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

Children, chickens, eggs, environmental enteric dysfunction and Campylobacter: the CAGED study

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Photos: UF IFAS, African Chicken Genetic Gains, Rod Waddington, Reuters

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FEED THE FUTURE INNOVATION LAB FOR LIVESTOCK SYSTEMS

- Rationale: Undernutrition (stunting) impairs brain development in under twos; animal-source foods, the best source of multiple stunting-preventing nutrients, are lacking in diets of the poor.
- Vision: To sustainably improve livestock productivity and consumption to improve human nutrition, health, and incomes.
- Countries: Eight in Asia (Nepal and Cambodia) and Africa (Ethiopia, Rwanda, Uganda, Kenya, Burkina Faso and Niger)
- Projects: 27 research for development projects on human and animal nutrition, disease, food safety, policy, gender, and capacity building.
- Funds: 49m from USAID (2015 to 2020) and 8.7m from BMGF (2017 to 2022)

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BILL & MELINDA GATES FOUNDATION AWARD

- **Equip project:** Strengthening smallholder livestock systems for the future

Subprojects:

- **FEED**: Improving supply of quality feed for dairy cows in Ethiopia and small ruminants in Burkina Faso
- **CAGED:** *Campylobacter* genomics and environmental enteric dysfunction
- **Project duration:** 5 years (2017-2022)
- **Target countries:** Burkina Faso & Ethiopia

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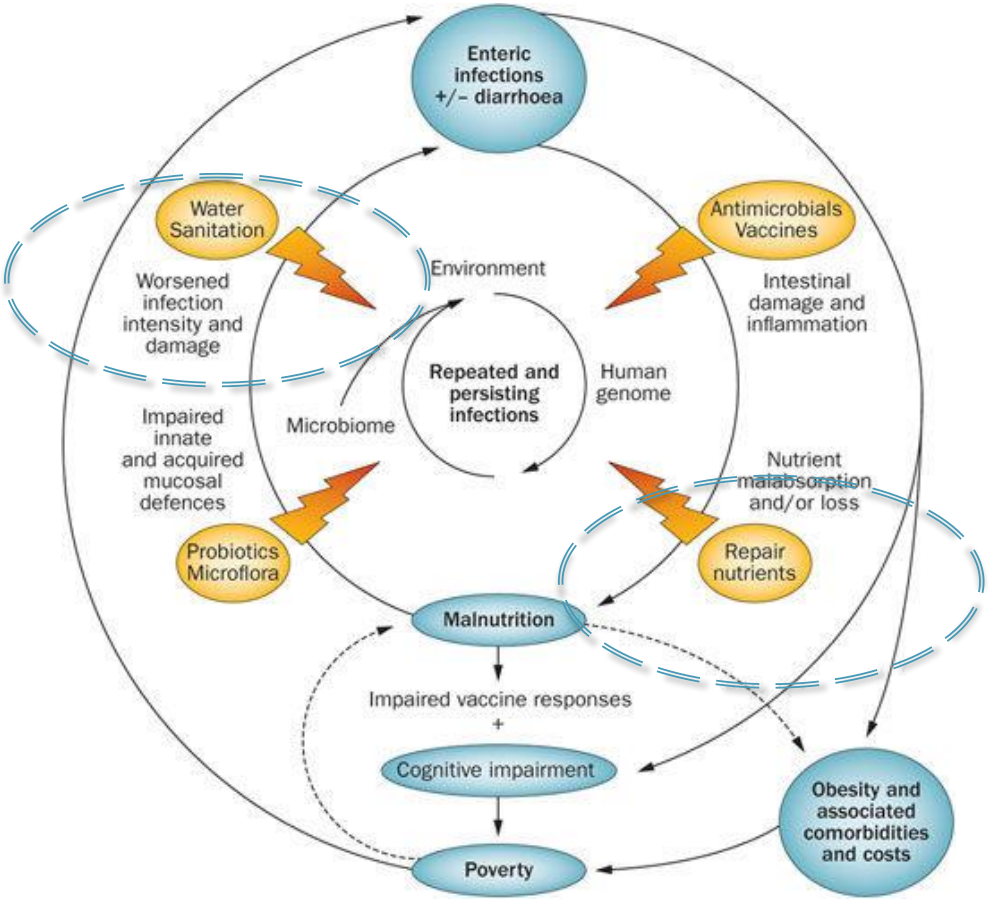
NUTRITIONAL INTERVENTIONS TO REDUCE STUNTING

- Micronutrients and plant-based foods have significant, but modest effects
- Animal source foods

  Best available sources of high-quality nutrients: proteins, vitamins (A, B12), zinc, iodine, iron, choline, docosahexanoic acid; high bioavailability

  Ecuador: providing one egg a day to children 6-9 months of age for six months LAZ by 0.63 and reduced stunting by 47%
- No nutritional intervention alone has fully prevented stunting
- Additional control of infectious disease agents is needed

THE VICIOUS CYCLE OF DISEASES OF POVERTY



HYGIENE INTERVENTIONS TO REDUCE STUNTING

- WASH Benefits
  - Cluster randomized trials in Bangladesh and Kenya
  - Can WASH and nutritional interventions prevent early life linear growth faltering?
  - Are combined WASH interventions more effective than single interventions?
  - Are there synergistic effects on diarrhea or linear growth?
  - Nutrition improved linear growth by 0.15 - 0.20 LAZ; no additional effects of WASH
- SHINE
  - Cluster randomized trial in Zimbabwe
  - Independent and combined effects of improved household WASH and nutrition on length and hemoglobin concentration among children at 18 months of age
  - Nutrition improved linear growth by ~ 0.20 LAZ; no additional effects of WASH
- Can exposure to animal excreta explain the limited effects of WASH?

ETHIOPIA LIVESTOCK MASTERPLAN

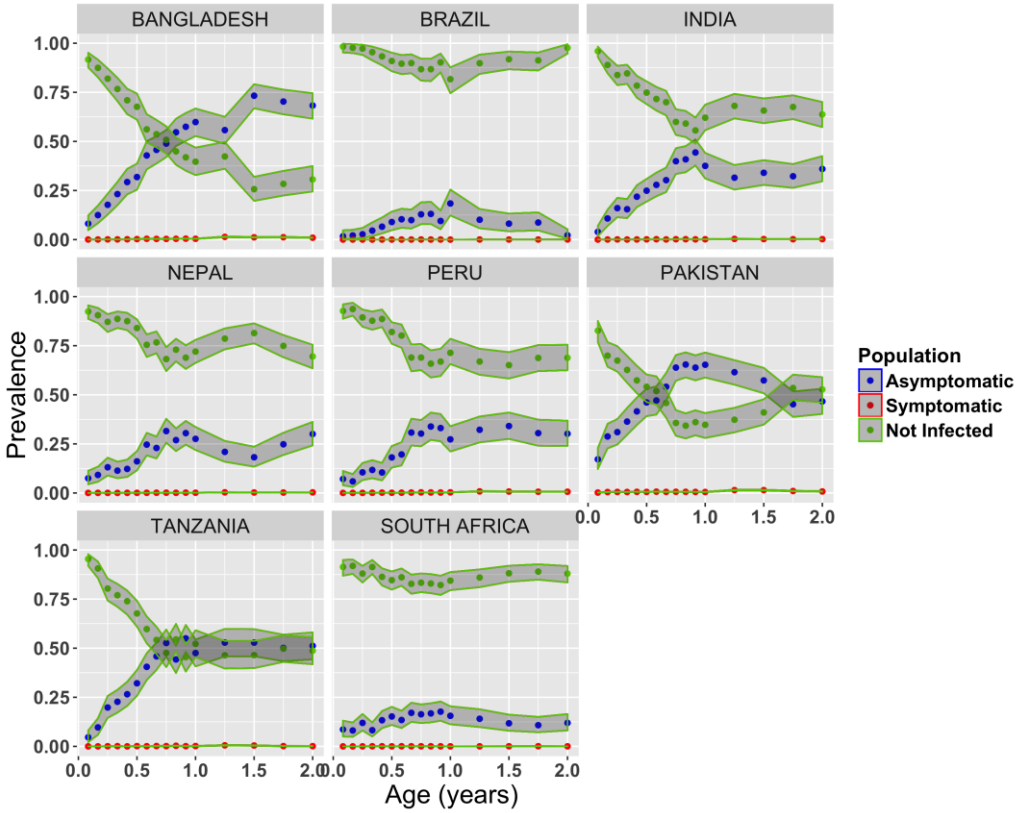
- In order to meet the increasing demand and nutritional need for animal source foods, the Livestock Master Plan (LMP), adopted by the Growth and Transformation Plan (GTP) of the GOE in 2015, aims to significantly increase poultry production by moving from traditional (scavenging) family poultry to improved (semi-scavenging) family poultry systems (IFP).
- In all production zones, the LMP envisions increases of 250% between 2014 and 2020 in the number of IFP keeping households (egg and meat production)
- The LMP may provide improved access of pregnant mothers and young children to animal source foods with nutritional benefits
- Higher poultry densities may negate the nutritional benefits through increased exposure to infectious disease agents chicken droppings

EXPOSURE TO CAMPYLOBACTER

- Chickens and other livestock are major reservoirs of human exposure to *Campylobacter* globally
- Transmission may occur by food, direct animal contact or environmental contamination
- Relative pathway contributions varies by settings; foodborne transmission more important in industrialized countries
- Very few data available for (children in) developing countries
- Most infections are asymptomatic (not associated with diarrhea) but do induce acquired immunity and EED
- Irrespective of transmission pathways, controlling reservoirs is expected to lead to reduction in (asymptomatic) colonization

MOST INFECTIONS ARE ASYMPTOMATIC

(re-analysis of MAL-ED data)



Beneficial effects of animal ownership and ASF consumption negated by EED?

Less Campylobacter?
Less EED?
Better growth?

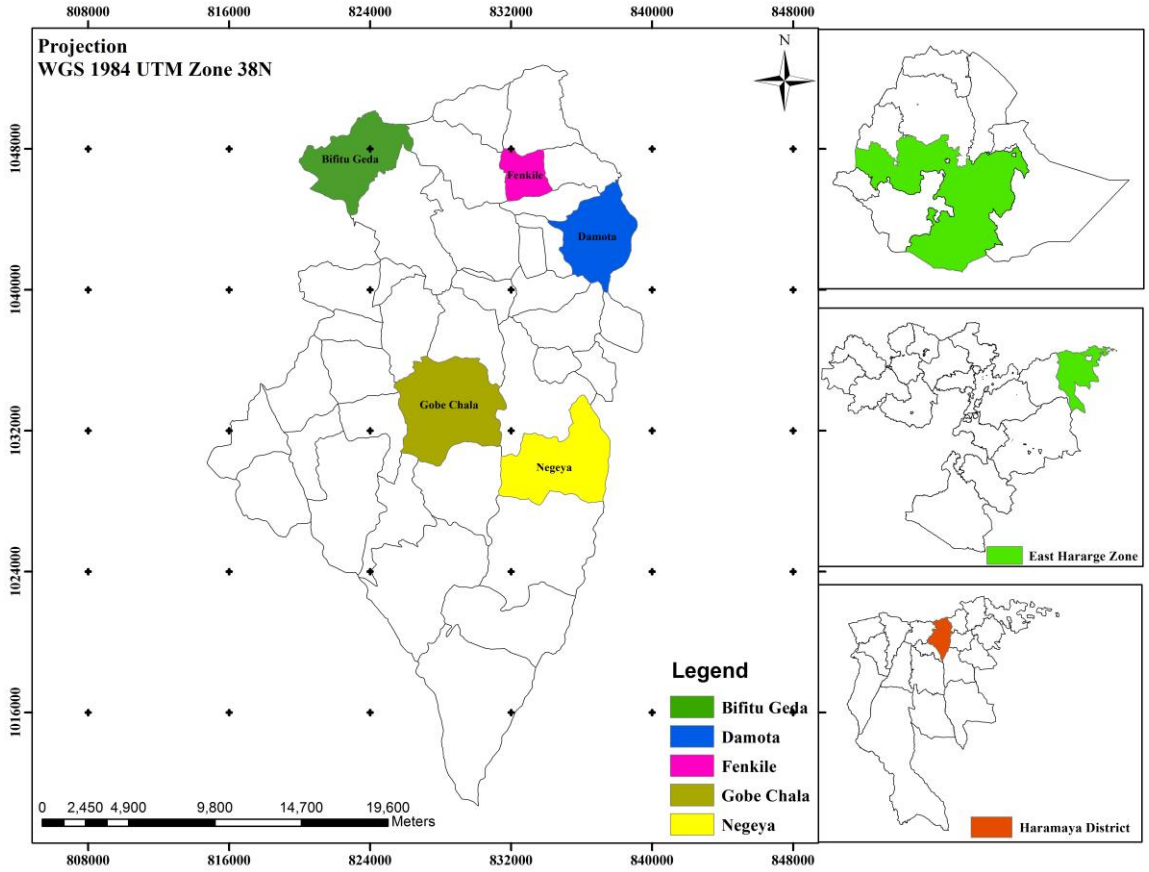
VISION

- Research has shown that young children who eat chicken eggs grow better and gain life-long benefits
- Our research in Ethiopia tests the benefits of improved poultry production by smallholders aiming to produce more eggs for their children
- We also examine the advantages of protecting their children from chicken droppings by using coops, which should further improve health and growth of the children

HYPOTHESES

- Against a background of increased chicken production by smallholder farmers, (a)symptomatic colonization with *Campylobacter* bacteria of children between 6 and18 months of age will be reduced by limiting their exposure to chicken excreta through animal husbandry interventions and hygiene training
- Reduced colonization by *Campylobacter* bacteria will reduce the prevalence of environmental enteric dysfunction in children, and, in combination with improved access to eggs within the household and basic nutrition and WASH training, will increase linear growth among children between 6 and 18 months of age

STUDY AREA – HARAMAYA WOREDA, ETHIOPIA



CLUSTER RANDOMIZED CONTROLLED TRIAL

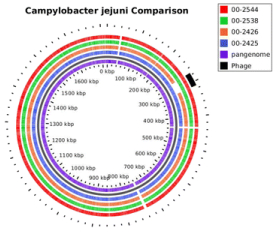
- Three treatment arms, hierarchical random approach
  - Random allocation of kebeles to treatment arm
  - Random selection of children in kebele
  - 100 children per treatment arm
- Full treatment
  - 10 chickens of improved breed (African Chicken Genetic Gains) in movable poultry house; vaccinations, health care, feed
  - Neighboring families receive 5 chickens in movable houses
  - Nutritional and hygiene training
- Partial treatment
  - As full treatment, no movable poultry houses
- Control
  - Current situation – scavenging chickens of traditional breed, often kept in the home overnight

FORMATIVE RESEARCH - ETHNOGRAPHIC

- March-May 2018
- Objectives
  - Understand local community contexts, socio-cultural beliefs and practices and social organization in relation to poultry, dietary intake, WASH, and child growth as they pertain to Campylobacter epidemiology
  - Explore community-level opportunities and barriers to possible interventions aimed at improving poultry biosecurity and zoonotic disease prevention, with a specific focus on caging poultry
- Methods
  - Informal rapid ethnographic approach, weekly visits
  - Animal feces, poultry management, poultry interventions, food safety, child health and growth, child nutrition and care, WASH, gender roles and community organization, poultry development projects, livelihoods and environmental change

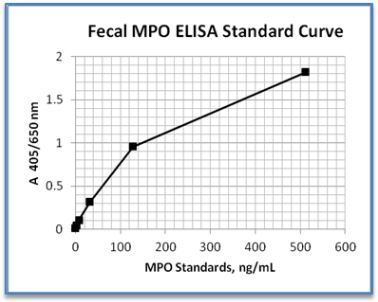
FORMATIVE RESEARCH - MICROBIOLOGY

- July-September 2018
- Research questions
  1. Prevalence of (thermophilic) Campylobacter in children 11-13 months
  2. Prevalence of Campylobacter in chickens
  3. Prevalence of Campylobacter in other domestic animals?
  4. Species and genotypic diversity of Campylobacter
  5. Genotyping as basis for attributing Campylobacter colonization of children to animal reservoirs?
  6. Performance characteristics of PCR and culture methods for Campylobacter in feces of children
- Study design
  - Cross-sectional study (100 children and animals in their environment)
  - Campylobacter culture and PCR; Whole Genome Sequencing



FORMATIVE RESEARCH - EED

- Research questions
  1. Prevalence of EED among children at 11-13 months of age
  2. Prevalence of stunting among children at 11-13 months of age
  3. WASH conditions of the home environment of targeted children?
- Study design
  - Cross-sectional study (100 children)
  - Anthropometric data (repeat after 4-6 months)
  - L:R test; fecal MPO (indicators for EED)
  - Observational study
  - Interview with mother / caretaker



FORMATIVE RESEARCH – AGRICULTURE AND ENVIRONMENT

- Research questions
  1. Domestic animals are present and numbers
  2. Management of chickens managed, specifically manure
  3. Contamination of the environment by chickens and other domestic animals
  4. Size of buffer zone around sentinel child's home is necessary to prevent (or minimize) exposure to neighbor's chickens
  5. Can chickens be housed all day in movable poultry houses
  6. How to stimulate families to accept containing chickens
  7. How to assure and monitor compliance with corralling
  8. Impact of chicken coops on prevalence of Campylobacter in the environment

FORMATIVE RESEARCH – AGRICULTURE AND ENVIRONMENT

- Study design

  Observational study (100 households)
  - GPS mapping
  - Presence of animals, feathers, feces, other visible signs of contamination

  Field trial (5 households)
  - Provide with10 chickens and house in movable poultry house for 1 month in summer
  - In-depth interviews and chicken health assessment
  - Observe chicken feces, feathers before and after
  - Campylobacter presence and numbers in drag sampling of floors in the home

RCT GO – NO GO DECISION

- Prevalence of stunting > 30% (WHO designated "high")
- Prevalence of EED > 30% (% lactulose excretion ≧ 0.2%)
- Prevalence of Campylobacter colonization in children > 30%
- Attribution of Campylobacter colonization of children to chickens > 40%
- Reduction of visible chicken droppings by coops > 75%

CONCLUSIONS

- Malnutrition causes a high disease burden in the developing world
- Stunting in early life condemns a child to a life of disadvantage
- Inadequate nutrition and environmental enteric dysfunction (EED) are major drivers of malnutrition
- Chronic (asymptomatic) infections with enteric pathogenic bacteria (specifically Campylobacter) are a major driver of EED
- Efforts to prevent stunting have to date had limited success
- Animal source foods are an essential component of diets of all children globally
- Sanitation efforts to prevent stunting should also focus on animal excreta
- The CAGED project will evaluate the effects of an intervention including feeding of eggs to young children in combination with improved hygienic management of chicken feces

STUDY TEAM

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ADDITIONAL ANALYSES

- Subject to incremental funding
  - Hemoglobin levels and serum zinc, iron and vitamin A at baseline and biannual follow-up
  - Metagenomics of child and animal feces to get a deeper understanding of the relationships between the microbiomes of children and animals, the extent to which they are shared and how this affects the gut health and growth of children
  - Metabolomics as a marker to measure egg consumption
  - Filtration/culture test to detect non-thermophilic Campylobacter
  - Detection of other zoonotic pathogens that can be causes of EED
  - Serology to measure long-term exposure to Campylobacter
  - Analysis of mycotoxin metabolites in urine or DNA adducts in serum
  - Allergy markers in serum

REFERENCES

- Stunting: FAO, 2017; NIPH, 2013; Grantham-McGregor et al., 2007; De Boer et al. 2012; Black et al., 2013; WHO, 2017b; Headey and Hirvonen, 2016
- Impoverished gut: Guerrant et al., 2013
- Stunting as an inflammatory disease: Milward et al., 2017
- ASF nutritional intervention: Ianotti et al., 2017
- EED: Trehan et al., 2016
- WASH trials: Arnold et al., 2013; SHINE team, 2015; ASTMH 2017 presentations; Luby et al., 2018; Nun et al., 2018
- Animals and growth: Headey et al., 2016a, b; Ngure et al., 2013; George et al., 2013
- LMP: Shapiro et al., 2015
- Campylobacter: Amour et al., 2015; Schnee and Petri, 2017; Platts-Mills et al., 2017

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