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Supplementation: An Effective Approach for Improving Nutrition and Health

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Introduction: The burden of micronutrient malnutrition

One of the major challenges to public health is that of quantifying the extent of micronutrient malnutrition in order to inform policy and program on effective response options. A study published in 2013 by Muthayya *et al.* (2013) represents a significant effort to collate the available data on key indicators of micronutrient deficiencies from national representative surveys. The major data sources were the World Health Organization's (WHO) Vitamin and Mineral Nutrition Information System (VMNIS), Demographic and Health Surveys (DHS) and Multiple Cluster Indicator Surveys (MICS).

Using these data, two hidden hunger index scores were created; the first index is based on national prevalence of iron deficiency anemia, zinc deficiency, and vitamin A deficiency, while the second is based on the Disability Adjusted Life Years (DALYs) attributable to micronutrient deficiencies. These index scores were used to create the hidden hunger index maps, which highlight hidden hunger hotspots around the globe. The maps highlight the significant burden of hidden hunger in Sub-Saharan Africa and parts of South Asia. They can be used as an advocacy tool to support the scale-up of micronutrient interventions, and as a surveillance tool to track progress towards reducing the burden of malnutrition in these areas of the world (Figure 1).

The study also examined the correlation between the hidden hunger index and the human development index, and found an association suggesting that hidden hunger decreases while human development index increases, and vice versa. This finding is of particular interest, as it indicates that in order for nations to advance prosperity, they must tackle malnutrition, a powerful message when advocating for increased action in the area of micronutrient malnutrition.

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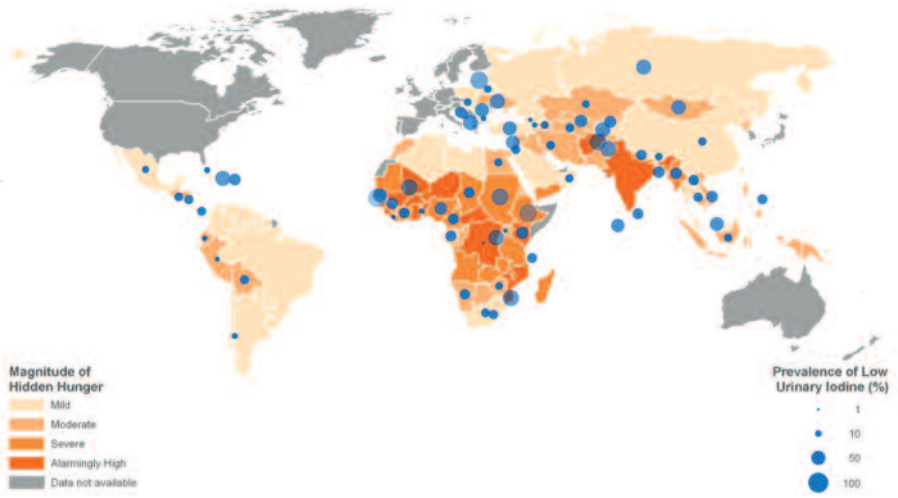

Figure 1. Global hidden hunger map (Muthayya *et al.*, 2013).

Strengthening evidence around the 1,000 days window

Since 2008, with the publication of the first Lancet Series on *Maternal and Child Undernutrition*, global consensus has been achieved that the period from a child's conception to his or her second birthday (often referred to as "the 1,000 days") represents a unique opportunity to ensure optimal outcomes on health and physical and cognitive development. When pregnant mothers and their infants and young children receive adequate nutrition in this critical period, they have a greater chance of surviving to their fifth birthday, and a lower risk of developing non-communicable diseases as adults. Some of the ways in which we can achieve good nutrition are through the use of micronutrient supplementation and fortification. As these interventions are relatively low cost to implement, they have the biggest returns on investment (see the chapter in this volume by Bjørn Lomborg on the Copenhagen Consensus).

Supplementation with micronutrient powders

Given that nutrient deficiencies usually coexist within the same populations, discovering innovative methods to tackle multiple micronutrient deficiencies simultaneously has been a priority for the nutrition field (Allen *et al.*, 2009). Since their original development in the late 1990s at the Hos-

pital for Sick Children, Toronto, Canada, the evidence around micronutrient powders (MNP) has advanced quickly.

MNP is a mix of vitamins and minerals that can be added to food just prior to consumption in the home, which is why it is also referred to as "home fortification". MNP improves the quality of the typically plant-based complementary food in developing countries, which is given to infants and young children who have very high micronutrient needs. This is typically accompanied by key messages to support optimal infant and young child feeding and caring practices. The product formulations can differ in terms of the number of micronutrients included; however, standard formulations usually contain 15 vitamins and minerals which are essential for a child's development and survival. One sachet is equivalent to 1 Reference Nutrient Intake (RNI) – the amount which will fulfill the nutritional needs of 97.5% of the target population. Thus, when 180 sachets are provided per annum, 50% of the child's micronutrient requirements over that 12-month period will be met by MNP.

A systematic review of complementary feeding by Dewey and Adu-Afarwuah (2008) found that the risk for anemia and iron deficiency was lower in children who received MNP, as compared to the controls [anemia OR: 0.54 (95% CI: 0.46-0.64); and that of iron deficiency was RR: 0.44 (95% CI: 0.22-0.86) for those using MNP compared with controls].

Subsequently, a Cochrane review conducted by De-Regil *et al.* (2011) found that MNP use was associated with a 31% reduction in anemia (RR 0.69, 95% CI 0.60-0.78) and a 51% reduction in iron deficiency (RR 0.49, 95% CI 0.35-0.67). It was noted that MNP was highly acceptable to mothers and children, there were fewer side effects with MNP than with iron drops, and the efficacy was not associated with the duration of the interventions (two, six or 12 months). However, both reviews suggested that more evidence was needed on the influence of MNP on malaria morbidity.

MNP and malaria interaction

Concerns about MNP use and malaria morbidity stem from the findings of a study conducted on the Island of Pemba, Zanzibar (Sazawal *et al.*, 2006). The community-based, placebo-controlled randomized trail provided prophylactic supplementation with iron and folic acid to reduce anemia risk. However, the study found an increase in both morbidity and mortality in the treatment group. Conversely, findings from Nepal providing the same supplements found no increase in mortality or morbidity in the treatment group (Tielsch *et al.*, 2006).

Following these studies, the WHO released a statement, which noted that untargeted iron supplementation is contraindicated, while targeted supplementation with concurrent protection from malaria and other infections was safe (WHO, 2007). Fortification programs and food-based approaches were deemed as being safe, but at that juncture home fortification with MNP held an unknown risk. However, in 2011 a revision of the evidence stated that MNP was safe for use (WHO, 2011).

Home fortification technical advisory group

The Home Fortification Technical Advisory Group (HF-TAG) is a global network comprised of organizations implementing or supporting the scale-up of home fortification programs. Comprised of United Nations (UN) agencies, non-governmental organizations (NGOs), manufacturers of home fortification products, and academic institutions, HF-TAG is an important platform for evidence gathering and technical information sharing on home fortification. This includes not only evidence collected from research settings, but also vitally important lessons from field studies, which are key to informing the continuing scale-up of MNP interventions. Moreover, expert members of the HFTAG have also been instrumental in analyzing negative results from MNP trials and providing an interpretation for donors, policy makers, and implementers.

The *Home fortification with micronutrient powders (MNP)* 2013 special edition published by HFTAG, which is freely available online, provides a summary of the successes and challenges around MNP programs in a variety of settings, such as refugee camps, schools, and market-based distribution (HF-TAG, 2013).

MNP program scale-up

In 2011, 14 million children aged six to 59 months were reached in 22 countries worldwide, and large-scale MNP programs have been implemented or planned in more than 40 countries. This success has been driven by a number of factors; an expanding evidence base has allowed nutritionists to advocate for programs scale-up, and has provided donors with the confidence to invest in MNP programs. Improved product formulation and packaging have been developed, while manuals, programmatic guidance briefs, and statements have facilitated the scale-up of national programs.

Vitamin A supplementation

Since the 1980s, decades of research in low-income countries provide substantial evidence that vitamin A supplementation (VAS) is an efficacious

solution to reducing child mortality and morbidity. The first of these studies was conducted in Aceh, Indonesia and showed a 34% reduction in mortality in the one- to five-year age group (Sommer *et al.*, 1986).

By 1993, a total of 8 studies, conducted in Asia and Africa, had been published, showing a significant decrease in child mortality (Sommer, 2008). In 2010, a Cochrane review of 17 trials with 194,795 children of six to 59 months of age found a 24% reduction in the risk of all-cause mortality for those receiving VAS compared with controls at follow-up [RR 0.76 (CI) 0.69, 0.83] (Imdad *et al.*, 2010). Seven trials reported a 28% reduction in diarrhea-related morbidity in those receiving VAS [RR 0.72 (CI) 0.57, 0.91]. VAS was also associated with a reduction in the incidence of diarrhea and measles morbidity.

Coverage of VAS programs

Given the significant impact that VAS has on children's risk of morbidity and mortality, the WHO recommends that pre-school-aged children at risk of vitamin A deficiency receive vitamin A capsules. The United Nations Children's Fund (UNICEF) collects data on national VAS program coverage. Currently, program coverage – determined as the number of children of six to 59 months of age receiving two doses of Vitamin A per annum – is vastly different, depending on region and country. In Eastern and South Africa the rate is as low as 72%, while in East Asia and the Pacific coverage reaches 85%. In Somalia, program coverage is abysmally low at 12%, while Afghanistan and Mauritania report 100% coverage (UNICEF, 2013). Improvements in program coverage will likely come when we improve access to program services; his requires a careful assessment of how programs are designed and implemented to reach the most vulnerable.

DEVTA Study: A case for delivery science

The Deworming and Enhanced Vitamin A (DEVTA) study was a cluster-randomized trial conducted in Northern India in the state of Uttar Pradesh under usual program conditions. The program provided periodic VAS in an area where children are known to be at risk of VAD (Awasthi *et al.*, 2013). With one million children in the study, it has been described as the largest drug trial ever to examine the impact of VAS on child mortality. The study, however, found a non-significant 4% reduction in child mortality among those children who received the vitamin A capsules.

Compared to the established evidence, the contradictory findings of the DEVTA trial have raised many questions about the methodology employed in the study. These points were addressed in a commentary by Sommer *et*

al. (2013), who suggested that the trial was not conducted in a manner rigorous enough to be deemed an efficacy trial, some of the issues being that children were not enumerated, consented, formally enrolled, or carefully followed up for vital events. Habicht and Victora (2013) and Habicht and Pelto (2014) raised a number of other issues relating to the program assessment design. In large-scale programs, the causal chains are long and complex, and documentation along the whole chain and process is essential to understanding the results (Habicht and Victora, 2013). In the DEVTA study, these questions were only answered in a non-random opportunistic sample of 2,106 children; furthermore, these children were likely to be easy to reach, and thus received both annual doses of vitamin A. The authors conclude that program assessments require more complex designs than randomized control trials.

Turning knowledge into action: Implementation research

Scientific advancements have provided public health nutritionists with the tools and products to tackle malnutrition. From earlier works involving micronutrient supplementation, such as the case of VAS discussed above, to new innovative methods such as MNP, it is largely recognized that we have the knowledge to tackle malnutrition. The next major challenge for the nutrition field is to take these interventions to scale, with our future success inextricably linked to our ability to deliver high quality programs to many people, particularly to those most difficult to reach.

So the major question is: How will this be achieved? There are a number of challenges that must be addressed. Delivering high quality supplementation programs is complex and requires an urgent investment in implementation research to elucidate the critical intervention and implementation components. Yet implementation research receives only 3% of research funds (Habicht, 2012). Improving program delivery requires program managers to systematically use a range of strategies across the program cycle, such as formative research, behavior change communication, market-based research, and robust monitoring and evaluation frameworks. Understanding the value of this process is the key to successful program implementation, and we need practitioners with skills in not only nutrition, but also social science, and who have strong management and leadership skills. At present, this is a major roadblock.

Another significant bottleneck to improving program delivery is a usable set of tools for frontline workers, especially for those implementing interventions within large-scale programs in health, agriculture, education, and social protection. A systems approach could help public health professionals

understand the complexities of delivering nutrition intervention across multi-sector platforms.

Conclusions

The examples of VAS and MNP show how supplementation can be used as an effective front line tool in the battle against micronutrient malnutrition. It is essential that, while acknowledging previous successes in the nutrition field, we move forward with scaling up nutrition interventions to reach those most in need and to ensure they will have the maximum benefit. We need to think beyond nutrition, and look over the fence to incorporate other disciplines to implement our programs more effectively.

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