Exploring the Anemia Ecology

Webinar Transcript

Yaritza Rodriguez

Good morning, good afternoon, good evening. Thank you for joining today's webinar to learn more about new thinking to address anemia on behalf of the U.S Global Nutrition Coordination Plan. We welcome you. My name is Yaritza Rodriguez and I'm a Communications Officer at USAID Advancing Nutrition. I'm going to get us started with some troubleshooting tips and norms for today's webinar.

Next slide, please.

If at any point during today's webinar you're unable to hear the speakers please make sure you've connected your audio by selecting the headphones icon. Please send a message to everyone as I mentioned before for those who joined a bit earlier. Please send a message to everyone in the chat box to introduce yourself. We'll also be using the chat box to collect your comments and you can also use the chat box to ask for support during today's webinar.

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We'll be using the Q&A box today, so please submit your questions for panelists in the Q&A box. Panelists will either reply back to you via text in that box or will answer your questions during the discussion portion of the webinar. Please also note that if you have any trouble staying on the webinar or seeing the slides or hearing the panelists, we will be recording this webinar so rest assured that it will be made available to you afterwards on the USAID Advancing Nutrition website.

It is now my pleasure to turn it over to Lindy Fenlason, Senior Nutrition and Capacity Building Advisor with USAID's Bureau for Global Health in the Office of Maternal and Child Health. Over to you Lindy.

Lindy Fenlason

Thank you Yaritza. Before beginning today's presentation I'd like to provide a bit of background on the US Government's Global Nutrition Coordination Plan or GNCP, which is now in its second iteration. The GNCP represents the US Government's commitment to applying a whole government approach to addressing malnutrition through interagency collaboration and coordination. And the GNCP houses multiple technical working groups, one of which is the Ecology of Parent Infant and Child or EPIC nutrition. And this is a subgroup that is sponsoring today's event.

This webinar is part of our knowledge sharing effort to learn about the key results of the recent anemia task force review and to discuss the implications of these findings on current and future efforts to address this high priority global health target. We have an exciting lineup of experts here to share findings from that report, as well as their perspectives on implications for program implementation. I would now like to hand it over to Dan Raiten, the co-lead of the EPIC nutrition group and also the Program Director of the Nutrition Pediatric Growth and Nutrition Branch of the Eunice Kennedy Schreiber National Institute of Child Health and Human Development, Division of the National Institutes of Health. So with that mouthful, I will hand it over to Dan.

Dan Raiten

Thank you Lindy and welcome everybody. I'm going to spend a couple of minutes just giving an overview of this project which I've been honored to chair. You're going to hear from the distinguished chairs of the subgroups that we have organized around this question but let's move ahead. So what is the problem? What are we talking about here?

Next slide.

There are lots of components to this and our efforts and the efforts that many of you who are involved in the global public health nutrition interface, we have this sort of a linear approach to addressing issues. So whether the crisis has to do with what we're experiencing as a result of Ukraine, what we've experienced as a result of Covid and other pandemic infections, social demographic issues and climate, they all have an impact on food nutrition security. That is then perceived as having an impact on malnutrition over and under the double burden, and many times that's interpreted as having an impact on global targets that we've established for ourselves to

address compelling issues in the global health arena like anemia or stunting. And then we move from there to addressing those problems by using the usual toolkit that we have at our disposal. This is an effective approach in many respects but it's also limited. And when we're talking about multifactorial issues like anemia, the limits are due to the fact that we're really not addressing biology and the real etiology of these conditions.

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So basically, our core premises is that 'one science fits all does it' and that we need a new approach to address a complex issue like anemia. We use the term ecology here and a very brief definition of ecology is the interaction of a complex biological system with its internal and external environments. In this case, that biological system where humans and the hematological system.

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We talk about the environment a lot and the environment is kind of like "beauty is in the eyes of the beholder"; what is an environment to some is not an environment to others. And there are multiple components of the environment. We are suggesting a holistic multi-dimensional view of the environment that includes the physical environment, the home environment, the health context, and of course the nutrition and food security/food system environment.

Next slide, please.

And this is the just to convey the complexity of the health context. That top line conveys that the issue of that linear logic where we often focus on issues of under nutrition, we're now dealing with the nutrition transition which is leading to other aspects of malnutrition, including the double burden. But the point here is that these aspects of malnutrition coexist in a world of multiple infectious diseases and non-communicable diseases. That piece in the middle is just to highlight, from a biological point of view, key intersecting systems that play key roles in all of these conditions. That is the inflammatory response to microbiome of course.

The line at the bottom is an acknowledgement that this is all occurring over the course of human development and that developmental trajectory has implications at each critical point.

Next slide, please.

We'll run through the next couple of slides really quickly. It's just to highlight the fact that anemia continues to be a massive problem that we're trying to deal with. This is some data from the

global burden of disease analysis done by Kassebaum in 2016. Some of these data have been updated but we still are faced with a very daunting and in many ways intractable problem.

Next slide.

One of the key issues here that we want to highlight is that while iron deficiency remains a leading cause of anemia, it's not the only cause by any stretch. And this is just a list of some of the multiple causes of anemia.

Next slide.

This slide again from Kassebaum sort of summarizes the issue. The core issue for us is that anemia continues to be a problem; iron deficiency anemia continues to be a major component. We've made some progress with iron deficiency anemia but the global numbers of anemia don't seem to be changing even though we're, in some respects, reducing iron deficiency. And that's because the system sort of compensates for itself on the increase in the prevalence of some of these other causes. So it really does make a case for a much more complex scenario than just a nutritional problem.

Next slide, please.

So, this is just a vein diagram to sort of convey the complexity of anemia and our approach to it. Anemia consists of sort of three primary causes: there's the nutritional cause that includes iron deficiency and other nutrients, genetics is a major factor and you'll hear about all this from Gary and the rest as we move forward, and of course the health context.

Next slide, please.

When we put this all together from an ecological approach, we have to consider the environment, the nutritional context, and the health context. These are all the components of the ecology. It is a daunting issue to deal with all these at once. We tend to deal with each of these sort of separately but the case we're trying to make is that we need to be able to do more than one thing at a time.

Next slide.

This just sort of highlights the key goals of the task force and what we're trying to do. We're really trying to address this issue of iron deficiency, recognizing that there are multiple causes, how can we be clear about what's iron deficiency and what's not, what's the contribution of other nutrients, how can we account for the other multiple causes of anemia, and how can we improve

the precision of assessment of both clinically and in surveillance to improve the development and scale-up roll out implementation of equitable context-specific interventions.

Next slide, please.

So the USAID response was to create this task force led by Omar Dary and Denise Murthy and some of the other folks that you'll hear from today, and certainly our team at Advancing Nutrition. We put this task force together to address the key aspects we've highlighted and that you'll learn about. We're intended to advise USAID in their efforts to address anemia and serve as a resource to the community. And you'll hear some of that later on as well.

Next slide.

This is just to highlight the fact that we understand these three components of anemia as a continuum but they're not linear. It's a circular interacting continuum and there's this continual feedback loop, both in terms of how we deal with it and interventions, but also how we do surveillance. We're constantly getting data and we're constantly getting feedback and we need to think about it in this interactive right.

Next slide.

This is just the process. We were asked to develop a report for delivery to USAID which we've done. We've been asked to publish that report which we're in the process of doing. The report will be published as a supplement to the Journal of Nutrition. And we've been asked to serve as a resource to the community which we are doing. You'll hear a little bit more about that later on. I think that's it.

I want to thank Omar and the USAID Advancing Nutrition team, Laura Hackel whom you will hear from next. We are privileged to have three chairs that you're going to hear from today, who have been critical in pulling this all together. I also want to acknowledge the contribution of all the members of the three working groups. There are five to eight members of each working group. They all work collaboratively together to pull these reports together. With that I'll turn it over to Laura and thank everybody for this opportunity.

Laura Hackel

Thank you very much then and also thank you Lindy for the introductions. It is a pleasure to be part of today's webinar. I am a Research Advisor at USAID Advancing Nutrition's Monitoring

Evaluation and Learning Team and in my role I had the distinct pleasure of working with an incredible team of experts to produce the USAID Advancing Nutrition Anemia Task Force Report under Dan's leadership. To get us started, I will now turn it over to Gary Brittenham, professor of pediatrics and professor of medicine at Columbia University for an overview of the biology of anemia. Gary, over to you.

Gary, in case you're speaking you are muted.

Gary Brittenham

This slide shows the members of the working group who are responsible for this report. It's their work that I'll be presenting briefly today. The next slide shows my financial disclosures just as the preface for the presentation. The next slide shows that enormous progress has been made in understanding the biology of anemia that can help guide effective assessment and interventions. This presentation will review the vital roles in anemia of the three components that Dan has mentioned: nutrient deficiency, infection, and genetics. These are described in the Anemia Task Force Report which I encourage you to read.

Anemia is present when circulating red cells are unable to carry enough oxygen to meet the body's needs. Clinically, it's detected by measuring hemoglobin. Normally, the biological system shown here maintains oxygen delivery. The circulating red cells carry the oxygen to tissues. If there's an insufficient supply of oxygen, special cells within the kidney produce a hormone (Erythropoietin) that then stimulates the bone marrow to produce more red cells if there are enough nutrients available. And the key ones are Iron, B12 and Folate that we'll hear more about later. So, to respond, the marrow needs these nutrients.

The next slide shows that normally, by using this system, red cell production is in balance with red cell loss.

On the next slide.

But anemia develops when there's an imbalance between these; when red cell production is inadequate to replenish red cells, or when red cell loss exceeds the capacity of the marrow to produce sufficient numbers of red cells.

We've gained tremendous insight into how this is controlled. A key nutrient for making new red cells is Iron. And in essence, the marrow needs circulating iron contained in the blood plasma to

produce red cells. The amount of this circulating iron is controlled by a switch, a hormone called Hepcidin, that controls the entry of iron into the circulation from the three main cells that can export iron: the iron recycling macrophage that takes up aging red cells and then promptly cycles back the iron contained in those cells into the circulation, the absorptive cells in the GI tract that control the total amount of iron absorbed into the body but contribute only a very small part of the total each day, and finally the liver storage cells that act as a sort of buffer to provide iron when needed and to take it up when an excess is present.

Now, the only normal way that iron enters plasma is through an exit protein called Ferritin. And Hepcidin works on Ferritin simply by blocking it and then leading to its degradation. So, there's no way for the iron to exit from these cells. It's a simple system in essence that iron can be moved into the circulation when needed by reducing the amount of Hepcidin it's circulating or it can prevent it from entering the circulation by increasing the amount of Hepcidin.

The next slide shows an overview of the body iron supply and where it's stored. On this slide, the red cells show the functional iron, the blue circles here show storage iron, the black arrows are the circulation of the iron, and the tiny little compartment in the middle is the plasma iron. And you see the GI tract and where the iron is absorbed. The width of the arrows shows how much of the iron is being recycled each day. And so I'd like to use these in the next slides to show the differences between Absolute Iron Deficiency and Functional Iron Deficiency.

The next slide shows normal ion storage to sort of calibrate you. On the left you see our diagram that we'll be showing and on the right a figure that shows that in iron homeostasis things are maintained in balance with red cell production and equity loss.

The next slide shows Absolute Ion Deficiency. You can see that the circulating red cells on the left have been reduced to an anemic level, and that the iron stores are absent; so there's not sufficient iron to go to the marrow and produce new red cells to maintain oxygen delivery. Contrast this with the next slide that shows Functional Ion Deficiency. Here you see that there's still not enough iron being delivered to the marrow to produce sufficient red cells, but stores are present. This is because Hepcidin produced by infectious inflammation is blocking the export of iron from the recycling cells, blocking absorption from the GI tract and blocking any iron from entering the system from the liver. This is Functional Iron Deficiency and it's very critical to the understanding of anemia because many or most infections perhaps produce cytokines that

stimulate the formation of Hepcidin that then blocks the circulation of iron. And if sustained and sufficient can then produce an anemia of a level that's equivalent to that where you see an iron deficiency. And absolute and functional iron deficiency can coexist as in this circumstance there are no stores to recirculate, but there's still a block from the increased levels of Hepcidin.

The next slide just shows that Absolute Iron Deficiency affects the most vulnerable; children under five and women during pregnancy, and women throughout their years of childbearing age.

The next slide reminds us that there are other nutrients, key of which are Vitamin 12 and Folate, which can also cause anemia through a different mechanism by limiting DNA synthesis. But these nutrients can also be affected by infectious inflammation because the inflammation that results from the infection can suppress the bone marrow even if there's a sufficient supply of nutrients.

I'd also like to mention Vitamin A deficiency. It's primarily a set of syndromes of which Anemia is simply a part, but it results in an interference with iron utilization. And like many of the disorders we'll be discussing in both infections and genetic disorders, it's prevalent in some of sub-Saharan Africa and in Asia.

The next slide.

I'm sorry this is the one showing the Vitamin A deficiency. Next slide, please.

This shows the global prevalence of certain infections. Chief of which is malaria, that we'll discuss further in a moment. Second among which we should mention hookworm that causes blood loss that also results in absolute iron deficiency.

The next slide shows the variety of mechanisms that can be responsible for anemia during infection. What I've emphasized earlier is the anemia of inflammation that's the result of chronic infections, hemolysis or the destruction of red blood cells is a feature that's prominent in malaria and other conditions, blood loss especially from hookworm and other ailments is present, and there are others than can also produce anemia through these various mechanisms. So there's not a simple way that infection results in anemia, but a whole complex of mechanisms that are operative. Just for a brief example, I'd like to show you the case of malaria. You see on the left how the mosquito transmitting the infection that then circulates within the infected red cells.

Next slide.

Then you see, it works through a variety of mechanisms; by causing hemolysis, by suppressing the bone marrow, by suppressing recycling of iron, and by suppressing iron absorption that

ultimately result in anemia. As a transition to genetics, I thought I would just show you the global map of malaria in endemicity in this slide because all of the genetic disorders that occur at a rate greater than random mutation coexists with the historical distribution of malaria. Their principal role for us is in assessing anemia because they can produce an anemia and microcytosis that is very difficult to distinguish from absolute and functional iron deficiency. And with that, let me transition back to Laura to introduce the next slide.

Laura Hackel

Thank you very much Gary for that very enlightening presentation. Now we'll hear about the ecology of anemia in the context of anemia assessment from Parmi Suchdev. He is a medical epidemiologist with the CDC Central American Regional Office in Guatemala and Professor of Pediatrics and Global Health at Emory University, and he's also a Practicing Pediatrician at the Children's Healthcare of Atlanta. Parmi, over to you.

Parmi Suchdev

Thanks Laura and thanks for the invitation to be with you all. Good morning from Guatemala. I'm going to talk about Improving Anemia Assessment in Clinical and Public Health Settings.

Next slide, please.

These are my disclosures.

Next slide, please.

So we're the assessment working group. We've talked about biology and we'll talk about interventions following me. Our goal of the assessment working group was to provide a practical approach to assessment of anemia, primarily in public health settings but also clinical settings, with the focus on evaluating the etiology of anemia.

Next slide.

This quote from Lord Kelvin "if you cannot measure it, you can't improve it", really is the core value that guided our work in the assessment group. Because if you want to really make an impact on anemia burden globally, we really got to better understand the ecology of anemia.

Next slide.

So we're going to pull up a zoom poll for you. It will be an opportunity for you to interact so please click on what you think is the answer to the question "how likely are we to meet the 2025 World Health Assembly target for 50% anemia reduction in women of reproductive age?"
Let's go ahead and look at the results. Okay, great!
Next slide.
So the answer was three percent and it's really striking how slow we've been to reaching these goals. So our most recent 2019 estimates that were published by the World Health Organization in the Lancet Global Health show that there was about 30% anemia prevalence in non-pregnant woman of reproductive age. And that orange line shows what we would need in order to cut that in half by 2025. But we're actually only declining within the green graph at only about 0.3 percentage points per year and only Guatemala and Philippines are on track to meet that target.
Next slide.
So this is what really led our working group and why we were put together. And really our objectives are to review how to assess anemia itself based on low hemoglobin, review assessment of causes of anemia in different settings, and then to propose a decision tree to systematically approach anemia assessment in surveys and populations, and then finally to discuss research gaps for priorities.
Next slide.
To diagnose anemia itself, Gary has already explained this a bit, is functionally defined as an inability for your red blood cells to deliver oxygen, but it's diagnosed by either a low hemoglobin or a low hematocrit. And clinical signs are not reliable in most settings.
Next slide.
So this results in us having to use some type of laboratory technology. And there are many different approaches; whether it's the point of care instrument, whether it's the goal standard or a culture counter, whether there are some novel non-invasive technologies. And there are also differences in these different approaches based on whether you're doing Phlebotomy to get venous blood or a Fingerstick to get capillary blood.
Next slide.
Even once you've decided on which technique you're going to use to measure hemoglobin, there are many pre-analytical and post-analytical factors you need to consider. To just give you some

examples on the pre-analytical side, an important factor is what type of blood you're going to use. Is it going to be venous or capillary? There was a recent study in Mexico for which there's a link provided here which showed that capillary samples were 20 to 30 grams per liter lower than venous samples. And that maybe pulling the capillary sample may approximately give less blood. So that's an important consideration. Then, on the post-analytical side, there are factors such as inflammation infection that can affect the hemoglobin concentration, altitude, and then the cut-offs you're going to use.

Next slide.

This is a recent evaluation done by the BRINDA Working Group which looked at the thresholds to define anemia. And this is a figure looking at anemia and healthy children using population-based surveys and defining a healthy subgroup of children who did not have Iron deficiency, Vitamin A deficiency, inflammation or malaria. And look at that 5% threshold, because that's how the anemia cut-offs are currently defined. And you can see in really all the countries besides Vietnam and the US that the 5% threshold is lower than the current WHO cut-off in children aged 11 which is shown in the dashed line.

Next slide.

So this is a statistical cutoff but more important is what happens to your body when you're getting anemic. One of the things your body does is your bone marrow produces more red blood cells, you get increased erythropoiesis. So using a serum soluble transplant receptor, which is a measure of erythropoiesis, and a cubic spline analysis we were able to also show that there's an exponential increase in transfer receptor at a hemoglobin concentration of about 9.6. Which really helped to collaborate the statistical cutoff that we also showed on the left.

Next slide.

So those are some of the ways to measure hemoglobin itself. But now, what about the causes of anemia. You heard from the biology group that there are many different causes of anemia and iron deficiency in this red box is just one of many causes. An iron deficiency can be both functional iron deficiency and absolute iron deficiency. But there are also causes such as blood loss, increased hemolysis, deficiency erythropoiesis and different micronutrient deficiencies. In our report, we go over each of these and why they can lead to anemia, and why they're important to assess. At the bottom line, anemia itself is not a disease. So if you've diagnosed a patient or you

diagnose the population as being anemic, that's not really helpful until you figure out what caused that anemia itself.

Next slide.

Really, the goal is to apply an ecological approach to assessing anemia. And this can be done by both individuals who are seeing patients in a clinical setting as well as researchers or public health professionals who are working in surveys.

Next slide.

So this is just one example of an approach to assessing an individual in a clinical setting. And this is a busy slide. I won't go into detail but essentially you would do an assessment of anemia and might do what's called a Complete Blood Count (CBC), and then if the patient is shown to have microcytosis or a low MCB, you would follow that up with some type of iron evaluation. Typically a ferritin and a measure of inflammation. And if the patient has a normocytic or macrocytic anemia you would do additional tests. But really when coming to the bottom line that's the red of diagnosing exactly what was the cause of anemia, then treatment can be given to that patient to address the anemia.

Next slide.

Our challenge then in populations is that 'what do we do to diagnose anemia in a population?' And really, no decision tree existed. And so our group spent a lot of time trying to think about how we can apply some type of decision tree in population. What biomarkers to include when conducting anemia survey so that it's not just hemoglobin itself but you're really getting at the determinants of anemia? It really comes down to understanding the data availability and underlying disease burden in that population to decide what measures you're going to do. So for example in in step two, our data available is to estimate the portion of the anemia that is due to iron deficiency. So if you don't have recent data on iron, then yes, you need to then measure iron with ferritin and some measure of inflammation. And then kind of going down this tree we ask the similar questions to have data on underlying infection burden, underlying inherited blood disorders, blood loss, additional micronutrients, and this will help guide you then from a population survey in terms of which biomarkers should be measured.

Next slide.

In summary, these are the conclusions or recommendations we compiled from our assessment working group. In terms of assessment and interpretation of hemoglobin, to utilize the venous or pool capillary blood and an automated analyzer or point-of-care Hemocue device to measure the hemoglobin itself. Once you have the hemoglobin to apply adjustments for altitude and smoking, and then finally to apply global age specific and physiologically validated cutoffs to define anemia. And we'll hear from the WHO later but there's some revision being considered and reconsiderations on these thresholds. It's an area of research.

And on the right side, once you have the etiology of anemia and the hemoglobin itself, then how do you assess the causes. It's important to assess all relevant causes of anemia surveys: infections, inflammation, blood loss, inherited blood disorder and not just measure hemoglobin itself. So doing a survey with hemoglobin alone is not going to be very useful. And then to apply analytical methods to measure the relative causes or the relative contribution of these different causes in the population to inform intervention. So if you have concurring iron deficiency, Vitamin A deficiency, malaria, inflammation, how do these each contribute together to cause anemia in that population so you can then prioritize your interventions.

Next slide.

Yes there's still many research needs in an assessment of anemia. On the side of assessing hemoglobin and anemia etiology there's needs to come up with non-invasive methods to measure hemoglobin or even point-of-care methods that are more precise; to consider point-of-care assessment of some of the causes of anemia such as iron, using ferritin, hepcidin and erythropoietin; the role of multiple micronutrient deficiencies anemia and then again like we've talked about re-evaluation of the hemoglobin thresholds themselves to define anemia.

And then on the population assessment side, statistical approaches and cost and logistical implications of a stepwise algorithm. We'll put another zoom poll up. I think we still have some time. So the zoom poll is just to ask you "which of these research needs would you prioritize based on where you're working in your current role?" All right let's see where we're at.

Okay as I suspected it's a good blend and I think this is helpful for the funders to see where we're much interested in the community. And this is something that we can discuss more in the discussion section on where should we invest and research.

Next slide.

My take home points.

- Anemia itself is not a disease, but a condition reflective of its diverse and overlapping causes.
- And we really need to broaden our focus from predominantly iron to better understanding the both nutritional and non-nutritional anemia determinants to both inform clinical care and anemia control programs
- And finally if we can adopt a practical systematic approach to anemia assessment as we've put forth in our report, this is an important first step to address data gaps which can then lead to our ultimate goal which is to reduce the burden of anemia globally.

And with that thank you.

Laura Hackel

Thank you very much Parmi for a truly great presentation. We will now hear from Cornelia Loechl. Cornelia is a Nutrition Specialist and Head of the Nutritional and Health Related Environmental Studies Section at the International Atomic Energy Agency, and she is also the chair of the Interventions Working Group in the Anemia Task Force. Cornelia, over to you.

Cornelia Loechl

Thank you Laura for the introduction. Good afternoon from Cornelia in Austria. I'm going to talk about the approaches on how to address anemia on behalf of my working group. And you see the members listed here. I have no conflict of interest to disclose.

Next slide, please.

But before I talk about the approaches themselves, I wanted to come back to something that you have heard from Dan earlier today. It's important to recognize that anemia is multifactorial. It has to be looked at as an ecology consisting of different components and here one of the components is diet and nutrition, which means production and consumption patterns then affected by social, behavioral, cultural and economic factors. And there's a challenge associated especially with plant-based diets of anti-nutrient compounds which reduce nutrient absorption. For example phytic acid is a potent inhibitor of iron, zinc and calcium absorption. So all these are really important considerations to inform the choice of nutrition-specific interventions.

Next.

So health status such as inflammation state, diseases, or genetics is another important component of the anemia ecology, which may or which might require actually to consider non-dietary interventions for anemia prevention and treatment. Which could be at individual level, population level, in a clinical context or a public health context.

Next.

Then there's the environment as part of the broader context. And here I would like to mention specifically climate change because it directly impacts food quality and quantity. The crop yields go down, nutrient composition changes, and higher CO_2 levels reduce the concentration of protein, calcium, iron and zinc in major crops.

Next.

So now, after looking again at this broader context, "how do we now select context-specific interventions that can address this complexity?" And we are proposing here the AAA framework that is a benefit from UNICEF to support such choices and help us to use a range of available interventions to address anemia in different etiologies. So this framework consists of a sequence and components of assessment, analysis and action as an interactive cycle which is then overseen by a monitoring and evaluation plan.

So for the assessment of needs, the basic sign is really important as you have just heard from Parmi, to understand potential ideologies, relevant aspects of the stages of the potential target population or potential implications of pre-existing interventions. And that really informs the selection of appropriate interventions.

The analysis is a continuous feedback loop involving data from different sources and action relies on the translation of research and evidence, and on implementation science. And then monitoring evaluation is a continuous effort to improve the implementation and the scalability of new and existing programs. A particular focus should be on potential unintended consequences.

Next please.

So now I'm starting with a presentation of an overview of the available approaches to address non-dietary anemia, either at individual or population levels. We have looked here at the interventions addressing disorders of the highest global burden of disease. Some of that we have heard in Gary's first presentation. For malaria, it is recommended to use intermittent preventive

chemoprophylaxis or insecticide-treated nets. WHO recommends, for intestinal parasites, mass drug administration or targeted chemotherapy or selective therapy. And then the inflammation associated with both tuberculosis and HIV impacts iron hemostasis and results in anemia. Here it's important for the selection of the treatment to differentiate between iron deficiency anemia from anemia of inflammation and to determine the etiology. Then other clinical conditions such as acute and chronic blood loss or inherited red blood cell disorders can be addressed through blood transfusions, iron supplements, iron chelating therapy or delayed core clamping for improved maternal and infant health outcomes.

Next please.

So here's an overview focusing on the efficacy or effectiveness and the scalability of some of these approaches that I have talked about. And you can see that the efficacy and effectiveness of these different interventions have been proven except for the management of acute and chronic blood loss and for the inherited blood disorders.

Next slide, please.

Key questions and the research gap remains in relation to these non-directory interventions. We have come up with many but I just want to mention a few here. To improve our understanding, we need to look at factors that relate to drug resistance, we need to better understand the drug interactions, safety of mass de-warming programs especially in the context of endemic malaria and HIV. We need to understand what the potential benefit of malaria vaccination is on the linear prevalence or what rich factors are actually impacting the compliance of large-scale de-warming programs and what is the true frequency of delayed cord clamping and it's cost benefit to scale-up. And we also need to understand better what the feasibility in the scientific merit is for a broad approach to reduce inflammation as an intervention for treatment of anemia.

We have also identified many actions that are needed and I'm just going to mention a few here. So, what we need is better tools for serological surveillance of malaria and pregnancy, we need empirical guidelines for the duration of delayed cord clamping and strategies to address new and emerging parasitic infections. Again, this is just a selection.

Next please.

Now, coming to the nutrition-specific approaches. Again, anemia is not iron deficiency and all iron deficiency is not anemia. You've heard this earlier from the previous speakers. But iron

deficiency remains a significant factor in our ability to comprehensively address anemia. So therefore the presented available nutritional-specific approaches here largely focus on iron but the concepts are applicable to other nutrients. So we distinguish here between food-based approaches and supplementation.

Next please.

So food-based approaches include improving dietary diversity, and dietary diversity is defined as a number of individual food items or food groups that are consumed over a given period of time and usually is reflected by computed dietary diversity score. Biofortification aims to increase the micronutrient content in crops through breeding and the addition of animal-source foods is helpful because it has a positive impact on nutrient absorption.

Next please.

Again here's some information on the evidence of the different approaches that is available. For improving dietary diversity and adding animal sources of iron to foods, we have seen mixed effects and there's more evidence needed. There's no information yet on effectiveness and there's more research needed on how to scale these up. Whereas, by fortification, we have proven efficacy and there's more and more evidence that it is effective and it has been integrated already into agriculture value chains and food systems.

Next please.

So I continue here with the traditional household level food preparation techniques such as dehulling, peeling, soaking, germination, fermentation or drying, and the presumed benefits here arise from the activation of enzymes such as amylases. And those techniques can reduce anti-nutrients by up to 90%. Then we have fruit fortification and we distinguish mass and targeted fortification. For mass fortification, the vitamins and minerals are added to commonly consumed food vehicles like salt, cereals, oil, milk, sugar whereas targeted fortification means the addition of micronutrients to foods consumed by specific population groups or specific age groups. Examples are the ready-to-use foods for the treatment of severe and moderate acute malnutrition.

Next please.

Again, here is the overview of the currently available evidence. For the food processing techniques there's limited information from small studies, mixed effects, no information on

effectiveness yet, and there is doubt about the scalability. So more research is needed. For mass and targeted food fortification, we have proven efficacy. The effectiveness has been proven but not sufficient yet and it has been scaled-up. And for targeted food fortification the effectiveness has been proven in a specific context but it's not yet widely used.

Next please.

For supplementation, we mean direct oral supplementation and consuming micronutrient supplements combined with foods. For instance micronutrient powders. So the focus here is on aspects of iron supplementation, as it is the micronutrient most difficult to deliver in sufficient amounts through other interventions. So oral iron supplementation is the first line treatment for iron deficiency or iron deficiency anemia in women. And WHO recommends daily oral iron folic acid supplementation. WHO also suggests multiple micronutrient supplementation which includes iron folic acid for pregnant women in the context of rigorous research. There's scanned evidence to date to support the supplementation of Vitamin A, Folate, Vitamin B12 for the purpose of reducing anemia.

Next please.

So, on my last slide, I would like to highlight a few research needs related to the nutrition-specific approaches. Here we need to improve our understanding on biological pathways through which climate change influences iron nutritional anemia, we need to understand better what the value of the traditional food processing techniques is for improving nutrient status, how the association is between those techniques and pathogen contamination, and what the implications are for scalability. We also need to understand better what the most appropriate food vehicles are for targeted fortification and how to better integrate bio-fortified crops into the food value chain on a large scale, and then what the benefits and risks of iron supplementation during pregnancy and on both outcomes are.

Again, this is just a selection of the research needs we identified. And what we need is to start with a systematic review on home-based dietary enhancement strategies. We need to model the impact of fortification concurrently with other interventions, and develop safer formulations and optimize protocols to reduce side effects.

Just to summarize, there is no one-size-fits-all as it has been mentioned already in terms of interventions because of the complex anemia etiology. The context matters, nutrition-specific

interventions might not always be the right or the only answer to address anemia. And therefore the assessment part that you've just heard about is really critical to help select the most effective interventions. Thank you and I'm handing back to Laura.

Laura Hackel

Thank you very much for a great presentation Cornelia and thank you to the other presenters for very interesting insights. We have now come to our discussion period and we have about 25 to 30 minutes for questions, and I will turn it over to Lindy to get us started. Thank you.

Lindy Fenlason

Thank you so much Laura and I'm echoing your thanks to all of our presenters for walking through those summaries of each section of the report. Now I'd like to introduce our respondents for today. We have Maria Elena Jeffords from the Center for Disease Control and Prevention, we have Sarah Cosick from the University of Minnesota and Lisa Rogers from the World Health Organization. We've had a lot of questions that have come in from the audience already, please do continue to add your questions to the Q&A section and we will answer as many as we can today. What I'm going to do though first is hand this over to our respondents. We'll go in the order of Maria Elena, Sarah and then Lisa. We would like you to take a few minutes to share your initial feedback on what stood out to you from this task force report and what do you see as potential implications for anemia programming within your organization, and even more broadly. I realize that's a huge question to cover in a few minutes but we're eager for your input. Again we'll go ahead and start with Maria Elena.

Maria Elena Jeffords

I appreciate the invitation to be here today. I really was very impressed by all of the presentations, these are incredibly complex topics. And it just reinforces to me how complex it is at so many levels and if this was a simple issue it would have been resolved by now. So I think it helps explain why we're still struggling so much with reducing anemia globally and in local contexts as well. One of the things that stuck out to me is I really would have liked to have seen the perspective

of people who are actually trying to run programs, who are trying to carry out national policies, reflect on from their perspective about how they view these presentations and the implications for them. That's something I would encourage the task force to consider. I think it would help them understand at a deeper level what some of the fundamental issues are. As I saw these presentations my mind kept going back to the issue of many countries having multi-sectoral plans and even anemia policies to address nutrition and really integrate and coordinate, and there's fundamental challenges with even trying to implement those national policies. And how do you coordinate, how do you integrate, how do you actually carry out these plans in the context of weak governance? The supply chains don't work. It really doesn't matter what you do or how do you manage that.

So I think those kinds of issues are fundamental to making progress and really reducing anemia. And we really have to focus on that as well, which is not easy. So I think the other piece of it is, as I've seen in many contexts, the guideline comes out and says "you have to be integrating or you have to do iron and malaria together. You always have to have both". And I think understanding what that actually means for implementing that in a given context or doing that in the country because then you don't want the nutrition program taking over the malaria program. So I think it's understanding how to operationalize which I think is really challenging and one of the fundamental drivers of the lack of progress.

I'll just make one other point, maybe two. I think understanding anemia clinically versus like from a population-based survey; like the ability to do this in LMIC's and even in low resource settings in high income countries, I think it's fundamental to the discussion and we can't get away from that. So I think trying to understand the complexity and how to reduce it into something simple and practical, that's again where I think having more input from others if we're actually doing this in that context would be helpful. The last point I have to make is what if it's all just a measurement issue. And it's already been reduced 50% and we just don't know because we're using bad assessment methods. So I keep coming back to that because we have too many surveys where it was a drop of blood versus a venous sample and it's a 20 or 30 percentage point difference. So ultimately there's a lot of work to do. Over.

Lindy Fenlason

Thank you so much for that. I really appreciate your points around the complexity of the issue and what that means for operationalizing this. And also what's needed to clear the fog and get a clear pulse check of where we're at with anemia. I'll go ahead and hand it over to Sarah.

Sarah Cosick

Apologies Zoom 101. Anyway, I was just saying that it was really an honor for the invitation to be here. When we're reading the report, I was struck by how comprehensive it was. It was really the most comprehensive report I've read on all the possible different causes of anemia, and how once and for all anemia does not equal iron deficiency. I really come from this from a research perspective and really appreciated the clear distinction made at the beginning between absolute iron deficiency and functional iron deficiency, and how they both interact and can both lead to anemia. We have some research in Uganda showing that, in fact, both of those are very much at play. And I guess this is a question to the speakers if the timing of any of these non-nutritional and nutritional interventions has been discussed. We've seen in several studies very clearly that addressing that inflammation first and resolving the functional iron deficiency first actually permits assessment of underlying dietary or absolute iron deficiency. To see if those stores are present or if reducing the inflammation is sufficient enough to mobilize body iron and get hemoglobin back up. And we've seen actually that, in some cases, the non-nutritional interventions are just as effective as getting the hemoglobin back up.

And finally, in malaria endemic areas where I predominantly work, this very well may avoid the need to even supplement with iron. If we can get anemia and iron back into functional compartments, back where it needs to be, perhaps the iron protect which is potentially risky may not be needed.

Finally, I don't know if this is a comment or just sort of an overall question for anyone and that is whether pre-anemic iron deficiency has been considered. Certainly, we know that there's a hierarchy of iron status markers. And in pre-clinical studies we've seen that the brain really gets torched or the brain loses iron or iron is kept from the brain to maintain the red blood cell mass. And so absolutely controlling anemia and measuring it is important, but I'm just wondering if there's been any … I know there's been some research, but any comment from the panelists

about any work done with pre-anemic iron deficiency which we know also can affect the long-term outcomes of neural behavioral outcomes. Over.

Lindy Ferlason

Thank you so much Sarah for sharing from your lens as well and highlighting those questions. Hopefully we'll get a chance to get to. If not we'll definitely get some feedback on those questions for you from the presenters and authors of the report. Now we'll go ahead and go to Lisa and hear her feedback.

Lisa Rogers

Great! Thank you so much. I agree with everyone that the work of USAID Advancing Nutrition and the Anemia Task Forces is an amazing amount of work and it's truly impressive. Just a huge thanks for all the work that's been done. And although a lot of work has been done, I think the real challenge is still ahead of us as Maria Elena highlighted. And that's how do we operationalize or implement some of this work and make real progress in reducing anemia. Countries should definitely be at the center and the foundation of our work because this is who we really want to support, and where impact is needed. And to be sure this work and the findings of the work that we're presented today really resonate with us very well and our approach going forward is very similar.

We've been building an interdepartmental working group of members of malaria, neglected tropical diseases, sexual reproductive health, and maternal, child & adolescent health as well as nutrition and food safety, precisely to try and tackle this comprehensive problem of anemia. And as Parmi had highlighted, we're really wanting to address the lack of progress on the world health assembly target on reducing anemia. So this group has been working also with HIV & TB health systems to try and develop a global action plan for the prevention and management of anemia. And we want to be able to provide strategic implemental implementable actions to reduce anemia, and it's also trying to really consider the different contexts that we're in. We want to ensure that we have that shared understanding of what is that multi-sectoral response that's needed, what are the different etiology of anemia, how do we together build commitment from both the political and the health leaders to drive efforts to address anemia in either multi-sectoral

or … I like how Dan phrased it … this ecological approach. And how do we provide that framework for not only the global community, but regional and country actions to guide their specific response to anemia. And this really includes understanding and addressing the context-specific causes of anemia, while we also simultaneously address some of the risk factors that are related to anemia. So I think really focusing on the women and children, who are the most vulnerable, are our priorities. But all this that we're doing has been highlighted in these presentations and in the report. So I think that this really helps us to look at it very comprehensively and I think this is the one thing that we're trying to really find. That happy medium to how do we not let the optimal get in the way of making any progress at all, but how do we make sure that we really build in the necessary components of the programs. I know there are so many competing priorities for countries - I mean really important priorities for countries. I feel our challenge is to be able to integrate the management of anemia into an overall health systems approach targeting women and children, adolescent girls, while we still recognize that there's a need to highlight that lack of progress towards anemia and understand that lack of progress. We also are establishing an alliance for anemia actions that's bringing together a really diverse group of people who are committed to working collaboratively from all different areas and disciplines, and it's the work that was just presented here. That's really going to help us in these endeavors to accelerate anemia reduction and we're really happy that some of the staff at USAID and many people on the call are contributing to these efforts. So I think it's together that we can try and make this happen but the implementation is going to be our challenge. So happy to work together to try and fix this. Thank you so much. Over.

Lindy Ferlason

Thank you Lisa for sharing from your context of where you're working and also highlighting aspects of the struggle between the ideal and the real, and also highlighting the alliance and the work that's going to be coming from there. So thank you so much for as well as your willingness to collaborate and eagerness to do so. It looks like we have so many questions to walk through. Thankfully we've got about 15 or so minutes to do so but we know that time's gonna go by very fast.

I'm going to go ahead and start us off with one question. I'm going to start with that just because we've got a lot of interest in it from the chat from different respondents around this particular question. This one I think will go primarily to Parmi but anyone else is welcomed to chime in as well. The question is that "there is always a tension between clinical assessment and public health assessment, how would you suggest readers navigate the two in the report?

Parmi Suchdev

Thanks Lindy and thanks for those who raised this question. I think it's an important question and we're fortunate in our working group to have folks who are on the clinical side as hematologists as primary care providers like myself, as well as those who work in populations. And I think that the clinical practice informs the public health and the public health informs the clinical. I think they inform each other and part of the goal is to get these two communities to work together on this problem. Because if you want to make a public health impact you have to understand the clinical impacts. And when you step back and think about it, they do go hand in hand and we even considered an example in assessing anemia in a population; can we take a similar approach that is done in a clinical setting where maybe in a subset of the population you actually look at red belt cell indices and you find out the proportion that are microcycotic. And then in that subset you do additional testing to look at etiologies, and that could maybe be cost saving. We considered this but couldn't recommend it because no one has really done it before. I think it's more of a research question.

So again, I think part of the goal of this task force was to bring these two groups together and to begin that discussion and to hopefully actually implement some very practical research. So I'd say more implementation science research, not basic research, to help address some of these challenges.

Lindy Ferlason

All right. Thank you so much for that. Let's go ahead and go to Gary. Gary we have a couple of questions for you. I'll start with this one. "At the population level, should we change our interventions if we find out that there is more functional rather than absolute iron deficiency, and how should we approach that change if warranted"?

Gary Brittenham

Let me refer you to Cornelia who I think dealt with this problem. To begin, in the case of malaria for example, there's a study that cleverly used the resistance that people with sickle cell traits have to malaria to estimate what would be the effect of eliminating malaria as a cause of iron deficiency and of iron deficiency in anemia. And the answer was surprising, it's almost half. So I think there has been insufficient attention to the control of infection as a means of enhancing both iron and other nutrient interventions. Maybe that's enough for the moment.

Lindy Ferlason

Thank you, Gary. Cornelia anything you want to add to that?

Cornelia Loechl

I'm just also one of the working group members and I'm not aware of where we have dealt with this distinction. We may have covered that under the non-dietary interventions but I'm not aware of anything at this point that we distinguished between functional and absolute anemia. Maybe others can help out.

Lindy Ferlason

Yeah, I'll leave it open for a little bit here and see if anyone else has something they want to add.

Maria Elena Jeffords

I'd just like to say I think at a clinical level that might be more feasible. I'm trying to imagine on a public health population level how that would be operationalized. So that's why I think there's this discussion of integration and coordination. You have to have malaria prevention control diagnosis available where you're delivering intervention simultaneously. So it's like it's foundational. You can't have that control there. So I think if you have a weak system then you're never going to make progress. And I think that gets back to the whole issue of just the weak implementation of all programs if you're in a system setting where the infrastructure is weak, the

delivery platforms are weak, it's a lot more challenging. But definitely you have to do both. You can't do one and then do it sequentially. At least for population interventions I don't think. Over.

Gary Brittenham

Lindy, let me just comment on another example. There's a recent study that was done in patients with tuberculosis that found that the majority who may have it, would not have benefited from iron supplementation. As soon as you cured the tuberculosis, the iron stores could be used to replete red cells and solve the anemia. So it's one example of how infections can really be an underlying cause. It's certainly complex because infections can also interfere with iron absorption and lead to iron deficiency as well.

Lindy Ferlason

Thank you for that Gary. And that builds I think also on Sarah's comments during her response regarding the roles of infection inflammation and iron. Let's go ahead and go to Dan for another question. Dan, climate change remains an influence on this as well, "how should we be thinking about this impact at the policy or institutional level or even on the individual level?"

Dan Raiten

Thank you for that. That's an important question. We dealt with it a little bit in that third section. Climate has implications on every choice that we will make with regard to interventions. It has implications in terms of the biology and etiology of the diseases. We know that climate is affecting vector-borne diseases. So we have scenarios where you have an increase in vector-borne diseases which has implications for iron status and then we look at our efforts to address iron efficiency in those settings - in areas where we know that the arable land for growing crops is limited, the quality of the crops is being affected by the CO_2 levels.

It becomes a very complicated set of issues. If it can't be a food based intervention in those contexts then what are your options if you're looking at iron supplementation. We know that iron supplementation is … Sarah pointed out this problematic in the context of malaria. So the real key here is to recognize that climate is important, and somehow build indicators of climate into our surveillance activities. If I could I just would respond to the questions with regard to

surveillance and some of the concerns that Maria Elena raised. We have multiple departments doing multiple things and they don't always talk together. So we'll have a malaria program that's doing surveillance but that doesn't include nutrition. And we have nutrition efforts that doesn't include malaria and infection. Perhaps if we can figure out a way to work together as Lisa pointed out, from a multisectoral point of view. Bringing those systems together more effectively in our surveillance that might be helpful. Hopefully Omar will discuss that a little bit in his closing remark with regard to things like the demographic and health surveillance system.

To the question, climate is critical it needs to be integrated. How we integrate that into surveillance is going to be critical because we may be attributing things to other causes that may in fact be due to climate - and certainly climate is playing a role. I'm sorry for rambling but it's a complicated set of issues and a really critical one. Thank you.

Lindy Ferlason

Thank you so much Dan. I'm glad that we're able to talk through that aspect of it initially here in this webinar. Thank you for the points that you made. For the next question, I'm going to hand over to Parmi first. But Parmi please feel free to redirect or anyone else to jump in. The question is "at what stage does cost enter into the consideration and is there any advice you can give regarding assessment capacity? Not all countries and settings have the ability to be able to follow all the steps of the algorithms. Are there any comments that you can make around that?

Parmi Suchdev

That's an important question, and I'll also defer to Maria Elena and others. I think it goes back to a bit of the comment Maria Elena made too. It's really seeking input from folks who are actually running these programs, doing these surveys and looking at their budgets and figuring out how it's able to be done. And in our experience, providing technical support for surveys around the world. There are several instances where it can be done. If you actually look at the budgets to really do all the things we've assessed and presuming you have no data, it's actually much cheaper than some other surveys in other sectors. I won't name them in particular. It is doable but of course you have to consider costs.

In our report we actually have a table where we roughly put some dollar signs along cost. But I think it's just a call to our private sector and laboratory science folks that if this is what is needed to improve assessment and to get a holistic picture of anemia, then let's come up with the technologies that are cost effective to do that. I think often we've kind of sat on our hands a bit and just say if we don't have the diagnostic test we can't do it, let's just stick with the hemoglobin only. But I think if we can put forward that this is what is needed, this is the algorithm that needs to be followed then the test will also come over. Thank you.

Lindy Ferlason

Maria Elena, anything you want to add to that?

Maria Elena Jeffords

The only thing I would add to what Parmi said is that there are people working on point-of-care devices for assessing different kinds of blood disorders or Ferritin or inflammation. So I'm optimistic that there will be, hopefully in the short term, easier laboratory techniques so that these could be done in countries routinely. At least as part of surveys if not for other reasons. So I do think we're going to see advances in the coming years with laboratory methods that will help us much better understand some of these issues on the causes and the context of anemia in these situations and being able to assess multiple factors at the same time.

Lindy Ferlason

Thank you for that. Let's go to another question around measurement of sorts. This one is going to go first to Gary. "Given that genetic conditions are immutable, why is it important to measure the prevalence of these mutations?"

Gary Brittenham

The main reason is that the most prevalent genetic disorders, alpha and beta thalassemia, produce a phenotype that resembles iron deficiency and produces anemia as well, and so can produce mistaken estimates of the prevalence of anemia. So that's one fundamental difficulty. I didn't deal

with the other kinds of genetic disorders that produce severe anemia themselves, because they're primarily more a clinical and medical concern than are things that can benefit from a public health intervention.

Lindy Ferlason

Thank you so much for that. I think we're getting close to the end of our discussion. I want to ask one more question that brings us back to something we were talking about a little bit more. I'll ask the question but then also leave it open for anyone to talk to this specific aspect of anemia, and this is around anemia, infection and inflammation. There was a question that was put into the chat around covid-19. "Is there any evidence of benefits and risks of iron supplementation in confirmed covid-19 pregnant women or in pregnancy with a confirmation of other infections?" So there's that specific question but also just leaving it open to anyone else who wants to make comments around the aspect of anemia and infection or inflammation. Actually I'm not quite sure who to hand this to first. I'm not sure if we have that information regarding Covid. Sarah, I think you can probably speak. If you want to speak more to the infection inflammation but I'll leave it open for anyone who wants to respond.

Dan Raiten

I can respond just quickly to the Covid relationship. There's been a patient-based meta-analysis that's been done starting under the auspices of a multisectoral effort initiated by WHO. That analysis took multiple cohorts around the globe and looked at the risk factors associated with Covid and pregnancy outcomes. And anemia was a risk factor. So we've learned that there is a relationship there. In terms of interventions, I don't think we've gotten to that point. We're now just exploring the nature of this disease and the impact that it has on various systems, but anemia is clearly a factor associated with Covid. What we do in terms of interventions remains to be seen.

Lindy Ferlason

Thank you Dan. With the one minute we have remaining does anyone else want to say anything on this topic?

Cornelia Loechl

I just want to thank Dan for taking that because I don't know anything about Covid and iron deficiency except what I read in the report yesterday. I guess my only question back to Dan would be … I think the answer is probably no because we don't yet know about interventions but "is iron deficiency somehow a risk factor for Covid or is it more about that the inflammation associated with Covid causes a functional iron deficiency?"

Dan Raiten

The data that was available only addressed the relationship with hemoglobin. They did not address the relationship with inflammation, they did not address any of the potential etiologies, and they didn't talk about iron specifically. This is the problem that we have without getting off on a tangent. Our ability to have a resilient response to challenges like Covid is limited by the limitations we have in the way we look at things. And hopefully efforts like this Anemia Task Force will enable the community to be more expansive and ecological, if you will, in how we design surveillance around whatever the issue may be. But because of the nature of the data that was collected we couldn't dive any deeper into it other than just assess the association between anemia, primarily hemoglobin and Covid, and the adverse risks during pregnancy.

Parmi Suchdev

Just to make one quick comment. There's some thought and a reason to [inaudible] that we need to wipe out infectious diseases and inflammation off the planet before we deal with the issue of iron deficiency and anemia. I think for certain severe infections, there's obviously a benefit to delay … as some of Sarah's work on tuberculosis. But in these settings we work with, kids and people are getting chronically infected with mild things like colds that could be resolved in a couple of days. And that alone can increase your aptitude to keep the iron out. Even non-infectious causes to inflammation. I think the research you need is how can we concurrently deal

with these issues at the same time and not kind of blame the other side saying this is an iron problem, a nutritional problem or an infection problem, and then wait.

There's work being done - like ways to actually down regulate Hepcidin and IV iron. So I think again the message that we've been giving this whole webinar is really the idea of integration and working across sectors. Thanks.

Dan Raiten

That's a really important point Parmi. I just want to also highlight the fact that nutritional iron deficiency remains a big problem for a number of reasons, and we have to continue to be vigilant about addressing nutritional iron deficiency. Its relationship with anemia is what we've talked about today. But there's no question that nutritional iron deficiency is the absence of a dietary source. Whether it's nutritional insecurity or whatever the case may be, it needs to be addressed. Some of those issues were covered in the section that Cornelia talked about in terms of fortification and food-based interventions. But also, back to the question of climate, how do we make decisions about the food system and how that food system is affected by things like climate. So whether or not we can rely on or use animal source foods, what's the impact of climate on animal source food systems and vice versa. And what's the role of animal source food systems in this complicated scenario that we have. But nutritional iron deficiency we should not lose sight of it. Thanks for that point. For me it's really important.

Cornelia Loechl

Lindy can I just add something because I'm screening through the chat. Just very quickly.

Lindy Ferlason

Yes, Omar only has two minutes for closing remarks right now but please if you want to add something quickly, please do.

Cornelia Loechl

Just to add to what Dan and Parmi were saying. I saw some of this in the chat. What if we don't have access to animal-source foods, plant-based diets, etc. We were, and there's more in the report, trying to look at other options of how you can improve iron absorption from plant-based diets. And there is another point that alluded to the climate change and the effect on the crops. Sure we'll get to genetic modification but I think we really need to explore iron fortification more looking at the climate. More climate smart crops like millet, sorghum and maybe alternative sources. Unfortunately insects have not proven to be a case for iron as a recent study showed. It's just not so far available, but I think you will find more information on these questions in the report. So please watch out for that. Thank you.

Lindy Ferlason

Thank you so much for tying that in with what was popping up in the chat as well. Omar, I'm sorry, you technically have about a minute left for your closing remarks. It's been a very rich discussion and thank you to everyone who's participated in that and anyone who's able to stay a little bit longer to hear Omar's full closing remarks. That would be wonderful. You're absolutely welcome to do so. So I will hand it over now to Omar Dary. He is a colleague of mine at USAID. He is a scientist in our Nutrition and Environmental Health Division and our Maternal Child Health and Nutrition Office. Over to Omar.

Omar Dary

Thank you Lindy. It was a really very good webinar and all these enthusiasm and that we are having a little more time to dedicate it to. I'm very glad also about the last discussion among all the panelists. First I would like to thank all members of the Anemia Task Force and today's speakers and panelists for their concepts and suggestions to improve our global effort to understand, prevent and treat anemia. Second, let me emphasize on some of the messages that we were hearing today. We human beings have colonized almost all ecosystems on earth. We have the capacity to modify the environment in our benefit. In this sense, for hundreds of years, we thought that everything in nature was for our own use and that we were separate from nature. It took several years for humankind to accept that the sun did not circulate around the earth, and later that our sun is no more than a tiny little star among millions of others. It has only until

recently that we have realized that the laws and forces of nature also affect us, and that is climate change.

In the case of anemia, for more than 40 years, we are explaining it based on the nature of our diets saying that if it does not contain sufficient iron or if the iron viability of the diet was low the anemia is going to appear. Although this is true, we will not really pay attention to other nutrients. We even use the term iron deficient anemia for naming any type of anemia. Around 20 years ago, we discovered a hormone that regulates the absorption and mobilization of iron, hepcidin. It withholds iron neutralization when we have sufficient stored iron, but also when we are suffering from infections or inflammation. This finding extended our attention to prevent and treat anemia to the physiological status of the individual. We learn that supplying iron is not going to be effective if diseases or parasites are prevalent. There is more, additional iron may be harmful because it favors the growth of pathogenic organisms. In this seminar we have also learned that in addition to the nature of the diet and the health status of individuals, some genetic traits; the microbiota that lives inside us, and our specific conditions of gender and age are also determining the concentration of hemoglobin in the blood.

Therefore it is difficult to have global and standardized criteria to diagnose anemia as everything depends on the context. Our international criteria about anemia are only basic reference to start the analysis of the meaning of the hemoglobin concentration. All the factors in these three spheres: the diet, health, and the genetic characteristics of our cells or our microbiota, are determined by environmental forces such as altitude over the sea, exposure to a smoke, climate, presence of parasites and pathogenic organisms, our own culture and beliefs. This means that the concentration of hemoglobin is no more than a steady-state condition in response to all these factors and the environment that defines them. If one of these factors is modified, the steady-state changes and so does the concentration of hemoglobin.

The important question to ask is "when is hemoglobin concentration normal and when does it negatively affect the physiological functions that are expected from hemoglobin?" For responding to these questions, we need to study the etiological factors of anemia and not simply measuring hemoglobin concentration. Today, we've reviewed several biomarkers and bioindicators to help us in this task. However, we are still learning. We still have knowledge gaps. Even though we already know it's frequently neglected for the anxiety of acting before first characterizing the

problem, motivated by our own good intentions to apply solutions that work in other contexts but we are not going to be sure that it works in ours. We need to remember that, first we need to assess then to analyze the measures with higher probability of acceptance and impact in our own specific conditions.

Finally, I would like to mention that we have also failed in applying the recommendations of Lord Kelvin as mentioned my Parmi, "if you cannot measure it, you cannot improve it". However, this recommendation must be completed with another one, "you need to use accurate, precise and reproducible methods". Otherwise … the criteria to diagnose anemia. We need to analyze how much of the no-progress in the progress of anemia prevention and control have been caused by erroneous practices. I hope that every one of us have now something more to think. Thank you to everyone and wishing you a very good rest of the day.

Lindy Ferlason

Thank you very much Omar for your closing remarks that were very insightful. I would also like to thank again all the presenters and panelists for sharing their work perspective and experience with us today, as well as all the participants for your interest, engagement and the rich questions that led to a very interesting discussion. Just for information, you will receive an email with a link to the recording of this webinar in the next few days and we hope to see you during future events. Thank you very much and have a great rest of your week.

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