



# FEED THE FUTURE

The U.S. Government's Global Hunger & Food Security Initiative

## Mycotoxins, EED, and Inflammation: Implications for Research and Programming on Child Growth and Nutrition

### Webinar Transcript

Katie Appel

Good morning afternoon and evening, thank you all for joining today's webinar to learn more about mycotoxins environmental enteric dysfunction and inflammation, and their implications for research and programming on child growth and nutrition.

My name is Katie Appel and I'm an assistant researcher for the Feed the Future Innovation Lab for Nutrition and will be your MC for this webinar today. As attendees are joining I'll begin by going over some housekeeping items. I'd like to direct all attendees to a few functions on the Zoom webinar. At the bottom of your screen, you should see a chat icon and the Q&A icon. Use the chat feature to engage in relevant conversation with other attendees. If you have a question for one of the panelists please use the Q&A feature. Panelists will respond to questions in the Q&A box throughout the webinar and we have allotted the final half hour of this webinar for Q&A. If you're experiencing any technical difficulties send a message on the chat box to all panelists so that our technical support staff can work with you to resolve them. This webinar is being recorded and will be made available on the Innovation Lab for Nutrition website and the USAID Advancing Nutrition website. There you can also register for upcoming webinars and view recordings and slide decks of previous webinars. We will repeat these technical housekeeping items in the chat throughout the webinar as people might join in later times.

Before I introduce today's moderator, I'll give a brief introduction to the Nutrition Innovation Lab and our webinar series. We are a Feed the Future Innovation Lab supported by USAID Bureau for Resilience and Food Security, and we are active in supporting research and capacity building, to build the evidence based around critical questions linked to agriculture, nutrition, and health. As you can see from this map- oh, next slide. We are active in Sub-Saharan Africa and South Asia. More information can be found on our website at [nutritioninnovationlab.org](http://nutritioninnovationlab.org).

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The Nutrition Innovation Lab is a consortium, led by the Friedman School of Nutrition Science and Policy at Tufts University, with US university partners including Purdue, Harvard TH Chan School of Public Health, Johns Hopkins School of Public Health, and Tuskegee University. In addition, we partner with government agencies in our host countries, UN agencies, local and international NGOs, as well as universities around the globe. Now it's my pleasure to introduce the moderator for today's webinar.

Dr. Ahmed Kablan is a senior science advisor in the Center for Nutrition, Food Safety Division, Bureau for Resilience and Food Security at USAID. He manages several research programs for nutritious and safe foods, including the Nutrition Innovation Lab, Food Safety Innovation Lab, and Post-harvest Loss Reduction Innovation Lab. Dr. Kablan has a doctor of pharmacy degree from Jordan University of Science and Technology, and a PhD in cellular and molecular biotechnology from the University of Bologna in Italy. He has worked for over 20 years in human nutrition, international development,

science policy, and regulatory research and is a well-published scientist. In 2012, Dr. Kablan was awarded the American Association for the Advancement of Science, Science Policy, and Technology Fellowship. Dr. Kablan, over to you.

### Ahmed Kablan

Thank you Katie, appreciate the introduction. And welcome everyone, good morning, good afternoon, or good evening. I know we are being joined with audience from all over the world. And it is my pleasure to moderate this webinar from the Nutrition Innovation Lab on mycotoxins, environmental enteric dysfunction and inflammation. And, as you can see from the title, it goes through a whole spectrum of topics that are related to several aspects of nutrition, from food safety and water, environmental safety, and the impact of these different factors on the overall health, and possible pathways that these factor could contribute to nutritional outcomes. As the new research has continued to emerge that reinforce the integral role for food safety in, for food safety and food security on nutrition, USAID recognize the need to build upon previous investments in food safety and elevate the priority of food safety and nutrition within USAID. In the past year or 2020 we were excited to announce the establishment of the first ever food safety division. Which is housed within the Center of Nutrition, and that housing or location is intentional to highlight the important link between food safety and nutritional outcomes. Prior to the establishment of the Food Safety Division, USAID has invested heavily in several research related to food safety, including aflatoxin research and the reduction of post harvest losses. Several of our innovation labs, including Peanut Mycotoxin Innovation Lab, Post-harvest Loss Innovation Lab, and, of course, our flagship research and nutrition program the Nutrition Innovation Lab that invested significant resources and time in researching the linkages between aflatoxin or mycotoxin and child development and birth outcomes. The Food Safety Division was established to build upon this work and to address the heavy and under-valued health and economic consequences of poor food safety practices in developing countries. When the food safety divisions, as well as many of other food safety investments, launched in the midst of COVID-19 and also the global pandemic have underscored the importance of addressing food safety to achieve food security and nutrition. One thing that we need to keep in mind to address food safety from all aspects, whether we're looking at mycotoxins, environmental factors such as WASH, for food safety hygiene and water hygiene that lead to environment and dysfunctions, we have to think about from a systemic approach. And that is very important to think through our food system linkages, how this, we can approach and achieve and reduce food safety factors. I am so pleased to be with you today and introduce our speakers that will talk about, not about what we have presented in the previous webinars on mycotoxins, environmental dysfunction, and inflammation, but what are the implications of these for research and programs on child nutrition going forward. What we know, what are the gaps or potential research opportunities to expand our knowledge as we are exploring and trying to establish what programmatic and policy guidelines in order to have more effective action towards reducing food safety or nutritional impact.

We have on our panel we have Professor Christopher Duggan. He is a pediatric gastroenterologist and a nutrition physician at Boston Children's Hospital, where he directs the Center for Nutrition and is also Professor of pediatrics and director for the Division of Nutrition at Harvard Medical School, and the Professor in the Department Nutrition and Global Health and Cooperation at Harvard TH Chan School of Public Health. Welcome Professor Duggan.

We have also with us, Dr. Shibani Ghosh is the research associate professor at the Friedman School of Nutrition Science and Policy. She's also associate director for the Feed the Future Innovation Lab for Nutrition with experience working in the Middle East, Sub-Saharan Africa, and South Asia. And I have the pleasure of working with Dr. Ghosh for over eight years now. Welcome Dr. Ghosh.

And finally, we have Dr. Patrick Webb. Professor Webb is director for the Feed the Future Innovation Lab for Nutrition, the Alexander MacFarlane Professor of Nutrition at the Friedman School of Nutrition Science and Policy, and the Principal Investigator of USAID Food Aid Quality Review Project, and until

2005 Professor Webb was the Chief of Nutrition at the United Nations WFP. Welcome Dr. Webb, and again I had the pleasure of working with Dr. Webb for over eight years now.

Next slide please.

And now we'll start with Dr. Christopher talking about the first mycotoxins, environment enteric dysfunction and inflammation. Over to you.

### Christopher Duggan

Well, thank you very much, Ahmed, and good evening, good afternoon, and good morning to all of our attendees at the seminar. It's really my pleasure to join this august group and discuss with you in and colleagues about the different roles of these different concepts. I will be focusing mainly on studies, recent studies, in our group and others that have addressed and defined this concept of an environmental enteric dysfunction. Next slide. I have no financial disclosures to make. I do want to explicitly thank my colleague, Dr. Jackie Lauer who led a similar topic on a Nutrition Innovation Lab seminar several months ago, Dr. Lauer, who's now at Boston University, has pioneered many of the assays that I will be describing in the assessment of environmental enteric dysfunction. Next slide.

In 2008 a very influential review article was published in The Lancet by Zulfiqar Bhutta and colleagues in the series of papers on maternal and child undernutrition. And, as the title of the paper points out, the focus of this publication was on identifying and highlighting specific and well-tested interventions to improve both maternal and child health. And they're listed in the table on this slide, which I won't review, but includes, as you can imagine, a number of different nutritional-sensitive and nutrition relevant interventions, as well as improvements in infectious disease therapies and preventions.

Next slide.

This modeling study went further and evaluated, how many deaths and reductions in stunting could be achieved by the global community if both the general nutrition micronutrient interventions and disease control interventions could be addressed throughout low and middle income countries. And in the lower half of this table, you can see that, furthermore, the authors hypothesized that if coverage was low at 70% of all of the interventions, moderate at 90% of all interventions, or very high at 99% of all the interventions, there was a concomitant reduction both in deaths before age 12, 24 and 36 months, but in the reduction in the prevalence of stunting. And that's the focus of our topic today, which is childhood growth.

Next slide.

You can see that if 99% of coverage, with all of the intervention summarized in the previous table, only a roughly a third of children, childhood stunting, could be prevented. And that really caught people's eye, to say well if that's all we know what explains two thirds of the effects of childhood stunting, how can we investigate other factors that might be related to childhood stunting. Next slide.

So let me turn to the idea that living in poor communities with high rates of enteropathogen exposure might be related to childhood stunting. And this was an ingenious study published by Francis Ngunjiri, Rebecca Stoltzfus, Johns Hopkins University, and colleagues in Zimbabwe. And what these groups did was visit 21 households in rural Zimbabwe. And two observers spent six to eight hours per day to examine how feces were disposed of and how people were performing in terms of WASH interventions and sanitizing and cleaning their hands before and after a meal preparation. Next slide. Table five of this paper points out that half of the people were disposing of feces in a garbage pit close to home.

Next slide.

In addition, the investigators cultured for E. coli, a common enteropathogen resident in the human gastrointestinal tract and animal gastrointestinal tract. They evaluated whether food, water, skin of the woman's breasts, hand swabs, kitchen floor included E. coli. Next slide.

50% of the caregivers dominant hand cultured positive for Escherichia coli. Next slide. 73% of the kitchen doorstep was positive for E. coli. Next slide. And not surprisingly, 100% of the chicken feces that were found in and around the house cultured positive for a bug that's known to be in the gastrointestinal tract of humans and animals. Next slide.

In addition to testing the fingers, food, and drinking water of infants, these observers noted that children were eating handfuls of soil, and two ingested actual chicken feces a couple times in the six hours of observations. And the calculation would be that if you eat one gram of chicken feces a day, they would expose their gastrointestinal tract to up to 23 million copies of E. coli species. So confirming in an ingenious observational way what we know intrinsically, that children who grow up in poor communities, next slide, unfortunately communities that look like this that have inadequate resources for waste disposal and use of good drinking water, have problems with their gastrointestinal tract. Next slide.

So the concept of environmental enteric dysfunction is not a new one, it's actually a concept that was discussed in the 1970s among US Peace Corps volunteers who were returning home and were found to have a reversible cause of enteric dysfunction or sometimes enteropathy or lesions in their gastrointestinal tract. Indeed, a few years ago, a group put together a diagnosis, or diagnostic description of this concept, environmental enteric dysfunction. And from a gastrointestinal standpoint it's helpful to review what the normal small bowel histology looks like under the microscope, which is figure A. You can see that the reason the gastrointestinal tract has such a high capacity for its two functions, namely gastrointestinal absorption of nutrients and a barrier function to prevent bacteria from getting access to the bloodstream, those functions are improved by having very nicely developed villi and crypts to increase surface area. With environmental enteric dysfunction, however, next slide, there is a distinct blunting of those nice finger-like projections into the bowel, and inflammatory infiltrate in the lamina propria of the tissue. Next slide.

Indeed, we conceive of environmental enteric dysfunction as a subclinical condition, in other words, people, young children and adults, may not have symptoms of gastrointestinal inflammation or infection. But they can have important alterations in mucosal barrier function and absorptive function.

Histologically, this consists of, as noted in panel B, atrophy of the villi, hyperplasia of the crypts, the crypts get longer. There's increased intestinal permeability, there's an inflammatory infiltrate, and we'll talk about systemic and gastrointestinal inflammation later in the talk, and malabsorption of nutrients. And the reason the group really didn't call environmental enteric dysfunction as environmental enteropathy, is that it's clear to me that even in the absence of histological changes, in the absence of true changes in pathologic specimens of the small bowel, there are functional changes that can occur.

Next slide.

I think we can still say that the exact cause is unknown, but it seemingly likely results from chronic fecal-oral exposures from enteropathogens that occur in poor sanitary conditions and in low- and middle-income countries, as illustrated by the data from Zimbabwe. Next. One of the advantages and disadvantages, I guess, I would say in the field of environmental enteric dysfunction, is that a number of different biomarkers have been proposed to diagnose the condition. Because obviously sampling of the small intestine is often an invasive procedure, although I will say that less invasive approaches to sampling have been, and continued to be, developed. But because the gastrointestinal tract, as I said, its role is both to absorb nutrients as well as to keep toxins and bacteria out of the body, it's not surprising that among the biomarkers include measures of intestinal absorption, as noted in the column B, as well as measures of mucosal permeability. Other markers, including those of enterocyte mucosal surface area, gastrointestinal inflammation, and microbial translocation have also been proposed as markers of environmental enteric dysfunction.

So that's the good news, is that there are a lot of different candidate biomarkers. Next slide. The disappointing news is shown in this slide, which is a bit confusing with a lot of numbers, but let me back

up and just say that these are data from Rebecca Campbell and Parul Christian and colleagues in rural Bangladesh. And in the setting of a cluster randomized trial of complimentary foods, they evaluated measures of environmental enteric dysfunction at 18 months of old age in children who have participated in their trial.

And what you can see here is a relatively poor correlation, this is the Pearson correlation coefficient among a variety of different candidate biomarkers. The top line, the top row, is the lactulose:mannitol ratio, which has been proposed to be, if you will, the gold standard of measuring environmental enteric dysfunction, and that was reviewed nicely by Dr. Lauer in the previous seminar. But, as you can see, stool markers for inflammation, which are the top three measures, myeloperoxidase, alpha one antitrypsin, and neopterin, correlated only fairly and not so significantly with a variety, with the gold standard of lactulose:mannitol ratio. And if we can just scan the Pearson correlation coefficients you can see that the highest one is probably .39, a correlation between total immune globulin M and total IGA. Obviously, this is a nonspecific relationship with markers of inflammation. So this is the challenge in our field, if you will, is that there was not the best correlation between different biomarkers of EED. This lack of specificity, I think, has hindered our ability to pinpoint which children, which mothers, which adults are suffering from this condition.

Next slide.

Well, our group has focused on another marker of environmental enteric dysfunction that is based on the cartoon shown here. On the left, you can see an example of a gram negative bacteria. And if you think back to your high school biology class you remember that bacteria are motile, and they're motile because they have a flagella at the end, as seen in the far left of this cartoon. And these allow the, for instance, E. coli, to swim through water and other fluids. In addition, there is a bilipid cell membrane, and an important component of this is shown as lipo polysaccharide, a complex component of both fat and carbohydrate. And this lipo poly saccharide, another name for it is endotoxin. And the classic experiments from the 1950s and 60s confirm that when a gram negative bacteria, such as E. coli, is broken apart or is attacked by the body's immune system, release of that endotoxin, as opposed to exotoxins, but release of that endotoxin leads to a very pro-inflammatory state with release of cytokines and, in extreme cases, septic shock. So we took advantage of the fact that antibodies to flagellin and lipo polysaccharides can be measured in the bloodstream, and preliminary data suggested that people with increased permeability, less well-structured and functional gastrointestinal tracts, had higher concentrations of these antibodies in their bloodstream.

Next slide.

The first paper that we published using serum anti-flagellin and anti-LPS antibodies was performed in the setting of a randomized trial we had recently concluded in peri-urban Tanzania. Next slide. And on this table we pointed out that, regardless of which antibody we were measuring, be it anti-flagellin IGA or anti-LPS IGA or IGG of these two components, next slide, there was a substantial doubling of the risk of subsequent underweight. So these antibodies were measured close to birth at six weeks of age, and the children were followed until 18 months of age. And what you can see in the red box is that, compared to people in the lowest quartile of any of these EED antibodies, children in the highest quartile, the fourth quartile if you will, have this exposure had approximately doubling of the risk of developing low weight for age Z scores over the course of follow up. So this was quite intriguing, and led us to consider whether evaluating this inflammatory response that's specific perhaps to the gastrointestinal tract, might be related to other health outcomes. I will say that people who, reviewers of this paper also pointed out that because these antibodies might be related to more systemic inflammation, a topic we'll talk about later today, the question is, were these specific for this effect or was this really reflective of a generalized inflammatory response.

Next slide.

So we basically did another experiment, and this is one that Jackie Lauer led, this was the birth cohort, which we performed with colleagues in Uganda and with support from the Nutrition Innovation Lab. So this birth cohort was performed, and at six months of age, a cross-sectional analysis of multiple markers of environmental enteric dysfunction were collected, including hemoglobin and measures of systemic inflammatory responses, including AGP and CRP measures of that. At six months of age I'll point out that this rural cohort had a 35% stunting prevalence and a 53% anemia prevalence. And controlling for these measures of systemic inflammation, markers of EED were still quite highly correlated with both length for age Z score, as well as hemoglobin. And the hemoglobin correlation shown in the figure on the right, shows a weak but statistically significant relationship, such that with higher concentrations of lipo polysaccharide antibodies, you can see lower concentrations of child, of infant hemoglobin at six months of age.

Next slide.

Dr. Lauer also performed another study, this time in Mukono District in the central region of Uganda, which is about 20 kilometers east of Kampala, among 258 women who were pregnant and attending clinic for the first antenatal clinic. Dr. Lauer and colleagues performed multiple measures of environmental enteric dysfunction, including the measure that I noted previously as the gold standard, the lactulose:mannitol ratio. Interestingly, the lactulose:mannitol ratio showed no relationship between important birth outcomes in these pregnant women, including gestational age, duration, or length for age Z score at birth. However, and is shown by the graph, the scatter graph again on the right of this figure, you can see that with higher concentrations of lipo polysaccharide antibodies, there was a sustained and weak but significant correlation between shorter gestational age. This was the first paper that we are aware of that linked measures of environmental enteric dysfunction with important measures such as gestational age. And in the next slide, you can see.

Next slide.

Again in the red box, you can see significant correlations between gestational age, length of the infant at birth, and length for age Z score at the birth, with a variety of different markers of environmental enteric dysfunction. Next slide. So in conclusion, a lot has been learned about environmental enteric dysfunction in low and middle income countries, but unfortunately key challenges persist. Specifically, we don't quite have an agreed upon case definition or specific diagnostic criteria. It's been proposed that, because there are multiple domains of gastrointestinal function including decreased absorption and increased permeability, that a mix of biomarkers might be a promising path. And we're moving forward on that with different studies we are setting up.

Next slide.

The idea that important WASH interventions and EED are related seems obvious to some, but indeed a number of WASH intervention studies have been performed without clear improvements in markers of EED or childhood growth. Next slide. But I think it's clear to say that there is a relationship between EED and linear growth in infants and young children. And we're interested in partnering with you and other colleagues to find out how EED might affect pregnant women, how it might affect birth outcomes, micronutrient deficiencies, and other forms of undernutrition. So we can help, next slide, children like this grow up to be as healthy as possible. Thank you very much.

Ahmed Kablan

Thank you, Professor. Again, I think the key message here, it is what we need to look at is not only the safety of the food but also the cleanness of the environment and the safety of the water. So it is looking at the micro and the macro environment surrounding the children and within the children and their families and household that is very impactful message that we need to work at comprehensive packages of intervention in order to achieve better nutritional outcomes. Thank you so much.

Now our next speaker is Dr. Ghosh who will speak about mycotoxins, microbiome, and environmental enteric dysfunction again. Dr. Ghosh, over to you.

### Shibani Ghosh

Thank you, Dr. Kablan, and it's my honor to be speaking with all of you today, and following Chris Duggan's fantastic presentation. So I'd like to go to the next slide please. So just as a reminder, I mean, this is a conceptual framework around the intergenerational elements of stunting where you have, this particular framework was developed by Andrew Prendergast and Jean Humphrey. And I think all of you are very familiar with this, where you have the effects or risks that are encountered by women in preconception and conception move over into outcomes in early life, but also in later life, and that this is a cyclical process.

So, within the Nutrition Innovation Lab we've tried to focus in, and I think Chris has highlighted some of the studies that have been conducted by our graduate students and postdocs such as Jackie Lauer, what we've looked at is that area within the green markers, and I'll ask Grace to please click on the next slide. Thank you, and we've looked at risk factors in pregnancy, including aflatoxins and other mycotoxins, we've also looked at EED and inflammation, some of which Chris has already presented. Next, please. And their correlations and their relationships with birth outcomes. And I think we are seeing a picture image, but as Chris has already outlined, that this is a pretty complex picture that emerges with respect to these different risk factors and the birth outcomes.

Next, please.

We've also looked at early life and up to five years of age at risk factors such as aflatoxins and other mycotoxins, EED, and inflammation, as well as assessing the microbiome in children who are moderately malnourished. And assessed these risk factors relative to outcomes, including anthropometry as well as recovery from malnutrition, particularly moderate acute malnutrition.

Next slide please.

And in a sense, and this has already been pointed out by Dr. Kablan, we've been able to conduct studies across different countries in sub-Saharan Africa and South Asia. And Southeast Asia as well, and some of them have been cross-sectional studies, like the study that was conducted in Timor Leste or in Mozambique. The Uganda studies that Chris has already outlined gave us an opportunity to collect longitudinal data, not just only on diets and anthropometry but also on specific EED markers as well as aflatoxins. We've also been able to collaborate with colleagues at Cornell on one of their longitudinal studies, called the prenut study which allowed us to assess aflatoxins relative to presence and absence of HIV infection in pregnant women, and the effects of those in early infancy. And in Nepal and Sierra Leone, we have been able to conduct studies that have allowed us to not just assess aflatoxins but also mycotoxins and the microbiome relative to risk of EED. So for the purpose of this presentation today, next slide please,

I'm going to try to ascertain, based on what we have as a data, some newly emerging analysis, as well as some analysis that has been presented by one of our other graduate students, Akriti Singh, for her work in Sierra Leone. I'm going to try to bring the elements of mycotoxins, EED and microbiome, and, as indicated by Ahmed, I think that we want to sort of put forward, what are the implications with respect to future research that is relevant for policy and programming. So for the purpose of this next series of slides, I'm going to focus on the Aflacohort study in Nepal and the Four Foods Study in Sierra Leone.

The Aflacohort study was supported by USAID Nepal, as well as USAID Bureau for Resilience and Food Security, and focused on assessing aflatoxin exposure in early pregnancy through early infancy up to two years of age. We had the opportunity in the study when the infants were around 18 months of age to add in assessments of other mycotoxins, as well as an assessment of the LM ratio, which, as Chris has already pointed out, is used as a sort of gold standard for measurement of EED. Similarly, the Four Foods Study, the Nutrition Innovation Lab was able to work with Akriti Singh, who implemented a



component of the Four Foods study for her dissertation. And this Four Foods study is a study supported by USAID Food Aid Quality Review. So it's a separate, outside the Nutrition Innovation Lab, but we were able to collaborate with FAQR and implement a small component of the Four Foods Study around EED and the microbiome. Next slide please. So, before I go into some of the results that I want to present, I think this is some of the questions that have come up with from the registrants as well as come up in some of the, in the chat box right now, like what is the possible mechanism by which mycotoxins could affect or lead to impaired growth. So this particular framework has been developed by Laura Smith and colleagues at Hopkins and was published in 2012. And essentially what you have in the red boxes are three mycotoxins, you have aflatoxin, you have DON or deoxynivalenol, and fumonisins, and these are the three mycotoxins that are implicated in impaired growth. And what Laura lays out is a very nice framework of how, based on literature, existing literature, what could be the proposed way in which these mycotoxins could affect growth. And essentially what you see in the yellow boxes is the process of environmental enteropathy, or environmental enteric dysfunction. So in a sense, what the authors are saying is that it's very possible that these mycotoxins affect growth and development in infants and young children through the process of affecting gut health and gut integrity. Which is sort of essentially defined as the the process of EED, if you will.

Next slide please.

In terms of sort of expanding that further, this was developed by Akriti Singh for her dissertation. And she expanded that sort of diagram as well as adapted from another diagram developed by the SHINE trial and colleagues at Johns Hopkins, in which sort of, in addition to aflatoxins and other mycotoxins, you could be exposed to poor WASH and environmental contaminants. And that could lead to changes in the microbiota profile, which then leads into changes in the small intestine that are similar to what has been described with EED. And that in turn translates into poor absorption of nutrients, systemic inflammation, which leads to increased nutrient needs and ultimately impaired growth. Of course, these are conceptual pathways and frameworks, but these are good guides for us to assess and understand using either existing data or conducting studies to ascertain if any of these, you know, which part of these pathways we can follow. As Chris has already mentioned, I want to sort of highlight the fact that EED is a process, and each of these red boxes, you can see, could have different markers that can be used to assess each of these boxes. And this was something that Akriti highlighted in her webinar that was conducted around the same time as Jackie's, and I welcome you all to go and look on the website for those webinar recordings. That essentially, what what you're seeing is the lack of correlations that might be observed with the EED markers could be a function of the fact that we are looking at a process, and a very complex process. And not all markers are measuring the same same red boxes, if you will.

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So let me move on to some of the sort of key findings, I have presented some of the descriptive statistics around mycotoxin exposure in young Nepali children aged 18 to 22 months, this is data from our Aflacohort study, but today I'm able to take it further into multivariate analyses. But just to sort of remind for those of you who were on the previous webinar and for those of you who are new, we assessed mycotoxins which include aflatoxin, ochratoxin A, fumonisin B1 and deoxynivalenol, and these are all different mycotoxins that essentially can exist in the food system, in different foods. Aflatoxins and fumonisins and DON usually exist, come in on maize, either food or feed, ochratoxins are present across all cereals and cereal grains, they're pretty prevalent, if you will, excuse me, across the the food system. And each of these mycotoxins have different affects, but most of them have been implicated in retarded growth or impaired growth. At least three of them are known carcinogens, and one is a suspected carcinogen, so that's also something very important to highlight here. Now in this slide, next, please, what I want to highlight is the fact that we measured in serum, we measured aflatoxin and ochratoxin in the serum of these Nepali infants, and fumonisins and DON in the urine. And we found very high rates of detection. So what you see in the parentheses that has been highlighted is the



detection rate that is there is detectable level of this mycotoxins present in the sample. And, whereas DON and aflatoxins were about 85 to 87%, all the samples that were assessed for ochratoxin and fumonisins had detectable levels of these mycotoxins. So pretty prevalent, but if you look at the right side of the table, you can see that there is a very wide range of minimum and maximum values with respect to the different mycotoxins.

Next slide please.

The next thing that we looked at, we were also able to collect, at the same time point, which is when the infants were 18 to 22 months of age, we were able to conduct an LM test, which is a lactulose mannitol test. And here we present the correlations between the LM, the EED markers that were developed or computed using the LM ratio, with this includes the LM ratio, it includes the percentage of lactulose excreted, it is percentage of mannitol excreted, and the lactulose mannitol excretion ratio. And what we found was three of the mycotoxins, aflatoxin, ochratoxin A, and DON, had significant very small correlations, but significant correlations. This is, this is a Pearson correlation coefficient.

Next slide please.

Using that, given that there were these relationships, we wanted to assess the individual mycotoxins relative to the LM ratio and anthropometry. So what I'm presenting here are four different models in which we looked at each mycotoxin relative to the LM ratio with the dependent variable being either stunting, so that's the first column, underweight, which is the second column, and low head circumference for age Z score, which is the third column. And what I'm presenting is all the odds ratios that were computed using logistic regression models. Now these models were adjusted for prior anthropometric status, either land or weight at birth or head circumference at three months of age. We also adjusted them for diet diversity at that time, as well as the mothers' education. So what you see here is that it was only the aflatoxin model where we found a significant odds ratio with children who had higher levels of aflatoxin were more likely to be stunted or underweight. So that was the only model where we found a significant association between a mycotoxin, in this case aflatoxin B1, and the specific anthropometric outcomes. None of the models was LM ratio significant.

Next slide please.

We then also looked at concurrent exposure, so we ran one single model per anthropometric outcome, and what you're seeing here is stunting, underweight and low head circumference. It is a single model where we inputted all mycotoxins along with the LM ratio. And what you can see here is for both stunting and underweight none of the mycotoxins, nor was LM ratio significantly associated with the risk of being stunted or underweight except for aflatoxin B1.

Next slide please.

And so the question is, are we able, is it possible that you know, based on that conceptual framework, the reason why we're not seeing these relationships is because these mycotoxins are mediating through the EED pathways. Now while unfortunately we don't have other markers of EED, and we had only the LM ratio, what we thought was we could look at individual mycotoxins and the LM ratio as the dependent. So we ran four different models, and these are linear regression models, and you can see that what we find is ochratoxin A and deoxynivalenol or DON were the two mycotoxins that were positively associated with LM ratio, indicating that the higher the level of the mycotoxins, the higher the LM ratio. Which indicates a higher sort of permeability, intestinal permeability, and higher impaired absorption, i.e., a higher risk of EED if you will. So what that's telling us is that at least in this sample, we're seeing two of the mycotoxins being significantly correlated with LM ratio, and it's very possible that they are mediating. That their relationship to grow is through the EED process. It's possible, right.

Next slide please.

So, so the next question really is what do we know about EED vis-a-vis, the microbiome. And this is, I'm just giving a snapshot of some of the findings that were presented by Akriti Singh, In which she looked at

EED microbiome and moderate acute malnutrition in Sierra Leone. It would have been interesting if we had mycotoxin data for this sample as well, but we don't so I'm just presenting this to sort of get us thinking about the microbiome, EED, and then where does that take us with respect to mycotoxins. So what did Akriti find? So Akriti assessed EED using many different markers, she used LM ratio, as well as she used fecal mRNA markers, and she used three different fecal protein markers. And what she found, depending upon what marker she used, she found that high inflammation and permeability were very negatively associated with length for age Z score and weight for length Z score in children with MAM. And this was even before they were exposed to the treatment foods, which was part of the Four Foods study. She also found that through the period of treatment that children who had high intestinal permeability when measured at baseline, they had lower length gain and lower weight gain. And finally, the children who had lower intestinal permeability were more likely to recover from moderate acute malnutrition. So this sort of emphasizes the issue that it's not just the treatment, but foods is going to help, is that cleaning the environment is going to be critical for these kids to recover from moderate acute malnutrition.

Next slide please.

Next.

So the next thing that Akriti looked at in her fecal samples was she did a sequencing to assess the microbiota and the microbiome composition of these kids with moderate acute malnutrition. And what she found was, next please. Next, sorry. That the gut microbiota of the children with MAM were very enriched with inflammogenic taxa. So on this figure that you're seeing, where you're seeing the red bars, those are the inflammogenic bacteria, and those were present in very high levels in the kids with MAM. And that the alterations in gut microbiota very associated with MAM. And it was also associated with inflammation as measured using different EED markers. And, as I said, we would have loved to have an assessment of mycotoxins relative to the gut microbiota as well as gut inflammation with the EED markers, but we don't have the data. And that's really where, what I'd like to see us thinking about in the future. That do we know about how mycotoxins interact vis-à-vis the microbiome. And does a varying or variable microbiota affect the sort of, does it does it remove the effects of the mycotoxins. So that's really a future area of research that needs to be explored.

Next slide please.

And what's very interesting is that is some, there is a recent review on this topic, particularly on mycotoxins and the gut microbiota. Because, to a certain extent in animal research, it has been shown that when you have an environment that is enriched by probiotics, so you have sort of, if you will, good bacteria, it is known to bio-transform mycotoxins to less toxic metabolites. And so that sort of highlights the fact that having a good microbiome might be supportive and might be protective of the effects of mycotoxins. Something that needs to be examined within human studies. On the flip side if you have changes in the microbiota composition as Akriti observed with respect to MAM, it is possible, as noted by this review that that could be a consequence, when there is mycotoxin exposure. Where you could have changes from a good microbiota to a bad microbiota because of the anti microbial properties of the mycotoxins itself, or the toxic effects that the mycotoxins might have on the the epithelial and the immune cells of the gut. So, essentially the flip side of this is that if you are, if you have a very good microbiome, you might be able to negate the effects of mycotoxins, but that if you have excessive exposure to mycotoxins, it might change your microbiota composition. So that's essentially what, in a nutshell, that needs to be explored and understood further within humans. And why is this important? Because we all know that we're not living in an enclosed environment where only one risk factor matters. What we are seeing is that often that i'm multiple risk factors that are going to be critical and that needs to be addressed. And I think, I wish I had used Chris's slide from the Lancet series where you could see that some of the interventions, even if you have those stand at 99%, they're going to only affect those specific outcomes, up to a certain degree. And so that's why it's really critical and important for us to consider the future of mycotoxins and microbiota.

Next slide please.

So I just I think I'm really way out of time here, but I just want to conclude that we've found some very interesting things with respect to multiple mycotoxins in Nepali infants. We're seeing some very interesting findings around EED and how it modulates recovery in MAM, and there is, there are reviews that are indicating the need for assessing the bi-directional relationships of mycotoxins and gut microbiota.

Next slide please.

So we really think that we should be looking at assessing interactions between these environmental toxins and microbes and the process of EED and the gut microbiota, and these are complex assessments, but they need to be done because it's going to help us drive future policy and program programming within the context of food systems, agriculture, nutrition and health. Thank you very much and I'm going to pass this back on to Ahmed.

Ahmed Kablan

Thank you so much, Dr. Ghosh, that's a very important message that you left us with, that factors contributing to child malnutrition, they are not one factor, there are multiple factors and you'll find some children, especially the population that you studied, they are exposed to bad environment in terms of poor hygiene, as well as unsafe food as well, which is contaminated with multiple things, including potentially several mycotoxins, different kinds of microbes. So that that's really share or bring the importance of the message, that the development community must work together in a unified voice advocating for food safety practices, linking food systems with the health systems in order to really deliver on improving child in nutrition and outcomes. Finally, we will move to Dr. Patrick Webb, Professor Webb, who will talk about what are the programmatic implications for all this knowledge that we have. Professor Webb, over to you.

Patrick Webb

Thank you, Ahmed. Those were two really important presentations, and I'm going to actually quite briefly bring us more to the level of programmatic and policy thinking around the implications of these things. Multiple factors, you just used that term Ahmed. I think we've heard so far, we've heard about mycotoxins of different kinds we've heard about EED and E. coli, we've looked at inflammation and gut microbiome. A lot of people would love to have simple answers to deceptively simple questions. You know how does EED affect stunting? How does inflammation impact linear growth and what can we do about it? But what we've been hearing so far is that these kinds of processes are not necessarily events they are processes within the body. They may sometimes be synergistic, they may be antagonistic, they may be additive and cumulative and their effects. Or, in fact, one maybe more important the other. That's really where I'm focusing in here is that we need to consider the multiplicity of possible threats or drivers or causes of the problems that we seek to resolve. That doesn't mean programmers have to measure them all themselves through the various highly complex techniques that were presented just now, but they do need to understand through theories of change how an intervention could potentially modify these risk factors, the term that Shibani just used. And, more importantly, did they?

Next slide please.

Did they actually succeed in modifying risk factors. Now I put this not expecting anyone to be able to read it, it's simply through The Lancet series and others, assessments of the global burden of disease. And that global burden, the relative contribution of elements to the global burden of disease, changes over time. So I think one important point we're trying to put on the table here is that these different risk factors we've been talking about, EED, aflatoxin, and so on, matter differently in different places and potentially over different times. This is two columns 1990 and then 2010, so 20 years later, the in the in terms of the red we see protein energy malnutrition, an old term for for undernutrition. In 1998 we're ranked ninth in the world in terms of contribution to the global burden of disease. By 2010 it's dropped

to 20th place and by 2030 it will almost undoubtedly have dropped still further. Iron deficiency anemia, on the other hand, 14th in 1990 was still 15th in 2010, and we know anemia remains one of the great challenges that's still there in nutrition. And we're struggling to make a lot of headway. Other things got worse over time, HIV/AIDS was 33rd in 1990, climb significantly to be fifth in 2010, may well have dropped a little in the meantime relative to others like diabetes, 21st in 1990, 14th in 2010, and almost certainly climbing higher in the meantime. So the point here is that the relative risk of different contributions to health outcomes and nutrition outcomes, they're not static. And so, in trying to understand the contribution of say EED to child growth, requires us to understand where that sits in the context of other risk factors in any particular environment. Next slide please. For example, well just keep going, I forgot those. For example, so in our study in Nepal we looked at a variety of risk factors related to, for example, low birth weight, one of the key birth, birth outcomes of interest because we know that low birth weight and, in particular, others, like being born small for gestational age, those are birth outcomes that are highly correlated with later stunting among children. Right so, being born with suboptimal outcomes at birth is itself setting in motion stunting, setting in motion the process of suboptimal growth. So, but in this particular sample in Nepal, risk factors for low birth weight, in a setting where, although there was widespread exposure to aflatoxin in this particular case, the levels of aflatoxin exposure were relatively low, but you take first.

Next slide.

What we see that, while- next slide, next click- while aflatoxin in the blood of mothers was predictive, you were more likely with higher levels of aflatoxin in blood, mothers were more likely to have low birth weight in their subsequent children. But lower maternal stature and smoking were more significant in that environment. Now what that means is not that aflatoxin in the blood is not important. What it means is that, right now, there are other factors that also contribute to low birth weight that need to be addressed. And smoking is a modifiable risk factor, one that we can change, indeed we have to change. In so many environments, low maternal height of course it's going to take longer intergenerational because we need to break the cycle, we need the next generation of girls to not be born with low birth weight and to grow more. Once those two problems have been resolved in this context, then the significance of aflatoxin in the blood, if we don't deal with it, will dominate. Right, so you get what I'm saying, these factors-- it's not this one is less important, it means, others are equally important and have to be addressed, but if we don't address the aflatoxin in the meantime, then its significance relative to others will grow over time, so we should address it immediately.

Next slide please.

I'm going to talk just very briefly about some of the some of the water issues, as opposed to aflatoxin. And really from the perspective of, in a sense, fixing the problem right. So we've heard that from Chris the more E. coli is linked to EED in the child, because of the leakiness, the amount of absorption in the child's gut, and we've also seen that more EED is associated with stunting in children and wasting, though wasting is not presented here, separately that's presented separately. But we have those links. E. coli is a problem in terms of EED, EED is a problem in that it is associated with certain nutrition outcomes. So what do we do, what's the fix?

Next slide.

Well there's been a long standing agenda of ensuring universal access to clean water, and I emphasize the word clean. It's not about universal access to water. It's universal access to clean water, and therein lies the problem, right. Because access to water has improved over time through a variety of interventions, through wells and boreholes, covered wells, uncovered wells, improved pipes and so on. Then- next slide- what we see, though, sometimes in treatment, direct treatment of water sources, next slide. Or improved or unimproved types of water access, you're still seeing roughly 60% of all kinds of the water access in this particular location in Southwest Uganda, having contamination, empirically contamination with E coli, right. So sometimes then not treated is worse, the unimproved is worse, but

not by a whole lot. But my point is even improved sources of water, treated sources of water, plastic jerry cans versus traditional pots, you're still seeing more than half of the samples contaminated with E. coli, right. So it's not just about, oh we've fixed the problem by ensuring a pipe.

Next slide please.

Sometimes it's the use and behavior of those things, next slide please. Next slide. In that location in Southwest Uganda, what you see the two columns there of safe versus unsafe, and you have you see that of the piped, there were only eight piped water sources in that particular community, half of them were deemed unsafe in terms of E. coli contamination. Public taps, more of them were safe than unsafe, but actually 42% of them were contaminated with E coli. Protected boreholes and protected wells, significantly more unsafe than safe right. So the what we're seeing here is that you cannot rest by dropping a borehole, covering a well, or ensuring access to a tap. That is not job done, that is just the first part of a job done. And the next slide shows that, next slide, showed that again correlation with EED, the lactulose mannitol ratio, showed a significant relationship with length for age and weight for height Z scores. Next slide. Now some of this can be related to obviously behavior. In the Uganda study, before I-- this slide relates to Ghana-- but before I leave, Uganda we've not published yet, but we've been looking at the impact of a multisector program in various parts of Uganda. One of those components was to improve sanitation and hygiene by teaching about hand washing behavior. And we've been looking, we're deep in the analysis of this, and a lot of things improved through that program. A lot of things were very positive, but what we've seen actually is that over time households most involved in the program actually reduced the frequency of handwashing. Reduced the frequency. With strong SBC messaging on quality, on how to wash your hands. And one possible solution to that conundrum, may be That the households heard the message about how to hand wash better, the whole two minute thing with soap or ash and so on, and as a result of that wash their hands less frequently. That's possible, we don't know we can't explain that. But these are some of the challenges that have to be faced. This is a map and a diagram relating to that map of a small township in Ghana. The orange pipes are standpipes, they're public pipes that theoretically are delivering clean water. But there's low consumption of water at those standpipes. The green ones further away from the River also notionally delivering clean water, have a high consumption overall. On average, much higher. And one can, the orange line on the graphic to the left, these are the consumption levels for the three pipes on the right. And what was documented through this particular study is that low consumption was related to proximity to the river. Why pay at all for water, if you have to pay, when it comes free from a river, right. So you have low consumption here. These communities around these much further away from the river, made much more sense to use the sandpipe. But click, next slide, what you see is that consumption level from those pipes drops during the periods of the rainy season by modal radius.

So the more rain there is, the much less consumption from the pipes there is. And again, one may say 'Oh well, that's logical, they may just catch rainfall.' In fact, during the rainy season what they're doing is collecting rainfall from surface water. Seasonal streams that develop during the rainy season, and taking water from there. And when asked 'well why are you doing that, normally you use the pipes.' And you know that that quality, the quality of water from those pipes is much higher. And the answer was, 'actually we prefer the taste. We prefer the taste of the groundwater.' Actually many of them prefer the taste of the river water than the water that was coming from the pipes, right. So the moral of the story here is that simply making clean piped water available doesn't mean that people will use it, or use it adequately on a systematic basis.

Next slide please.

So the relative risk of these different threats, these risk factors, is going to change on context. So really one of the messages for programming is it's not black and white. You've got to know the context. Which foods in your context are known to be high carriers of various mycotoxins. What do you know about the water quality, even have the supposedly clean water sources in your context. What are the disease parameters on a seasonal basis, yeah. We all know this, but it needs to be reiterated, because

what we're understanding through this kind of research that is pushing the boundaries of understanding is the variety of stressors, inflammation, mycotoxins, E. coli, and diseases like HIV, which themselves stimulate inflammatory processes, they are clearly interacting, or not, in important but not always predictable ways. And so we need to understand more about how those interactions take place, how humans react to the stressors in their environment, and what, therefore, we as development agents of change can do to either modify those behaviors in positive ways, or change the cleanliness of the setting. Access to universal clean water matters as much as access to clean food environments and clean health environments. Programs themselves shouldn't be seeking to measure everything. We're not asking people to measure blood serum aflatoxin levels or even lactulose mannitol tests, but theories of change do need to be much more rigorous and transparent in their assumptions. I've looked at a lot of theories of change, programmatic design over many, many years. And I don't see this happening, I see far too many assumptions and a fairly hand-waving approach to the links between boxes. And what we need to understand here is the dynamics and the potential net interactions among these various stressors. Of course, knowing more matters. Field-friendly metrics, there are better quick ways of assessing proxies for E. coli or cleanliness of the water using water colored bags. There are proxies for assessing food, mycotoxins in food as opposed to in serum, but we still need to go a long way more in that direction. Field-friendly techniques are going to help us all a great deal. But last message, these stressors matter hugely, physiologic among nutritionally vulnerable populations. They're not linear relations between mycotoxin and stunting. But the processes that contribute to sub-optimal growth of children, adolescent girls, and then pregnancy outcomes are all somehow related to these stressors. And we do need to know how they interact and what we can do to change that situation.

I'll end on the terrible note that I just heard in the news that the UK, my government, has just announced it's going to cut funding for water and sanitation interventions in developing countries by 80% in the coming few years. Which I think is shameful, and based on what we've just been seeing, extremely short sighted. So I hope we can change that around in the near future. And thank you, back to you Ahmed.

### Ahmed Kablan

Thank you, Dr. Webb, and appreciate the programmatic messaging that you left us with, and the complexity of the issue. But I really appreciate the one message that you mentioned, the importance of transparency of the fear of change and to have it built on testable assumptions and not on assumption that could not be validated. This is very critical to establish and build programs. Especially if you want to go back and to some of these assumptions, in a searchable methodological way. We have received, as you can see, a lot of questions through the live Q&A, but also we have a good list of questions that have been submitted during the registration. And about 22 questions have been answered already by the speakers, thank you so much for that. I will ask some of the questions from the live portion as well as some question from these question that have been submitted. What, we'll start with one of the easy questions.

In terms of aflatoxin, and this might be for you, Shibani. How long does aflatoxin remain in the gut of children under two years, and does it last long enough to influence the composition of their gut microbiota. Yeah that's a very good question I, I can say that the serum aflatoxin, which is what we use as the measure or the marker in our studies, has a half life of 90 days. If you measure aflatoxin, a metabolite of aflatoxin, AMFI, in the urine, that's usually a much faster turnaround. It's 24 hours. So it really depends on the marker you're using with respect to exposure. Whether it's a serum marker or a urine marker. In terms of the absorption of aflatoxin, and is it sufficiently long enough? In one instance in the gut I don't know the answer, but I do know that what we find in the populations we are working in is that is consistent chronic exposure to aflatoxin. So, even if it has a very fast transition in terms of absorption through the gut, what I can tell you is that they are being exposed aflatoxins on a daily basis. And that that is, yeah so, there might be others on this webinar who might be able to answer specific question on gut absorption of toxins like aflatoxin in the gut.

## Ahmed Kablan

Thank you, Dr. Ghosh, and a question for Christopher related to the environment and enteropathy, how fast the condition will be reversed if you improve the environment, improve the environment, food and water, etc. And is there a long lasting damage?

## Christopher Duggan

That's, it's a great question and the short answer is, we don't know. The early studies in this field suggested that when adults left an environment that was correlated with high enteropathogenic exposure, that their absorption of nutrients improved, so leading people to think that it was a temporary issue. But of course most people living in low and middle income countries can just exit their environment, that's where they live. And so chronic exposure likely is correlated with chronic effects. Whether short term exposure leads to chronic effects is hard to know. But it's an area of great interest, because it seems early studies, and some which we've done, have suggested that, for instance depending on what marker of EED is used, are, for instance neurodevelopmental effects of early infancy EED.

## Ahmed Kablan

Thank you. A question submitted during registration period, and I'm going to ask it to the panel, and this is related to climate change impact on, the question submitted from Principal and Food Security officer from ministry of animal, agriculture and fisheries in Uganda, the question how can government mitigate the effect of aflatoxins on children growth, under the conditions of climate change, but I want also to expand this to look at other factors that could lead to negative impact on child growth and environmental conditions environmental enteropathy, to look at how you anticipate also climate change could impact the spring of microbial contamination or contaminants that could lead to a condition like EED and others. Over to you. Who wants to start it.

## Patrick Webb

Well okay I'll jump in I guess. Very forward looking and good question obviously. And there's very likely to expansion of mycotoxins contamination threats into new geographies with climate change. And maybe intensification of those threats in areas where they already are, simply because of the temperature, humidity, rainfall effects. And, therefore, attempts have to be made to prevent the problem from growing. And that means improved seeds, improved management on farm, but especially improved storage and improved processing. And therefore knowledge and awareness. Not just of the smallholder farmer but of the marketplace, and that means governments have to play their role, not assuming this is just something the farmers have to deal with. The regulations, testing, food testing and safety standards, are all going to matter a great deal in future. So you combine that with the potential lowering of water tables and water stresses, which are already manifest in many low income countries. And that combination of water stress and food stress is pretty scary when you look down the future. So we better start acting on it right now to prevent the worst. Over.

## Ahmed Kablan

Thank you Dr. Webb, any other of the speakers would like to add to it, or should we move to the next question. I have an interesting, several other interesting questions. One of them, I really want to pick on it came in terms of looking at, thinking about environment enteropathy and impact on the microbiome as well as potentially aflatoxin impact on the microbiome. Now, what are your thoughts about adding pre- and probiotics to diets along with the other WASH interventions, as well as the other nutrition packages to support the health, or the assembly of a healthy microbiota in the gut. Any thoughts on that, Christopher you want to take stab with?

## Christopher Duggan

Oh sure, I'm, I don't mind saying that I'm very much a probiotic skeptic. There have been many, many different trials evaluating probiotics and I always think back to the composition of human milk, which is



very rich in prebiotics, right. The oligosaccharides in human milk are in part responsible for the development of the intestinal flora, a healthy diverse intestinal flora in the colon of breastfed infants. So I think the most important role of prebiotics are the naturally occurring ones that are included in human milk. It does beg the question of course of this really cutting edge idea that Jeff Gordon and Tamid Ahmed and others have proposed, which is are there certain patterns of diet that can be used for the treatment of malnutrition to improve weight gain and engender a better, if you will, microbiome pattern. And I think I, in the chat, had sent some some references for some new recent New England Journal papers on this very topic. So it's a very exciting area, but I think still we have a lot more to learn.

Ahmed Kablan

Thank you, Chris. Ahmed Kablan: Another question. To the speakers from, Where is the audience or Sarah Maklan is interested to hear more about the policy implications based on what evidence we currently have. More specifically, any thoughts on conceptualizing the basic or the most basic packages of intervention that consider with mycotoxins and nutrition linkages. What that could look like, and I think that question to be you Patrick.

Patrick Webb

Well, but also Shibani. Well, I think it's so easy to say, well, you of course we have to have multisector integrated programming that ensures that the water is clean and keeps children or infants away from livestock and chickens in particular, and ensures access to clean food. And, when appropriate, hand washing and sanitation environment, right. I mean none of these are actually quite that new. But the evidence, scientific evidence, on just how important these things are, and how much they can strain investments from having the impacts you'd like to see, suggest that we really need to do a lot better. And test and measure what we're doing to ensure that it is really actually achieving the outcomes that we assume it's achieving. And so you know I'm not, again I'm not suggesting much more testing by programmatic or policymakers of the drivers necessarily of these challenging interactions, but, we you know, evidence, we all call for evidence based programming, right. Evidence based policies, but we absolutely need evidence at the other end, that those policies and programs based on evidence, are doing what we expected them to do, and if not, why not. And how to how to make changes accordingly, right. So cost effectiveness, benefit cost analysis, and testing of hypotheses and assumptions in programming, I think, are all really quite important to need to play a bigger role in programming M&E systems and investments that donors make. Over.

Shibani Ghosh

Ahmed? So I think I have actually from the previous question, as well as this one, I wanted to just make two comments, one is that I think I would say that, we're not at the point where you can say that this is the intervention that is going to support a healthy biome and we're going to remove EED and that's going to translate into better growth. I think there's a lot more in this space that needs to get done, whether it's on the metrics within the context of EED, whether it's in the metrics of what is a healthy microbiome and can even sort of sequence the biome itself. So there's a lot on the upstream end of research around this topic that still needs to get done. So there's no sort of 'yes a probiotic' or 'give a prebiotic.' The other point that I wanted to make was that in terms of package of interventions, actually what we do know is that keeping a clean food system, having a clean environment, a good diet, so there's the basic tenets of these interventions do exist. But to Patrick's point, I think we don't do enough in understanding whether those policies that are targeting these specific tenets are actually translated into action, and if that has an effect. And, and I think so that's, so there's two different ends to where I'm looking at this. One is what still needs to be done on the upstream and research to sort of push new innovative interventions, and two is what needs to be still done on the existing a package of interventions and approaches. So that that really, so to me there's a duality to this, there's no one single way of going on with these, with these two questions.

Ahmed Kablan

Thank you Shibani. And another question related to this from Dr. Debendra Adihkari from USAID Nepal. He's asking about the linkages and implications you'll see between food system, health system, and nutrition policies and overall programming, based on the more generic. Now, I think this is a question I want to relay on the whole panel, because each one of you bring different perspective from health and nutrition system, as well as food system point of view. Anyone would one would like to start?

[Shibani Ghosh](#)

Patrick.

[Patrick Webb](#)

No, not me. I actually didn't catch the question, so.

[Ahmed Kablan](#)

Sorry, the question is implications of the data that we have, or the evidence that we have so far, and on the linkages or potential linkages between on food systems, health systems, and nutrition policies.

[Christopher Duggan](#)

Well, I mean I don't have any great answers, except to point out that obviously it's, to focus too much for instance on the Ministry of Health in low and middle income countries and not thinking about other ministers, including agriculture ministers, environmental health ministers, and others whose policies have a direct effect on the problem, is not the way to go. And I think what you've heard, not just from the panelists but from the questions in the audience, really this idea has to be a holistic approach. To go back to my first slides, if we make all of the interventions that we know are effective, we're only going to reduce childhood stunting by 36% or so. So indeed a trans governmental approach to these problems is really important.

[Patrick Webb](#)

I think. Mycotoxins are, let's see it as an opportunity. For encouraging that kind of dialogue, right, as we've seen in several countries aflatoxin threats have been known and tackled by ministries of agriculture primarily for decades, for very, very long periods, because they are known to affect livestock productivity and survival, and so on. And there are very strict limits, regulations through Codex on the movement of contaminated foods across borders, right. So it affects trade. Right, so the Ministers of Agriculture, Ministers of trade have long understood the threats from an economic perspective of aflatoxin. A lot of this new research is bringing on board the medical and public health perspectives to understand that this isn't just about dying of cancer through eating contaminated foods. There's something here that affects basically the physiology, and birth outcomes, and children's growth and development, right. So what this does is serve as a reminder of the interconnectedness of development activities, or how they should be. And there are countries like Nepal, like other parts of the world where they're making efforts to better link into actions across sectors, across ministries, in ways that can do better than they've done in the past. So I think these kinds of findings matter, but you have to get these findings not just to scientific journals, you have to get it into the hands of the policymakers and to the donors who can make a difference.

[Ahmed Kablan](#)

Thank you, Patrick. I think we are almost out of time, and I just want to say before we hand it back to you, Katie for closing out. This this whole presentation, and looking at the complexity of the factors that contribute to the nutritional outcomes that has several linkages to food safety, the quality of the diet as a whole, the environment surrounding water linkages- it's really been it back to the importance of how much we really want to say we have to think on a systemic level. Rather than an individual household or personal level or single intervention, as Patrick, Christopher, and Shibani mentioned, we need to look at it as a holistic approach from all angles. And what could be the most effective packages, maybe not also not looking at one size fits all because one size fits all does not really work everywhere. And that's why

we have to be thinking more broadly, and again I want to emphasize one of the points, the importance of tested or testable, potential to be validated, assumption to be built, that should be used. And finally, I want to say this, to say unsafe food is not only undermining the children's wellbeing as we have seen. It also threaten their lives. We can't afford not to invest and to look at food safety from all aspects, from microbial or mycotoxins or others. Unsafe foods impede our ability to achieve in nutrition and other development targets, they are a disease and number one cause of children under five deaths. And up to 70% of their diseases are caused by unsafe water and food. So we can't just do nothing, and Christopher put it nicely, if we implement 90% of the nutrition-specific interventions or improved interventions, we're achieving 35% efficacy. With that, I thank all the audience Thank you so much for being being with us for about an hour and a half, and I will hand it back to you, Katie.

### Katie Appel

Alright, well, thank you so much, and thanks to the presenters for the wonderful presentations and to all the panelists , sorry the participants, for a great discussion. And hope you have a wonderful rest of your day.

### Patrick Webb

Thank you all, thank you.

### Shibani Ghosh

Thank you, thank you, everybody.

### Christopher Duggan

Thank you.



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Implemented by:  
JSI Research & Training Institute, Inc.  
2733 Crystal Drive  
4<sup>th</sup> Floor  
Arlington, VA 22202

Phone: 703-528-7474  
Email: [info@advancingnutrition.org](mailto:info@advancingnutrition.org)  
Web: [advancingnutrition.org](http://advancingnutrition.org)

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