Perspectives in Nutrition Science

New Allies Accelerate the Fight against Malnutrition

A discussion of field-friendly diagnostics, screening devices, and tools

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Key messages

- Despite progress, malnutrition remains a major health concern worldwide.
- Effective efforts to address malnutrition, in all its forms, have long been hindered by a lack of affordable, effective, and field-appropriate diagnostics, screening devices, and tools to measure and track nutritional status.
- Thanks to entrepreneurs from across sectors, a new crop of innovative products promises to dramatically improve field-based measurement of nutritional status, particularly in low-resource settings.
- > This article introduces five exciting products; outlines their use and potential impact; and highlights the continued need to champion the partnerships and investment that make breakthrough health innovation possible.

The challenge of field-based nutrition measurement

Despite tremendous progress, malnutrition remains a major barrier to health and wellbeing worldwide. Undernutrition among children and mothers remains the leading underlying cause of child morbidity and mortality, contributing to 3.1 million child deaths each year. Globally, 155 million children under five are

stunted due to chronic undernutrition, and 52 million suffer from wasting from acute malnutrition. Concurrently, a growing epidemic of overweight and obesity affects an estimated 40.6 million children under age five.²

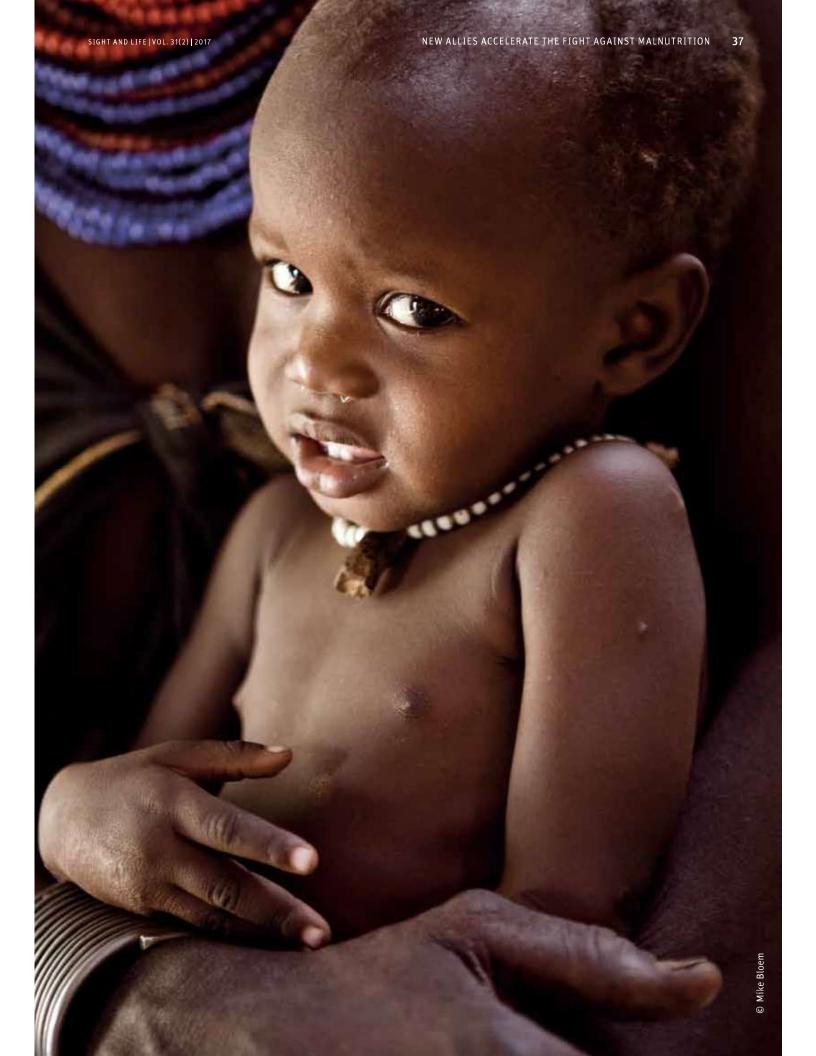
Recognizing the prevalence and persistence of this burden, the global health community is increasingly striving to identify and address the complex causes and impacts of malnutrition. Yet measuring and assessing nutritional status and outcomes in low-resource settings (LRS) has often proven expensive, time-consuming, and difficult.

Fortunately, a new generation of field-friendly diagnostics, screening devices, and tools is poised to help address these challenges. Here, we present a sample of these promising innovations. We hope that greater familiarity will increase interest in these and other products; prompt greater use and better health outcomes; and inspire leaders to champion the partnerships and investments that make innovation possible.

"There is a new generation of field-friendly diagnostics, screening devices, and tools for assessing nutritional status and outcomes in low-resource settings"

1. Pooled enzyme-linked immunosorbent assays: A fast, affordable test for multiple biomarkers of nutritional status

Although global leaders rely on population-level testing to build a broad picture of community health and develop coordinated





and effective responses, vitamin and mineral deficiencies in par-

To close this gap, PATH, a leading global health organiza-

in a sample of human serum derived from a finger-stick.

ticular have proven challenging to assess.

tion (Seattle, WA, USA), the University of Washington (Seattle, WA, USA), and private-sector manufacturer Quansys Biosciences (Logan, UT, USA) collaborated on the Q-Plex™ Human Micronutrient Array, currently available from Quansys.³ The tool is more affordable and efficient than current technologies because it can simultaneously measure up to seven biomarkers for vitamin and mineral status in a sample of human serum derived from a finger-stick. This minimally invasive sampling method facilitates easier field collection than most current methods for micronutrient surveillance. Using pooled enzyme-linked immunosorbent assays (ELISA), the Q-Plex[™] detects biomarkers of iodine (thyroglobulin), iron (ferritin, soluble transferrin receptor), and vitamin A (retinolbinding protein 4) deficiencies, as well as inflammatory status (C-reactive protein, α_1 -acid glycoprotein) and malaria infection (histidine-rich protein II). Currently packaged in up to a 7-plex configuration, the tests can be customized, allowing researchers to choose which tests to include. Iterations in development will add biomarkers for vitamins B₁₂ and D, envi-

ronmental enteropathy, and exposure to infectious diseases.

For more information, visit: www.quansysbio.com.

2. Automatic anthropometry:

A rapid scan for accurate and objective body measurement

Health workers use anthropometric measurements to assess the nutritional status of children during their early years of development. In most LRS, the current standard for measuring child length or height to monitor stunting and wasting is the ShorrBoard®. When users are trained appropriately, board measurements are accurate, 4.5.6 but the board is cumbersome, requires multiple people to use, and is often uncomfortable for children. This can limit correct use by researchers and health workers.

To address this challenge, the private company Body Surface Translations (BST, Athens, Georgia, US), has developed AutoAnthro. This technology derives child stature (length/height), head circumference, and mid-upper arm circumference (MUAC) from 3D scans and a 3D model. An occipital structure sensor, attached to a smart phone or tablet, generates a series of 3D images to create a model, and then generates measurements from the scans using custom software.

BST, in collaboration with Emory University (Atlanta, Georgia, US), has evaluated the tool in a 500-child study within the United States. Early data are promising and suggest the option may be easier to use, more accurate and consistent, and more efficient for large-scale data collection and analysis. Now, the team will field validate AutoAnthro in LRS with a goal of making



AutoAnthro, a new mobile device from Body Surface Translations (Athens, Georgia, US), derives child stature, head circumference, and mid-upper arm circumference from 3D scans and a 3D model.



may help expand reliable access to hemoglobin screening.

it commercially available by late 2018. For more information, contact: Gene Alexander, PhD: gene.alexander@gmail.com.

3. A noninvasive tool for point-of-care hemoglobin screening

Iron deficiency anemia is one of the most common and widespread global nutritional disorders, causing fatigue, dizziness, headaches, and shortness of breath, and contributing to chronic infections. Pregnant women with anemia (low hemoglobin [Hb]) are at increased risk of complications and death if they experience uncontrollable bleeding (hemorrhage) during childbirth.8 Among children, low Hb levels can hinder brain development.9

The amount of Hb in whole blood, expressed in grams per deciliter (g/dL), is commonly used to diagnose anemia and is relatively easy to assess using a blood sample. Blood draws, however, can be difficult and painful for patients and increase the risk of infection and disease transmission. Effective screening programs have been hampered by the lack of a safe, accurate, and affordable solution.

Noninvasive Hb measurement devices, such as the portable handheld Pronto® developed by Masimo (Irvine, CA, USA), may help. Using wavelengths of light, a sensor placed on a patient's finger provides readings of total Hb (g/dL), oxygen saturation, and pulse rate. The sensors are pre-loaded with spot-check measurements in quantities of up to 1,000. Simple and easy to use, Pronto® provides accurate results in as little as 40 seconds and measures through motion and low perfusion conditions. With its lower cost and accuracy specifications, and because of the safety of noninvasive measurement, Pronto® may help expand reliable access to Hb screening. 10,11 For more information, visit: www.masimo.com.

4. Dried matrix spots (DMS): A new look at dried blood spot sampling

Dried blood spot (DBS) testing is currently used to test infants for HIV, phenylketonuria, and other diseases. Using this method, drops of whole blood are collected from a finger- or heelstick on a special type of card stock. Once dried, these samples are biosafe, small, and lightweight. Most do not require refrigeration or electricity to remain viable, so they can easily be transported or stored for testing. Although DBS is widely accepted by clinical communities, it continues to face gaps in accuracy and stability.

Now, researchers are developing more sophisticated sample collection approaches for dried matrix spots (DMS), which can test more than just whole blood, for example, blood serum or breast milk. 12 This opens the door for new uses - including nutrient biomarker testing. To explore this potential, Craft Technologies Inc. (CTI, Wilson, NC, USA) is evaluating sample collection



devices by measuring the accuracy and stability of 11 nutritional biomarkers in blood samples. ¹³ The group has been working with ViveBio (Alpharetta, GA, USA) to optimize a collection card (PRISM[™]) to separate plasma and red blood cells. CTI is also evaluating collection and analysis methods for biomarker stability and reliability in LRS. ¹³ For more information, visit: www. crafttechnologies.com and www.vivebio.com.

5. Enhanced tape measures to improve health

Not every new innovation is complex. MUAC tape measures are considered the standard tool to identify moderate or severe acute malnutrition and elevated mortality risk among children six months to five years old. ¹⁴ Yet although MUAC tapes are simple tools, health workers need training and practice to use them properly. Common errors, such as placing tapes incorrectly along a child's arm or pulling them too tight, limit the reliability of measurements, hindering referral and treatment.

These challenges have prompted two teams to develop improved tapes. Intellectual Ventures' Global Good Fund (Seattle, WA, USA) has developed a wider tape that reduces pressure applied to the arm and corrects for error incurred by the strap's thickness. Another effort, led by *Médecins Sans Frontières* (MSF), in collaboration with Brixton Health (Llawryglyn, Wales) and a group of nutrition experts, has developed a "Universal"

MUAC" (uniMUAC) strap that is double-sided for both adults and children. This adaptation also has a broader strap width, a triple-slit design for greater stability, and a wider reading window. 16 Both designs require less training to use than previous iterations. For more information, contact: Global Good, David Bell, MD, PhD (dbell@intven.com); MSF, Bhargavi Rao, MD, PhD (bhargavi.rao@london.msf.org).

"Today, the nutrition community has an unprecedented opportunity to champion innovative approaches and tools to measure nutrition outcomes"

Conclusion

Even as a new generation of diagnostics, screening devices, and tools reach commercial markets, others are undergoing development and revision for accuracy, affordability, and ease of use. These products have the potential to save lives by helping the public health community better assess and track mal-

nutrition, predict trends, and create and target more effective programs and policies.

Just as exciting is the increasingly global – and cross-sector – nature of health innovation. Today, the nutrition community has an unprecedented opportunity to champion innovative approaches and tools to measure nutrition outcomes, and to participate actively in their use and improvement.

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References

- **01.** Black RE, Victora CG, Walker SP, Bhutta ZA, Christian P, de Onis, M et al. Maternal and child undernutrition and overweight in low-income and middle-income countries. Lancet 2013;382(9890):427–451.
- O2. World Health Organization (WHO) and the United Nations Children's Fund (UNICEF). Joint Malnutrition Estimates: Levels and Trends. 2017. Internet: http://www.who.int/nutgrowthdb/jme_brochoure2017. pdf?ua=1 (accessed 21 July 2017).
- O3. Brindle E, Stevens D, Crudder C, Levin CE, Garrett D, Lyman C et al. A Multiplex Immunoassay Method for Simultaneous Quantification of Iron, Vitamin A and Inflammation Status Markers. PLoS One 2014;9(12):e115164.
- 04. Mwangome MK, Berkley JA. The reliability of weight-for-length/ height Z scores in children. Mat Child Nutr 2014;10(4):474–480.
- 05. Mwangome MK, Fegan G, Mbunya R, Prentice AM, Berkley JA. Reliability and accuracy of anthropometry performed by community health workers among infants under 6 months in rural Kenya. Trop Med Int Health 2012; 17(5):622–629.

- **06.** Ulijaszek SJ, Kerr DA. Anthropometric measurement error and the assessment of nutritional status. Br J Nutr. 1999;82(3):165–177.
- **07.** World Health Organization [WHO]. Micronutrient deficiencies: iron deficiency anemia. Internet: http://www.who.int/nutrition/topics/ida/en/ (accessed 30 August 2017).
- **08.** AbouZahr C. Global burden of maternal death and disability. Br Med Bull 2003:67:1–11.
- **09.** Glazer Y, Bilenko N. Effect of iron deficiency and iron deficiency anemia in the first two years of life on cognitive and mental development during childhood. Harefuah 2010;149(5):309–314.
- 10. Levy TS, Méndez-Gómez-Humarán I, Morales Ruán MdC, Martinez Tapia B, Villalpando Hernández S, Hernández Ávila M. Validation of Masimo Pronto 7 and HemoCue 201 for hemoglobin determination in children from 1 to 5 years of age. PLoS One 2017;12(2): e0170990.
- Hsu DP, French AJ, Madson SL, Palmer JM, Givani-Diaz V. Evaluation of a noninvasive hemoglobin measurement device to screen for anemia in infancy. Matern Child Health J 2016;20(4):827–32.
- **12.** Sturm R, Henion J, Abbott R, Wang P. Novel membrane devices and their potential utility in blood sample collection prior to analysis of dried plasma spots. Bioanal 2015;7(16):1987–2002.
- 13. Arredondo FX, Craft NE. Screening of dried matrix spot collection to be used for nutritional biomarker analysis. FASEB J 2017; 31(1): Supplement 786.18
- 14. World Health Organization (WHO) and United Nations Children's Fund (UNICEF). WHO Child Growth Standards and the Identification of Severe Acute Malnutrition in Infants and Children: A Joint Statement by the World Health Organization and the United Nations Children's Fund. 2009. Internet: http://www.who.int/nutrition/publications/severemalnutrition/9789241598163_eng.pdf (accessed 3 August 2017).
- 15. Hess SY, Hinnouho GM, Barffour MA, Bounheuang B, Arnold CD, Bell D, et al. First field test of an innovative, wider tape to measure mid-upper arm circumference. Food Nutr Bull, in press.
- 16. Rao B, Roby R, LeBeau K, du Cros P, Briend A, Fritsch P et al. Comparing the accuracy and sensitivity of a double-sided universal MUAC strap ("uniMUAC") with the UNICEF MUAC strap. 2017. MSF Scientific Days 2017–Innovation Conference. Internet: https://f1000research.com/documents/6-885 (accessed 2 August 2017).