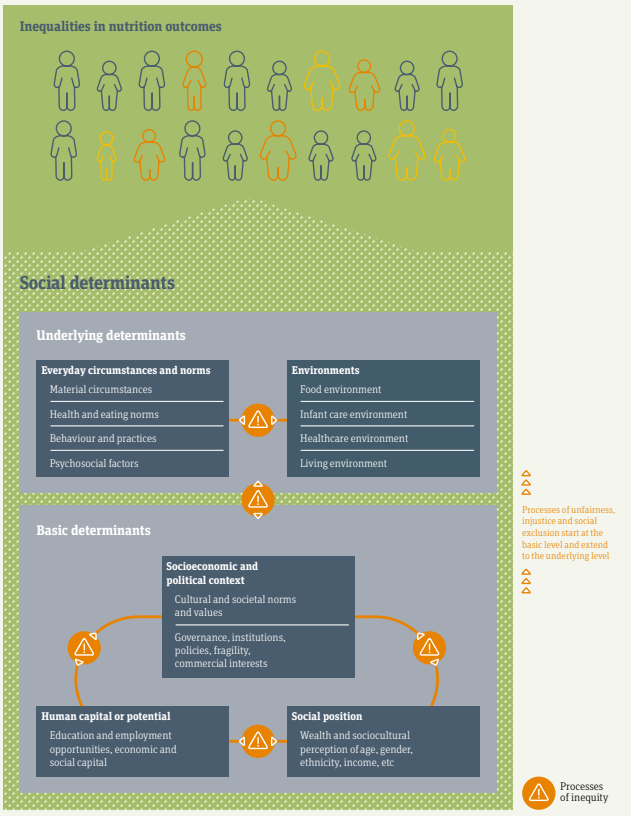
Early life micronutrient interventions: Short- and long-term outcomes

In this session, presenters aimed to show evidence for addressing MNDs in the first 1,000 days to prevent or reduce noncommunicable disease (NCD) risk. Furthermore, they presented results from their studies to determine whether early life nutrition interventions increase the risk of adiposity and/or NCDs.

Chittaranjan Yajnik, King Edward Memorial Hospital & Research Centre, presented on the developmental origins for health and disease. He presented on the concept of developmental origins of health and disease (DOHaD), and gave examples of micronutrients affecting the DOHaD phenomenon. The DOHaD concept came about because of an understanding that fetal undernutrition was associated with increased risk of long-term hypertension, diabetes and heart disease. He presented how NCDs are a result of epigenetic factors and challenged the conventional idea that NCDs are the result of only genetic predisposition and lifestyle-precipitating factors. Yajnik highlighted that it is never too early, and never too late, to intervene. He presented results of neural tube defect predisposition by MNDs.[15] He also presented results from the Pune Maternal Nutrition study – a follow-up study that followed infants from birth to 24 years of age.[16–20]

In the same session, Kristen Hurley, Johns Hopkins University, presented on results from a study conducted in Malawi. Researchers were tasked by the Malawian Government to evaluate the impact of a comprehensive nutrition program (monthly distribution of a lipid-based nutrient supplement [LNS] for 6–23 months) plus social and behavior change communication (SBCC) in reducing undernutrition in children aged 6–23 months.[21] The objectives of the study components were to assess the impact of: (1) the programs on the nutritional status of children aged 6–23 months, (2) full program exposure from 6 to 23 months on growth, and (3) the extended effects of early program exposure on growth later in childhood. Results from the first study indicated that, at baseline compared with the comparison district, the program improved weight indicators

FIGURE 4.2: Nutrition equity framework



Source: Global Nutrition Report: Action on equity to end malnutrition[25]

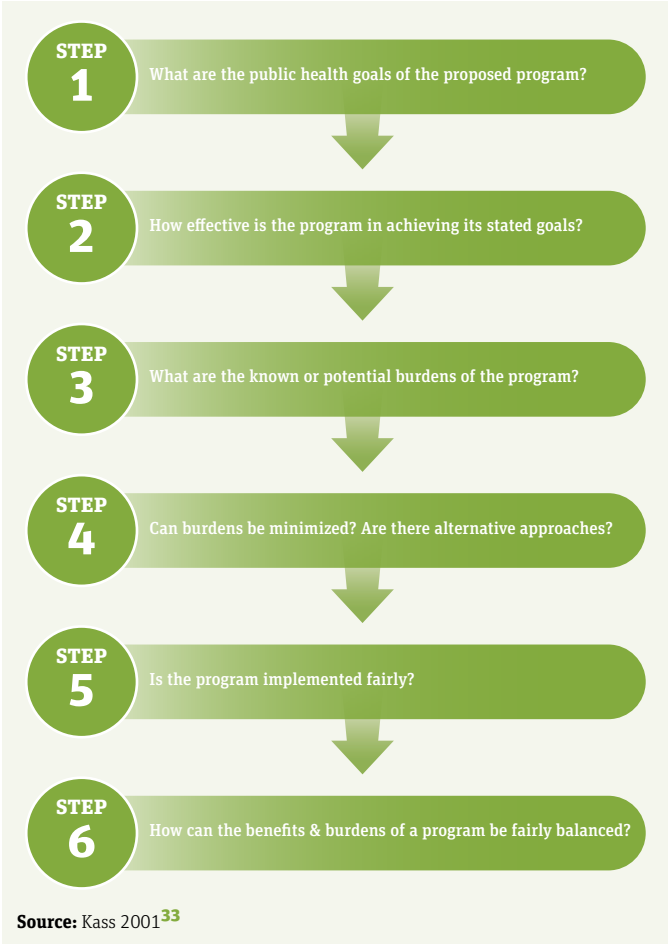
and reduced the prevalence of wasting and moderate acute malnutrition at a population level; however, there were no differences at the population level for indicators of child linear growth or stunting across the districts.[22] For the second study, the prevalence of stunting was higher in the program (44.8 percent) versus the comparison (39.5 percent) district at enrollment, with corresponding lower length-age-z (LAZ) scores. However, growth velocities favored program children such that LAZ scores, weight-age-z (WAZ) scores and MUAC increased, leading to comparable distributions across the districts by 23 months of age. Program exposure after 18 months reduced child morbidity (fever and malaria) and improved child diet (minimum dietary diversity). In the third study, by the age of 3–4 years, children in the program district had higher weight-height-z (WHZ) scores and BMI-z scores and lower height-age-z (HAZ) scores than those in the comparison district – i.e., they were heavier and shorter. The reasons for these post-program changes are unknown, but may be related to sustained increases in appetite and continued gains in fat tissue over lean body mass, as children rapidly transitioned at 24 months from a nutritionally balanced diet to a low nutrient-dense maize-based diet. Hurley suggested that in order to promote sustained linear growth, future research might consider developing and evaluating nutrition programs that target the first 2,000 days (conception to 5 years) and continue to focus on dietary quality past the age of 23 months.

Jessica Fanzo, Johns Hopkins University, presented on the ethics surrounding research, and highlighted the four core principles of ethics: autonomy, beneficence, non-maleficence and justice. Her first ethical question was: "Do we really know the true number of people who suffer from micronutrient deficiencies (MNDs) and what those deficiencies are?" She pointed out that the statistics and data used in research on MNDs are outdated estimates such as zinc deficiency prevalence data. Other ethical questions were: "Are we potentially causing harm by not knowing who is suffering from MNDs?" and "Who are the women targeted in the women nutrition interventions?"[23,24]

> **"Are we potentially causing harm by not knowing who is suffering from MNDs?"**

Fanzo emphasized the need to use the right words and terms in nutrition, for example vulnerability versus marginalization (**Figure 4.2**).[25] This is important because each term when put into context influences the types of programs and priorities that are made. Reconciliation of these terms and kinds of programs is therefore important to ensure that no one is left behind. The question of whether we are aiming for either equality or social change when we are implementing programs and policy was discussed. Fanzo also discussed whether interventions to address MNDs are sufficient/appropriate, and if they should be scaled up or out and taken as the best approaches for addressing MNDs.[26] She gave examples of ethical questions surrounding food fortification,[27,28] ready-to-use therapeutic food (RUTF) and the long-term health complications that may result from their intake,[29,30] and the prioritization of biofortification over biodiversity.[31] She encouraged us as the nutrition community to take an ethical framing in decision-making before undertaking an intervention. The framework involves asking whether effectiveness, proportionality, necessity, least infringement and public justification will be addressed by an intervention (**Figure 4.3**).[32,33]

FIGURE 4.3: Ethics framework for public health



Source: Kass 2001[33]

Fanzo posed Nisbett and colleagues' 2014 question to the nutrition community: "Shifting agendas in nutrition: Do they help us as nutritionists? Do they leave policymakers confused?"[34] Fanzo then pointed out that regardless of nutrition requiring multisectoral commitment, there is an absence of fixed responsibilities and accountability. Perhaps nutrition is not visible enough for actors to care if they have other competing priorities, she said. To conclude her presentation, Fanzo asked: "How do we better position nutrition in international development, how do we stay focused and not confuse policymakers, how do we make nutrition everyone's responsibility, and when responsibility is acknowledged, how do we hold them accountable?"

Anne Walsh, Power of Nutrition, presented on the donor perspective on early micronutrient interventions and the challenges faced. She highlighted the barriers to the scaling up of MMS, which include communicating the benefits of MMS on birth outcomes in LMICs, which in turn makes it difficult to justify the additional cost to governments and funders with constrained budgets and competing priorities. Another barrier highlighted by Walsh was that of compliance with current IFA supplementation: although many countries are managing good coverage, compliance is still low. She cited Liberia as a case study. In this study, a survey performed in 2018 found ANC visits to be high, which resulted in 81 percent of pregnant women receiving IFA. However, the consumption of supplements by these pregnant women for more than 90 days was low (33 percent). A repeat survey in 2019 revealed that although ANC visits were high, the consumption of IFA for more than 90 days had decreased to 30 percent. Walsh recommended that the nutrition community must continue working collaboratively to generate evidence of impact, improve IFA compliance (i.e., not just in supply but also in demand), and involve government from the start – as government buy-in ensures long-term sustainability. In addition, Walsh emphasized that we need to engage with the private sector and other suppliers to ensure MMS is more accessible and push for collaborative solutions.

Meeting essential needs in humanitarian and livelihood programs: Accounting for the cost of a nutritious diet

In a session chaired by Saskia de Pee, World Food Programme (WFP), panelists presented examples of how estimates of the cost of a nutritious diet (COD) and essential needs assessments were used in programming and in determination of support packages.

Nora Hobbs, WFP, emphasized that food security and nutrition objectives can be met only if other essential needs (food, water, hygiene, shelter, medical care and education) are adequately met. She introduced the two assessment tools that are used to assess the food needs of populations: cost and affordability of a nutritious diet (COD) and minimum expenditure basket (MEB). When COD and MEB assessments are combined, they provide complementary information from different perspectives that inform policy and promote advocacy and programming to meet essential needs. Hobbs suggested that a systems approach to food and nutrition should be adopted. She also highlighted that in households that face a wider gap to meet nutrient requirements, there is a need to help individuals with the highest nutrient requirements. Looking first at specific interventions that can mitigate the nutritional risks of vulnerable groups by reviewing all of the health services that are available to them (including access to IFA, and other options such as school meals, optimal breastfeeding and household interventions) was suggested. To inform coordinated, complementary programming and responses, Hobbs recommended the use of assessment tools that work across sectors, because meeting essential needs requires a multisectoral approach.

Piet Vochten, WFP, presented the results of a 2019 Fill the Nutrient Gap (FNG) analysis conducted in Bangladesh. The aim of the study was to investigate barriers to adequate nutrient intake, and inform WFP and government policy decisions. Results from the analysis demonstrated that, at the national level in Bangladesh, the cost of meeting nutrient requirements throughout the life cycle is twice that of meeting energy-only requirements; it is three times higher in Cox's Bazar. Additionally, one in eight households at the national level and one in two households in Cox's Bazar cannot afford a nutritious diet. An important finding was that the inclusion of fortified rice in social protection programs has the potential to reduce the COD. By comparing the COD with the MEB, the study found that, compared with the local population's access to 50 commodities, Rohingya refugees have access to 20. Vochten also noted that interpretation of the results to inform programs and policies must consider that people do not make perfect choices for many reasons. He suggested that further studies are needed to understand the efficiency factor of transfers and to consider contextual factors such as nonfood costs that are not covered by other interventions or own income, existing market inefficiencies, time constraints and food preferences beyond staples. Vochten further showed how key findings from the FNG analysis were used to support the Bangladeshi Government to develop a SBCC strategy to promote nutritious diets, limiting the consumption of snacks and the high intake of rice. Results were used to advocate for higher transfer values in social safety net programs and to revise the composition of food packages for emergency responses. Furthermore, findings strengthened national school feeding programs by designing and piloting recipes that maximized micronutrient intake. In addition, results from the analysis were used to respond to, and ease pressures from, the COVID-19 pandemic. Vochten concluded that the FNG analysis helped the WFP and Bangladesh to better understand key barriers and limitations to availability and access in meeting nutrient needs. Additionally, it helped them to better understand and anticipate changes to packages of interventions.

Raisul Haque, Save The Children, presented results from the COD analysis that was conducted in the Suchana graduation progress model. This analysis aimed to quantitatively assess the effect of livelihood interventions in Bangladesh on improving people's affordability of, and access to, a nutritious diet. From standard analysis based on a six-member household, the cost of four diet types was assessed. The energy-only diet and macronutrient diet did not meet all nutrient requirements but were the cheapest. The most expensive diet was the food habits diet, which met all nutrient requirements. The analysis indicated that an affordability gap exists, as Bangladeshi families could not afford their food and nonfood costs on their existing incomes. The analysis showed that project interventions such as home food production packages improved household-level accessibility to nutritious foods, as they affected the cost of the diet, reducing affordability gaps and annual diet costs. In poor households, the affordability gap reduced from 17 percent to 1.5 percent, and in very poor households from 57 percent to 14.4 percent, between 2013 and 2018. In addition, households that received income-generating interventions had lower affordability gaps compared with households that received home food interventions only.

In the question and answer session, Tracy Dube, WFP, discussed how the WFP is using results from the FNG analysis to provide e-vouchers to households that include children aged 3–5 years and pregnant women so they can procure acceptable locally produced food. Additionally, exploration programs resulted in the development of a program called 'a farmers' market.' Dube emphasized that they are moving from in-kind targeted assistance to cash assistance, so that targeted households have the option to choose what they want to buy and consume. During the COVID-19 pandemic, results from the 2019 FNG analysis helped the WFP to lobby the government at national level to include fortified rice in open-market sales at a subsidized price for lower-income households, and to pilot programs to inform national social protection programs. In Cox's Bazar, they adjusted food rations and provided fortified high-energy biscuits and super cereal. To counter international supply problems, they explored local production of nutrition commodities.

Cost and affordability of healthy and nutrient-adequate diets: Impact of COVID-19 pandemic and data needs for design of interventions to protect the most vulnerable

The question of food security in terms of the cost and affordability of nutrient-adequate diets was addressed in this session chaired by Jane Badham, JB Consultancy.

> **"Existing food systems and assistance programs do not fulfill long-standing aspirations for global food security"**

Anna Herforth, Harvard TH Chan School of Public Health, said it is important to monitor the cost and affordability of nutrient-adequate diets in order to design response options. Healthy diet monitoring metrics are needed, and because nutrient-rich, non-staple foods tend to be high-cost, there is need to invest in more affordable food sources. She emphasized the need during emergencies to protect access to nutritious foods because any disruption and deprivation may have long-term consequences, especially in vulnerable populations. Herforth noted that existing food systems and assistance programs do not fulfill long-standing aspirations for global food security. Before COVID-19, more than 3 billion people, mainly in sub-Saharan Africa and Southeast Asia, could not afford a healthy diet, and 1.5 billion of them could not afford a nutrient-adequate diet as recommended by national dietary guidelines.[35] Three diets were described: the energy-sufficient (US$0.79 per day), nutrient-adequate (US$2.34 per day) and healthy (US$3.75 per day) diets. On average, the cost of a nutrient-adequate diet is nearly 63 percent of the cost of a healthy diet. Herforth also noted that changes in affordability during the COVID-19 pandemic resulted in a 17 percent increase (+220 million) in people who cannot afford a nutrient-adequate diet, resulting in more and more households getting further from the affordability line for nutrient-adequate diets. Herforth highlighted the fact that because of the magnitude of the non-affordability gaps, poverty lines may need to be adjusted if we as a community are serious about food security.

De Pee showed how a food systems approach can be used to assess the impact of COVID-19 on nutritious diet accessibility. Consideration of the characteristics of food systems in fragile settings should be considered when designing a response to mitigate the impact of non-affordability of healthy diets. De Pee emphasized the need to look not only at the proportion of people who cannot afford a diet but also at the gap – i.e., by how much they fall short of being able to afford the diet. She highlighted that the cost of a healthy diet sets an economic benchmark at which people can afford to get a healthy diet. This economic benchmark helps in understanding the extent to which the needs of people can or cannot be met, and what kind of support is required to get people closer to meeting a healthy diet. She presented results from the FNG assessment in East Africa. During the pandemic, there was a 10 percent increase in costs in Burundi, and a 15 percent (rural) and 12 percent (urban) increase in Rwanda. In Uganda, the yearly increase of the COD was twice as high in April 2020 as in previous years, while an 11 percent increase from February to May 2020 was noted in Ethiopia. De Pee noted that the impact of COVID-19 on an essential diet was exacerbated by a greater loss of income in urban areas than in rural areas. She showed how scenario modeling can help to understand the proportion of people unable to afford a nutritious diet, where the vulnerabilities may be greater and where actions are required to protect the consequences of increased unaffordability of nutritious diets.

As presented by Aregash Samuel, Ethiopian Public Health Institute, lack of affordability in Ethiopia was already high before the COVID-19 pandemic. In Ethiopia, the cost of an energy diet (US$4.30 per month) is four times less than the cost per capita of a nutritious diet (US$16.60 per month). She noted that 93 percent of Ethiopian households can afford an energy-only diet and only 26 percent can afford a nutritious diet. Filipe da Costa, SUN Movement Focal Point Prime Minister Office, addressed the question of affordability of a nutritious diet. He highlighted that in Timor-Leste, the cost of an energy-only diet is 3–5 times less than that of a nutritious diet. He noted that one in four households could afford a nutritious diet, which costs ~US$177 per month.

In the panel discussion, de Pee and Samuel emphasized the need for concise country-based bulletins that can be used as advocacy tools in multisectoral environments. Numbers can be used for sensitization and to create awareness as well as for programming during emergency shocks. De Pee further suggested the need to engage civil society and the private sector, and to inform parliamentarians of the importance of nutrition. Finally, she suggested that we need to convince people at all levels and ensure everyone is aware of the importance and centrality of nutrition. Samuel mentioned that nutrition is not a one-organization task and that it is everyone's responsibility. De Pee also highlighted that, to cope with an increase in food prices and a reduced income, households increased their intake of calorie-dense food and reduced their intake of micronutrient-dense food; they also consumed less food away from home.[36] David Laborde, International Food Policy Research Institute, added that coping mechanisms during the pandemic included: the use of savings to stabilize intake, reduced purchase of perishable food, shopping differently and increased intake of cheaper calorie sources.

Emergency nutrition and nutrition in emergencies: Rethinking our approach in extreme cases

In this session, presenters showed how interventions can be adapted to effectively meet nutritional needs in the most extreme

cases. The session assessed how services can be adapted to prevent nutritional deficits in extreme contexts (e.g., humanitarian emergencies), and how services in more developmental contexts can be adapted to routinely care for children with extreme nutritional deficits (e.g., wasting).

Luz Tagunicar, Department of Health, Government of the Philippines, presented the Philippine Integrated Management of Acute Malnutrition (PIMAM) program. The Philippines is a disaster-prone country, and wasted children are at a higher risk during times of disasters and emergencies. During the integration of PIMAM, challenges included the decentralized health system in the Philippines, the change in local chief executives and legislators every 3 years, other health programs competing with PIMAM for national funding, and a lack of wasting data disaggregated by province or municipality. The challenges faced during scale-up were reporting delays in the procurement of, and delivery of, community-based management of acute malnutrition (CMAM) commodities and the delayed approval of moderate acute malnutrition guidelines in 2017. A rigorous consultation and data collection process at all implementation levels was conducted in 2018. To counter challenges faced during scale-up, a bottleneck analysis for PIMAM was initiated in 2019. Two laws were passed while CMAM was being scaled, thus ensuring sustainability of CMAM within the healthcare system. Despite the many challenges, the PIMAM program managed to reduce the prevalence of wasting from 7.1 percent in 2015 to 5.6 percent in 2018. Lessons learnt include: severe acute malnutrition and moderate acute malnutrition guideline development must go hand in hand, as limitations in one will affect implementation of the other; and because PIMAM is a multisectoral program, it is paramount that stakeholders are involved in the development process as early as possible. Tagunicar pointed out that comprehensive stakeholder consultation can be a long and drawn-out process, but that it is vital to get the support and collaboration of all stakeholders.

Mohamed Yattara, Helen Keller International, presented the results of the PROMIS project conducted in Mali and Burkina Faso. In children aged 6–23 months, the aims of the study were to investigate if integrating a preventive intervention package (small-quantity lipid-based nutrient supplements [SQ-LNS]) into a platform for screening and treating acute malnutrition increased screening coverage and treatment coverage. The study also aimed to investigate whether the preventive intervention package reduced the prevalence and incidence of global acute malnutrition as well as child anemia, improved infant and young child feeding practices, and led to better child linear growth. The study revealed a lack of improvement in the coverage of treatment for acute malnutrition, which could be due to the many barriers to seeking treatment at health facilities. There was a program difference between Burkina Faso and Mali, which could reflect variations in the potential to benefit versus the potential to respond as well as differences in the management of infections and inflammation in young children. Yattara concluded that the preventive package implemented in PROMIS was an important motivator that helped to improve participation in preventive counseling and services. In addition, SQ-LNS had an important impact on child growth and anemia. He noted, however, that further efforts are needed to strengthen the use of CMAM.

> **"Further efforts are needed to strengthen the use of community-based management of acute malnutrition"**

Saul Guerrero, UNICEF, presented on UNICEF's new integrated, systems-based approach to addressing wasting in all contexts. The systems approach to nutrition aims to make national systems better equipped, and more accountable, for improving the nutrition of children, adolescents and women, and for addressing malnutrition in all its forms. He highlighted that during the past 10–15 years, stunting and overweight have been reduced but the proportion of the world's children who are wasted has remained persistently high. Guerrero suggested that this is due to the unsustainable approach of treating wasting only in humanitarian and emergency settings. He highlighted that the increased number of wasted children results in an imbalance between the need and the financial resources available. In 2019, UNICEF started to shift their approach to wasting towards prevention. This preventive approach will be possible if there is an improvement in early detection together with the optimization and simplification of treatment protocols for child wasting. To this end, on 18 September 2020, UNICEF and WHO agreed to update global and national guidelines on child wasting by the end of 2021 and 2023, respectively. These updates are expected to lead to an increase in demand for RUTF. UNICEF will therefore support governments to determine demand based on the number of wasted children at the greatest risk of dying, strengthen supply chain systems, and increase domestic and long-term financing for RUTF. To address the financing of RUTF, UNICEF donors and partners will set up a multi-donor Match Fund focused solely on RUTF, expand UNICEF's Bridge Fund for RUTF and provide support to 10 priority countries for supply chain strengthening.

What's the value proposition? How to engage new partners along the value chain for micronutrient nutrition outcomes

In this session, presenters showed the importance of attracting new partners into the nutrition value chain as well as ways in which to engage them. In addition, presenters showed how to successfully leverage social protection systems, the retail sector, technical partners and innovation platforms.

In his presentation, Paul Newnham, SDG2 Hub, noted that the ease with which information is shared and consumed through social media often results in competing claims and vested interests. He noted that it is not only vital that new partners should be engaged in the micronutrient value chain, but also that the nutrition messaging should be credible, understandable, relatable and context-specific. He suggested four areas to consider for strengthening communication across the value chain: (1) clear and consistent messaging, (2) information must be context-specific, (3) investment in the rollout of communication, and (4) language that people can understand.

Kalpana Beesabathuni, *Sight and Life*, presented on the engagement of new partners through competitions such as the Elevator Pitch Contest. From running the contest for several years, five learning experiences have been discovered: (1) investment in young entrepreneurs is important, (2) connecting youth with multidisciplinary experts improves their chances of success, (3) it is better to frame the competition around a specific need, (4) the pitch format compels innovators to focus only on the key features required to build, pilot and scale-up solutions, and (5) the contest offers an environment for collaboration.

Janosch Klemm, WFP, presented on how cash-based transfers (CBT) can contribute to improving micronutrient intakes. He showed the different types of cash programming, and how to conceptualize the value-add of CBT within a food systems framework, for example using market functionality assessment, needs estimation, modality comparison and gap analysis. He gave the example of the social protection program (PSNP) in Ethiopia.[37] To conclude, he said: "It's important to ensure that a nutrition objective is included in CBT programming. When transfer amounts are calculated, there is a need to reflect nutrition and modality choices. Include nutrition-sensitive targeting criteria for vulnerable individuals. Assess the market situation from a nutrition perspective, including retailers' interests, then consider what households prefer and how they utilize the transfer. Lastly, use social behavior change (SBC) models to support community engagement, empowerment, gender, and demand creation to make the most of the CBTs."

David Cummings, Partners in Food Solutions, presented on their aim to expand and increase the competitiveness of the food processing (forgotten middle) sector by linking food businesses that need technical/business assistance with cooperative volunteers. This is because food processors are the economic engine that provides markets for the farmers and provides affordable and nutritious foods for the consumers. Strengthening the processing sector improves the whole system, and thereby helps programs such as fortification. Cummings gave the example of the Strengthening African Processors of Fortified Foods (SAPFF) program, which aims to improve the compliance of mandated food fortification regulations in Nigeria, Kenya and Tanzania. With the help of corporate volunteers, this program builds processor commitment by utilizing the Trojan Horse Change Model.

Solutions to engagement with the private sector (small and medium-sized enterprises) to invest and support high-quality foods

Small and medium-sized enterprises (SMEs) are essential for the provision of affordable, safe and nutritious food, but the policy environment does not usually provide the required incentives for them. Exploration and creative solutions with SMEs can set a transformative agenda to increase the demand for, and supply of, nutritious foods for all. In this session chaired by Patrizia Fracassi, Food and Agriculture Organization, policies, incentives, enablers and barriers (including market failures) to support investment and the production of safe and nutritious foods in an ethical and sustainable way were addressed. This session also looked at what has worked and how these successes can be scaled up.

> **"SMEs are essential for the provision of affordable, safe and nutritious food"**

Uduak Igbeka, Global Alliance for Improved Nutrition, noted that SMEs are the backbone of the food system in Africa. Igbeka presented results from a rapid online assessment conducted in 17 countries in May 2020 to determine the impact of COVID-19-associated control measures on businesses and SME support needs. The survey revealed that lockdown measures, while necessary, had negative effects on access to safe nutritious foods. The measures reduced production, increased food prices, limited access to markets, and resulted in food waste/losses and disruption of the supply and distribution chains, all of which ultimately impact consumption. Igbeka recommended that governments should support food systems in production sectors and SMEs by providing tax breaks for input and food production. Productive capacity can be facilitated through grants to SMEs or subsidies, lower interest rates, or policies that facilitate or incentivize investment. In distribution, governments and other stakeholders can support market links for SMEs that provide nutritious food. Support initiatives will result in the reduction of food loss and waste, technology adoption and minimal disruptions in the distribution chain. For import countries, trade disruptions should be minimized, as this will affect access to food. In retail, market links can be established between nutritious food-producing SMEs and community or government feeding programs to provide safe nutritious food to vulnerable populations. In addition, raw materials suppliers and processors can partner with logistics providers and retailers to ensure that food is kept on the move in order to reach low-income consumers. In conclusion, Igbeka recommended that governments and other development partners should take steps to support these crucial yet vulnerable SMEs, and to ensure that they remain in a position to provide nutritious, safe foods in the future.

Daniel Amanquah, *Sight and Life*, presented on the OBAASIMA seal, which was created as a trusted symbol for fortified foods in Ghana, in an attempt to increase the availability of, and access to, affordable, nutritious fortified foods. He noted that in order to create demand, deep consumer knowledge is required. In Ghana, the key component of demand creation for particular products was good branding that was grounded in the local context. To create interest in the fortified products and increase demand for them, the OBAASIMA scheme conducted above-the-line teaser campaigns on digital platforms and ran below-the-line campaign market activation programs. Amanquah also noted that to create an effective demand activity, there must be a consistent supply of products on the market.

Maya Stewart, Lenziemill, presented on how to create a sustainable value chain in the poultry industry through the egg hub model. In this integrated model, Lenziemill works with smallholder farmers to achieve commercialization. Lenziemill provides a holistic cycle whereby the ecosystem works flawlessly, and results in the farmer, processor and consumer all being content. They use an innovative business model to organize smallholder farmers into groups of five with a 3-year break-even. These farmers receive training, extension services, high-quality input and consistent market support. The support helps smallholder farmers because they usually cannot compete with commercial farmers on quality, price and efficiency of production. Through the program, smallholder farmers have increased their flock sizes and turnover, and increased their income as a result. Stewart noted the challenges faced by Lenziemill during the pandemic. As in most organizations, core activities were disrupted, and in order to survive uncertainties, business decisions had to be made quickly and realistically. Fortunately, they managed to transition into shift operations and lobbied the Malawian Government to ensure that their business was considered an essential service. Transition was easy, as the system was already in place. The lessons Lenziemill learnt were that SMEs should be open to new ideas and learn from other examples. Stewart remarked that sustainability should make room for dynamism: what is sustainable today might not be sustainable tomorrow.

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TRACK 5

Food Systems

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Introduction

COVID-19 and food systems

The COVID-19 pandemic has negatively affected the ability of current food systems to provide nutritious food to populations around the globe. The pandemic has influenced all sectors that are part of the food system (agriculture, nutrition, health, transportation, education), and triggered a global economic and social crisis. The economic collapse is destabilizing people's income and increasing food prices. Moreover, global lockdowns have led to food systems disruptions by reducing the affordability and accessibility of healthy food. Likewise, social protection mechanisms such as school feeding programs and antenatal care services are being interrupted.

The impact of the COVID-19 pandemic on food and nutrition security is enormous. The most recent projections by the Food and Agriculture Organization (FAO) indicate that an additional 83–132 million people will suffer from food insecurity as a direct consequence of the current pandemic.[1] The use of a food systems approach is key when estimating the impact of COVID-19 on people's nutritional status. Data from economic, health and food systems services are being brought together by numerous experts to fully understand the impact of the pandemic on people's health and wellbeing. A systems approach is essential to understand how to best mitigate the short-, medium- and long-term consequences of the current pandemic on people's nutritional status, and how to get back on track to meet the 2030 SDG agenda.

"Food system transformations to fight micronutrient malnutrition are high on everyone's agenda"

Insights and challenges from the Micronutrient Forum 2020 CONNECTED conference

The complexity of food systems with their numerous players and the dynamic linkages between sectors is not easily represented in a conference. However, there is no doubt that food system transformations to fight micronutrient malnutrition are high on everyone's agenda. The UN Food Systems Summit is approaching fast, and a couple of takeaway messages should be kept in mind when moving the food systems agenda forward.

First, there are no magic bullets. Food systems are complex, diverse and highly context-specific. There is no single solution or intervention that will transform 'the' food system. Multisectoral programs are needed to implement and integrate simultaneous interventions in a specific context. Leaders and decision-makers need to be prepared for this task.

Second, we need to work together. Nutritionists alone cannot fix failing food systems, and neither can agronomists, economists or climate experts. Also, governments cannot do it alone, and neither can civil society or the private sector. However, by combining our knowledge, skills and expertise, it is possible to tackle the complex and multifaceted challenges we are currently facing.

However, as we move toward the UN Food Systems Summit, we should be aware of certain challenges that remain. These include, for instance, micronutrient malnutrition related to the rising levels of overweight and obesity around the world and the affordability of healthy diets. Although these challenges were recognized by many, there were few discussions about practical tools, as well as examples of how to address these issues. In general, more attention to the translation of scientific knowledge into practical tools and concrete actions might facilitate the uptake of this knowledge by policymakers and other action-oriented players.

A major challenge when working within food systems is to be inclusive and to involve all stakeholders equally. Although the MNF CONNECTED conference engaged a wide range of stakeholders with different backgrounds, the presence of the less visible stakeholders in the food system should be recognized. These include representatives from the retail sector, the transportation sector and small and medium-sized enterprises (SMEs).

Moreover, an often-neglected stakeholder in the food systems dialogue is the consumer. During the conference, several speakers mentioned constraints and difficulties faced by the consumer. However, consumers are not yet fully recognized as active players in the food system, especially in low- and middle-income countries (LMICs). Emerging consumer consortia or associations should be acknowledged and integrated as soon as possible into the food systems conversation.

Lastly, when working with a food systems approach, one should be able to clearly identify the 'winners' and 'losers' of implemented actions in order to ensure that these actions achieve the desired outcomes. That is, overseeing all actors involved in a food system, their interrelations and the inevitable trade-offs that may exist might be challenging. It is therefore crucial to recognize who is benefiting from a certain intervention or policy, and who is not. This needs to be considered in both research and policymaking.

"Track 5 aimed to connect and inspire key experts all working toward a common goal: improved micronutrient status for all"

Aim of Track 5 and rationale

As stated above, current global challenges regarding malnutrition and other development goals call for integrated and multisectoral approaches that focus on the entire food system. Moreover, transforming the food system to address the current challenges will require many people working in nutrition to do things differently. **Track 5** of the MNF CONNECTED conference aimed to connect and inspire key experts all working toward a common goal: improved micronutrient status for all.

The broad and complex nature of food systems was well presented in **Track 5**, with presentations ranging from climate change to food environments for children and biofortified rice. For this reason, the report on this track was approached differently from those covering the other tracks. Rather than reporting on each of the different sessions, the overarching themes that emerged from **Track 5** were identified. These themes include: current gaps and challenges, key stakeholders, multisectoral linkages and innovations in food systems. By doing so, an attempt was made to refer to the latest insights and challenges in food systems thinking, from a systems perspective.

Food systems: Current gaps and challenges

Introduction

Our understanding of food systems is rapidly growing, and a broad range of stakeholders are committed to the positive transformation of these food systems. During the conference, speakers pointed out several existing gaps and challenges that hinder the development of healthy and sustainable food systems. These gaps relate to our current understanding of food systems and the enabling environment, to data, or to the policy/governance level needed to support and implement innovations.

However, the direction of this transformation and the priorities given to different elements within food systems vary. Moreover, food systems contain many elements and interconnections that we need to understand more deeply. Because of the complexity of food systems, all actors (and their diverse areas of expertise) are required to commit to this challenge.

"Several challenges hinder the development of healthy and sustainable food systems"

Challenges of current food systems

During the session 'Efficacy and effectiveness of food system value chain interventions,' Inge Brouwer pointed out that there is a broad agreement that current food systems are not sustainable. Moreover, despite many innovations and complex interventions designed to transform food systems, many challenges still need to be addressed. For instance, definitions of food system components, boundaries and interactions differ across stakeholders and sectors.[2] The priorities as seen from a nutritional point of view differ from those seen from an agricultural perspective. Furthermore, highly cited reports and frameworks often approach food systems from a supply (production)-, midstream (markets)-, demand (consumers)- or system (governance)-oriented angle. Few reports on sustainable food systems focus primarily on diet and nutrition.[3] This is a huge gap in the current work on food systems. Brouwer proposed that diets should, in fact, be the starting point of food systems analyses. This reversed analysis, from diet to impact, helps to better understand some of the key trade-offs. According to Brouwer, these trade-offs include: (**1**) healthy diets and consumer demand, (**2**) healthy diets and profitability, and (**3**) healthy diets and affordability.

Data and evidence

During the same session, Brouwer mentioned a gap in context-specific evidence for food systems interventions. According to Brouwer, very little evidence is available on the dietary impact of successful food systems innovations or interventions in low- and middle-income contexts. The main reason for this gap is the lack of rigorous evaluation of such interventions at the local level. Furthermore, for interventions that are successful in a high-income setting, we often do not know whether they are also effective in a low- or middle-income setting. Similarly, there is very little evidence of the potential of scaling these interventions and related challenges. This last point was confirmed by Francesco Branca, who emphasized the lack of monitoring within food fortification programs. According to Branca, this lack of data poses serious constraints to innovation and scale-up.

Another data gap hindering innovation was indicated by Mourad Moursi. He pointed out that in many LMICs the food composition databases are incomplete and outdated (or else completely absent). These databases are used in nutrition research to translate consumed food to the actual nutrient intake. Developing these databases is an intensive task, but with climate change altering the nutrient composition of foods, there is a huge need to update these databases. Similarly, Ashley Aimone called for more updated nutritional data collection in the light of the changing nutrient content of staple foods due to climate change. Aimone stressed the importance of collecting real-time data to assess nutrient alterations in staple foods. This data could aid the development of adaptation strategies and help evaluate the effects of climate change on nutritional issues.

During the on-demand session 'Measuring progress and impact of actions to improve food systems for nutrition,' Christopher Turner focused on evidence from food environment research in LMICs. He stated that during recent years global interest has grown in food environments and in drivers of food choices in response to the need for improved dietary and health outcomes.[4] This is reflected in the development of several conceptual frameworks for food environments. Despite the existence of these frameworks, there are many gaps in our knowledge and understanding of the food environment in LMICs. A systematic scoping review showed that food environment studies generally focus on overweight and obesity rather than undernutrition.[5] Also, food environment research covering the African continent appeared to be largely absent. We should improve theoretical concepts, study design methods and metrics to assess the food environment in LMICs. Improving the quality of food environment research will be critical to the design of feasible interventions to improve public health nutrition.

Finally, during the session 'How socio-economic factors influence dietary patterns and nutrient intakes,' it was suggested that dietary intake data is collected from a wider range of family members than is current practice. Jaya Jumrani discussed how collecting dietary data from only women and children fails to allow the detection of intra-household and food distribution inequities. Without fully understanding these inequities, it is difficult to target interventions that could ensure a healthy diet for all household members.

Despite the many data gaps, a significant amount of data is at our disposal. As pointed out by Aimone, it is important that this data is used, translated into knowledge and delivered to decision-makers who can take concrete actions where needed.

"Despite the many data gaps, a significant amount of data is at our disposal"

Food systems governance

One of the identified gaps in food systems governance became apparent in the session 'Exploring the intersection of climate/environmental change, food systems, nutrition and health.' During this session, Wolfgang Pfeiffer discussed conventional plant breeding with the purpose of raising mineral and vitamin densities in staple food crops. He stressed that biofortification should be mainstreamed into the food system to improve the nutrient density of staple crops, and mentioned a successful example from India. Mandatory iron and zinc levels for a pearl millet variety were implemented by the Government of India in March 2018.

According to Pfeiffer, the biggest challenge in mainstreaming biofortification into the food system is not on the technical side (once the 'parent' plants are biofortified, the offspring will also be biofortified), but rather on the policy side. He stressed the importance of investing in biofortification and advocating scale-up at all levels. Biofortification should be included in public and private policies and programs. Finally, when aiming to mainstream biofortification into the food system and to improve micronutrient density, a regulatory framework for biofortified crops is necessary. Donald MacKenzie additionally emphasized that technical solutions and a supporting policy environment are necessary for the development of climate-resilient crops. Climate change is affecting food production as a result of floods, droughts and other natural disasters, as well as affecting the nutrient content of crops. Lastly, he explained that only four breeding cycles are left to develop nutrient-dense and climate-resilient rice varieties before 2050.

During the same session, Adegbola Adesogan pointed to a gap in policy that might improve micronutrient availability in LMICs. He discussed the role of animal-source food in meeting micronutrient requirements, especially in LMICs. Animal-source food production in Africa remains low, while the evidence of the importance of this food source for many nutrition outcomes in children is growing. Adesogan recommended the promotion of sustainable intensification of livestock production in LMICs, using existing strategies. For instance, feeding seaweed to cows results in a 50 percent decrease in methane production.[6] Efforts in (bio)fortification have been effective, but at the same time we should promote the production and consumption of animal-source foods in LMICs. This will require animal-source food subsidy programs. For instance, programs promoting the consumption of animal-source foods (especially milk) have enriched children's diets in high-income countries for decades, and similar efforts are urgently needed in LMICs.

Brouwer pointed to the need for food systems governance. Food systems are complex, and interventions are generally targeted toward a single component of the food system or else aim to improve a single specific factor (i.e., behavior change, diversified agricultural production). Food systems governance should create

the possibility for coherent, connected and simultaneous interventions, addressing many components of the food system at once to create a multiplier effect.

> **"Food systems governance should create the possibility for coherent, connected and simultaneous interventions"**

Everyone has a role to play

Introduction

The MNF CONNECTED conference enabled a wide range of stakeholders with different areas of expertise to come together to address the multisectoral challenges of micronutrient deficiencies. Bringing stakeholders together is the first step to meet this challenge. In addition, the Food Systems Summit and Nutrition for Growth events are expected to strengthen partnerships and engage more stakeholders to transform the food systems. Experts from multiple disciplines therefore need to work together. Multistakeholder and multisectoral partnerships need to amplify food system transformations that are inclusive of the most vulnerable people and that also ensure healthy and sustainable diets, for people and planet.

As important as celebrating successes is the ability of all stakeholders to acknowledge and communicate failures. Sharing failures with relevant stakeholders might speed up our learning process and greatly contribute to achieving SDG2: Zero Hunger.

According to Sufia Askari (CIFF), maternal nutrition is one of the major challenges of the nutrition community in which more progress needs to be made. In fact, the inability of the nutrition community to scale up maternal micronutrient supplementation (MMS) was pointed out as a failure by Askari. Despite MMS being more effective than iron and folic acid (IFA) supplements, IFA remains the most delivered supplement. Askari referred to Jim Kim, the World Bank's President, as saying that: "The world has invested too much in what to deliver and too little in how to deliver it, with the result that 'it' often fails to reach and benefit people." Askari closed her speech by stating that as a scientific community we are ready to shift our focus toward implementation strategies based on the abundance of data and knowledge we have acquired.

Multisectoral experts

During the live session 'Strengthened food systems and food environments for children,' several experts with different backgrounds shared concerns about children's diets. The session, facilitated by Corinna Hawkes, involved different stakeholders and discussed how to integrate child nutrition into the food system instead of addressing it as a separate component.

During the live session 'Transforming the food system for nutrition while progressing on the unfinished agenda of nutrition-specific actions,' the speakers highlighted two key concepts regarding stakeholder engagement. Askari opened her speech by reminding the attendees of the need to celebrate the successes achieved so far. In fact, 59 million fewer children were stunted in 2019 compared with 2000. The numbers of stunted children are still unacceptable. However, emphasizing and acknowledging the progress made can motivate stakeholders to be further engaged and to address this multisectoral global burden.

Furthermore, Purnima Menon (IFPRI) underlined the importance of stakeholders sharing the same goal. We aim to provide diverse and nutritious food for every human being, every meal and every day of her/his life. From this long-term goal, we should extrapolate simple actions that can be achieved by the various stakeholders. Menon provided an example from India. The Indian National Nutrition Guidelines were recently translated into 'MyPlate guidelines.' This easy format can better support people and stakeholders in everyday food choices.

Public–private partnerships

Public–private partnerships represent a key pathway to help deliver sustainable and healthier diets.

Hana Yemane Wodajo presented a case study from Ethiopia on how to leverage public–private partnerships to deliver healthy diets for children and adolescents. Wodajo emphasized how purchasing power and consumer behaviors are changing because of increasing urbanization. For instance, in Ethiopia 83 percent of food is purchased in urban areas, whereas only 43 percent is purchased in rural areas. Local SMEs are involved in 70–100 percent of total food sales in urban settings. These local SMEs therefore play a crucial role in the food system that cannot be neglected. We should embrace them as contributors to healthy dietary solutions. Engagement with SMEs should aim to reduce sales of unhealthy food as well as to provide opportunities to build public–private partnerships that support the delivery of healthy food. The main challenges that emerged from the case study included the differing priorities and timescales between private and public sector partners, and the low preparedness on the part of the Ethiopian Government to provide technical assistance to SMEs.

Lastly, Alan de Brauw discussed the importance of trust between stakeholders of the food systems. Lack of trust on the part of consumers can inhibit the purchase of healthy food. For instance, the trade-off between 'safe' processed food and 'unsafe' fresh food can affect people's food choices.[7] Among producers, trust can influence input purchases, certification schemes, methods of selling crops and choices regarding which foods to produce. Interventions should therefore increase and ensure

trust across the food system, especially regarding the output of the markets to achieve healthier diets.

> **"Local SMEs play a crucial role in the food system that cannot be neglected"**

4. Connecting the silos: How multisectoral linkages could transform food systems

Why do we need multisectoral linkages?

Nutritional problems are broad and complex, and without addressing the underlying determinants of nutrition we will not achieve SDG2: Zero Hunger. These underlying determinants of the many forms of malnutrition are, for instance, embedded in agricultural, climate and economic sciences. As pointed out by Daniel Raiten (NIH): "How do we make sure that while advancing on one issue we do not unintentionally worsen another? This is a challenge that requires a multisectoral approach."

The importance of linking different sectors that have diverse perspectives on malnutrition became apparent in the session 'Biofortification from discovery to delivery: A case study of rice for Bangladesh.' The session provided both a nutritional and an agricultural perspective on the potential of rice fortification. Two researchers, Joanne Arsenault and Rita Wegmüller, shared their findings on the effects of biofortified rice on either nutrient adequacy or plasma zinc concentration. Overall, rather modest effects of iron- and/or zinc-fortified rice on nutrient inadequacy or plasma zinc were found. However, Khairul Bashar showed the elaborate implementation and delivery strategies for zinc-fortified rice that have been implemented in Bangladesh since 2013. These efforts appear to be based on the beneficial agricultural properties of zinc-fortified rice, such as early maturation and high yields, rather than on the impact on micronutrient malnutrition in the population. This example demonstrates that stakeholders might approach the same problem from a different angle, and shows the importance for these stakeholders to coordinate their efforts to tackle malnutrition in the most effective way possible.

What kind of linkages became apparent?

Nutrition – agriculture

Linkages between nutrition and agriculture were mainly discussed during the on-demand session 'Agriculture and nutrition: recent learnings and future directions.' The objective of this session was to present new evidence on how agricultural interventions across the food value chain can improve micronutrient status and other nutritional outcomes.

Marie Ruel shared the findings from the International Food Policy Research Institute (IFPRI)'s review (2018) on nutrition-sensitive agriculture.[8] On the basis of this review, she concluded that, although lots of learning is still to be done, nutrition-sensitive agriculture programs do work. Such programs improve a variety of dietary and nutrition outcomes, especially when programs also include behavior change communication, women empowerment, WASH or micronutrient-fortified product components. She recommended that programs should focus on increasing the intake of high-quality diets for all household members (rather than focus on childhood stunting), and that they should be carefully tailored to the local context.

The need for more nutrition-sensitive agriculture was also expressed by Ismail Cakmak. He stated that: "Crop production and farming systems are not designed with the aim of improving human health." Consequently, current crop production and farming systems fail to meet human needs for micronutrients, and there is a need for them to become more nutrition-sensitive. As stated by Cakmak, human-induced depletion of nutrient reserves in the soil might be responsible for micronutrient deficiencies in populations, especially in African countries.[9,10] Cakmak discussed the HarvestZinc program, which explores the potential of various micronutrient-containing fertilizers to increase micronutrient concentrations in various staple crops. Ultimately, this approach should contribute to an increased dietary intake of micronutrients. Foliar zinc fertilization of wheat (involving the application of liquid fertilizer to the leaves of the crop) was found to positively affect grain zinc concentrations in the crop.[11] Furthermore, soil fertilization with nitrogen was found to significantly increase zinc and iron concentrations in wheat grain.[12] This effect has also been demonstrated in field experiments in China and Turkey.[13] Cakmak concluded that to combat malnutrition, hidden hunger programs should be complemented with plant nutrition solutions.

Gordon Prain discussed the contribution of urban agriculture to nutrition. He described how, in several large cities in Africa, women are found to be important players in urban agriculture. In five large cities in Latin America, sub-Saharan Africa and Asia, own-food production through urban agricultural practices was perceived to contribute to household food security. Respondents from these cities indicated that own-food production saves money for food purchases and provides extra food.[14] However, there seems to be an ideological opposition between 'urban' and 'agriculture.' Urban and rural areas are subject to sectoral policies and divided mandates of ministries and donors. This is affecting urban food production and the potential of urban agriculture in general.

Nutrition – climate

The effects of climate change on nutrition and health were widely discussed during two live sessions. As pointed out by Kristie Ebi,

rising CO_2 concentrations in the atmosphere affect all forms of malnutrition. Although CO_2 promotes plant growth, it alters the nutritional quality of many crops by increasing the proportion of carbohydrates and reducing the proportion of protein and essential micronutrients. She presented a study that estimated the global availability of dietary iron, protein and zinc in 2050, while considering the effects of climate change. A decrease in the availability of protein (19.5 percent), iron (14.4 percent) and zinc (14.6 percent) in 2050 was predicted.[15] Besides causing a decrease in nutrient density, climate change could also increase food safety risks. For instance, elevated soil temperatures increase arsenic uptake in rice. The challenge is to manage the decline in nutrient density, and Ebi presented four options that could help to achieve this: (1) biofortification, (2) dietary diversity, (3) oral nutritional supplements, and (4) postharvest fortification. Finally, the importance of maintaining a focus on the quality of children's diets was stressed (manuscript in preparation by Ebi and colleagues).

Stuart Gillespie (IFPRI) presented a recent study that mapped the relationship between climate change, equity and nutrition outcomes.[16] In this study, the trends in interdisciplinary literature were mapped, equity dimensions were characterized (fairness, justice, inclusion) and the findings were applied to a conceptual framework. As stated by Gillespie: "We don't know enough on how the different dimensions of equity (especially justice and inclusion) affect the relationship between climate and nutrition outcomes. This is something we need to know when responding and adapting to climate change from a nutritional point of view."

"In many African and Asian countries, the cost of the EAT–Lancet diets is not affordable for most of the population"

Nutrition – economics

In the session 'How socio-economic factors influence dietary patterns and nutrient intakes,' the key economic factors influencing dietary patterns were discussed. Derek Headey (IFPRI) explained the relationship between income and prices as drivers for food consumption patterns. A meta-analysis of studies in Africa (Colen et al. 2018) showed that as income increases, the consumption of animal-source foods is likely to increase as well. However, demand for fruits, vegetables and nuts only weakly increased with rising income.[17] This means that income increases are not necessarily followed by an increase in nutritious food intake. Headey referred to a study by Hirvonen and colleagues demonstrating that in many African and Asian countries, the cost of the EAT–Lancet diets is not affordable for most of the population, as presented in **Figure 5.1.**[18] Based on the relationship between income, food prices and food choices, Headey invited nutritionists to pay more attention to the relative costs of different foods and recommended diets. At the same time, Headey encouraged economists to rethink the poverty line and social protection strategies, based on the real costs of healthy diets.

Innovations in food systems

Introduction

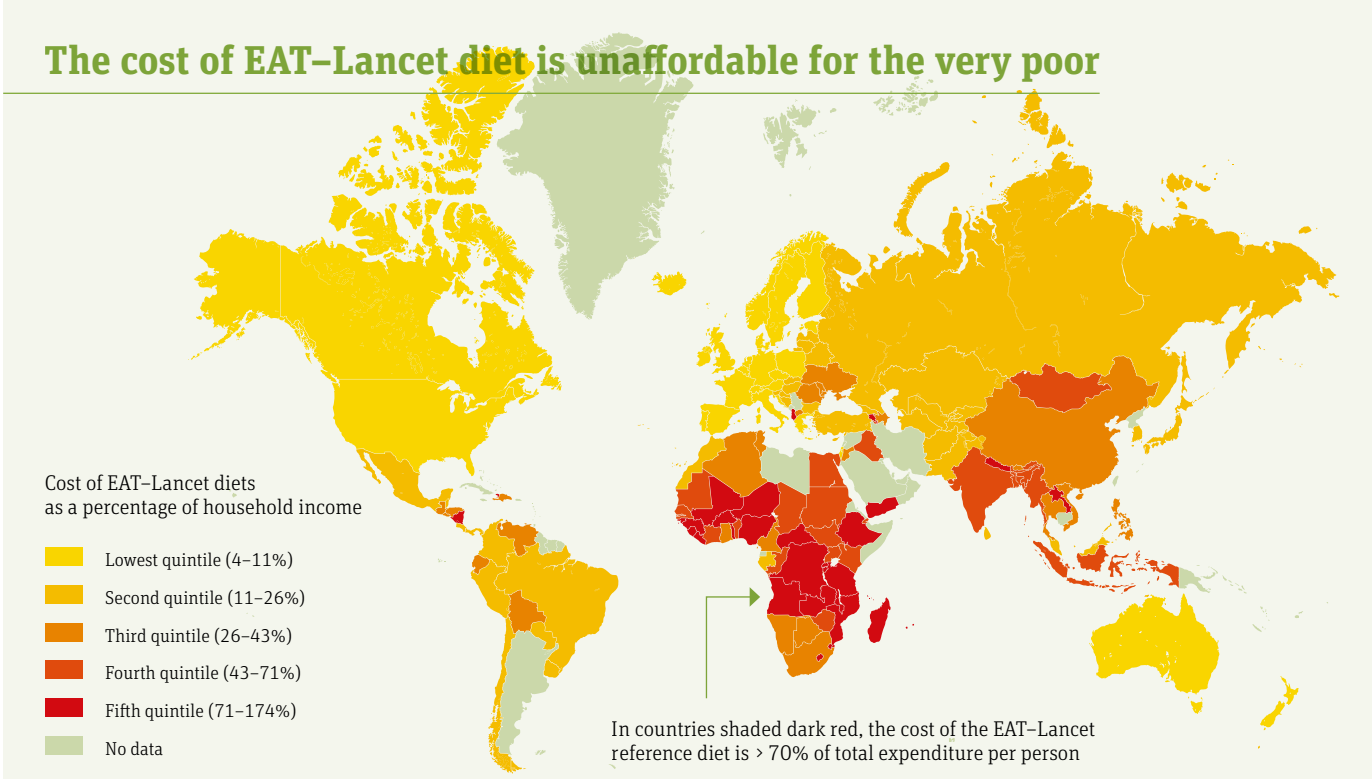
Innovations can appear in many forms, large or small. The conference saw a high interest in innovative frameworks, data, tools and indicators to accelerate progress among the stakeholders. It follows that innovations should always consider the possible trade-offs within the food system to avoid compromising the work of other actors. Innovations could fill existing gaps with new tools or methodologies, but could also simply serve to improve the existing programs, interventions or methodologies. In recent years, innovations have mainly focused on the food supply chains, aiming to increase production. However, the focus has since shifted, and it is recognized that innovations should aim to deliver high-quality and sustainable diets for all.

Key innovations for food system transformations

During the conference, the necessity of reaching out to vulnerable population groups emerged as a key part of the SDGs' strategies. Today, because of the global COVID-19 pandemic, the number of vulnerable people has sharply increased. It is estimated that in 2020 an additional 7 million children will suffer from acute malnutrition.

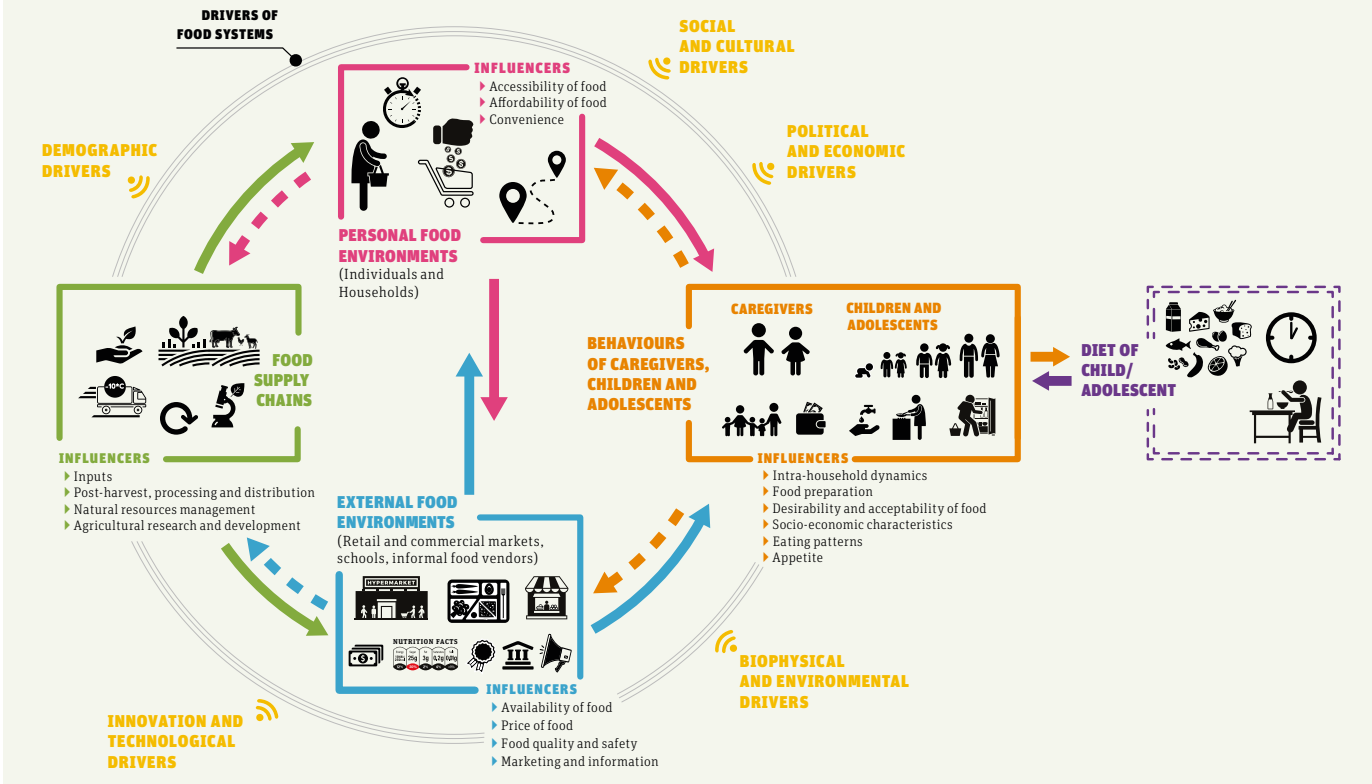
Children are a vulnerable group. In 2019, more than one in three children under 5 years old did not grow well because of the burden of some kind of malnutrition. Besides, at least one in two children suffered from hidden hunger.[19] During the session 'Strengthened food systems and food environments for children,' Roland Kupka explained the steps that led the United Nations Children's Fund (UNICEF) and the Global Alliance for Improved Nutrition (GAIN) to launch the innovative Innocenti Framework[20] (**Figure 5.2**). This conceptual framework sought to overcome the general lack of focus on the special needs of children and adolescents in food systems. The Innocenti Framework builds on the Agriculture, Nutrition and Health Academy's Food Environment Framework (2017)[21] with an additional determinant, the behavior of caregivers, children and adolescents. This particular consideration covers the specific influencers of children's and adolescents' diets. Overall, the Innocenti Framework better addresses the determinants of children's diets, thereby improving our understanding of the drivers of child malnutrition worldwide.

FIGURE 5.1: The cost of the EAT–Lancet diet*



*Presented by Derek Headey during the session 'How socio-economic factors influence dietary patterns and nutrient intakes'. Reproduced with permission.

FIGURE 5.2: The Innocenti Framework on food systems for children and adolescents*



*Presented by Roland Kupka during the session 'Understanding the determinants of child diets' and reproduced with permission of UNICEF

> "Only 18.9 percent of children worldwide meet the Minimal Acceptable Diet"

In the same session, Elizabeth Fox shared the latest data on child diets. Only 18.9 percent of children worldwide met the Minimal Acceptable Diet (MAD).[22] Fox pointed out the urgent need for food system innovations to match the special needs of children and adolescents, especially in two areas. The first refers to the peculiar dietary needs essential to satisfy healthy growth. The second relates to the dynamic and different interactions of children with the food systems, which are highly influenced by age group and the choices made by caregivers. Acknowledging the special needs of children and adolescents in the food system is the first step to accelerate innovations that should aim to build a food environment capable of delivering healthier diets for this vulnerable category. Fox highlighted some opportunities for innovations, which included raising awareness of marketing techniques and creating innovation to support the development of preferences for healthy food from the earliest years of life.

Lastly, Shauna Downs provided a package of actions required to create a child-centered food system. The novel six-step assessment tool includes questions (**Table 5.1**) and methodologies designed to achieve healthy diets that are affordable, appealing, available and aspirational (AAAA) in support of children's needs.[4]

Data and tools to accelerate innovation

Data is essential to spark innovation and transformations that address the multifactorial crisis (climate, nutritional, environmental). Currently, nutrition emergency responses caused by, for example, natural disasters are largely limited to focusing on the treatment of acute malnutrition rather than focusing on improving the diet quality of vulnerable groups, as described by Joan Matji. She presented innovative approaches implemented by UNICEF to address the consequences of climate change on nutrition. These included a social protection system to strengthen the resilience of mothers and children in Kenya, and a climate-informed country program approach in Madagascar. Moreover, Matji pointed out the need to improve the quality of diets by making use of a climate-informed approach. That is, past and future context-specific climatic trends need to be analyzed. This will increase the amount of contextualized data on the impact of climate change on food security, and will allow for more effective program design and decision-making.

> "The process of decision-making can be made more effective through the use of tools that present data in a clear and concise manner"

The process of decision-making can be made more effective through the use of tools that present data in a clear and concise manner. Some of these innovative tools were discussed during the conference. For instance, GAIN and Johns Hopkins University, in collaboration with partners, developed the Food Systems Dashboard. The dashboard combines data from multiple sources to help users visualize and understand different components of food systems worldwide.

Mourad Moursi presented two other new initiatives: the Global Diet Quality Project and the Global Diet Quality Score. Initiated by Harvard University, GAIN and the Gallup World Poll, the Global Diet Quality Project aims to monitor diets worldwide. The project will generate data and tools that facilitate routine, valid and comparable data collection on diets across different countries. The

TABLE 5.1: Steps to identify a package of actions to create a child-centered food system[4]

Steps	Assessment question
Step 1	What is the prevalence of underweight, stunting, overweight, obesity and micronutrient deficiencies in the population of concern?
Step 2	Which foods should child-centered food systems make more AAAA* to address the relevant forms of malnutrition, and which ones less so?
Step 3	Why are children eating, or not eating, these foods, and how does this relate to the food environment they are in?
Step 4	Taking account of these contexts, which aspects of food environments should be changed to make these foods more or less AAAA* in the short and long term?
Step 5	What incentives and disincentives are needed in the food supply chain, and where, to create healthier food environments for children?
Step 6	What is the package of mutually complementary actions, and what are implementation opportunities and challenges?

*AAAA: affordable, appealing, available, aspirational

Global Diet Quality Score, developed by Intake and partners, is a new metric of diet quality that is appropriate for use in LMICs. Both initiatives integrate the relationship between diets and diet-related noncommunicable diseases.

Furthermore, Rahul Rawat (BMGF) stressed how we need tools to assess and optimize the cost-effectiveness of interventions in the food systems and health arena. The example of the Optima Nutrition tool (launched by the World Bank in 2019) was mentioned. This tool can assist governments by providing practical advice on how a given budget can be allocated across programs and geographical regions to minimize malnutrition.

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Second Global Summit on Food Fortification: Launch event

Food fortification and biofortification are two important public health strategies to address micronutrient malnutrition. With COVID-19 further compromising people's access to healthy diets, the scale-up of food fortification and biofortification has become essential in order to deliver essential nutrients to populations. The aim of this event was to mobilize high-level political will to pursue the unfinished agenda on large-scale fortification and biofortification, and to show high-level attention and commitment to the fortification agenda across sectors and stakeholders.

Fortification: A food system game-changer hiding in plain sight?

Andreas Blüthner (BMGF) set the scene with some opening remarks during the first panel of the event. He emphasized that this event was a moment to celebrate large-scale food fortification. Governments and their partners have achieved great successes since the introduction of food fortification programs in the 1920s, as is reflected by the fact that ~130 countries have mandatory salt fortification, ~80 countries have mandatory wheat fortification and 35 countries (and counting) have edible oil fortification. However, challenges surrounding regulatory frameworks, the delivery of fortified products to the 'base of the pyramid,' and compliance and quality control remain. The large-scale food fortification agenda is still unfinished and, especially in times of COVID-19, it is important to highlight and rethink this agenda.

The panel members each presented a short statement, addressing many aspects of the unfinished agenda of food fortification. One aspect that several panel members pointed out was the importance of social protection programs (e.g., school feeding programs), which reach 1.8 billion people worldwide. There is a great opportunity to link social protection programs with food fortification programs. Furthermore, it was stressed that to further impact populations, food fortification should be rolled out on a large scale. Axton Salim (Indofood) stressed that food fortification has been around for nearly 100 years, and that it is time to speed the process up. The experience in Rwanda with fortified high-iron beans was mentioned many times as a successful example.

When asked what, in one word, is needed to scale up food fortification, the panelists mentioned the following aspects: (**1**) leadership (at governmental, private and societal level), (**2**) political will, (**3**) contributions from the private sector, (**4**) partnerships, and (**5**) diversifying the food basket. Lawrence Haddad (GAIN) concluded that: "Successful scaling requires constant innovation," a theme that was further elaborated on during the second panel of this event.

Pursuing the unfinished fortification agenda: Opportunities and innovations

This panel was moderated by Saskia Osendarp, and discussed the key opportunities presented by large-scale food fortification and biofortification. Where is more investment and more attention needed to overcome barriers and maximize impact?

Penjani Mkambula discussed who should invest in the scale-up of fortification. He pointed to two main stake-

holders: national governments and their partners, and the private sector. That is, investments from national governments and donors are necessary to get a project started. Investment should be made in monitoring and evaluation (M&E), digital technologies, standards and regulations, and overall program management. As a program matures, the biggest investor should be the private sector. It is seen that generally 90 percent of the ongoing program costs are borne by the private sector. These costs relate, for instance, to the procurement of premix and quality control.

Alok Ranjan shared the key enablers influencing the effectiveness of innovations in food fortification. These included: (1) social safety net programs, (2) coordination between partners in the entire development sector, and (3) a government approach focusing on engaging, exciting and enabling the involved stakeholders. He mentioned that although COVID-19 is a huge barrier to current programs, it can also be an enabler for the scale-up of food fortification. It forces us to rethink the system, especially regarding the use of digital technologies.

Ekin Birol shared innovative technologies, tools and mechanisms used by HarvestPlus for the scale-up of biofortification. These included: (1) mobile apps to enhance the spread of information among farmers, or to link farmers to input suppliers, (2) working with local SMEs and supporting them with capacity-building and financing opportunities, and (3) blockchain technology.

As a concluding remark, Osendarp stated that: "If you are stubbornly pursuing a dream of innovation, then you can overcome technical barriers, skepticism and funding challenges, and can impact the lives of millions." Haddad closed the panel by stating that: "Innovation, sometimes glamorous but often unglamorous, can help the scale-up of fortification."

A resilient food system for a time of crisis: The role of fortification

The final panel discussion of the event revolved around the role of national leadership in the scale-up of food fortification. This panel included high-level representatives from Bangladesh, the African Union, The Gambia, Mozambique, India, Nigeria, Indonesia and Kenya. The panelists represented a broad range of sectors, from industry to health and agriculture, and highlighted the importance of adequate nutrition and the efforts made in food fortification and biofortification. As mentioned by Josefa Leonel Correa Sacko, scaling up biofortification to mitigate malnutrition is a strategy endorsed by many African heads of state. The importance of national standardized food fortification guidelines was recognized by most of the panelists, and commitments and progress related to this matter were shared. As observed by Haddad: "The willingness of these leaders to navigate traffic is a telling indication of their commitment to this issue."

Haddad closed the session by raising the question of how food fortification and biofortification could be better integrated in the Nutrition for Growth Summit and the Food Systems Summit in 2021. How can we help governments to make strong commitments? Finally, he stressed that to move forward on the fortification agenda: "Everyone, no matter who they are or where they are, needs to show leadership."

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