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Inclusion of Micronutrient Biomarkers in National Surveys and Surveillance Systems: Barriers and Enablers

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ABBREVIATIONS

AGP	α -1-acidglycoprotein
CDC	Centers for Disease Control and Prevention
CHORI	Children's Hospital Oakland Research Institute
CHSU	Community Health Services Unit, Ministry of Health, Malawi
CRP	C-reactive protein
DFID	Department for International Development, United Kingdom
DHS	Demographic and Health Survey
DNHA	Department of Nutrition, HIV and AIDS, Ministry of Health, Malawi
FCDO	Foreign, Commonwealth & Development Office, United Kingdom
GAIN	Global Alliance for Improved Nutrition
ILSI	International Life Sciences Institute
INCAP	Instituto de Nutrición de Centro América y Panamá
IZiNCG	The International Zinc Nutrition Consultative Group

IRD	Institut de Recherche pour le Développement
LMIC	Low- and middle-income countries
MRDR	Modified Relative Dose Response
NIN	National Institute of Nutrition, Vietnam
NSO	National Statistical Office, Malawi
PSC	Pre-School Children
RBP	Retinol-Binding Protein
RBC	Red Blood Cell
RSSPMCE	The Republican Specialized Scientific Practical Medical Centre of Endocrinology, Uzbekistan
sTfR	Soluble Transferrin Receptor
ThDP	Thiamine Diphosphate Concentrations
UBOS	Uganda National Bureau of Statistics
USDA ARS	United States Department of Agriculture
WHNRC	Agricultural Research Service, Western Human Nutrition Research Center
WFP	World Food Programme
WRA	Women of Reproductive Age

EXECUTIVE SUMMARY

Background

Including biomarkers of micronutrient status in existing or planned national surveys or surveillance systems would dramatically improve capacity to promote, design, monitor and evaluate micronutrient policies and programmes. Ultimately, investing in better data would yield healthier populations, safer programs and cost savings.

The predominant approach for collecting national-level data on micronutrient status is to conduct stand-alone nutrition and/or micronutrient surveys. Unfortunately, many low- and middle-income countries (LMICs) lack routinely collected data on micronutrient status. Although a lot of attention has been devoted to technical aspects of micronutrient status assessment, such as the selection and analysis of appropriate micronutrient biomarkers, less attention has been given to implementation-related experience of micronutrient status assessment at the population level.

Objectives

The objectives of this study were to identify barriers to, and enablers of, the inclusion of micronutrient biomarkers in national surveys and surveillance systems. We sought to identify challenges throughout the process, including financing, planning, collection, processing, transport, storage, and analysis of blood/urine samples. We also aimed to review experiences using different platforms to collect micronutrient biomarker data. This project was part of a wider collaborative effort aimed at increasing the availability and utilization of high-quality data on micronutrient status at the national/sub-national levels in LMICs.

Participants and methods

With support from the Micronutrient Forum, the International Zinc Nutrition Consultative Group (IZiNCG) conducted a series of key

informant interviews with in-country and external representatives from six countries where national-level data on micronutrient status had been collected in the past five years: Cambodia, Pakistan, Malawi, Uganda, Ghana and Uzbekistan. In addition, representatives from the US Centers for Disease Control and Prevention (CDC); GroundWork; ICF, the lead implementing organization of the Demographic and Health Survey (DHS) Program; Institut de Recherche pour le Développement (IRD); and UNICEF were interviewed to capture their perspectives as supporting agencies to a particular survey, or to a wide range of countries.

Findings

Three of the surveys were initiated by the Ministry of Health in the respective countries. UNICEF advocated for the need for two of the surveys, and a local champion played a critical role in convincing donors of one of the surveys. External technical support was provided by CDC and GroundWork in two surveys each (Malawi and Uganda, and Ghana and Uzbekistan, respectively). IRD provided technical support in Cambodia, and Aga Khan University provided technical support in Pakistan. In two countries, micronutrient biomarkers were included in a DHS survey. In three countries, stand-alone nutrition surveys included micronutrient biomarkers. And in one country, micronutrient biomarkers were collected as part of a National Panel Survey. The level of representativeness was urban-rural and/or macro-region in four surveys, and district or micro-region in two surveys.

Blood samples were fully or partially exported for analysis in four of the surveys, and analysed domestically in two of the surveys. Biomarkers of iron, vitamin A, folate and vitamin B12 status were assessed in one or more population groups in all surveys. Five surveys included assessment of urinary iodine. Micronutrients whose biomarkers were collected in three or fewer surveys included

zinc, vitamin D, calcium, thiamine, and selenium. The VitMin Laboratory, which analyses five biomarkers in a small amount of serum at an

exceptionally low price, was used in all four surveys where samples were exported for analysis.

Overview of the six surveys:

	CAMBODIA	MALAWI	PAKISTAN	UGANDA	GHANA	UZBEKISTAN
Survey year	2014	2015-6	2019	2018	2017	2017
Domestic lead agency	UNICEF	Ministry of Health NSO	Ministry of Health Aga Khan University	Ministry of Health NBOS	University of Ghana	UNICEF
External agency	IRD	CDC Emory University	UNICEF, WFP	CDC	GroundWork	GroundWork
Funding sources	UNICEF, World Vision, IRD, WFP, ILSI	Irish Aid, World Bank, UNICEF, USAID	DFID, USAID, Australian Aid	USAID, UNICEF,	UNICEF, Global Affairs Canada	UNICEF
Model	“Follow-on” from DHS	“Follow-on” from DHS	Broader nutrition survey	National Panel Survey	Broader nutrition survey	Broader nutrition survey
Representativeness	National Urban-rural	National Urban-rural Regional: 3 zones	National Province District	National Urban-rural Regional: 5 regions	National Urban-Rural Regional: 3 zones	National Regional: 14 regions
Laboratory analysis of micronutrient biomarkers	International, Regional, and Domestic	International and Domestic	Domestic	International	International	Domestic
Micronutrient biomarkers assessed	Haemoglobin Ferritin sTfR RBP U. iodine S. folate Vitamin B12 Zinc Vitamin D Calcium RBC ThDP CRP AGP	Haemoglobin Ferritin sTfR Retinol RBP MRDR U. iodine S. folate RBC folate Vitamin B12 Zinc S. folate RBC folate Vitamin B12 Zinc Selenium CRP AGP	Haemoglobin Ferritin Retinol U. iodine S. folate RBC folate Vitamin B12 Zinc Vitamin D Calcium CRP AGP	Haemoglobin Ferritin Retinol RBP MRDR U. iodine S. folate RBC folate Vitamin B12 CRP AGP	Haemoglobin Ferritin sTfR Retinol S. RBP MRDR S. folate Vitamin B12 CRP AGP	Haemoglobin Ferritin Retinol U. iodine S. folate Vitamin B12 CRP AGP

Agencies: IRD, Institut de Recherche pour le Développement; WFP, World Food Programme; ILSI, International Life Sciences Institute; DHS, Demographic and Health Survey; NSO, National Statistical Office; CDC, Centers for Disease Control and Prevention; FCDO, Foreign, Commonwealth & Development Office (FCDO) United Kingdom (formerly DFID, Department for International Development); UBOS, Uganda National Bureau of Statistics. Micronutrient biomarkers: U., urinary; S., serum; sTfR, soluble transferrin receptor; RBP, retinol-binding protein; MRDR, modified relative dose response; vitamin D, 25-hydroxy-vitamin D; RBC, red blood cell; ThDP, thiamine diphosphate concentrations; CRP, C-reactive protein; AGP, α-1-acid glycoprotein.

Micronutrients associated with specific public health programmes were always prioritised for inclusion in the survey. If funding, time, and/or logistics allowed, other considered micronutrients were also included. In Uzbekistan, a ban on the export of blood samples for analysis meant that domestic capacity determined which biomarkers were included. The most important and frequently reported barrier to inclusion of a more comprehensive panel of micronutrient biomarkers was inadequate funding to cover the analysis cost for all micronutrients considered at the planning stage. Analyses for serum and red blood cell folate, along with the modified relative dose response test for vitamin A, were the most expensive laboratory analyses. For countries where export of blood samples was prohibited, a key barrier for micronutrient biomarker assessment was the capacity of domestic laboratories.

Difficulty obtaining funding was only discussed in detail for two of the countries, because funding had typically been obtained prior to the key informant's involvement in the survey. However, the lack of funding sources was cited quite simply as "there aren't many apart from UNICEF to turn to." Lack of funding for micronutrient surveys was attributed to limited awareness of the need for the data by development partners, and specific funding earmarked by micronutrient programs.

Government support and commitment was stressed as the most important enabling factor by all key informants. Having experienced the value of micronutrient data from earlier surveys, the Malawi government wanted to track progress and understand what was driving the high stunting and birth defect rates in the country. When implementation in Malawi got challenging, the government's vision was the motivation to keep going. And external support agencies echoed the need for government support and commitment: "It doesn't work well any other way." In-country advocates, often individuals who drove the agenda of the need for securing funding for a micronutrient

survey, were also consistently mentioned as an enabling factor.

The interviews examined perspectives on using existing survey platforms to collect micronutrient biomarker data. The idea of including micronutrient biomarker assessment within a DHS survey was initially thought to have major cost-saving potential and logistical benefits. So far, two countries, Cambodia and Malawi, have implemented and published variations of a micronutrient survey that has "followed on" from the DHS. Because separate survey teams and vehicles were used, cost savings were considered to be minor. However, several logistical and other substantive advantages were mentioned such as a reduced burden on the respondents and the implementing organisation in-country. For future surveys combining micronutrient biomarker assessment with a DHS survey, all stakeholders wanted enhanced integration and simultaneous planning. In Uganda, the pilot inclusion of micronutrient biomarkers in the National Panel Survey demonstrated that this platform was feasible and relatively cost effective. There are other existing survey platforms, such as UNICEF's Multiple Indicator Cluster Surveys, which could also be used for inclusion of micronutrient biomarkers.

Recommendations

Ideas for the steps the international community could take to increase and/or expand the inclusion of micronutrient biomarkers in national surveys were discussed by CDC, ICF, the DHS Program and UNICEF key informants. The discussions revolved primarily around how funding could be made available to pay for laboratory analyses, and the advocacy needed to achieve this, but also the required short- and long-term efforts on the laboratory side.

Advocacy: Work to create demand; donors and policy makers in-country need to understand the value of having the data. Advocacy is "about the face time, not about developing a brief." There is a need to identify effective 'advocacy mechanisms'

and partners, building on existing advocacy efforts and movements.

Finance: Work to establish a funding mechanism for micronutrient status assessment, which includes increasing the number of people with the necessary expertise. Funding must be accessible for countries to cover local costs and technical assistance.

Laboratory analysis: Work to develop global contract labs that have the staff, equipment and capacity to do several analyses in a low cost, timely

manner, with routine quality assurance testing. Strengthen efforts to develop field-friendly, micro-volume, multiplex methods for biomarker analysis.

Survey integration: Pursue the integration of micronutrient biomarker assessment in pre-existing survey platforms, e.g. DHS, Multiple Indicator Cluster Surveys (MICS), and national surveillance systems. Continue dialogue with countries and agencies involved in upcoming case studies of different integration models to develop lessons learned.

1 | BACKGROUND AND RATIONALE

A. Background

There is an increasing commitment to addressing malnutrition globally. However, many low- and middle-income countries (LMICs) lack routinely-collected high-quality data on micronutrient status.

“Micronutrient deficiencies are estimated to impact a significant number of people around the world, but there remains far too little information on micronutrient status and deficiencies. More essential information and surveillance need to be gathered to make substantial progress on global targets.”

2018 Global Nutrition Report (1)

Collecting high-quality data on a regular basis will dramatically improve capacity to promote, design, and monitor micronutrient policies and programmes. Such data enables the most vulnerable subgroups to be identified, programs to be targeted effectively, and changes in micronutrient status to be monitored over time. The documentation of change in micronutrient status also facilitates efforts to enhance, scale-up, scale-down, and/or replicate effective policies and programs to reach other populations. In other words, investing in better data would ultimately yield healthier populations, safer programs and cost-savings.

Unfortunately, too much of our current micronutrient malnutrition information is based on proxies of micronutrient status. Using zinc as an example, it is estimated that at least 17% of the world’s population is at risk of inadequate zinc intake (2). This estimate is based on two proxy indicators: the amount of zinc in the food supply and the prevalence of stunting among children under 5. However, these two indicators tend to underestimate the prevalence of zinc deficiency among vulnerable population groups such as infants, young children, and women of reproductive age (3). Measuring the best available biomarker of zinc status (i.e. plasma/serum zinc concentration

(PZC)(4) would enable a more precise estimate of nutritional zinc deficiency in vulnerable populations. To date, PZC has only been measured in pre-school children in a national survey by 26 LMICs. Current, high-quality, population-based biomarker data is similarly limited for micronutrients such as folate, vitamin B12, thiamine, and vitamin D.

The predominant approach for collecting national-level data on micronutrient status is to conduct standalone nutrition and/or micronutrient surveys, with frequency varying from a one-off attempt to once every 5-10 years. National-level data on indicators of micronutrient status are also collected as part of various national surveillance systems (5), and in recent years some countries have collected micronutrient biomarker data using such platforms. Although significant effort has gone into publishing recommendations on technical issues related to micronutrient biomarker assessment (6), less is known about the main barriers that prevent countries from conducting a comprehensive micronutrient status assessment and/or the enabling factors that promote the successful assessment of micronutrient status at the population level. Similarly, countries’ experiences of different approaches to collect micronutrient status data have not been comprehensively assessed in a systematic way.

B. Scope and goal

Several factors may prevent a country from conducting a comprehensive micronutrient status assessment. An awareness of the importance of key micronutrients may be limited by those involved in planning the survey. Technical expertise regarding survey design, as well as the collection, storage, and analysis of samples may be limited in-country. Financial resources may also be constrained, which often leads to the de-prioritisation of micronutrients that are

more expensive to collect or analyse. Further, the necessary supplies for sample collection and processing may not be readily available.

In 2017, IZiNCG formed a working group to monitor and promote the inclusion of zinc status assessment in national surveys. Because the issues under consideration were relevant to other micronutrients, the scope of work was expanded, and IZiNCG approached the Micronutrient Forum to co-lead the effort. The Working Group to Promote the Inclusion of Micronutrient Biomarkers in National Surveys consists of representatives from the Bill & Melinda Gates Foundation, CDC, the Global Alliance for Improved Nutrition (GAIN), GroundWork, HarvestPlus, ICF, the New York Academy of Sciences, Nutrition International, OpeN-Global, PATH, Sight & Life, UNICEF, USAID and WHO. The overarching goal of this wider collaborative effort is to *increase the availability and utilization of high-quality data on micronutrient status at the national/ sub-national levels in low- and middle-income countries.*

C. Objectives

As an initial step in achieving this goal, IZiNCG was supported by the Micronutrient Forum to conduct a series of interviews with representatives from countries where national nutrition survey or surveillance data had recently been collected, including the collection of at least some biomarkers of micronutrient status. The interviews were designed to achieve the following objectives:

- To identify barriers behind the inclusion of biomarkers of micronutrient status in national surveys and surveillance systems;
- To identify factors that enabled the inclusion of biomarkers of micronutrient status in national surveys and surveillance systems;
- To identify the main challenges faced during collection, processing, transport, storage and analysis of blood/urine samples;
- To identify experiences and perspectives regarding the assessment of biomarkers of micronutrient status as part of DHS surveys as an example of the use of an existing platform to collect micronutrient biomarker data.

2 | PARTICIPANTS AND METHODS

A. Country selection

Representatives from six countries were interviewed, selected for inclusion based on the following characteristics:

- A national nutrition survey or surveillance had been carried out in the past 5-10 years (**Appendix A**), with emphasis on surveys in the past five years. These countries were drawn from a global inventory of completed and upcoming surveys which had been compiled and maintained by IZiNCG over the past year;
- The selected countries captured a variety of geographical regions;
- The surveys were provided with support from a variety of external agencies;
- At least one survey collected micronutrient biomarker data as part of a DHS.

Because the interviews were initially planned with a focus on assessment of PZC, three countries were selected because PZC was assessed in their national survey, and three countries were selected because they did not assess PZC. For the purpose of this report, this distinction will not be further discussed.

B. Key informant selection

Country key informants were identified with the help of the main external support agency of the survey in question. Two informants were contacted directly because they were known to the investigators. The aim was to interview one in-country representative and one representative from the external agency that provided technical support to the survey, primarily CDC and GroundWork, for each country where feasible.

Key informants for the overview perspective from CDC, UNICEF, and ICF were selected from the *Working Group to Promote the Inclusion of Micronutrient Biomarkers in National Surveys*.

ICF implements the DHS Program in partnership with Blue Raster, the Johns Hopkins Bloomberg School of Public Health Center for Communication Programs, PATH, Vysnova, Avenir Health, and EnCompass.

C. Interview guides

The primary interview guide for the in-country representatives (**Appendix B**) was developed with a focus on PZC and subsequently expanded to encompass all micronutrient biomarkers. Representatives from the Micronutrient Forum and the IZiNCG Steering Committee contributed to the development of the final interview guide.

For the purpose of interviews with representatives from external agencies that provided funding or technical assistance to the surveys, the primary interview guide was modified slightly to encompass specific prompts about the role of the external agency and how it became involved in the survey. Barriers and enablers were discussed from their experience working with several countries, and questions included steps the international community could take to expand the inclusion of micronutrient biomarkers in national surveys and surveillance systems.

D. Interviews

The interviews were conducted between September and November 2019. The main questions of the interview guide, i.e. without interviewer probes, were shared with the informants one week prior to the interview. All interviews were conducted by the first author (MSM), with the second author (CM) participating in two of the interviews. The interviews were conducted by conference call using GoToMeeting and were approximately 90 minutes in duration. Due to time zone constraints, in-country key informants and supporting agency informants were

typically interviewed separately rather than in pairs. All interviews were recorded after obtaining informed consent from the informants.

E. Data analysis

Detailed notes were taken from the recorded interviews. A mixed methods approach was then used to analyse the interview data. First, major themes for barriers, enablers, and challenges were drawn from each interview, and in the case of surveys for which there were two key informants, collated for that survey. Next, the themes from all country interviews were categorised and the categories were named. The categories were further reviewed and refined by going back to the detailed notes. Barriers reported by the respondents were classified according to importance, as emphasised and/or ranked by the respondent and the frequency (per country) with which the barrier/enabler was reported. The perspectives of external technical support agencies were checked against country perspectives.

3 | FINDINGS

A. Countries and key informants

A total of 12 interviews with 13 key informants were conducted. In four countries, both in-country and external perspectives were captured, and in two countries, only one key informant was interviewed.

The ‘overview’ interview with the UNICEF India representative partly captured a 7th survey-specific experience, that of the recent Comprehensive National Nutrition Survey in India (**Table 1**).

Table 1. Key informants interviewed in country- and overview-interviews.

COUNTRY	KEY INFORMANT(S)	INSTITUTION
Cambodia 2014	Frank Wieringa	Institut de Recherche pour le Développement, France
Malawi 2016	Anne Williams	Centers for Disease Control and Prevention, USA
	Eunice Nyirenda & Dalitso Kang'ombe	World Food Program (EN) & Ministry of Health (DK), Malawi
Pakistan 2019	Zulfi Bhutta	Aga Khan University, Pakistan, & SickKids, Canada
Uzbekistan 2017	Fakhriddin Nizamov	UNICEF, Uzbekistan
	Fabian Rohner	GroundWork, Switzerland
Ghana 2017	Seth Adu-Afarwuah	University of Ghana, Ghana
	James P. Wirth (email only)	GroundWork, Switzerland
Uganda 2018	Sarah Ngalombi	Ministry of Health, Uganda
	Andrea Sharma	Centers for Disease Control and Prevention, USA
Overview	Maria Elena Jefferds	Centers for Disease Control and Prevention, USA
Overview	Sorrel Namaste	ICF, USA
Overview	Robert Johnston	UNICEF, India

B. Characteristics of the included surveys

i. General characteristics

The characteristics of the six included surveys are shown in **Table 2**. In Malawi, Uganda, and Uzbekistan, the surveys were initiated by the country’s Ministry of Health. In Cambodia and Ghana, representatives from UNICEF advocated for the need for survey data. In Pakistan, a local champion played a critical role in convincing donors to support the survey. UNICEF was the primary donor in three surveys. External technical support was provided by CDC and GroundWork in two surveys each (Malawi and Uganda, and

Ghana and Uzbekistan, respectively). In the case of Cambodia, IRD provided technical support. In the case of Pakistan, Aga Khan University provided technical support internally. Two countries assessed micronutrient biomarkers in association with a DHS survey; three countries conducted standalone nutrition surveys including micronutrient biomarkers; and one country collected micronutrient biomarkers as part of a National Panel Survey. The level of representativeness was urban-rural and/or macro-region in four surveys, and district or micro-region in two surveys. Blood samples were fully or partially exported for analysis in four of the surveys and were analysed domestically in two of the surveys.

ii. Micronutrient biomarkers

In general, biomarkers of iron, vitamin A, folate, vitamin B12, iodine status, and inflammation were most commonly assessed (Table 3). Haemoglobin, serum ferritin, and the inflammatory markers, C-reactive protein (CRP) and α -1-acid glycoprotein (AGP), were assessed among pre-school children and women of reproductive age in all surveys. Haemoglobin was also assessed among adolescent girls in Pakistan and among pregnant women in Ghana. Serum soluble transferrin receptor (sTfR) was assessed in four of the surveys in addition to serum ferritin.

For vitamin A, serum retinol was assessed in five surveys, but as a sub-sample together with MRDR in three surveys. Retinol-binding protein (RBP) was assessed in four surveys; in three of these surveys it was accompanied by a measurement of serum retinol in a sub-sample, and in one of these surveys it was the only biomarker of vitamin A status. Serum folate was assessed in all six surveys, but only among WRA in three surveys. Red blood cell (RBC)

folate was assessed in three surveys, in Malawi, Pakistan, and Uganda. Vitamin B12 was assessed in all six surveys, but only among WRA in three surveys.

Five surveys assessed urinary iodine, but among WRA only in Malawi, Uganda, and Uzbekistan. Ghana did not include urinary iodine assessment because iodine status had recently been assessed in a nationally representative survey. Biomarkers of the following micronutrients were collected in three or fewer surveys: zinc, vitamin D, calcium, thiamine, and selenium. As per selection criteria, three surveys assessed PZC. Plasma/serum vitamin D and serum calcium were assessed together in two surveys, and RBC, thiamine diphosphate, and plasma selenium were assessed in one survey each.

None of the surveys measured biomarkers of riboflavin or niacin status, however assessment of urinary niacin metabolites was being discussed as a post-hoc analysis for the Malawi survey.

Table 2. Characteristics of the six micronutrient surveys for which key informant interviews were carried out

	CAMBODIA (7)	MALAWI (8)	PAKISTAN (9)	UGANDA¹	GHANA (10)	UZBEKISTAN (11)
Survey year	2014	2015-16	2019	2018	2017	2017
Domestic lead agency	UNICEF	Ministry of Health NSO	Ministry of Health Aga Khan University	Ministry of Health UBOS	University of Ghana	UNICEF
External agency	IRD	CDC Emory University	UNICEF, WFP	CDC	GroundWork	GroundWork
Funding	UNICEF, World Vision, IRD, WFP, ILSI	Irish Aid, World Bank, UNICEF, USAID	DFID, USAID, Australian Aid	USAID, UNICEF	UNICEF, Global Affairs Canada	UNICEF
Model	“Follow-on” from DHS	“Follow-on” from DHS (closer in time)	Broader nutrition survey	Uganda National Panel Survey (surveillance)	Micronutrient survey	Broader nutrition survey
Representativeness	National Urban-rural	National Urban-rural Regional (North- Central-South)	National Province District	National Urban-rural Regional (5 regions)	National Regional (South- Middle-North)	National Regional (13 regions)
Laboratory analysis	International Regional, and Domestic	International and Domestic	Domestic	International	International	Domestic

IRD, Institut de Recherche pour le Développement; WFP, World Food Programme; ILSI, International Life Sciences Institute; DHS, Demographic and Health Survey; NSO, National Statistical Office; CDC, Centers for Disease Control and Prevention; FCDO, Foreign, Commonwealth & Development Office (FCDO) United Kingdom (formerly DFID, Department for International Development); UBOS, Uganda National Bureau of Statistics..

¹Report expected end-2020.

Table 3. Micronutrient biomarkers assessed in selected population groups in the six surveys

Micronutrient	Biomarker	CAMBODIA		MALAWI		PAKISTAN		UGANDA		GHANA		UZBEKISTAN	
		PSC	WRA	PSC ¹	WRA	PSC	WRA	PSC	WRA	PSC	WRA	PSC	WRA
Iron	Haemoglobin	☑	☑	☑	☑	☑ ³		☑	☑	☑	☑ ⁵	☑	☑ ⁵
	Serum ferritin	☑	☑	☑	☑	☑	☑	☑	☑	☑	☑	☑	☑
	Serum sTfR	☑	☑	☑	☑			☑		☑	☑		
Vitamin A	Serum retinol			☑ ²	☑ ²	☑	☑	☑ ²	☑ ²	☑ ²	☑ ²	☑	☑
	Serum RBP	☑	☑	☑	☑			☑		☑	☑		
	MRDR			☑ ²	☑ ²			☑ ²	☑ ²	☑ ²	☑ ²		
Iodine	Urinary iodine	☑	☑		☑	☑ ⁴	☑		☑				☑ ⁶
Zinc	Plasma/serum zinc	☑	☑	☑	☑	☑	☑						
Vitamin D	Plasma/serum vitamin D		☑			☑							
Calcium	Serum calcium		☑			☑							
Folate	Serum folate	☑	☑	☑	☑	☑	☑		☑		☑		☑
	RBC folate				☑	☑	☑		☑				
Vitamin B12	Plasma/ serum vitamin B12	☑	☑	☑	☑	☑	☑	☑	☑		☑		☑
Thiamine	RBC ThDP	☑	☑										
Selenium	Plasma selenium			☑	☑								
Inflammation	Serum CRP	☑	☑	☑	☑	☑	☑	☑	☑	☑	☑	☑	☑
	Serum AGP	☑	☑	☑	☑	☑	☑	☑	☑	☑	☑	☑	☑

PSC, pre-school children; WRA, women of reproductive age; sTfR, soluble transferrin receptor; RBP, retinol-binding protein; MRDR, modified relative dose response; vitamin D, 25-hydroxy-vitamin D; RBC, red blood cell; ThDP, thiamine diphosphate concentrations; CRP, C-reactive protein; AGP, a1-acidglycoprotein.

¹The same micronutrient biomarkers were also assessed in school-aged children.

²Measured in a subsample

³Also assessed in adolescent girls

⁴Urinary iodine only for children 6-12 years

⁵Also assessed in pregnant women

iii. Laboratories used

The laboratories used in each of the surveys are shown in **Table 4**. Haemoglobin was measured in the field using HemoCue 301 in all surveys, but with venous blood in four surveys and capillary blood in two surveys. In Cambodia, the reason for using capillary blood was that haemoglobin assessment was carried out by the DHS teams and not the micronutrient teams. In Ghana, capillary samples were used for the majority of children with the exception of those selected in the subsample for MRDR assessment.

In the two countries where all analyses were carried out domestically, Aga Khan University carried out all micronutrient biomarker analyses for the Pakistan survey, and three domestic laboratories carried out the analyses in the Uzbekistan survey.

In the four countries where survey samples were exported for analysis, samples were sent to five different laboratories in two surveys, to three laboratories in one survey, and to two laboratories in one survey. Juergen Erhardt's VitMin Laboratory was used for analysis of serum ferritin, sTfR, RBP, CRP, and AGP in all surveys where samples were exported for analysis. Peking University analysed six micronutrient biomarkers for the Uganda survey.

Table 4. Laboratories used for analysis of micronutrient biomarkers in the six surveys.

	CAMBODIA	MALAWI	PAKISTAN	UGANDA	GHANA	UZBEKISTAN
Haemoglobin	Field: HemoCue 301 (capillary)	Field: HemoCue 301 (venous)	Field: HemoCue 301 (venous)	Field: HemoCue 301 (venous)	Field: HemoCue 301 (capillary)	Field: HemoCue 301 (venous)
Serum ferritin, sTfR, RBP, CRP, AGP	VitMin Laboratory, Germany	VitMin Laboratory, Germany	Aga Khan University, Pakistan	VitMin Laboratory, Germany	VitMin Laboratory, Germany	Vitamed Laboratories, Uzbekistan (not sTfR & RBP)
Urinary iodine	Mahidol University, Thailand	CHSU, Malawi	Aga Khan University, Pakistan	Peking University	-	RSSPMCE, Uzbekistan
Serum retinol and MRDR	-	INCAP, Guatemala	Aga Khan University, Pakistan	Peking University	University of Wisconsin, USA	Medstandart Laboratories, Uzbekistan (not MRDR)
Serum and RBC folate; serum vitamin B12	Pasteur Institute, Cambodia (not RBC folate)	CDC, USA	Aga Khan University, Pakistan	Peking University	USDA ARS WHNRC, USA (not RBC folate)	Vitamed Laboratories, Uzbekistan (not RBC folate)
Plasma/serum zinc	NIN, Vietnam	CHORI, USA	Aga Khan University, Pakistan	-	-	-
Serum vitamin D, calcium	Pasteur Institute, Cambodia	-	Aga Khan University, Pakistan	-	-	-
RBC ThDP	Abbott Laboratories ¹	-	-	-	-	-

NIN, National Institute of Nutrition; CDC, Centers for Disease Control and Prevention; INCAP, Instituto de Nutrición de Centro América y Panamá; CHORI, Children's Hospital Oakland Research Institute; CHSU, Community Health Services Unit, Ministry of Health; USDA ARS WHNRC, United States Department of Agriculture Agricultural Research Service Western Human Nutrition Research Center; RSSPMCE, the Republican Specialized Scientific Practical Medical Centre of Endocrinology; sTfR, soluble transferrin receptor; RBP, retinol-binding protein; CRP, C-reactive protein; AGP, a1-acidglycoprotein; MRDR, modified relative dose response; vitamin D, 25-hydroxy-vitamin D, RBC, red blood cell; ThDP, thiamine diphosphate concentrations.

¹Thiamine was reported separately from the UNICEF-funded report due to the laboratory used

C. Survey contexts and timelines

Rough timelines from conception through planning, implementation, and dissemination for each survey are shown in **Figure 1**. Each survey came about in a different manner due to varying contexts and partners involved. The time from the start of discussions about a survey to field implementation of the survey varied from 3 months in Ghana to 3 years in Uganda. The time from completed field implementation to the publishing of the first report varied from 3 to 5 months in Pakistan and Cambodia, respectively, to 12 months in Malawi. Uzbekistan had a longer time period between completion of field work and reporting due to time spent building the in-country quality-related capacity for laboratory analyses.

The **Cambodia** survey came about with UNICEF contacting IRD about the possibility of including some measures of micronutrient status in the upcoming DHS. Next, UNICEF and IRD started discussions with ICF, which finally settled on a follow-on approach in November 2013. Both the UNICEF and IRD representatives had practical experience from the micronutrient survey in Vietnam. The driving force for the government was determining the cause of the high prevalence of anaemia in the country, which could not be treated with iron supplements. As long as this question was answered, the government was happy to give UNICEF and IRD autonomy as to which micronutrient biomarkers to select for inclusion in the survey.

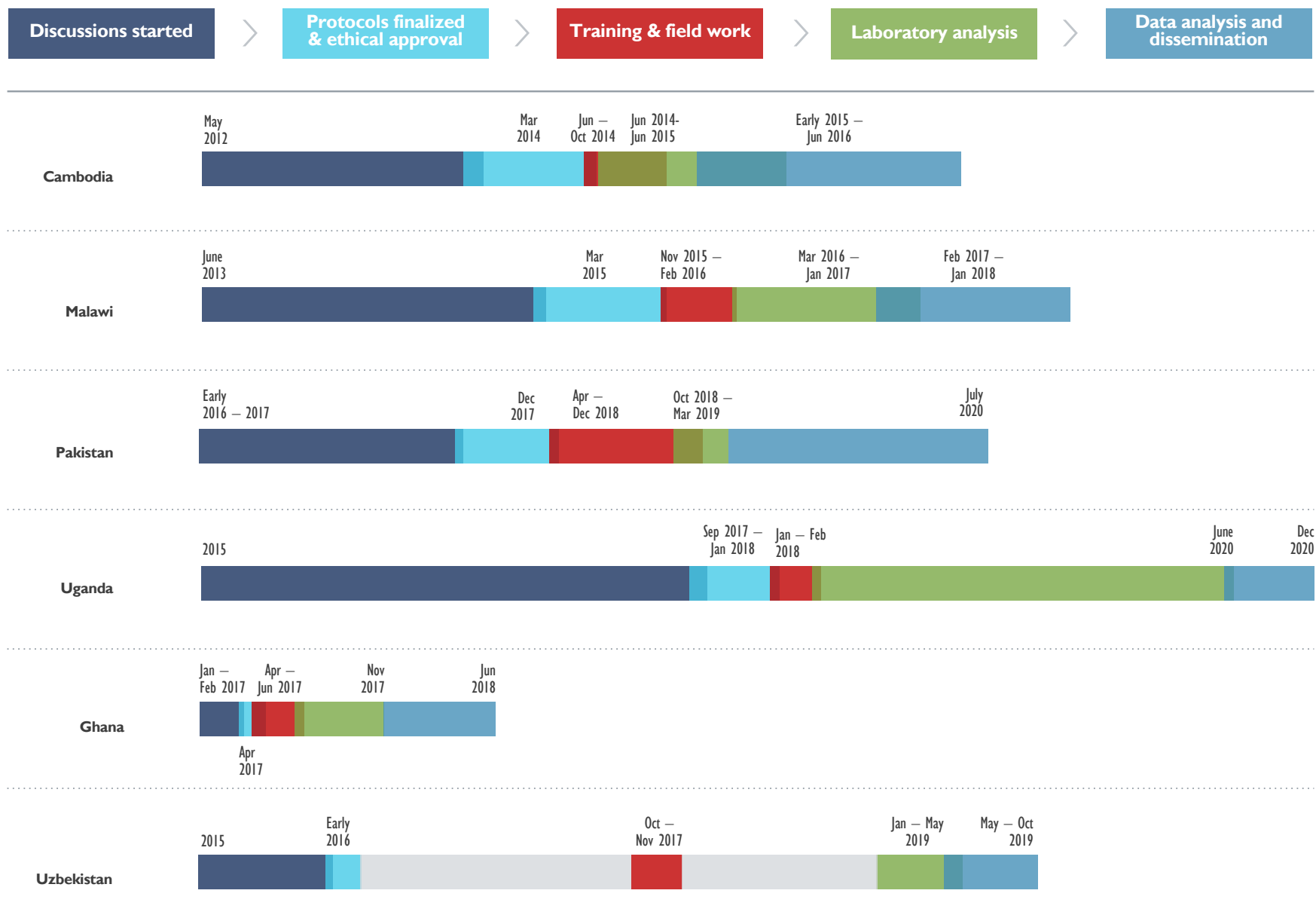
In **Malawi**, the 2015-2016 micronutrient survey was the third national micronutrient survey. The first two surveys had “informed us greatly in terms of how we [were] doing,” and this time around the survey organizers wanted “to see if they could marry a micronutrient survey with a DHS.” The survey was initiated by the Department of Nutrition, HIV and AIDS (DNHA) at the Ministry of Health, and stakeholders included the National Statistical Office, the Community Health Services Unit (CHSU) at the Ministry of Health, UNICEF, Irish Aid, USAID (who funded the Malawi DHS) and CDC.

The micronutrient biomarkers considered were in response to the 2009 survey “to see what [was] happening,” and to understand what was causing the high prevalence of stunting and birth defects.

The **Pakistan** survey was also the third nutrition survey where biomarkers of micronutrient status were assessed. Zulfi Bhutta, from Aga Khan University, had been advocating the Department for International Development, United Kingdom (DFID; subsequently replaced by the Foreign, Commonwealth & Development Office (FCDO)) to finance the survey for several years. It took 2 years to plan the survey, for FCDO to obtain approval from headquarters, and to get the government onboard. Zulfi Bhutta was the principal investigator of the survey. The other stakeholders were part of the technical advisory committee for the Government and included FCDO, USAID, AusAID, technical staff from UNICEF and WFP, and national experts. The committee considered the biomarkers measured in the preceding surveys, building on findings and lessons learnt.

The **Uganda** 2018 micronutrient assessment was a pilot to assess the feasibility of integration within the Uganda National Panel Survey (UNPS), a nationally and longitudinally representative survey which collects data primarily on agriculture and economics on an annual basis. Data are collected over a period of 12 months each year. Discussions as to whether a baseline micronutrient survey should be a standalone survey or add-on started as early as 2010, and integration with DHS had been considered. They wanted to try utilising an existing survey platform because they were “looking for a cost-effective way” to include micronutrient biomarkers in a nationally representative survey. The selection of biomarkers reflected the pilot focus, but, as with many other surveys, the starting point for the selection process was the existing nutrition programmes in the country. The UNPS was implemented by the Uganda National Bureau of Statistics (UBOS). Other stakeholders included the Nutrition Division of the Ministry of Health, other Ministry of Health

Figure 1. Survey timelines for six countries



divisions, USAID, UNICEF, and various NGOs, with technical assistance provided by CDC.

The Ghana micronutrient survey was initiated by UNICEF, which issued a request for proposals that prioritised the survey as an in-country activity, but with acceptance of collaboration from other countries. The University of Ghana-Legon and GroundWork formed a consortium and were selected to design and implement the survey. The list of which micronutrient biomarkers to assess was specified in the call from UNICEF and was informed by the nutrition programmes being implemented in country. In addition, the stipulated implementation timeframe in the request for proposals was shorter than most other surveys, which impelled the survey team to equip all teams with equipment to process and freeze samples independently.

The main stakeholders in the Uzbekistan survey were the Ministry of Health, UNICEF and GroundWork. The survey was initiated by the Ministry of Health, who requested UNICEF to implement the survey. Nutrition and micronutrient indicator data were either not available or were of uncertain quality. At the same time, the government was initiating several nutrition-related programs with the support of UNICEF, and the Ministry of Health wanted to assess nutritional status to inform what the focus areas for the government, UNICEF, and other stakeholders should be in Uzbekistan. UNICEF issued a request for proposals for protocol design, to which GroundWork bid on and won.

A list of priority micronutrients for assessment was provided in the RFP after discussions between the Ministry of Health and UNICEF, and additional micronutrients and their biomarkers were suggested by GroundWork. However, the main factors in the decision-making process for the micronutrient biomarkers to be included in the Uzbekistan survey were related to the prohibition of exporting biological specimens and to challenges related to domestic analytical quality.

D. Barriers to inclusion

Barriers to the inclusion of micronutrient biomarkers focused on including *a more comprehensive panel of micronutrient biomarkers*. However, throughout the in-country interviews and particularly in the overview interviews, barriers to assessing micronutrient status at all were also discussed.

Nearly all survey committees considered a more comprehensive set of micronutrient biomarkers than what was ultimately included in the final survey. Five main categories of experienced/perceived barriers to inclusion of a more comprehensive set of micronutrient biomarkers emerged. These barriers were: financial, programmatic, laboratory, awareness/knowledge, and contextual. The barriers are presented in **Table 4** according to the frequency by which the barriers were reported, and the importance placed on the factor as reported by the respondents.

Table 5. Importance and frequency of reported barriers to inclusion of micronutrient biomarkers in national surveys in six countries¹.

	LOW FREQUENCY	MEDIUM FREQUENCY	HIGH FREQUENCY
High importance	<p>Contextual:</p> <ul style="list-style-type: none"> • Export of blood samples prohibited. • Domestic capacity dictated which biomarkers were selected. • Limited time available to conduct survey. • Micronutrients were ‘competing’ against desired precision of the survey. • Lack of available laboratories for some micronutrients. 	<p>Laboratory:</p> <ul style="list-style-type: none"> • Lack of laboratories capable of multiple analyses, within available resources. • <i>Lack of field-friendly multiplex methods.</i> <p>Awareness/ knowledge:</p> <ul style="list-style-type: none"> • <i>Lack of awareness of need for the data among donors/ development partners.</i> 	<p>Financial:</p> <ul style="list-style-type: none"> • Available funding not adequate to cover the analysis cost for all micronutrient biomarkers. • High laboratory analysis costs. • Difficult to obtain funding. • <i>Limited human resources globally to support countries.</i> <p>Programmatic:</p> <ul style="list-style-type: none"> • Micronutrient not associated with a programme.
Medium importance	<p>Laboratory:</p> <ul style="list-style-type: none"> • Complexities in collection for some micronutrients. 	<p>Awareness/ knowledge:</p> <ul style="list-style-type: none"> • Government concerned survey would put them in a bad light or that they would be held accountable. • Lack of understanding of the need to analyse samples abroad, or of analysis quality. 	

¹In italics: additional barriers noted by external support agencies.

i. Financial barriers

All six surveys reported lack of sufficient funds to cover the cost of assessing all considered micronutrient biomarkers as a major restricting factor in the decision-making process. Within the available funds, countries did their best to include assessment of as many biomarkers as possible, and they were advised by the external supporting agency on how to do so. The in-country experiences were echoed in the interviews with the external technical support agencies:

“it’s always, always money”

“Countries not having the funding for what they are requesting”

“If a micronutrient biomarker is cheap, then it is a lot easier to include it than if it is expensive.”

In cases where the inclusion of micronutrient biomarkers at all was discussed, the additional

field costs in terms of phlebotomists, vehicle and mobile processing, and cold-chain set-ups, were also a barrier. The CDC informant also noted that, after cost, there is a limited pool of people with the technical expertise required to support these surveys globally – human resources are limited at both CDC and GroundWork. However, ultimately limited human resources was a question of funding; with more funding, more technical experts could be made available.

Approximate analysis costs for some of the frequently included biomarkers from laboratories commonly used by CDC, e.g. for the Uganda survey, are shown in **Table 5**. Based on these costs, a minimum cost per individual for ferritin, at least one inflammation biomarker, vitamin A (serum retinol), RBC folate, and vitamin B12 comes to approximately USD 65 – before including urinary iodine, other micronutrient biomarkers, or malaria tests needed in malaria endemic environments.

Table 6. Approximate analysis costs per sample for selected micronutrient biomarkers.

MICRONUTRIENT BIOMARKER	APPROXIMATE ANALYSIS COST /SAMPLE
RBC folate	USD 25
Serum folate	USD 25
Plasma/serum vitamin B12	USD 18
Serum retinol	USD 12–15
MRDR	USD 25–30
Ferritin, sTfR, RBP, CRP, AGP (VitMin Laboratory)	USD 6-7
Plasma/serum zinc	USD 12

Costs in Pakistan were “rock bottom” because all biomarkers were analysed in the laboratory at Aga Khan University at-cost. Similarly, pricing of analyses of the Cambodia survey was at the lowest end, including USD 9 for serum folate and USD 4 for plasma zinc.

Difficulties in *obtaining* funding for a survey were discussed in only two of the country interviews, because the funding had typically been obtained prior to the key informant’s involvement in the survey. In Pakistan, focused advocacy towards a specific donor over several years paid off, and the basis of the support was largely the nutrition-related work Aga Khan University had done with FCDO and the Government of Pakistan over the years. When asked about the biggest obstacle for measuring plasma/serum zinc and other micronutrient biomarkers in a national survey again, the Cambodia informant said without hesitation:

“Funding. It is always a problem. People aren’t really interested in surveys anymore.”

The remainder of the surveys were all co-funded by UNICEF, with UNICEF being the primary donor of three of these surveys. The difficulty in obtaining funding for micronutrient status assessment was a major theme in the external support agency interviews and cited simply as “there aren’t many apart from UNICEF to turn to.” A comparison was made to malaria, for which substantial funding was set aside in the US President’s Malaria Initiative, and to population-based HIV impact assessment surveys funded by the US President’s Emergency

Plan for AIDS Relief. Nutrition, on the other hand, was assumed to be included under health, with little finance earmarked specifically for it.

ii. Programmatic barriers

Some micronutrients were included for assessment in nearly all surveys despite high analytical costs for some of their biomarkers. Micronutrients associated with specific public health programmes, such as vitamin A supplementation for young children, iron-folic acid supplementation during pregnancy, and salt iodisation, were consistently shortlisted for inclusion in the survey. This was true regardless of whether specified by UNICEF in the request for proposals, or by the country government itself with or without consultation with partners. Vitamin B12 was often included because it “went with folate,” and because there was support for its assessment from CDC.

In surveys where funding was less restricted, less commonly assessed micronutrients were also included in a quest to either address a particular health problem with which they were associated or to generate baseline data if deficiency was suspected. This included carrying out zinc status assessment as part of understanding the high prevalence of anaemia in Cambodia and understanding “the stunting problem” in Malawi. However, in other countries, the lack of historical data for a particular nutrient was identified as a barrier: “Really the main reason not to include [riboflavin] was lack of data ...but I could not convince the donors on this one....”

In Ghana, a combination of budget constraints and a very limited timeframe meant that ‘non-programmatic’ micronutrients such as vitamin D, thiamine, riboflavin and zinc were not discussed. In Uganda, they stuck to the ‘must have’ biomarkers because they were piloting the integration of micronutrient biomarker assessment in UNPS.

iii. Laboratory analysis barriers

Despite exporting the majority of samples for analysis, informants from Uganda and Malawi reported “we’d want our labs to be able to do this.” External technical support agencies also reported that countries conveyed a desire to gain the capacity to carry out laboratory analysis domestically. Even if agreeing to advice from external supporting agencies such as CDC regarding quality and cost, government officials interviewed would often face questions from superiors about “why it couldn’t be done in-country.”

A major barrier for frequent micronutrient biomarker assessment at-scale was reported in all overview interviews as the lack of field-friendly, microvolume, multiplex methods. Such methods would enable in-country analysis without considerable investments.

As was the case for three of the surveys, shipping samples to up to five different labs globally complicated logistics and added cost to the survey, and survey investigators had to defend this strategy to stakeholders within the country. Preference was given to laboratories that could analyse many biomarkers at acceptable quality, at reasonable cost, with as few shipments as possible. CDC informants reported that there was a limited pool of such laboratories. For example, due to government barriers limiting the importation of specimens, the CDC could no longer send samples to INCAP in Guatemala for a range of micronutrients. In addition, a barrier reported by CDC at the global level was the very limited availability of laboratories for analysis of certain micronutrients such as niacin.

Despite a preference for export of samples for analysis as the cost-effective option, at least two of the countries experienced major delays caused

by difficulties in obtaining approvals for shipping samples. GroundWork informants also noted that many university-based laboratories have complicated contractual agreements, including clauses requiring data access, which are difficult for UNICEF and Governments to sign, and which have caused considerable delays.

MRDR was the biomarker most frequently mentioned as harder to collect, because it required administering the analogue dose and a delayed blood draw. Plasma/serum zinc was mentioned as a little more complicated because of the precautions needed to prevent contamination. However, “harder to collect is ultimately a question of money.”

iv. Knowledge/awareness factors

Government concern for being seen in a bad light was mentioned for two of the surveys, and from the perspective of external support agencies:

“You know no government really likes surveys because it shows them in a bad light if things don’t go the right way.”

This perspective contrasted with the nutrition community’s emphasis on the importance of data to establish a baseline, and the use of data to intervene effectively and to track progress.

In one country, the survey investigator came to realise that there was low knowledge about micronutrient biomarkers among stakeholders, even at the local universities, which were more focused on other aspects of undernutrition such as wasting or stunting. In the interview with ICF it was emphasised that during some design visits, the topic of micronutrient biomarkers “isn’t even coming up” as a priority by country stakeholders involved in the DHS.

v. Contextual barriers

1) ***Export of biological samples was prohibited***

In Uzbekistan, the major barrier was the prohibition of exporting human biological samples, combined with limited capacity of domestic laboratories. There were several technical- and cost-related

issues from the start which prevented UNICEF from considering micronutrients that extended beyond a limited panel. In addition, when UNICEF encountered the restrictions on sample exportation, and the need to work with domestic laboratories on quality improvement, there was “enough to deal with”. For example, the decision of which vitamin A biomarker to use stemmed from available laboratory capacity within the country: A pharmaceutical lab experienced in HPLC was able to set up a serum retinol analysis to acceptable quality. Much time and effort went into capacity development, which included technical expertise from CDC and GroundWork.

2) Time pressure

Ghana was unique for having a very short timeline for the entire survey. Combined with funding restrictions, this added time pressure was a barrier for inclusion of micronutrients whose status were more complicated to assess, such as plasma/serum zinc. Country time constraints were also mentioned as a barrier from the perspectives of CDC and ICF.

3) Statistical factors

In two of the surveys, micronutrient biomarkers were in “competition” with the desired precision for the survey. In other words, despite smaller sample sizes being required for biochemical assessment of micronutrient status compared with other nutrition indicators (e.g. anthropometry), larger sample sizes were required when representativeness beyond urban/rural or macro regions were desired. For example, the Uzbekistan survey required results that were representative at the level of 13 oblasts (regions) and the survey in Pakistan was carried out with district-level representativeness:

“when you survey 115,000 households from every district in Pakistan you have to be parsimonious in terms of what you can feasibly do and justify.”

E. Enablers of inclusion

The three countries most clearly demonstrating/reporting enabling factors were those which were

selected for their inclusion of plasma/serum zinc assessment in the survey. The categories of enabling factors are reported below. Country perspectives and overview perspectives are reported separately.

i. Political factors

All key informants stressed the importance of government support and commitment. It was mentioned that the government wanted to “establish a baseline,” or “track to see what is happening,” in other words measure the success of their programmes. In some cases, the government was highly committed to ‘solving’ a certain health condition where a micronutrient was implicated. In Malawi, the government wanted to understand what was driving the high stunting rates, and also the high birth defect rates despite a policy of iron-folic acid supplementation during pregnancy. This commitment enabled the measurement of plasma/serum zinc, folate and vitamin B12 in addition to iron biomarkers.

In Cambodia, the driving force for the government was finding out what was causing the high prevalence of anaemia, which could not be resolved by provision of iron supplements. The government gave autonomy to IRD and UNICEF to add more micronutrient biomarkers to the survey as long as this question was answered.

Having experienced the value of collecting data on micronutrient biomarkers in previous surveys was a motivating factor: in Malawi, the two previous micronutrient surveys “informed us greatly in terms of how we are doing.” The government wanted to see if salt fortification with iodine, or interventions with iron and vitamin A, were “making a difference in the people’s lives.”

The government was also a driver in two of the countries where a potentially cost-effective model was used, both in the case of including micronutrient biomarkers in the Uganda National Panel Survey, and in the Malawi DHS. When faced with several challenges during data collection in Malawi, “the solution to the challenge laid in the

motivation from the government's vision, which was clear: 'we are going to do this.'

ii. Advocacy factors

There were several examples of the importance of in-country advocates. In Pakistan, Zulfi Bhutta had been actively advocating over time for financial support from FCDO to carry out the survey. At the time of the Malawi survey, the Department of Nutrition, HIV and AIDS (DNHA) was in a powerful position directly under the office of the President's cabinet. In addition, funding agencies were highly motivated to capitalise on the unique opportunity of including micronutrient assessment in a DHS survey.

In Cambodia, IRD and UNICEF were highly experienced with assessment of micronutrient biomarkers in a similar context (Vietnam) and could capitalise on the government's drive to understand the identified anaemia problem.

iii. Programmatic factors

All countries reported the selection process as starting with the micronutrients that were associated with large-scale nutrition programmes in the country. However, the importance of this enabler was less strong; all informants reported that they would have included other micronutrients if additional funding, time, or laboratory capacity were available. The starting point for CDC when advising a country on which micronutrient biomarkers to include was asking, "what are all the large-scale nutrition interventions in the country?"

iv. Laboratory analysis-related factors

Savings were made by using contract laboratories which could carry out many analyses, thereby preventing multiple shipments. Juergen Erhardt's VitMin Laboratory was used by all four surveys where samples were exported because of his ability to measure five biomarkers at an exceptionally low price and with a minimal amount of serum (100 µL). Apart from the unique case of the VitMin Laboratory, Peking University laboratory, where serum vitamin B12, serum folate, RBC folate, serum retinol, MRDR,

and urinary iodine from the Uganda survey were analysed, stood out among the laboratories used for exported samples (see **Table 3**).

Savings were also made on laboratory analysis by assessing expensive biomarkers such as serum retinol and MRDR on a subsample (see Table 3) or by only analysing certain biomarkers for the population group for which it was considered most critical, e.g. RBC/serum folate for WRA only.

In two of the country surveys, analyses were done at-cost within the country or region because of the resources available to the Principal Investigator, or because of collegial networks.

v. Enabling factors as listed by CDC, UNICEF and ICF

Echoing the country interviews, the most important enabler listed by CDC and UNICEF informants was having in-country support and government commitment:

"It doesn't work well any other way"

"When there is political leadership and trusted labs available, then funds can be mobilised"

Likewise, from the DHS Program perspective, the main reason micronutrient biomarkers would be included in a DHS was if it was requested by the government. For the subsequent important enabling factors, the CDC, UNICEF, and ICF perspectives vocalised what was implied by the country experiences but not explicitly reported by the informants.

The second most important enabler from the CDC perspective, which reflected the most commonly reported major barrier, was adequate funding. Third, CDC stressed the importance of having a local survey organization with expertise in implementing population-based surveys. The specific biomarker-related expertise was considered less of a prerequisite because this could be provided by the supporting agency. Fourth, from the CDC perspective it was important that the local organisers were communicative and

responsive. The combination of enabling factors was described for the inclusion of zinc in the Malawi survey: Malawi had a flexible government and strong donor participation; they could argue that no data were available, that zinc deficiency was likely, and that zinc interventions had the potential to reduce stunting; and they were willing to ship samples abroad.

From UNICEF's perspective, two more factors were added: the availability of in-country advocates and experts, and the designation of nutrition as a priority. It was a clear priority for Victor Aguayo as Chief of Nutrition in India to implement a national micronutrient survey first in India, and later in Nepal. Driven by UNICEF, sufficient resources were obtained to "do it properly," i.e. collect micronutrient biomarkers for the most important micronutrient deficiencies in addition to biomarkers for non-communicable diseases across the age range 1 to 19 years.

UNICEF advocated that the India survey was a priority through documentation of the paucity of robust data from previous surveys, which could not be used to make national or state-level estimates of micronutrient deficiencies. In addition, "everyone kept talking about it" from a programmatic perspective, saying that if they knew what they were facing, they could better know how to adjust funding demands and programme priorities, and that there was a clear cost-benefit in this. Throughout the process, there was strong national ownership among the Indian academic community, who are some of "the best in the world." There

was never a question about their involvement, and these academics are still involved today, taking leading roles in analysis and advocacy for policy based on the results.

F. Challenges during survey implementation and their solutions

The country survey teams were by-and-large prepared for the challenges they might face, as quoted: "that's what you get from experience." In some cases, the experience was in-country (e.g. Pakistan), and in the majority of the surveys, it was provided by the external technical support agencies (e.g. CDC and GroundWork).

The challenges faced during data collection, processing, transport, and storage have been summarised in **Table 6**. Ensuring that the cold chain was maintained with appropriate solutions to variable availability of electricity was mentioned as the first or second challenge for nearly all surveys. However, all countries were well-prepared with necessary mobile solutions. In the surveys where micronutrient biomarker data collection followed a DHS survey (Cambodia, Malawi) or was included in the National Panel Survey (Uganda), the coordination with the main survey team was reported as challenging with several lessons learnt for the next time around. Obtaining the blood samples was reported as a major issue for two surveys, either because of misperceptions or refusals, or because it was an addition to surveillance which previously had only used fingerstick sampling.

Table 7. Main challenges faced during collection, processing, transport, and storage of blood and urine samples

CHALLENGE	FREQUENCY	SOLUTIONS AND ENABLING FACTORS
Ensuring cold chain was maintained	5	Cold boxes, freezer in car, car battery for mobile freezers, mobile field labs or district hospitals for processing and/or temporary storage Feedback from lab technicians to field staff
Coordination with DHS or panel survey	3	Dedicated coordination and persistent communication Leadership and support from government Gathering all teams and agreeing on a plan
Obtaining the blood sample (major issue in 2 surveys)	2	Establishing rapport with study population Competent & experienced staff
Long lead times for supplies (major issue in 2 surveys)	2	Allowing long timelines, circumventing UNICEF Supply Division for specific supplies
Obtaining approvals for shipment of samples	2	Lesson learnt: factoring in time and resources for this
Rainy season, snow, security	2	“keep going”
Short duration of training or varying quality of staff hired	2	Hiring field workers with nutrition/ health background

G. Using existing survey platforms to collect micronutrient biomarkers: experiences from Cambodia, Malawi, and Uganda

i. Country experience

The interviews aimed to explore country experiences in combining a micronutrient survey with a DHS survey as an example of using existing platforms. In addition, Uganda piloted micronutrient biomarker assessment as part of a national surveillance system, and experiences from both the government and technical support (CDC) sides were obtained.

An overview of the two published DHS surveys which included a micronutrient component is provided in **Table 7**. The country motivation to

“marry a micronutrient survey with a DHS” was primarily to learn whether it could be a cost-effective way of obtaining nationally-representative micronutrient status data, and also for the opportunity to link this data with a larger, more comprehensive data set. Coordination challenges were experienced in both Cambodia and Malawi, but Malawi in particular expressed that they would conduct a micronutrient survey in association with a DHS survey again. However, they would “need to start the discussions at the same time and have stakeholder agreement from the start.” Informants for Cambodia and Malawi said they would strongly prefer integrated data collection, including visiting the clusters at the same time and accessing DHS electronic forms.

Table 8. Summary of two examples of micronutrient biomarker assessment in a DHS

	CAMBODIA 2014	MALAWI 2015-16
Technical assistance	IRD provided technical assistance	CDC provided technical assistance.
Data collection	<ul style="list-style-type: none"> • “Follow-on:” Micronutrient team visited household 2 weeks – 2 months after DHS team • Concern from DHS that venous blood collection would disrupt DHS procedures in the field. 	<ul style="list-style-type: none"> • “Follow-on,” closer in time: Micronutrient team visited household 2 weeks after DHS team. • Intention was simultaneous data collection. This was not possible when supplies did not arrive in time for DHS training.
Country experience	<ul style="list-style-type: none"> • If doing it again, preference would be to visit households at the same time as DHS 	<ul style="list-style-type: none"> • Would do it again, but starting discussions at the same time, have stakeholder agreement from the start, and with integrated data collection.
DHS perspective	<ul style="list-style-type: none"> • Micronutrient biomarker assessment perceived as feasible because implementing DHS in Cambodia was routine. • Limited ICF involvement in micronutrient component. Only provided household information and help with analysing the data. 	<ul style="list-style-type: none"> • From the DHS viewpoint the MN survey “was just tacked on” and ICF involvement was very limited beyond linking data sets and posting the survey on their website.
Challenges	<ul style="list-style-type: none"> • Difficulties with coordination, e.g. micronutrient survey was assigned households where Hb had not been collected. 	<ul style="list-style-type: none"> • Difficulties with timelines, funding streams and coordination. Elements of duplication.
Haemoglobin assessment	<ul style="list-style-type: none"> • Hb was only measured by DHS (capillary). 	<ul style="list-style-type: none"> • The micronutrient survey measured Hb from venous blood, and the DHS from capillary blood.

Uganda piloted a national surveillance system, the UNPS, to collect nationally representative data on micronutrient status. The key informants viewed it as a relatively cost-effective model. Compared to a standalone survey the micronutrient biomarker component could utilise some of the staff and logistical structures. In addition to the flexibility of the platform, which would allow phasing of collection of micronutrient biomarkers, the unique advantage of the UNPS is that it can assess longitudinal trends, with each household and split-offs being followed for 10 years. A key disadvantage was the relatively high burden placed on households year after year. As for Cambodia and Malawi, a challenge was coordination between the lab team and the interview team.

ii. Supporting agencies’ perspectives

The ICF informant reported that countries are increasingly requesting micronutrient biomarker surveys combined with DHS surveys because the national statistics offices are overburdened. A third case study is in progress is Rwanda, where the micronutrient biomarker data and the rest of the DHS survey data are being collected at the same time, and a fourth is planned for Tanzania. If moving in the direction of developing and supporting a micronutrient module, ICF’s preference would be to take the lead in providing technical assistance in order to achieve streamlined communication and integration.

A concern within the DHS Program is that adding micronutrient status assessment will overburden the traditional survey, and that this could compromise the quality of the survey as a whole. In addition, having a cold chain is not part of the regular procedures for the core data collected

in DHS surveys. However, there is an increasing recognition that dried blood spots and finger pricks may not be the best platform for micronutrient status assessment.

The biggest barrier for this model is laboratory analysis. Countries have a strong ownership of their DHS survey, which may include a desire to carry out laboratory analysis in-country. The ICF informant noted that if countries were amenable to shipment, ICF would be amenable. However, it was noted that some form of country capacity strengthening should be considered as ICF's role is to provide technical assistance to countries to eventually do surveys on their own. The ICF informant also noted it would be extremely helpful to have a back-up plan which enabled samples to be exported, but acknowledged the “many mixed feelings about this within the DHS Program.”

From the CDC's perspective, since a cold chain is not part of the regular procedures for the core data collected in DHS, and if countries are not willing to ship samples abroad, a micronutrient module is not realistic until a lab method implemented in-country is functional and cost-effective.

ICF has not conducted an analysis to examine the potential cost-savings of a micronutrient module compared to a standalone survey. However, the ICF informant reiterated that the main advantage of a combined survey is the platform, not the (small) cost savings. Ultimately, the overarching barrier to micronutrient biomarker assessment as part of a DHS survey was not DHS Program capacity, which could be developed to meet the need, but rather inadequate funding to perform the analyses

of interest and the risk of overburdening the DHS survey.

In addition to Uganda, CDC highlighted Guatemala as another example of a country which uses a national surveillance system to collect micronutrient biomarker data. The national epidemiological surveillance system in health and nutrition (SIVESNU) has since 2015 collected different biomarkers from round to round, including core biomarkers for iron, vitamin A, and iodine, but also biomarkers of vitamin B12, folate, zinc, and vitamin D status.

iii. CDC perspective

It was also noted that to efficiently conduct the number of surveys DHS undertake annually, they would need the process much more standardised. From a CDC overview, since DHS would prefer not to have a cold chain and not to ship samples, a micronutrient module is not realistic until a lab method that can be easily done in-country exists. These were however acknowledged as barriers which could be overcome. Remaining barriers would be working out the quality of internal labs and figuring out which lab to use each time. It was noted that analysis in-country would “change the game”, e.g. when QuanSys had been validated.

It was also noted that USAID's interest is to help increase nutrition surveillance. The interagency agreement with CDC is about identifying surveys or platforms that were already in place and how one could capitalise on these by adding a nutrition module. This is how piloting a nutrition module in the UNPS came about.

4 | DISCUSSION AND TAKE-AWAY MESSAGES

This study captured the perspectives of key in-country and external agency informants involved in six national-level assessments of micronutrient status. Each country had a unique set of circumstances, and every survey was different. However, some universal barriers and enablers of the inclusion of biomarkers of micronutrient status were identified, and interviews with informants from key global supporting agencies confirmed and added to the country experiences.

Several barriers and enablers reflected each other. The lack of available or sufficient funding was reported as the most important barrier, and a survey being adequately funded was a key enabling factor. Being associated with a programme was an enabling factor for micronutrients to be included in the surveys, notably iron, vitamin A, iodine, and folate, and a barrier for those nutrients not associated with a programme, such as zinc, vitamin D, and thiamine. Government support was a key enabling factor, and the lack of awareness of the importance/need for the data was reported as a barrier. A lack of moderately-priced laboratories where several biomarkers could be analysed was cited by some countries, and cost savings made on laboratory analyses in various ways was an enabling factor in many countries. Challenges during implementation were exactly that, challenges: they could be overcome, and countries/partners were by-and-large prepared for what they would face. A clear message from those who work to support surveys was this:

“They need money. They need money to pay for the lab analyses - just give them money rather than reinventing the wheel.”

It was not possible to discern how funding came about for all countries, but it was evident that UNICEF plays a key role by either funding or mobilising/advocating for funding surveys.

Some country representatives expressed that they wanted capacity strengthening to be able to analyse samples in-country in the future. It appeared that further engagement and discussion on how to meet both country goals and global goals of more and higher quality data would be needed. Regardless, improving laboratory capacity within nations that want to regularly monitor micronutrient status would require commitment of funds.

Perspectives on the most cost-effective way of doing laboratory analysis was a theme throughout the interviews. The proposed solution of regional laboratories, intended to increase regional capacity, was discussed with CDC key informants. It was not considered unreasonable to have one or two laboratories serving each region, but “World Courier goes everywhere” and criteria such as willingness to accept specimens from other countries and ability to analyse multiple indicators at a reasonable price and in a timely way were more important:

“Building capacity is great, but if those labs don’t work as contract labs, it’s not going to help improve the amount of data in the world.”

In the long term, there was a clear message from all informants that field-friendly, micro-volume, multiplex methods would be a key enabling factor.

Including micronutrient biomarker assessment in existing survey platforms has been suggested as a potentially cost-saving approach to collecting national-level data on micronutrient status. The perspectives shared by in-country and external agency informants on including micronutrient assessment in the Cambodia and Malawi DHS surveys corresponded well with a more comprehensive evaluation of the Malawi experience. More integration was needed and planning for integration had to start well in advance (12). The potential cost savings appeared to be small, but due to several other advantages of linking with the DHS platform, Malawi reported

that they would do the same again. However, the concerns from DHS about the potential impact on the quality of the survey data as a whole requires further attention, and the issue of country ownership of laboratory analysis discussed previously would need to be resolved:

“But can DHS build enough capacity in each country to do a micronutrient survey every 5 years? I don’t think so. This is a challenge for the nutrition community to work out.”

Uganda used another platform, the Uganda National Panel Survey to collect micronutrient

biomarkers. A key advantage of this model was the flexibility: survey teams visit households annually, making it possible to collect different biomarkers from round to round, as demonstrated in the more established collection of micronutrient biomarkers in Guatemala’s SIVESNU.

The two examples of platforms explored in these interviews are not an exhaustive list of survey or surveillance platforms available. UNICEF’s Multiple Indicator Cluster Survey (MICS) is another potentially suitable option, and was used for the 2018 Gambia National Micronutrient Survey (13).

5 | PROPOSED NEXT STEPS

Ideas for steps the international community could take to increase and expand the inclusion of micronutrient biomarkers in national surveys were discussed with CDC, ICF, and UNICEF key informants. Suggestions are provided under the headings below.

A. Advocacy efforts

There is a need to advocate towards policy makers in-country about why data on micronutrient biomarkers are needed, a “policy-level technical assistance” if you will. Donors and development partners have to feel there is a need for the data. And high-level nutrition champions are required. From ICF, the DHS Program implementer’s perspective, it is not DHS champions that are needed, but donors and policy-makers in-country. Showing what other people have done and how the data has been used was suggested in order to get buy-in, “but it’s about the face time, not about developing a brief.”

The UNICEF informant also pointed out that UNICEF is good at putting together broad appeals and building on work started by other agencies, and referred to the great work the Global Nutrition Report is doing in defining what malnutrition looks like.

Ideas for advocacy:

- The Nutrition for Growth (N4G) summit presents a unique opportunity to advocate towards donors about the importance of micronutrient status data.
- Partnering with existing advocacy efforts and movements, such as Scaling Up Nutrition, and building on successes, such as the control of iodine deficiency disorders.
- Potential donor or organisational partners could include Advancing Nutrition, the WHO-UNICEF TEAM group (Technical Expert Advisory Group

on Nutrition Monitoring) and the Bill & Melinda Gates Foundation.

- Prepare examples of how countries have used the data and how it has saved lives and money.
- Focus on the double burden of malnutrition and emphasise that a “poor diet” (whether it is causing NCDs or undernutrition) can be assessed through micronutrient deficiency prevalence.

B. Funding mechanism efforts

There is a clear need to have funding allocated specifically for micronutrient status assessment, including increasing the number of qualified people with technical expertise. Finance was considered a quick win: “if money is made available, countries can do it” and technical support can be mobilized to some extent. By infusing moderate amounts of money, external support agencies were confident that this would translate into data being collected and analysed for a handful more surveys.

Informants were less certain about what a funding mechanism should look like but suggested either having specific groups to contact for financial support for assessment of specific micronutrients, or the equivalent of the President’s Malaria Initiative equivalent for micronutrient status assessment. Important criteria for a funding mechanism were that funding must be accessible for countries to cover local costs and technical assistance. It was also suggested that governments could build survey budgets into their loans, and that UNICEF regional nutrition advisers should be engaged for thoughts on how UNICEF could raise funds for more micronutrient status surveys.

C. Laboratory efforts

i. Contract laboratories

There is a clear need to develop reasonably-priced contract laboratories which have excellent

capacity to analyse several indicators. The VitMin Laboratory was used in all four surveys where samples were exported for analysis because it analysed five biomarkers at a low cost using only a small amount of serum. Other laboratories used by the CDC for analysis of several indicators include Peking University, INCAP (currently under embargo), and UC Davis.

Suggested criteria for such contract or resource laboratories include:

- Multiple contract laboratories are needed, and they need to be doing routine quality assurance testing for any biomarker being considered for that laboratory.
- The laboratories must have a process for accepting funds, and through different mechanisms.
- The laboratories should be based in politically stable countries.
- The laboratories must have the staff, the equipment (and keep it working), and the capacity to do analyses at a low cost. This could imply a middle-income setting.
- The laboratories need to have multiple, highly-trained staff in order to perform analyses in a timely way.
- Contractual agreement must be feasible for UNICEF and governments to sign.

A very first step in this effort should be to map out available laboratories that are willing to perform fee-for-service work, have been used previously, and are participating in external quality assurance programs. Also laboratories considered as having potential for this role should be included. The currently available biomarkers with their corresponding price should be listed for all laboratories, as partly done with the information collected in these interviews. Opportunities to engage with private sector laboratories should also be explored, leveraging global knowledge, technology, and capacity. With a large volume of samples processed, there are opportunities for

making the analysis costs affordable for countries and profitable for the laboratory.

ii. Technology efforts

The availability of field-friendly technologies using small blood volumes and analysing many biomarkers at once would “change the game.” Efforts initiated in this area should be strengthened and continued.

Work has already been initiated around the development of technical product profiles for multi-analyte methods developed by companies such as Quansys. Work is in progress on the potential for using capillary blood for assessing plasma/serum zinc, and the use of portable X-ray fluorescence for assessing zinc and selenium status from nail clippings.

The UNICEF informant also mentioned the importance of technology in data collection from experience in recent years using tablets, including the CNNS in India, pointing out that “in the past, implementation using paper has been slowing us down.” It is also suggested that international guidance be provided regarding the level of population stratification that is considered adequate for a micronutrient survey. Cost savings could be possible if district-level representativeness was not required.

D. Existing platform integration efforts

BFor DHS, because countries are requesting combined surveys, and countries that tried would do it again, it is recommended to develop a micronutrient module in DHS surveys based on experiences from these and upcoming case studies. Despite reservations, the DHS program is obliged to be responsive to what countries are requesting and is able to respond if there is an enabling environment with adequate funding and the issue is considered a priority by USAID. Other existing survey platforms such as MICS and national platforms are also potential candidates.

However, the issue of in-country laboratory analysis must be resolved as a medium-term strategy before valid field-friendly methods become available. Enabling the use of international contract labs for DHS micronutrient surveys in countries which allow the export of samples (the majority) would be a more cost-effective option, but would

be a trade-off for countries, since in-country lab capacity strengthening would not be carried out. The DHS Program expertise in micronutrient status assessment needs strengthening or partnership with another agency that is capable of providing technical support, e.g. CDC or GroundWork.

6 | CONCLUSION

The call for more and better data has been sounded by the nutrition community and deemed critical by the Global Nutrition Report. The “countries who want the data, who want to build evidence-based decision making” are champions of micronutrient status assessment. However, assessment of biomarkers of micronutrient status is expensive, and the major barrier for countries is insufficient funds to pay for the analyses. Advocacy to establish a funding mechanism specifically for micronutrient biomarker assessment, and in particular for the development of global contract laboratories, is needed as a first step to increase the availability of high-quality data on micronutrient status in LMICs, and ultimately improve population health.

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About IZiNCG

IZiNCG is the International Zinc Nutrition Consultative Group whose primary objectives are to promote and assist efforts to reduce global zinc deficiency through interpretation of nutrition science, dissemination of information, and provision of technical assistance to national governments and international agencies. IZiNCG focuses on identification, prevention and treatment of zinc deficiency in the most vulnerable populations of low-income countries.

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8 | APPENDICES

A. Countries with surveys or surveillance systems collecting micronutrient biomarker data from 2015 to 2019 - 20¹

REGION	COUNTRY	SURVEY YEAR	MICRONUTRIENT BIOMARKERS
Africa	Burkina Faso	2020	P/S Zinc, Ferritin, sTfR, Hemoglobin, Vit A (RBP, Retinol, MRDR), Vit D, Urinary Iodine, Serum Folate, RBC Folate, Cobalamin, CRP, AGP
	Ethiopia	2015	P/S Zinc, Ferritin, sTfR, Hemoglobin, Vit A (Retinol), Urinary Iodine, Serum Folate, RBC Folate, Cobalamin, CRP, AGP
	Gambia	2018	Ferritin, sTfR, Hemoglobin, Vit A (RBP), Urinary Iodine, CRP, AGP
	Ghana	2017	Ferritin, sTfR, Hemoglobin, Vit A (RBP, MRDR), Serum Folate, Cobalamin, CRP, AGP
	Malawi	2015-16	P/S Zinc, Ferritin, sTfR, Hemoglobin, Vit A (RBP, MRDR), Urinary Iodine, Serum Folate, RBC Folate, Cobalamin, Selenium, CRP, AGP
	Nigeria	2020	<i>Ferritin, sTfR, Hemoglobin, Vit A (Retinol, RBP, MRDR), Urinary iodine, Serum Folate, RBC Folate, Cobalamin, Whole Blood Thiamin, Whole Blood Riboflavin, CRP, AGP</i>
	Rwanda	2019	<i>Ferritin, Hemoglobin, Vit A (Retinol), Urinary Iodine, RBC Folate, Serum Folate, Cobalamin, CRP</i>
	Uganda	2018	Ferritin, sTfR, Hemoglobin, RBP, Vit A (Retinol, MRDR), Urinary Iodine, Serum Folate, RBC Folate, Cobalamin, CRP, AGP
	Zambia	2019-20	P/S Zinc, Ferritin, Hemoglobin, RBP, MRDR, Serum Folate, Cobalamin, CRP, AGP
South-East Asia	Bangladesh	2020	<i>P/S Zinc, Ferritin, Hemoglobin, Vit A (Retinol), Urinary Iodine, Serum Folate, Cobalamin, Vit D</i>
	India	2016-18	P/S Zinc, Ferritin, Hemoglobin, Vit A (Retinol), Urinary Iodine, RBC Folate, Cobalamin, Vit D, CRP
	Myanmar	2017-18	P/S Zinc, Ferritin, sTfR, Hemoglobin, Vit A (RBP), Urinary Iodine, Serum Folate, Whole Blood Thiamin, Vit D, CRP, AGP
	Nepal	2016	P/S Zinc, Ferritin, Hemoglobin, Vit A (MRDR), Urinary Iodine, RBC Folate, CRP, AGP
Western Pacific	Kiribati	2017	P/S Zinc, Ferritin, sTfR, Hemoglobin, Vit A (RBP), Plasma Selenium, eThDP, Plasma Folate, Cobalamin, CRP, AGP
	Mongolia	2016	Hemoglobin, Ferritin, sTfR, Vit A (Retinol), Urinary Iodine, Vit D, CRP, AGP
	Viet Nam	2019	P/S Zinc, Ferritin, Hemoglobin, Vit. A (Retinol), Urinary Iodine, Serum Folate, Cobalamin, Vit D, CRP, AGP
Eastern Mediterranean	Pakistan	2018	P/S Zinc, Ferritin, Hemoglobin, Retinol, Vit D, Iodine, Folate, Cobalamin, Calcium
	Jordan	2019	P/S Zinc, Ferritin, Hemoglobin, RBP, Retinol, MRDR, Vit D, Folate, Cobalamin, CRP, AGP
	Somalia ²	2019	P/S Zinc, Ferritin, sTfR, Hemoglobin, RBP, serum retinol, Iodine, Folate, Cobalamin, CRP, AGP
Europe	Uzbekistan	2017	Ferritin, Hemoglobin, Vit A (Retinol), Urinary Iodine, Folate, Cobalamin, CRP, AGP

1 For Americas, micronutrient biomarker data was collected in Guatemala in 2015, 2016, 2017 and 2018, but not included here; 2Micronutrient biomarkers were assessed in capillary blood.

2 sTfR, soluble transferrin receptor; RBP, retinol-binding protein; MRDR, modified relative dose response; vitamin D, 25-hydroxy-vitamin D, RBC, red blood cell; ThDP, thiamine diphosphate concentrations; CRP, C-reactive protein; AGP, α -1-acid glycoprotein.

Micronutrient biomarkers in italics were tentative at the time of reporting.

B. Interview guide: The measurement of biomarkers of micronutrient status in national surveys

Background

Including micronutrient status in existing national surveys would dramatically increase the ability to promote, design, and monitor micronutrient policies and programs. In an effort to increase the availability and utilization of high-quality data on micronutrient status at the national level in low- and middle-income countries, IZiNCG and the Micronutrient Forum are seeking inputs from countries that have recently carried out a national nutrition survey.

As you know, micronutrients are essential nutrients for our health, and deficiencies of several micronutrients are likely to be a public health problem in many low-and middle-income countries. We want to learn how and why you decided on which biomarkers of micronutrient status to collect, and get a sense of your overall experience with collecting information on these indicators. By identifying factors that have enabled assessment of biomarkers of micronutrient status along with challenges that remain, we hope to facilitate the sharing of knowledge between countries and to promote the more frequent and systematic inclusion of diverse biomarkers of micronutrient status in future surveys.

We are kindly seeking your responses to the following questions.

We anticipate that this interview will take 60-90 minutes.

Do we have your consent to continue? Yes___ No___

Do we have your consent to record this interview? Yes___ No___

Introductory

1. From the report of your national survey, I noted you collected *list the biomarkers reported on* – is this the complete list?

Prompts/follow-ups:

1.1 In which population(s) did you measure these indicators?

1.2 What was the size of this population/sub-group? How did it compare to the total sample size of the survey?

Early planning stage and fundraising

2. Which biomarkers of micronutrient status did you *consider* for inclusion in your survey and how did you decide which to include?

Prompts/follow-ups:

2.1 Can you tell us about the ‘selection process’ and key deciding factors for inclusion? In other words, how did you decide which biomarkers would be included and excluded?

2.2 What led to the decision not to include *list those considered but not included* in your survey? If you had to rank these, which factor would be most important/deciding?

2.3 Did the inclusion of certain micronutrient biomarkers come at the cost of excluding other micronutrients? If so, which micronutrients were excluded?

- 2.4 What type of support/resources (financial, technical, logistical, training, other?) may have changed the outcome for those excluded?
 - 2.5 Which stakeholders were involved in the discussions and making this decision?
 - 2.6 When did you start the process of selecting the micronutrient biomarkers to be included in the survey? When did you make the final decision about which micronutrient biomarkers to include? (How did this timing relate to the initiation of data collection?)
 - 2.7 Apart from the micronutrients considered, there are also *list those not considered*. Why were these not considered? Which information/insights/factors would have caused you to consider these?
- 3. Were micronutrient biomarkers “competing” for resources with other indicators? If so, which other indicators were under consideration?**
- 3.1 How did these overall decisions influence your final list of micronutrient biomarkers to be included?
- 4. What were your sources of funding?**
- Prompts/follow-ups:
- 4.1 Did you need to seek separate funding to include any of the micronutrient biomarkers?
 - 4.2 Which were your ‘most expensive biomarkers’? Would you be willing to share any costing data with us?
 - 4.3 What strategies did you use to raise funds?
 - 4.4 How did the various funding sources compare in terms of magnitude and flexibility?

Survey planning

5. How were data collection personnel trained for the collection and processing of blood (and maybe urine) for the micronutrient biomarkers in question?

Prompts/follow-ups:

- 5.1 What special training was given to account for specific factors that can affect the analysis or interpretation of micronutrient biomarkers?
 - 5.1.1 For example, contamination for zinc, or light exposure for vitamin A
- 5.2 Which types of resources or tools were helpful in this regard?
 - 5.2.1 For example, did the institution responsible for implementing the survey have its own protocols or did you refer to e.g. international technical documents?
 - 5.2.2 Or did you rely on the experience of the supervisor team?
- 5.3 Which additional resources would be helpful in the future?

Survey implementation

6. What were the main challenges faced during collection, processing, transport and storage of blood (and maybe urine) samples for your micronutrient biomarkers?

Prompts/follow-ups:

- 6.1 Did you collect venepuncture or capillary blood samples or both?
 - 6.1.1 With which method were challenges mainly associated?
- 6.2 Were any of these challenges specific to a certain micronutrient? (e.g. zinc, vitamin A, thiamine)

- 6.3 Were any of these challenges specific to a certain target group?
- 6.4 How were these challenges addressed?
- 6.5 Can you describe any specific routines or technical solutions put in place?
- 6.6 Did you experience any challenges related to supplies/consumables?
- 6.7 If applicable, what were the challenges associated with transport of samples from the field to the lab, including (maybe) international transportation?
 - 6.7.1 Were there any rules prohibiting the export of human samples to laboratories outside the country?
- 6.8 What would you do differently in a future survey to avoid these obstacles?

Sample analysis

7. Where did you have the samples analysed?

Prompts/follow-ups:

- 7.1 How were the decisions made regarding the location of analysis for each biomarker?
- 7.2 If applicable, how were laboratory personnel trained for analysis of the micronutrient biomarkers in question?
 - 7.2.1 Was any capacity building or laboratory support received from external labs? Did any external labs provide QA/QC?
- 7.3 What were the main challenges faced during sample analysis?
 - 7.3.1 Were any particular micronutrient biomarkers more challenging than others?
- 7.4 If sent to an external lab, what were the reasons this lab was chosen?

8. Were any remaining plasma/serum samples stored for future analysis of micronutrient biomarkers?

Prompts/follow-ups:

- 8.1 Where did you store the samples?
- 8.2 What plans are there for analysing these samples in the future?

Data analysis

9. How did you assess the quality of the data obtained?

Prompts/follow-ups:

- 9.1 Please include whether any criteria or guidelines were used, and whether any assistance was received from external agencies.

Dissemination

10. After the survey was complete, how/where did you make the data available?"

Prompts/follow-ups:

- 10.1 When did you make the results available?
- 10.2 How did you make the results available?

10.3 Is the micronutrient biomarker meta-data (individual data) available?

10.3.1 Would you be willing to make it publicly available?

10.4 Did you communicate with the WHO to ensure the results were incorporated into the WHO Micronutrient Database?

11. How have the findings from the survey been used since the survey?

Prompts/follow-ups:

11.1 What value did you see in having data on the *insert the less common/more difficult to assess biomarkers they assessed*?

11.2 Were the findings used to advocate for /lead to interventions to improve micronutrient status. Any micronutrients in particular?

Survey summary

12. Interviewer summary of key issues and challenges throughout the process.

Prompts/follow-ups:

12.1 Does this sound like a correct impression of events? What would you add?/Why not?

12.2 You mentioned challenges A, B, and C—which do you see as the biggest obstacles for measuring the micronutrient biomarkers in question again?

13. To aid our understanding of measuring micronutrient biomarkers in your survey further, can you please share a rough timeline of decision-making, fundraising, survey planning, survey implementation, sample analysis, data analysis and dissemination?

Looking ahead

14. Are there plans to assess these micronutrient biomarkers again in the future?

Prompts/follow-ups:

14.1 If applicable, when and in what format? Please include whether it will be in a national nutrition survey or associated with another survey or system.

14.2 If applicable, in which subgroups?

14.3 If not, why not?

Your two cents

15. What advice would you give to colleagues in other countries who might be interested in assessing a variety of micronutrient biomarkers in a national survey?