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LIVESTOCK, CAMPYLOBACTER AND CHILD NUTRITION: FINDINGS FROM THE FORMATIVE RESEARCH OF THE CAGED STUDY IN RURAL ETHIOPIA

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

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STUNTING

- Affects 25% of children under 5 years of age globally, 35% in Africa, 38% in Ethiopia
- Stunting is associated with:
  - Increased mortality from diarrhea, pneumonia, other infectious diseases
  - Impaired cognitive development
  - Reduced income (by up to 22%)
  - Reduced life expectancy by up to 17%
  - Increased risk of chronic diseases later in life
- Need for interventions to reduce this important cause of morbidity and mortality

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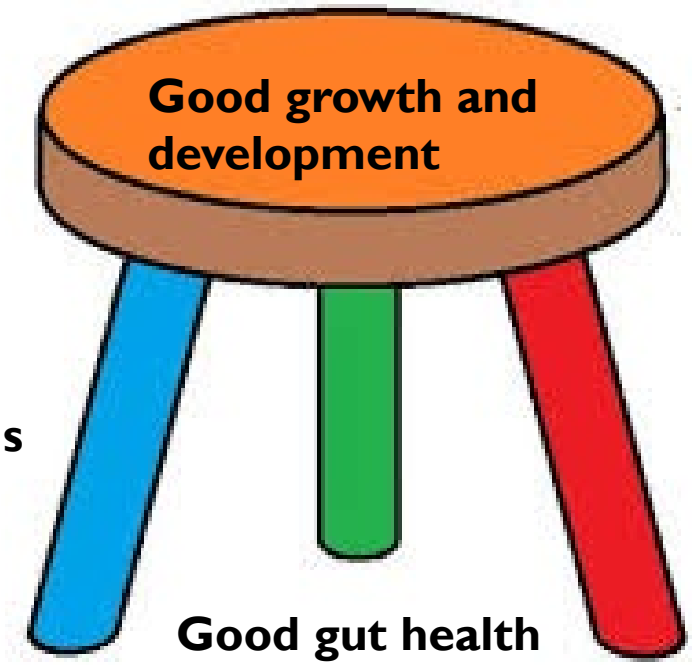
FOR NORMAL GROWTH AND DEVELOPMENT 3 CONDITIONS MUST BE MET



No excess of symptomatic common infections such as malaria, diarrhea, or lower respiratory tract infections

Diet provides adequate macro- and micronutrients in bioavailable forms

Dr. Mark Manary
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INTERVENTIONS TO REDUCE STUNTING

- Micronutrients and plant-based foods have significant, but modest effects; typically 0.2 – 0.3 Length-for-Age Z score (LAZ)
- Animal source foods are the best available sources of high-quality nutrients; some studies suggest greater impact on LAZ
- No nutritional intervention alone has fully prevented stunting
- Additional control of infectious disease agents is needed
- Three recent randomized controlled trials showed no impact of WAter, Sanitation and Hygiene (WASH) interventions

- Can exposure to animal excreta explain the limited effects of WASH?
- Increasing livestock production may increase exposure of young children to animal excreta, negating positive effects of improved diets

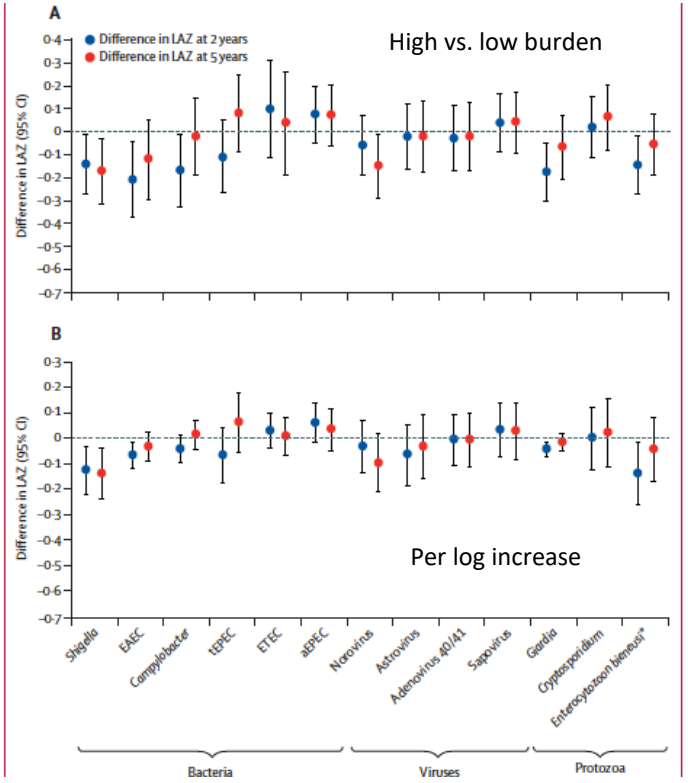
ENVIRONMENTAL ENTERIC DYSFUNCTION

- Condition found in children in LMIC that develops in the first three years of life.
- Characterized by a chronic inflammation of the small intestine, abnormal villous architecture, and reduced intestinal mucosal surface area.
- Etiology of the disease is complex; it is associated with unsanitary living conditions, colonization by intestinal pathogens, and malnutrition.
- Increasing evidence of involvement of (asymptomatic) colonization by enteropathogenic bacteria in causation of EED
- Colonization with *Campylobacter* spp. is very common in children in LMIC (prevalence up to 75%)

CAMPYLOBACTER AND STUNTING

- MAL-ED study
- 24-month length-for-age Z (LAZ) score associated with:
  - Complementary food (+)
  - Diarrhea (-)
  - (Asymptomatic) colonization by specific enteropathogens (-)

The work here suggests modifying the longstanding UNICEF framework of malnutrition by adding enteropathogen infection in the absence of diarrhea



Platts-Mills et al.. BMJ Glob Health 2017; 2:e000370
Rogawski et al., Lancet Glob Health. 2018;6(12):e1319-e1328

EXPOSURE TO CAMPYLOBACTER

- Chickens/livestock are major reservoirs of *Campylobacter*
- Transmission: food, direct animal contact, environmental contamination
- Pathway varies by setting: foodborne in industrialized countries
- Very few data available for children in low- and middle-income countries
- Controlling reservoirs should reduce colonization of children

HYPOTHESIS

- *Campylobacter* species, a natural inhabitant of the gastrointestinal tract of livestock and poultry, are among the main pathogenic bacteria involved in the causal chain of stunting, due to the exposure of young children directly or indirectly to feces of these animals

FORMATIVE RESEARCH 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
- Measure the prevalence of *Campylobacter* spp., EED and stunting and associated risk factors in young children in rural Ethiopia

FORMATIVE RESEARCH METHODS

- Ethnographic research (March-May 2018)
  - Informal rapid ethnographic approach, weekly visits
- Cross sectional study (October-December 2018)
  - Household survey, child and environmental samples, anthropometric measurements of children

STUDY AREA – HARAMAYA WOREDA, ETHIOPIA

FORMATIVE RESEARCH - ETHNOGRAPHIC

- Themes investigated:
  - 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
  - Environmental change

QUALITATIVE FINDINGS

- Islam dominant religion
- Agricultural production dominated by chat
- Eggs not consumed, "too luxurious".
  - Explained by extreme poverty, dietary norms, parental fatalism, and a lack of awareness of benefits of dietary diversity
- Livestock dominant on most homestead landscapes
  - Often one cow, few small ruminants, some chickens
- Homesteads were highly contaminated with human and animal feces
- Shared human-animal housing and care practices place children at high risk of exposure to pathogens in animal manure
  - Divided houses; animals brought inside at night

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VILLAGE CHICKEN PRODUCTION

- Households keep local indigenous chickens (average of six per household, unstable numbers due to seasonality and disease)
- Both exotic and improved breeds have been introduced, but indigenous preferred
- Chickens are women's domain, though interest among young men
- Benefits: Eggs, meat, sale of roosters, and fertilizer
- Land pressures make chicken production more attractive
- Lack of feed is problematic

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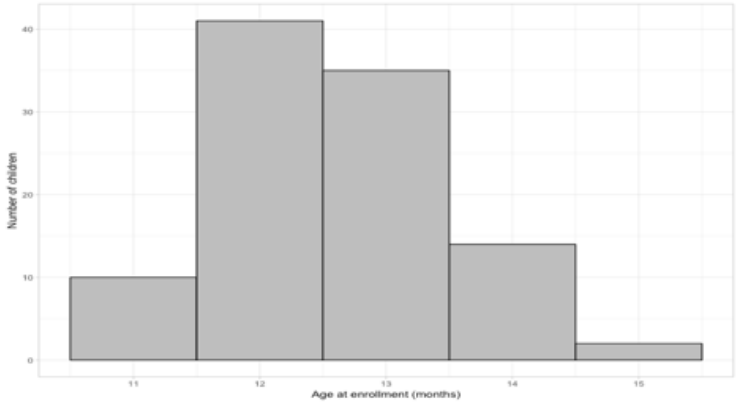
CROSS SECTIONAL STUDY DESIGN

- Randomization based on HDSS survey
  - Five randomly chosen kebeles, maximized distance
  - Parent-reported birth dates inaccurate; used calendar approach to estimate actual birth date
- High participation despite social unrest

  1 declined consent, 5 declined after consent but 2 reintroduced
- 102 children, median age 12 (11 -15) mos.



CHILD HEALTH AND DIET

Variable	Number (%)
Female	52 (51%)
Breastfed at birth	100 (99%)
Currently breastfeeding	90 (90%)
Only breastmilk in first three days	55 (56%)
Minimum Dietary Diversity – IYC (5 out of 8)	9 (9.4%)
Animal source food consumption (previous day)	57 (56%)
Milk	*53 (52%)*
Egg	*5 (5%)*
Diarrhea (past 15 days)	48 (47%)
Current diarrhea	12 (12%)
Fever (past 15 days)	51 (50%)
Current fever	5 (5%)
	Mean (IQR)
Dietary diversity score (out of 8)	3.5 (3 – 4)

ANIMAL OWNERSHIP AND HYGIENE

Variable	Number (%)
Any livestock ownership [Average Tropical Livestock Units]	96 (94%) [1.6]
Chicken ownership	55 (54%)
Small stock (sheep, goat) ownership	82 (80%)
Large stock (cattle) ownership	64 (63%)
Chicken nighttime location	
0 (no chickens, or not kept inside at night)	47 (46%)
1 (chickens kept in house at night, confined)	26 (26%)
2 (chickens kept in house at night, unconfined)	28 (28%)
Sanitation	
Open Defecation	79 (77%)
Limited	23 (23%)

NUTRITIONAL STATUS AND EED

	Number of children	Prevalence (95% CI)
Stunted (LAZ < -2)	42	41 (32-51)%
…Severely stunted (LAZ < -3)	19	19 (12-27)%
Wasted (WLZ < -2)	5	5 (2 -11)%
…Severely wasted (WAZ < -3)	1	1 (0-5)%
Acute malnutrition (MUAC < 125 mm)	31	30 (22-40)%
…Severe (MUAC < 115 mm)	8	8 (4-15)%
EED*	50	50 (40-60)%
…Severe EED**	17	17 (11-26)%

*EED = %L>0.45 or MPO>11,000 ng/mL or %L>0.2 and MPO>2,000 ng/mL

**Severe EED = %L>0.45 and MPO>2,000 ng/mL or %L>0.2 and MPO>11,000 ng/mL

CAMPYLOBACTER PREVALENCE IN CHILD FECAL SAMPLES BY PCR

Taxonomic group	# samples	Prevalence
Campylobacter genus	51	50 (41-60)%
C. jejuni	13	13 (8-21)%
C. coli	2	2 (0.5-7)%
Other *Campylobacter* species	36	≥ 36%

METAGENOMIC TOTAL RNA SEQUENCING OF CHILD FECAL SAMPLES (ID-SEQ)

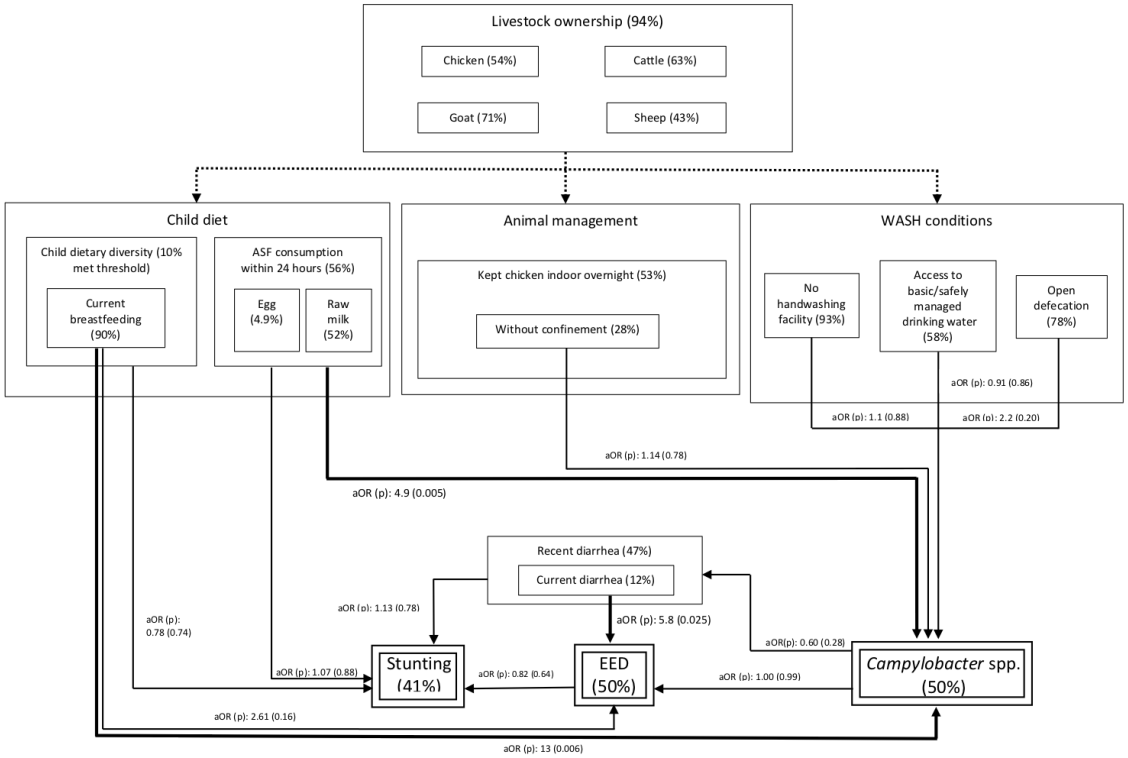
Campylobacter species	Prevalence	Mean (sd) log_{10}(RPM)
Campylobacter genus	88%	3.42 (0.98)
C. jejuni	68%	2.19 (1.12)
C. hyointestinalis	65%	2.75 (1.13)
C. coli	62%	1.76 (1.16)
Campylobacter sp. RM6137	53%	2.08 (1.00)
C. upsaliensis	50%	1.79 (1.03)
Uncultured *C.* species	46%	1.85 (1.05)
Campylobacter sp. RM12175	41%	2.79 (1.24)

Exclusively breastfed infants with diarrhea exhibited high *Campylobacter* abundances. Although *C. jejuni* and *C. coli* are prevalent among these infants, the second most abundant Campylobacter species was a new species, which we named "Candidatus *Campylobacter infans.*"

Bian et al., mSphere 2020;5(1)

Current breastfeeding	13 (0.006)	Not significant
ASF consumption	4.9 (0.005)	Not significant
Current diarrhea	Not significant	5.8 (0.025)
Drinking water	Not significant	0.38 (0.035)
Age (≥ / < median)	*0.37 (0.06)*	*2.1 (0.097)*
Sex (female vs. male)	*0.54 (0.23)*	*0.85 (0.71)*
Kebele group	*(< 0.001)*	*(0.47)*
Two vs. One	*0.03*	*0.53*
Three vs. One	*0.02*	*0.59*

CONCEPTUAL MODEL



LONGITUDINAL STUDY (2020-2021)

- What is the prevalence, species composition, and genomic diversity of thermotolerant and non-thermotolerant *Campylobacter* species in young children, adults, livestock and other reservoirs (i.e. drinking water, soil) in the Haramaya woreda?
- What is the attribution of *Campylobacter* infections in young children to humans, livestock, and other reservoirs) based on the genetic population structure of Campylobacter species circulating in these reservoirs?
- What are the associations among the presence of *Campylobacter* species, gut microbiota, and the health status of children?

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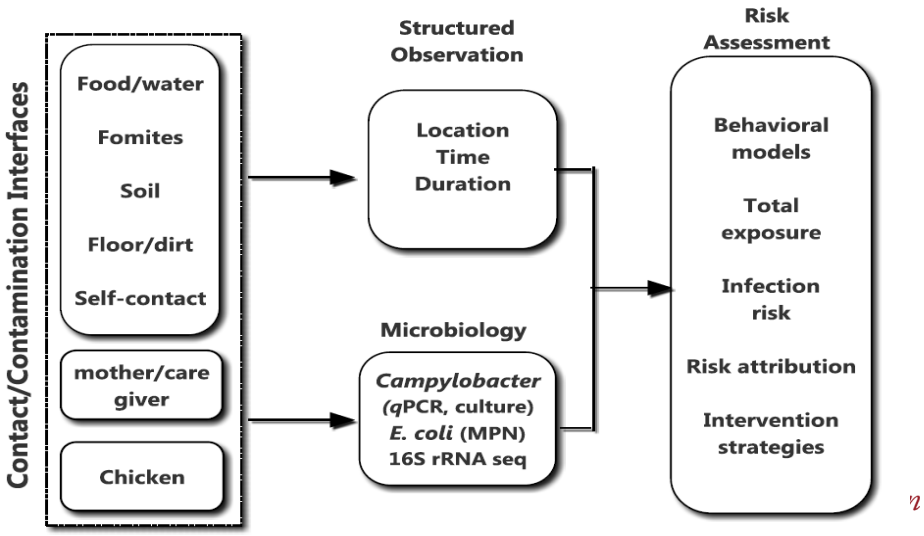
EXPOSURE ASSESSMENT OF *CAMPYLOBACTER* INFECTIONS IN RURAL ETHIOPIA (EXCAM)

- Characterize space-time patterns of children's behaviors in their living environment
- Detect, quantify, & characterize *Campylobacter* at key contact/contamination interfaces
- Assess the children's exposure to *Campylobacter* & infection risks



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CONCLUSIONS

- Traditional society of smallholder farmers with recent evolution towards cash economy (chat production)
- Low level of sanitation, cohabitation with livestock
- High level of breastfeeding, poor complementary diets
- High prevalence of stunting, EED and (asymptomatic) *Campylobacter* spp. infections
- Common occurrence of "emerging" *Campylobacter* spp.
- Reservoirs, transmission pathways and health impacts of these species unknown
- Potentially related to ruminants and other livestock, human-human transmission cannot be excluded
- *Campylobacter* colonization positively associated with ASF (raw milk) consumption and current breastfeeding
- Improved drinking water supply protective against EED
- Further studies planned to better understand *Campylobacter* reservoirs, transmission pathways and impacts

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Disclaimer

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