Reducing environmental enteropathy and child growth faltering: An intervention trial update

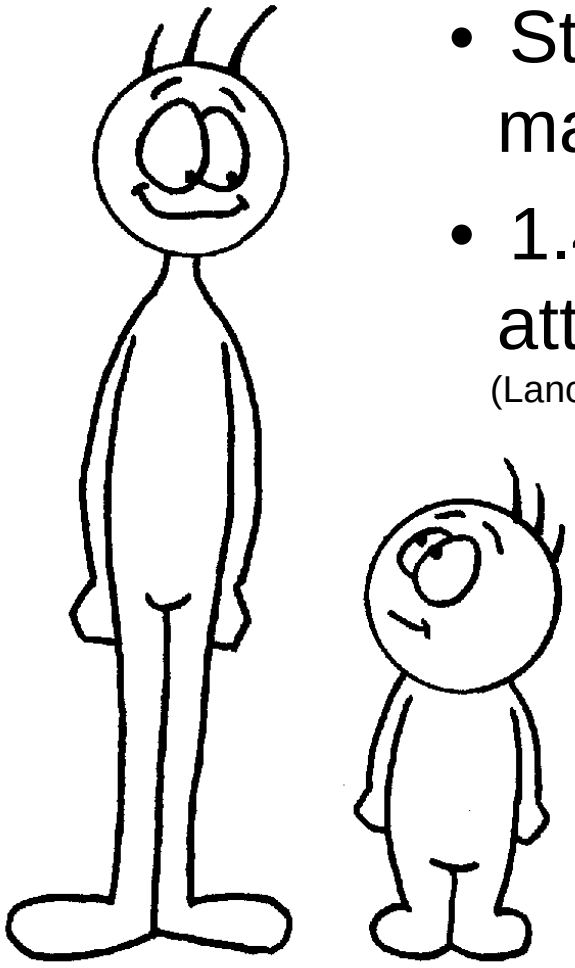
Steve Luby, MD
FHI-360
Washington, DC
19 June 2014

Photo: Faruqe Hussain

Outline

- Environmental enteropathy
- Update on WASH Benefits
- Recent evidence on environmental contamination
- Implications for research and programs

Why worry about stunting?



http://printablecolouringpages.co.uk

- Stunting is a marker of chronic malnutrition
- 1.4 million child deaths annually attributable to undernutrition.

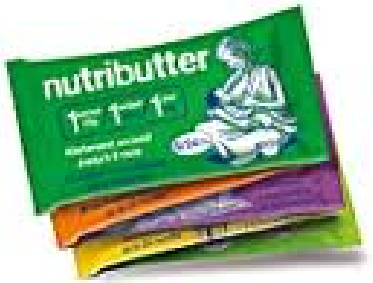
(Lancet 2012; 380: 2224–60)

- Malnourished children face:
  - increased mortality
  - cognitive impairment
  - decreased wages
  - increased chronic diseases

Photo: Mubina Agboatwalla

If children are malnourished

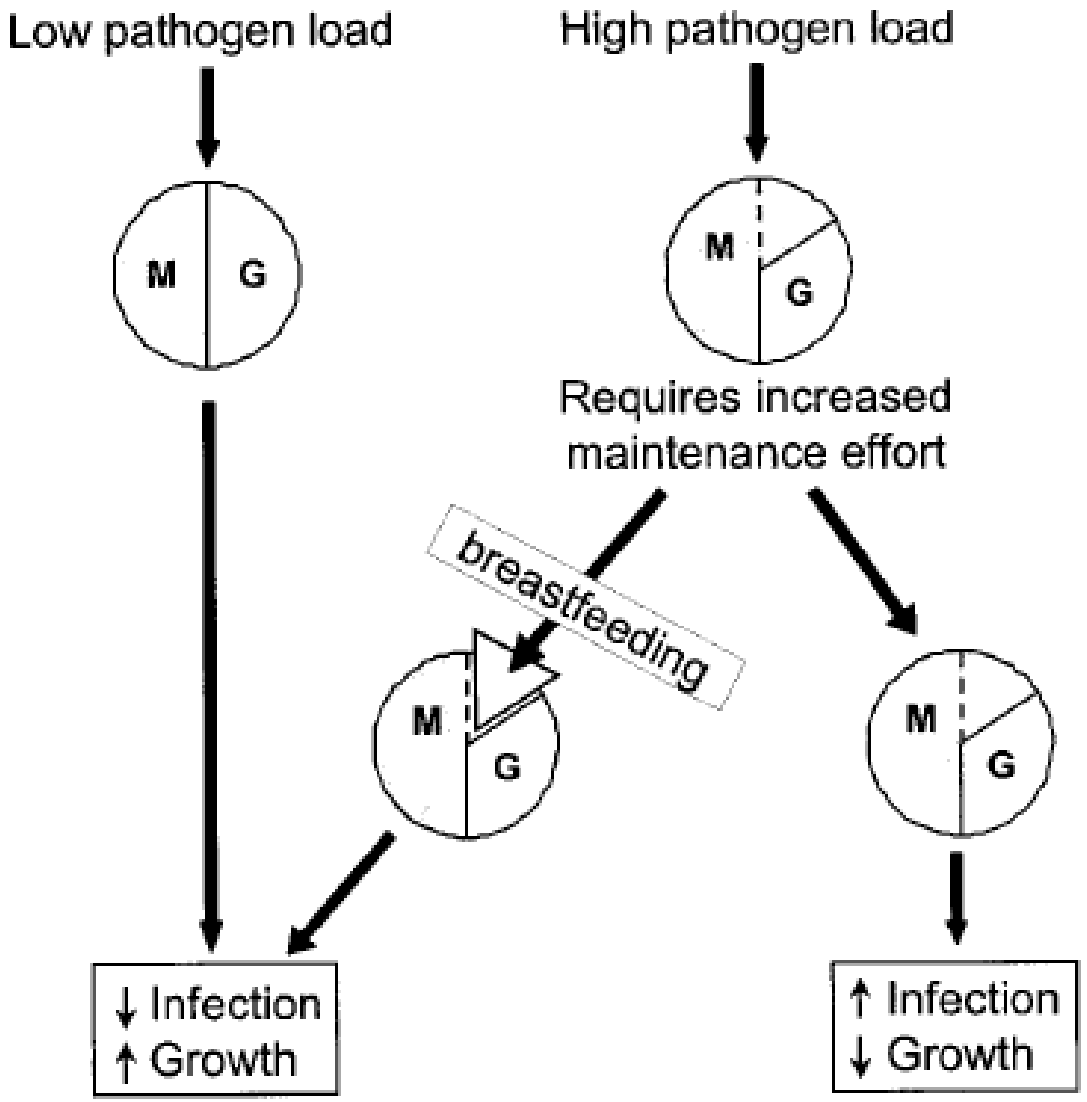
- Feed them more
  - But more calories are insufficient; need nutrient dense food
- Supplement with nutrient dense foods
  - only correct 1/3 of growth faltering (0.69 SD)
  - Mean effect (0.28 SD)
  - (Dewey K. *Matern Child Nutr* 2008, 4 Suppl 1: 24--85)



- 118 Kcal
- 9.6 gm fat
- 2.6 gm protein
- ≥100% RDA of 12 vitamins
- 9 minerals

If lack of food is not the sole common underlying sufficient cause of stunting, what else is driving this?

Impact of child infections on growth

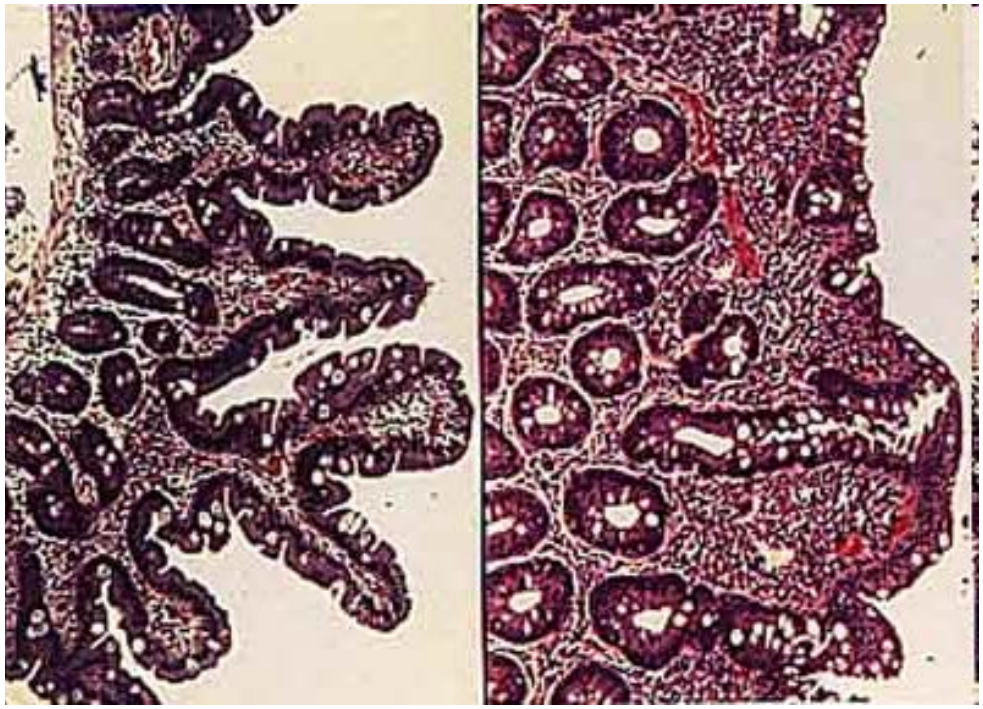


M – Maintenance
G – Growth

From: Thomas McDade. *Yearbook of Physical Anthropology*, 46:100-125 (2003)

Environmental Enteropathy

- Change in small intestinal villa architecture
  - Flattened; Reduced villous height
  - Increased
    - crypt depth
    - mitosis per crypt
- Inflammatory cell infiltration
  - Increased intraepithelial lymphocytes
  - Mucosal T-cell activation
    - CD3+ CD69+
    - CD3+HLA-DR+

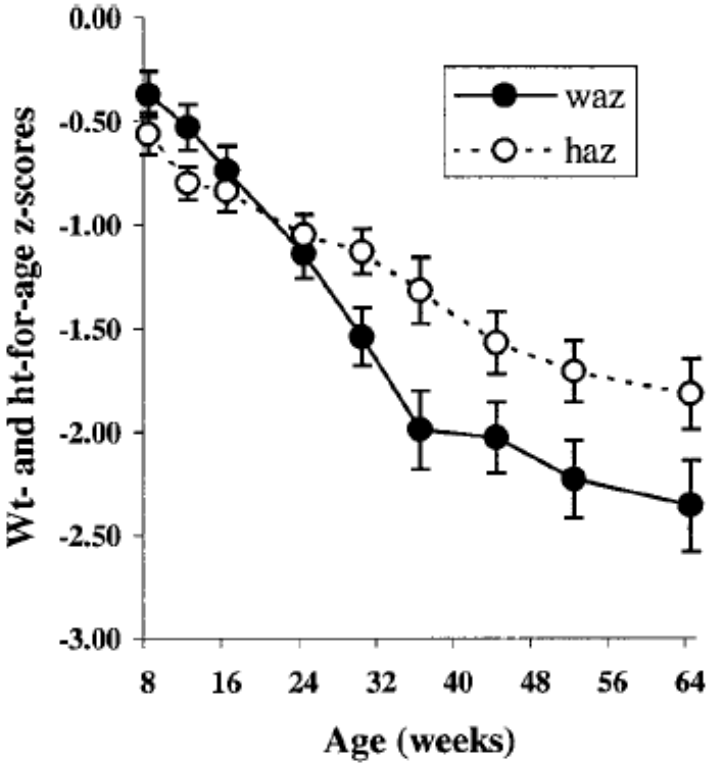


Normal **Environmental Enteropathy**

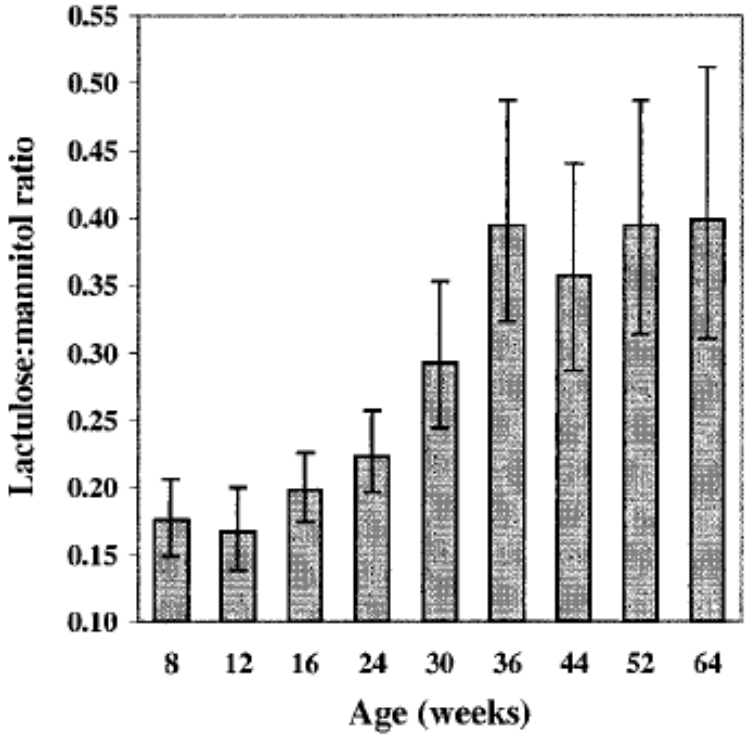
http://www.bio.davidson.edu/courses/Immunology/Students/spring2006/Mohr/Villi%20Atrophy.jpg

Veitch AM, *Euro J Gastro Hepatology* 2001, 13:1175-1181

Growth and intestinal permeability



Deterioration in weight and height by age (N = 71)



Worsening intestinal absorption by age (N = 71)

22% of the variability in growth was explained by variability in intestinal permeability

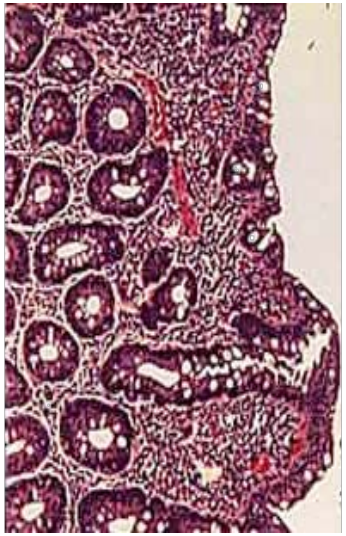
Campbell DI, Elia M, and Lunn PG, *J. Nutr*. 133: 1332–1338,2003.

Epidemiology
Environmental Enteropathy

- Widespread in
  - low income tropical countries
  - where food, water and environment are commonly contaminated with feces
- Acquired in early childhood
  - Stillborn children in endemic countries have normal intestinal cellular structure
  - Resolves with migration to developed countries (after 2 – 5 years)
- Peace Corps workers, U.S. soldiers in Vietnam acquired environmental enteropathy within 3 – 6 months.
  - Resolved within 12 months of returning to developed country

Suggests an environmental cause

Photo : UNHCR / G. Akash



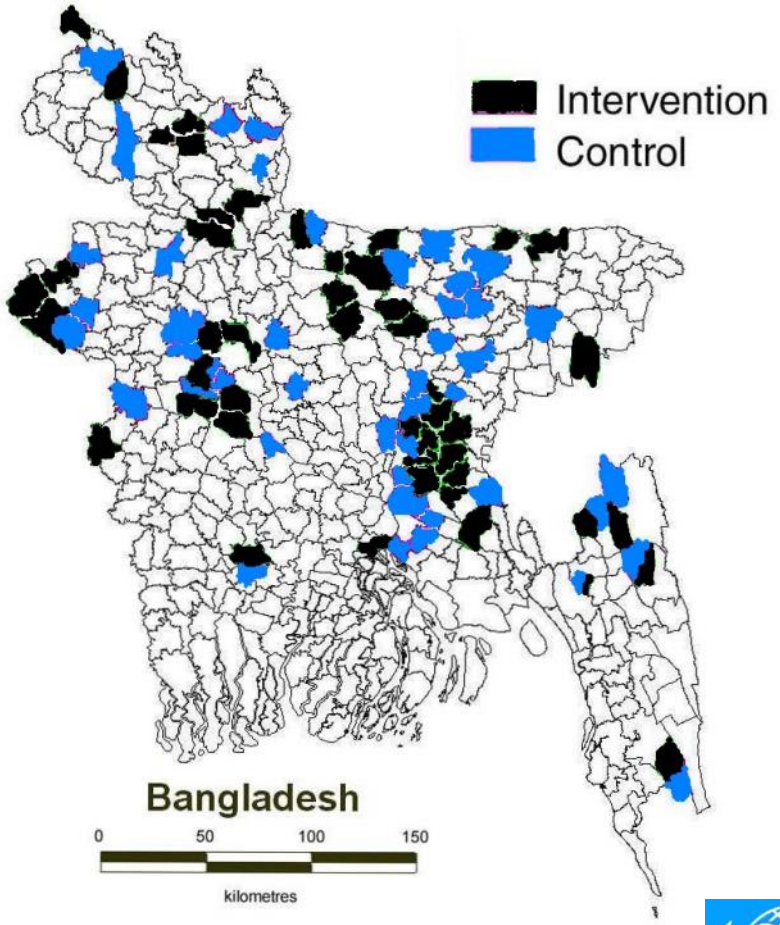
Study question

Would children living in relatively clean households have less environmental enteropathy than children in dirtier households?

SHEWA-B Evaluation

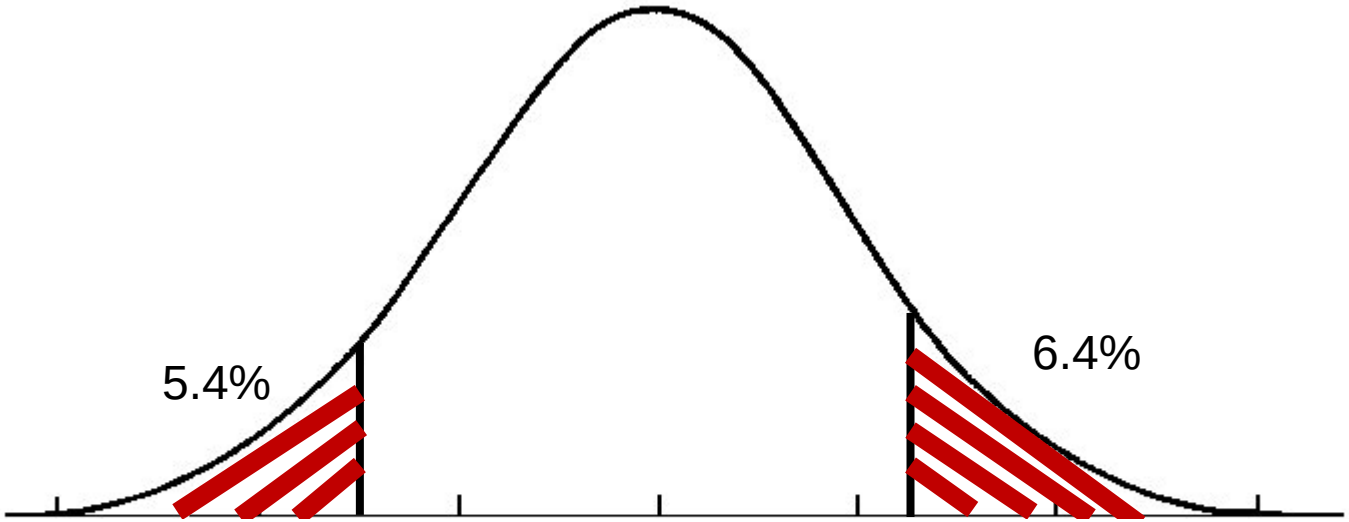
Sanitation Hygiene Education and Water Supply, Bangladesh

- Government of Bangladesh / UNICEF program
- Targeting 20 million people
- icddr,b contracted with the evaluation
  - 50 intervention and 50 **matched** control clusters
  - Clusters randomly selected
  - Probability proportional to size sampling
  - 10 households **per cluster**
  - Monthly follow up for 2 years



icddr,b
KNOWLEDGE FOR GLOBAL LIFESAVING SOLUTIONS

unicef



Dirty

- open defecation or toilet that did not separate feces from the environment
- median [*E. coli*] ≥ 10/100 ml
- No handwashing station *or* handwashing station w/o water and/or w/o soap

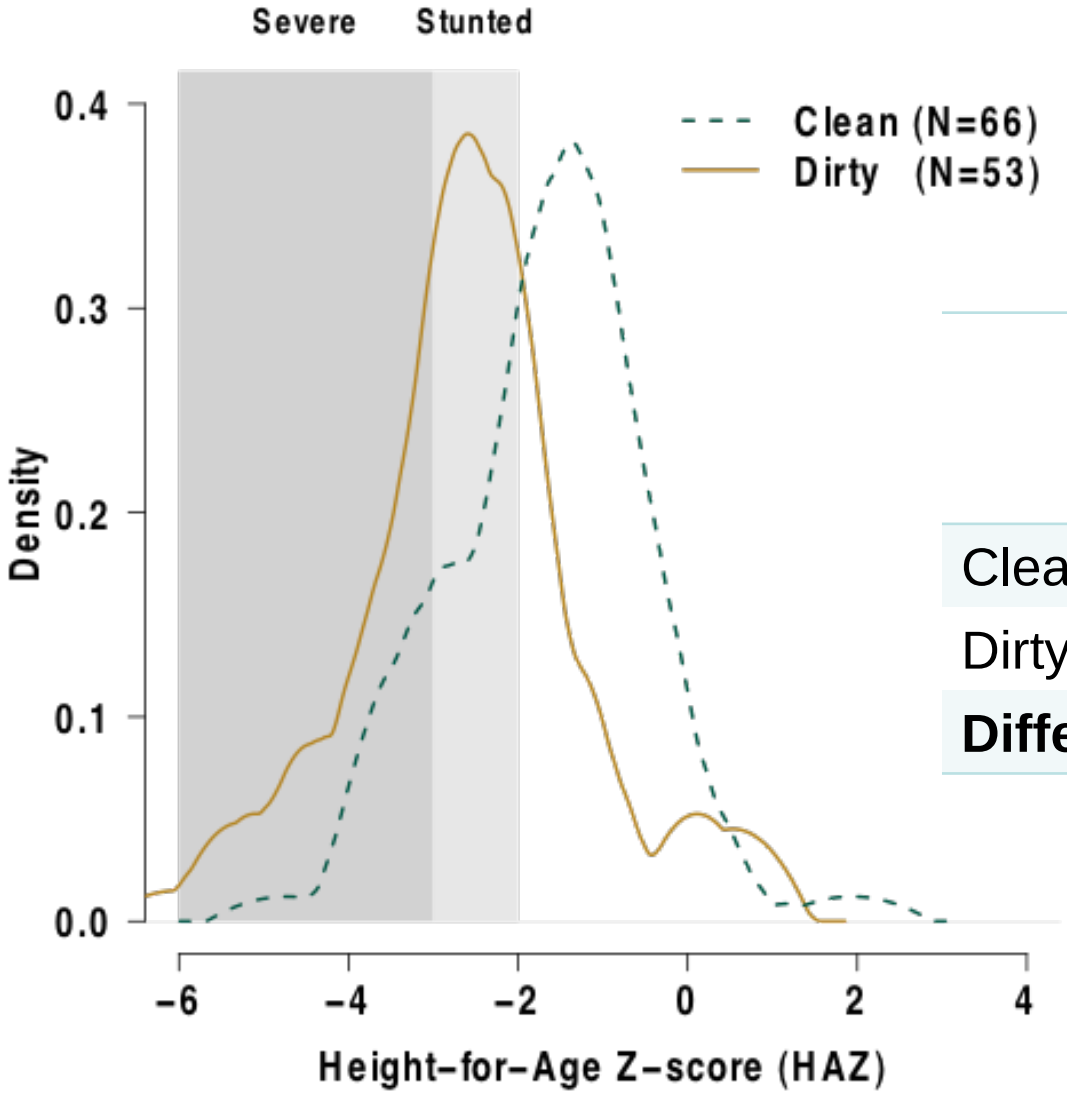
Clean

- Toilet that separated feces from the environment
- median [*E. coli*] < 10/100 ml
- handwashing station w/ water and soap

Household Characteristics

	Clean (n=67)	Dirty (n=55)	P-value
female	0.54	0.58	0.62
age in months at enrollment	10.5	12.5	0.39
have electricity	0.72	0.36	<0.01
Own	0.3	0.16	0.08
radio	0.3	0.16	0.08
b/w television	0.31	0.15	0.04
color television	0.24	0.05	0.01
refrigerator	0.07	0	0.02
home	0.94	0.87	0.25
people live in the household	5.91	6.31	0.47
rooms	2.94	1.8	<0.01
earth/bamboo floor	0.69	0.93	0.001

Children from cleaner households 0.9 SDs taller



	Mean HAZ (2010)	Stunting % (2010)
Clean	–1.66	33%
Dirty	–2.57	74%
Difference	**0.91**	**– 40%**

Outcome differences: clean versus dirty

Outcome	Unadjusted Difference		Adjusted* Difference
HAZ (Stunting)	0.91 (0.17, 1.65)	↓ 41%	0.54 (0.06, 1.01)
WAZ (Wasting)	0.42 (0.02, 0.83)	↓ 95%	0.04 (-0.48, 0.55)
WHZ (Underweight)	-0.12 (-0.54, 0.30)		-0.19 (-0.61, 0.24)
Ascaris, proportion infected	-0.14 (-0.30, 0.02)		-0.12 (-0.30, 0.06)
Trichuris, proportion infected	-0.05 (-0.18, 0.09)		0.02 (-0.13, 0.17)
Giardia, proportion infected	-0.02 (-0.20, 0.16)		0.01 (-0.21, 0.23)
Standardized Ln Total IgG	-0.50 (-0.86, -0.14)		-0.47 (-0.85, -0.08)
Standardized Ln EndoCAb	-0.29 (-0.64, 0.07)		-0.24 (-0.63, 0.16)
Standardized Ln L:M ratio	-0.42 (-0.77, -0.07)		-0.32 (-0.72, 0.08)

Lin A, Am J Trop Med Hyg. 2013 Jul;89(1):130-137

*adjusts using ordinary least squares for age, age squared, sex, household head occupation, land ownership, number of people in the household, number of rooms in the house, house floor materials, house wall materials, house electricity, and asset ownership (tables, watches, beds, radio, television, bicycle)

Conclusions : Descriptive Study

- Rural Bangladeshi children
- With somewhat
  - Cleaner water
  - Better toilets
  - Better equipped handwashing stations

?

- had
  - Less environmental enteropathy
  - Better growth

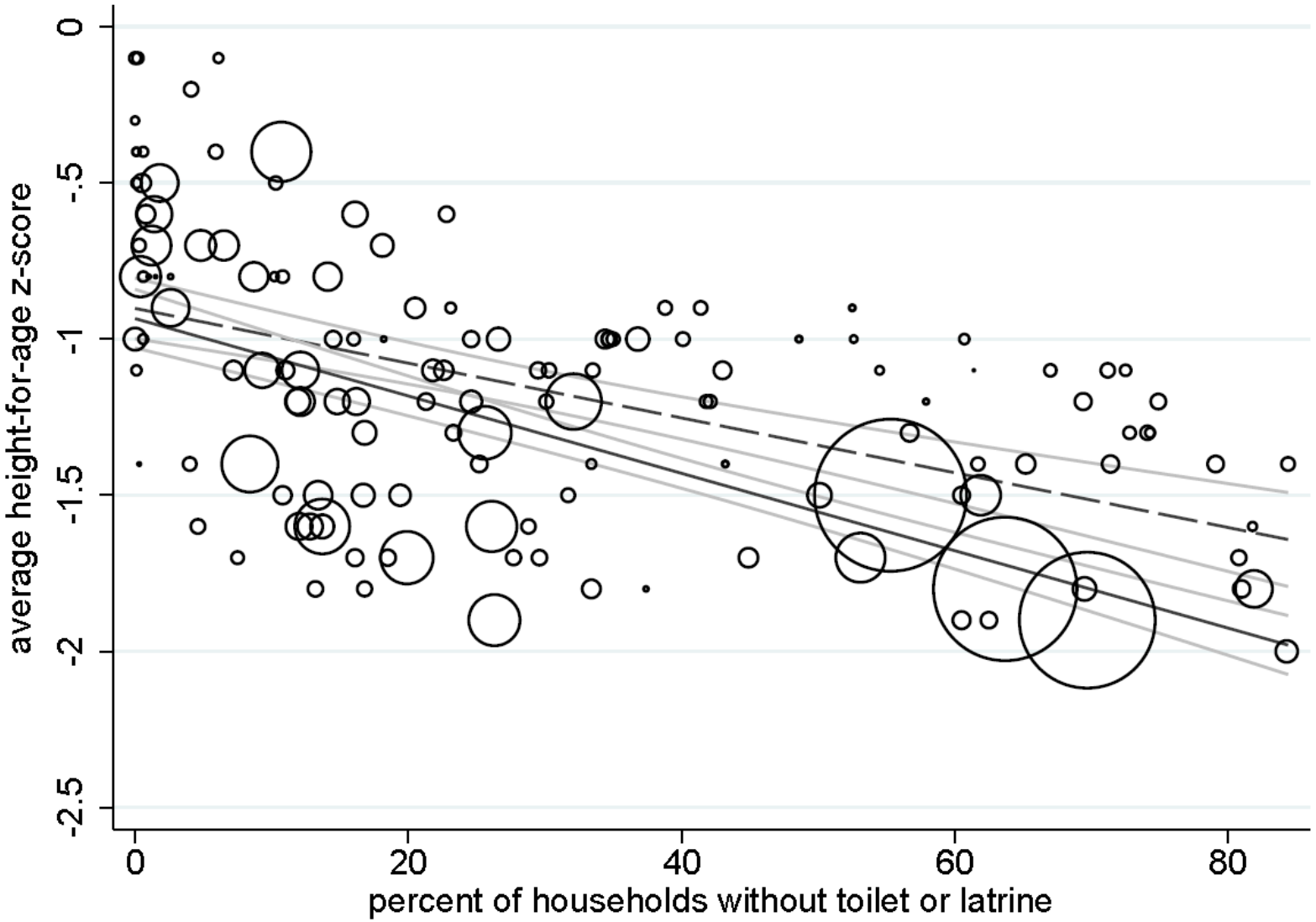
Lin A, *Am J Trop Med Hyg*. 2013 Jul;89(1):130-137

What is the evidence that fecal environmental contamination causes stunting?

- Stunting is more common where there is more environmental fecal contamination
- Animal husbandry
- Biological plausibility

Child height versus open defecation

150 national assessments



Spears D. How much international variation in child height in sanitation explain? Working paper www.riceinstitute.org

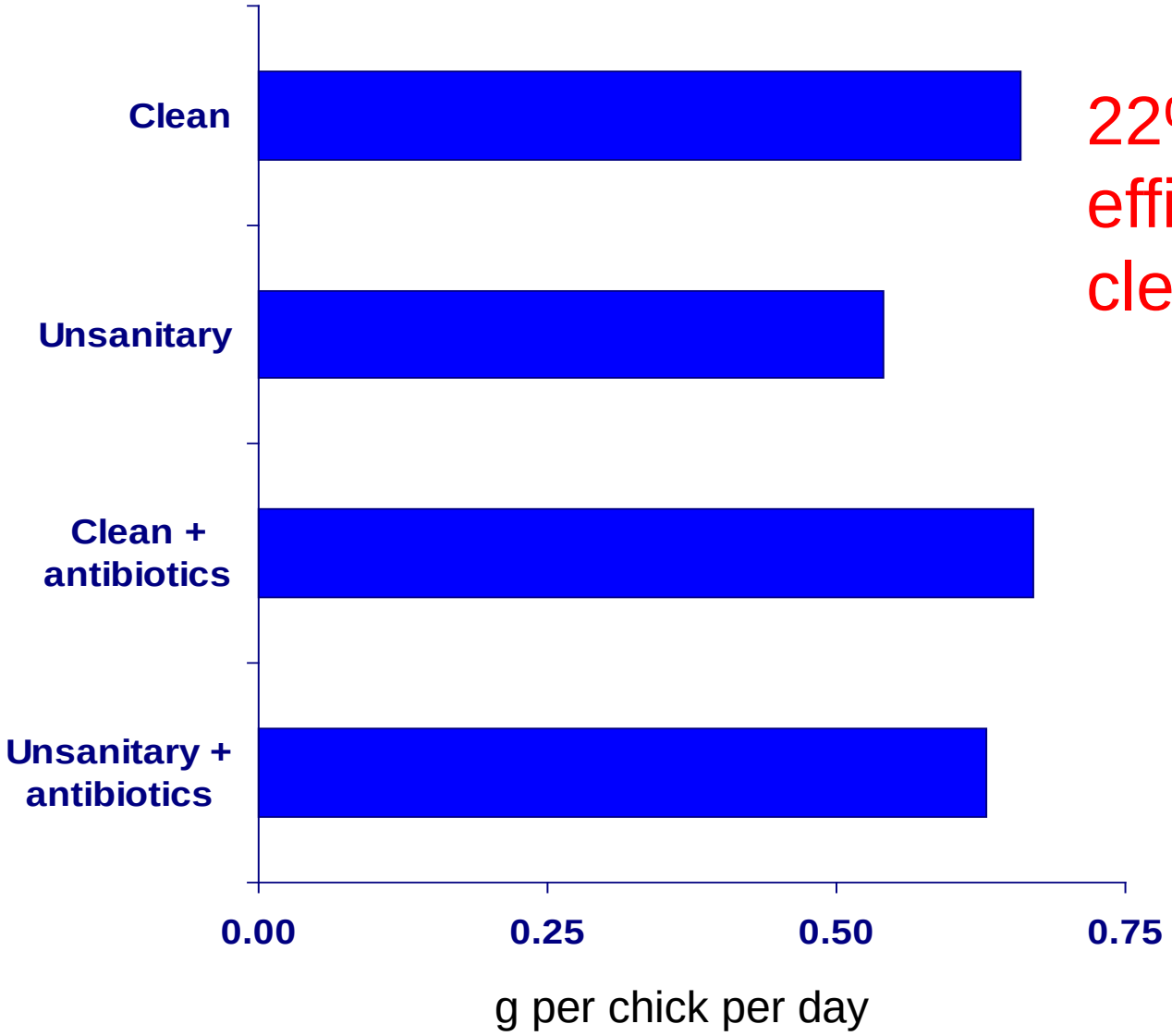
Animal husbandry experiment
2 by 2 factorial design

- Clean vs. unsanitary cages
  - Unsanitary
    - Raising multiple cycles of chicks in the same battery cages
    - Let feces, dust and dander accumulate
  - Clean
    - Steam cleaning the cages
    - Changing the bedding 3 times per week
- Antibiotics vs. No antibiotics
- 64 chicks per arm

www.farmsanctuary.org

Roura E. *J Nutr*. 1992 Dec;122(12):2383-90.

Feed efficiency of chicks



22% gain in feed efficiency with a clean environment

Roura E. *J Nutr*. 1992 Dec;122(12):2383-90.

Proposed pathophysiology of EE
a dysfunctional microbiome

- Malawian monozygotic twins
  - One with severe malnutrition (WHZ < 3)
  - One without
- Transplanted fecal sample to germ free mice
- Fed standard mouse chow for 21 days
  - Mice with feces from malnourished twin: lost 7% of body weight
  - Mice with feces from non-malnourished twin: gained 2% of body weight

J. B. RUSSELL/PANOS

Smith M, *Science*. 2013 Feb 1;339(6119):548-54.

WASH Benefits Hypothesis

- Improvements in:
  - Drinking water quality
  - Sanitation
  - Hygiene
  - Nutrition

  - Less diarrhea
  - Fewer parasites
  - Less environmental enteropathy
  - Improved child growth
  - Improved child development

Design Overview

- Two highly comparable (but standalone) cluster-randomized trials
  - Bangladesh
  - Kenya
- Enroll children before birth, and follow them for two years
- A large number of village clusters and children, with infrequent outcome measurement

WASH Benefits interventions

	Children	
	Bangladesh	Kenya
Water quality	630	1000
Sanitation	630	1000
Hand washing	630	1000
Water + Sanitation + Handwashing	630	1000
Nutrition	630	1000
Water + Sanitation + Handwashing + Nutrition	630	1000
Control	1260	3000
Total	5040	9000

Primary outcomes

1. Height-for-age measured after 2 years of intervention (children will be between 20 and 27 months old)
2. Diarrhea in children < 36 months at enrollment

Other outcomes after 2 years

1. Child development scores for verbal ability, motor ability, and social skills
2. Parasitic infections
   - Protozoa by multiplex rt-PCR
     - *Giardia, Cryptosporidium, Entamoeba histolytica*
   - Soil transmitted helminths by Kato Katz
     - *Ascaris, Trichuris*, hookworm
3. Environmental enteropathy markers

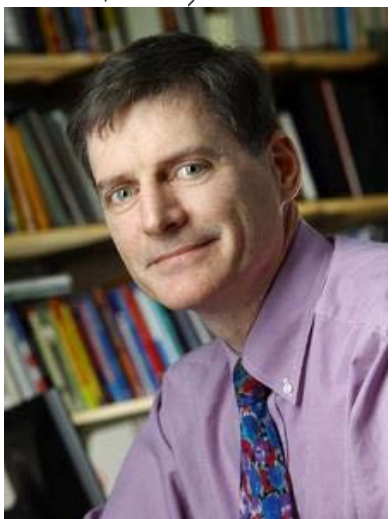
Dreibelbis et al. BMC Public Health 2013, 13:1015
http://www.biomedcentral.com/1471-2458/13/1015

BMC Public Health

RESEARCH ARTICLE Open Access

The Integrated Behavioural Model for Water, Sanitation, and Hygiene: a systematic review of behavioural models and a framework for designing and evaluating behaviour change interventions in infrastructure-restricted settings

Robert Dreibelbis[1*], Peter J Winch[1], Elli Leontsini[1], Kristyna RS Hulland[1], Pavani K Ram[2], Leanne Unicomb[3] and Stephen P Luby[3,4]



IBM-WASH

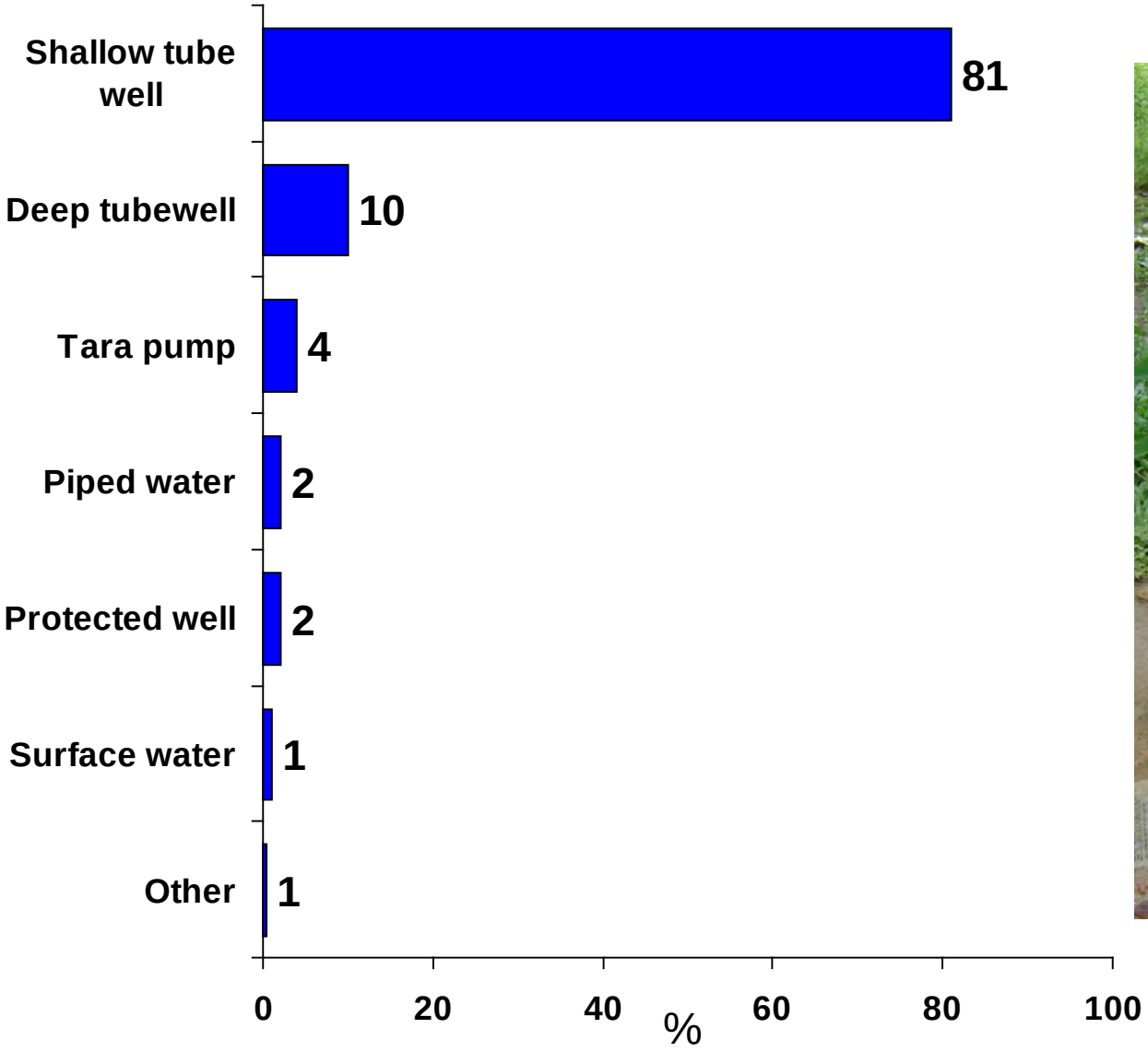
Integrated Behavior Model for Water Sanitation and Hygiene

Levels	Contextual/ environmental	Psychosocial "Software"	Technology "Hardware"
Societal / Structural	Policy and regulations, climate and geography	Leadership / advocacy, cultural identity	Manufacturing, financing and distribution of the product, current and past national policies and promotion of products
Communal	Access to markets, access to resources, built and physical environment	Shared values, collective efficacy, social integration, stigma, local leadership	Location, access, availability, individual vs. collective ownership/access and maintenance of the product
Relational / Interpersonal	Roles and responsibilities, household structure, division of labor	Injunctive norms, descriptive norms, aspirations, shame	Sharing of access to product, modeling/ demonstration of use of product
Individual	Wealth, age, education, gender, livelihoods/ employment	Self efficacy, knowledge, disgust, perceived threat	Perceived cost , value, convenience and other strengths and weaknesses of the product
Behavioral/ habitual	Favorable environment for habit formation, opportunity for repetition of behavior	Existing water and sanitation habits, outcome expectations	Ease / Effectiveness of use of product

Dreibelbis R, *BMC Public Health*. 2013;13(1):1015.

Primary Drinking Water Source

N=993 (SHEWA-B)



Water Quality - Bangladesh

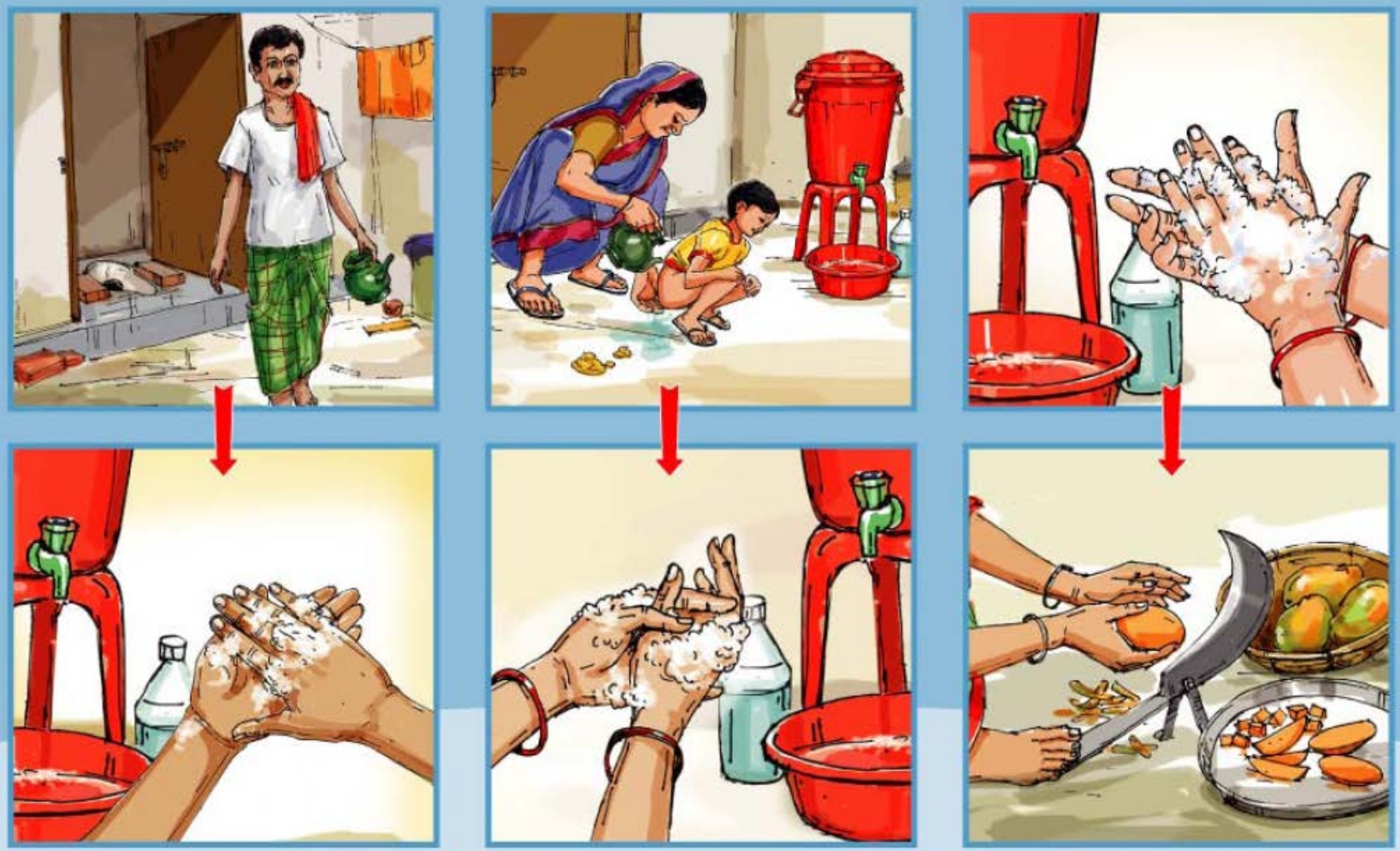
Aquatabs (NaDCC)

+

Safe Storage

(www.aquatabs.com)

icddr,b



icddr,b

WASH Benefits Trial Latrine

dual pit latrine

- Two pits
  - (5 feet depth)
  - Each pit contains 5 concrete rings
- Durable superstructure
- Water seal

Water seal

Slide from : Faruqe Hussain

Best potty model: rabbit headed

- Durable
- Animal shaped/toy for children
- Child can hold the ear as grip
- Mother can add water to removable pot before child defecates
- Can remove the pot when child uses the potty to sit on or play with
- Removable pot make it easy to dispose of feces

Slide: Md Faruqe Hussain

Sani-scoop

Men's agricultural hoe

- Purpose
- Lifted edges
- Angle
- Weight
- Front edge
- Handle
- Thickness

Women's sani-scoop

My daughter says, "My father has one scoop (agricultural hoe) and now I have my own (sani) scoop".

Sultana R, *Trop Med Int Health*. 2013 Jul;18(7):854-60.

Sanitation - Bangladesh

Dual Pit Latrines + Child Potties + Sani-scoop

Nutrition : Bangladesh

Nutritional Promotion

- Exclusive breastfeeding through 6 months
- Continued breastfeeding with LNS (6 – 24 months)
- Encourage preparation of micronutrient-dense food
- Feed child at least 2-3 times per day (6-8 mos) and 3-4 times per day (9-24 mos)

+

Daily LNS (6 – 24 mos)

- Next-generation Nutributter (iLiNS project)
  - 118 Kcal
  - 9.6 gm fat
  - 2.6 gm protein
  - ≥100% RDA of 12 vitamins
  - 9 minerals
- 10-gm sachet twice daily

Community Health Workers: Interactive dialogues and activities

Slide: Farzana Begum

Early stage

- Negotiate hardware
- Help adopt new technology
- Identify problems
- Immediate solution
- Early habit formation

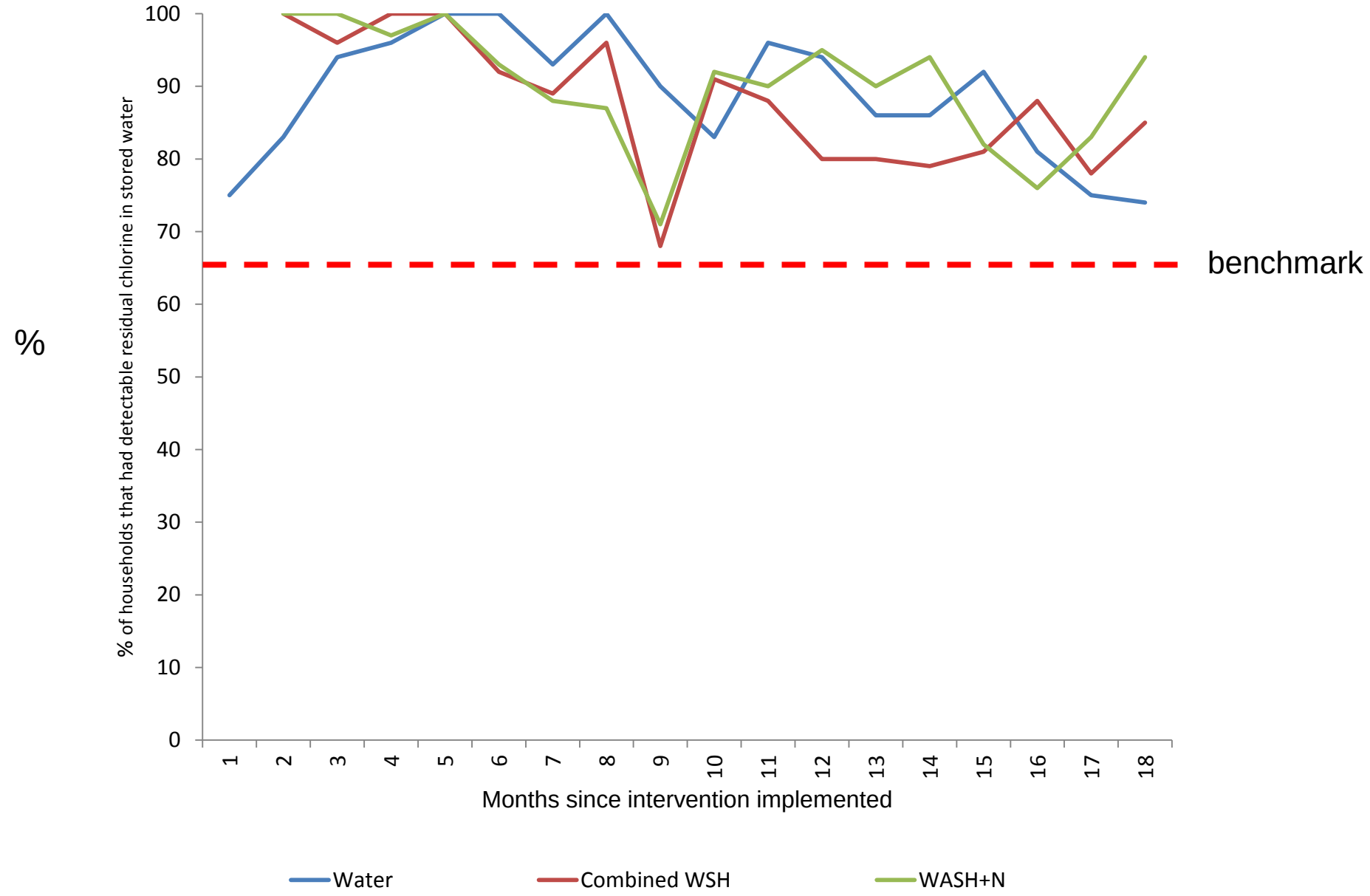
- Focus-Parents of index child, caregivers
- Households visit

Later

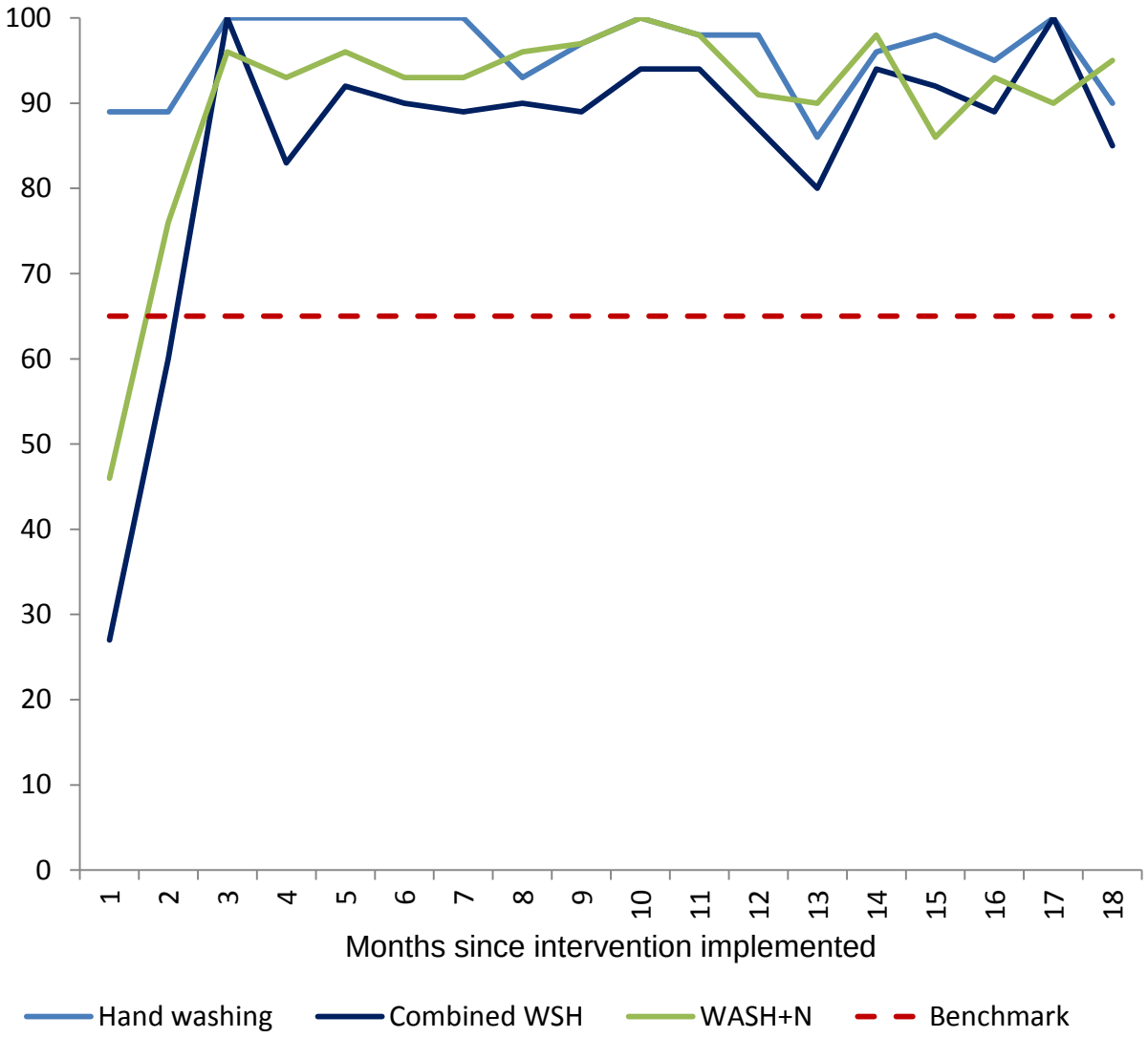
- Follow up Behavior change
- Motivate continuation of improved behavior

- Inclusion of wider Group-
- Male, children and adolescent, elderly
- Varied activities

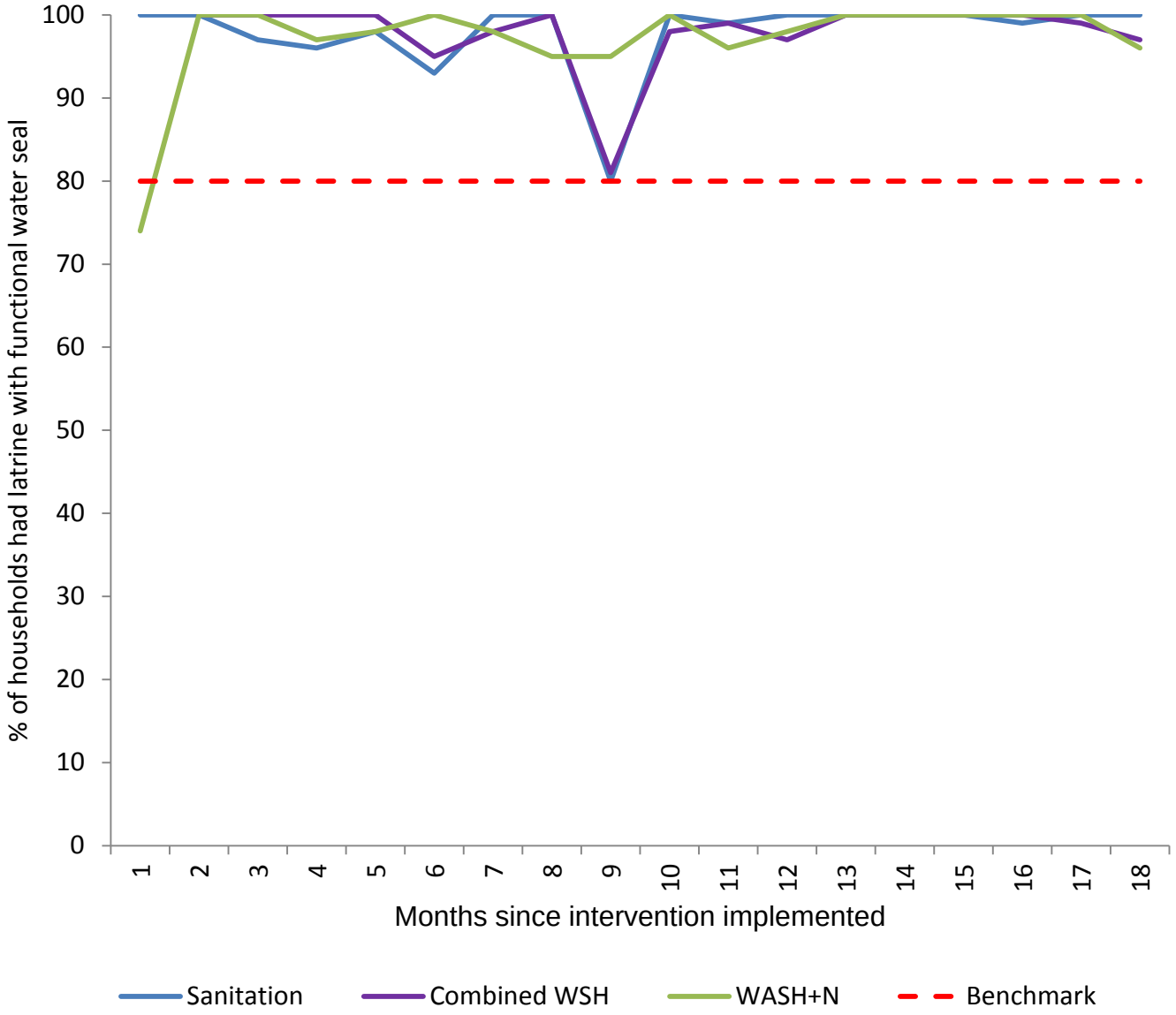
Stored chlorinated drinking water



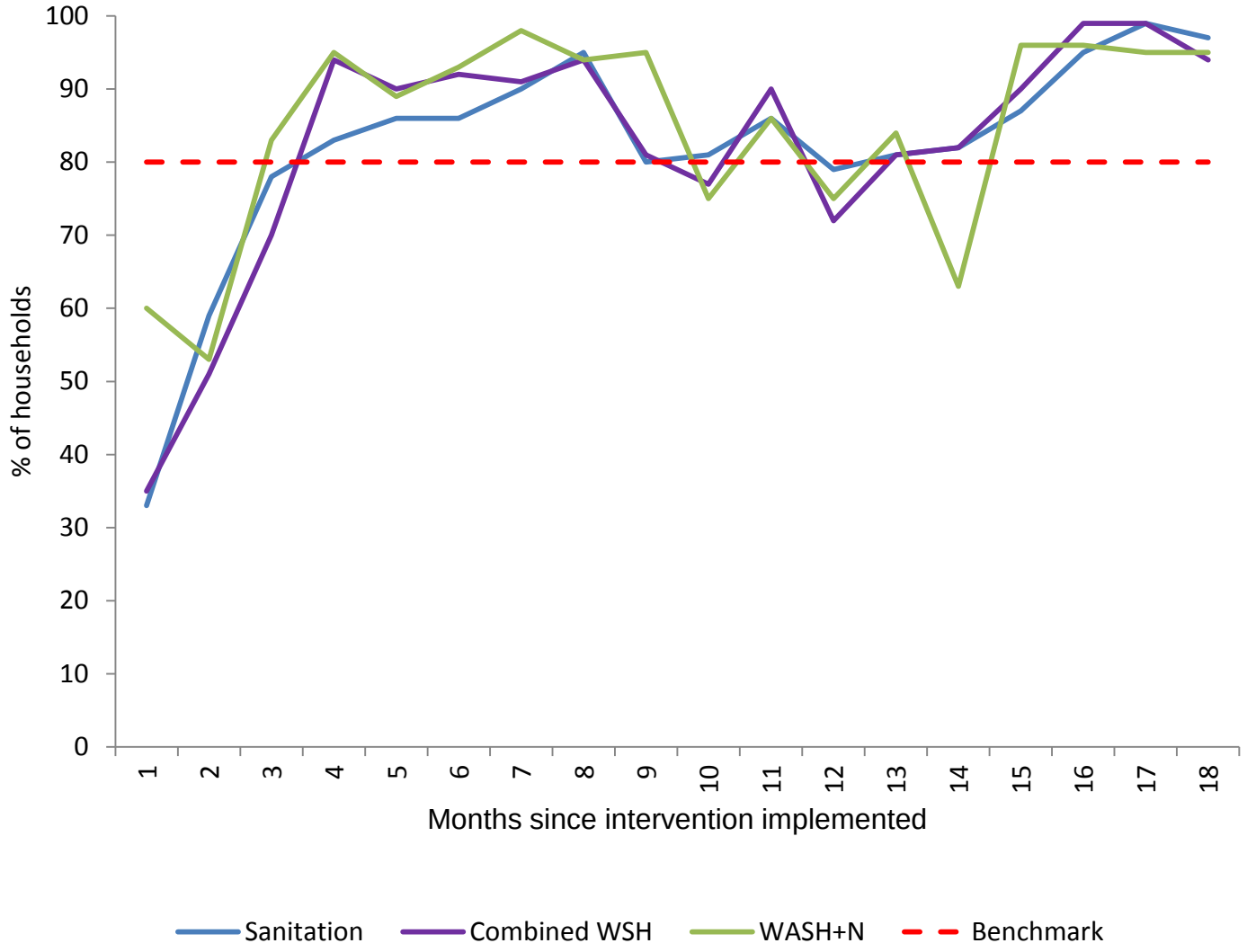
≥1 handwashing station with soap and water present



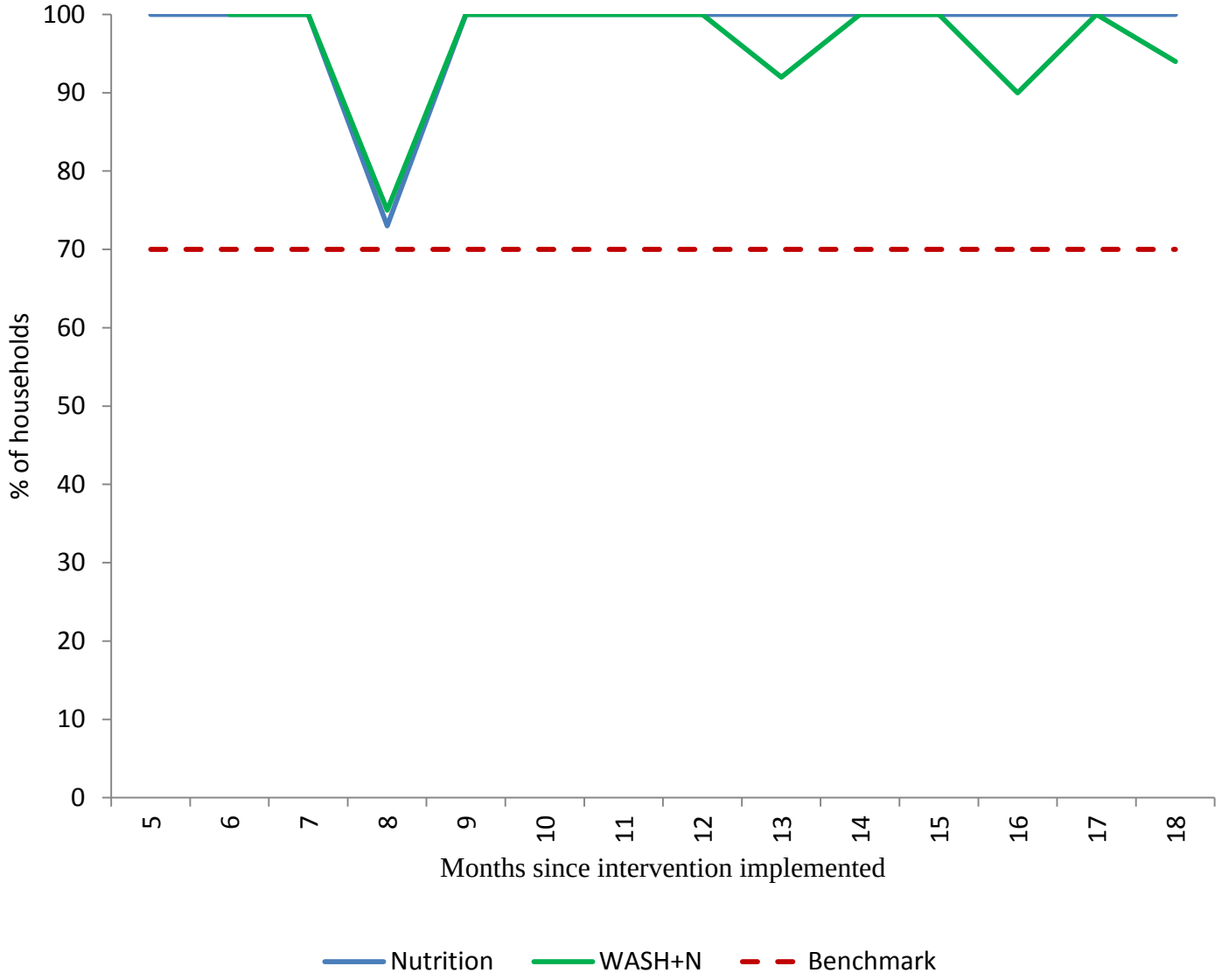
Presence of icddr,b provided latrine with functional water seal



Presence of hygienic latrine among compound residents

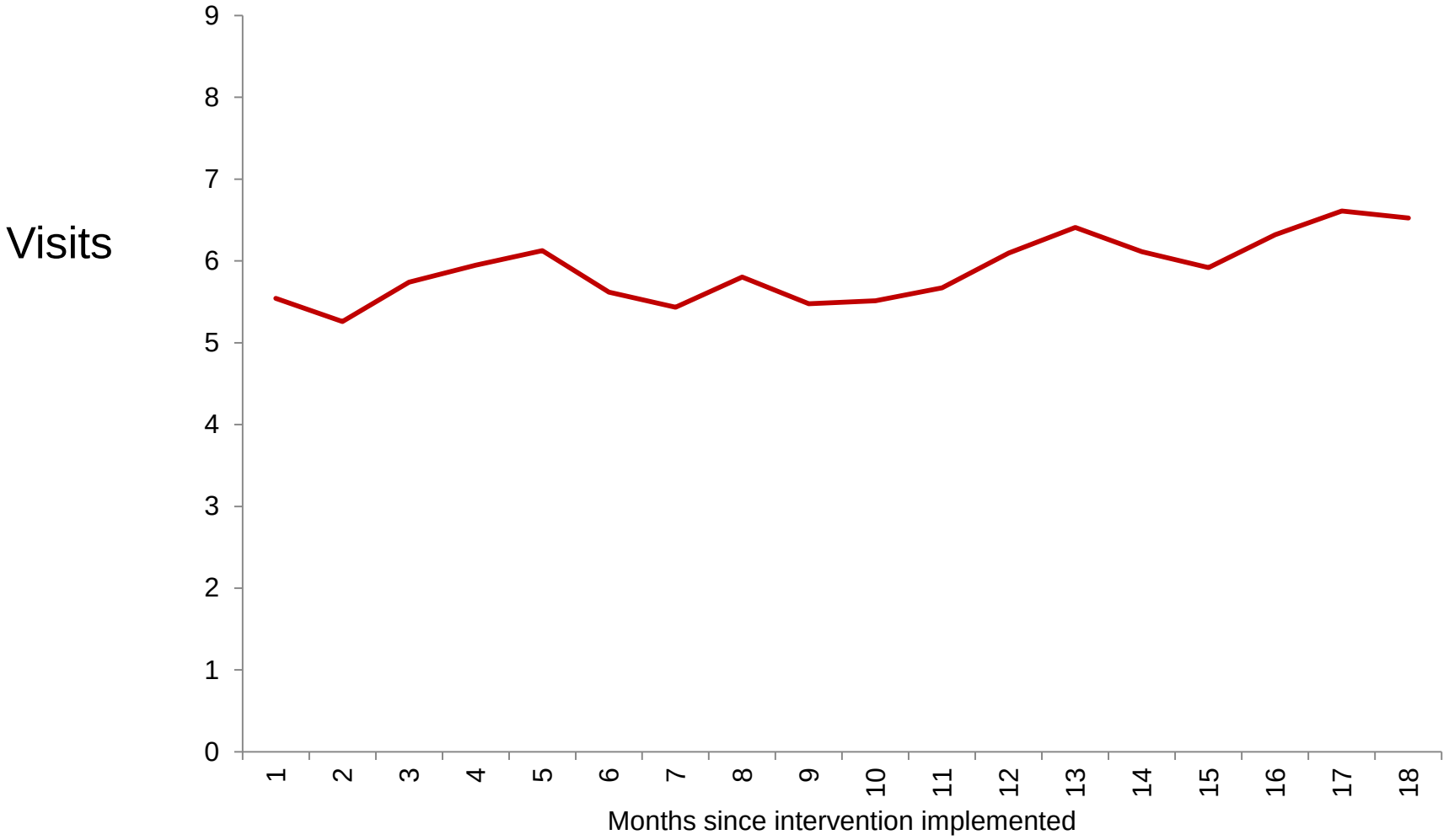


LNS sachet stock consistent with 2 sachet per day consumption



Average promoter visits per month

through April 2014

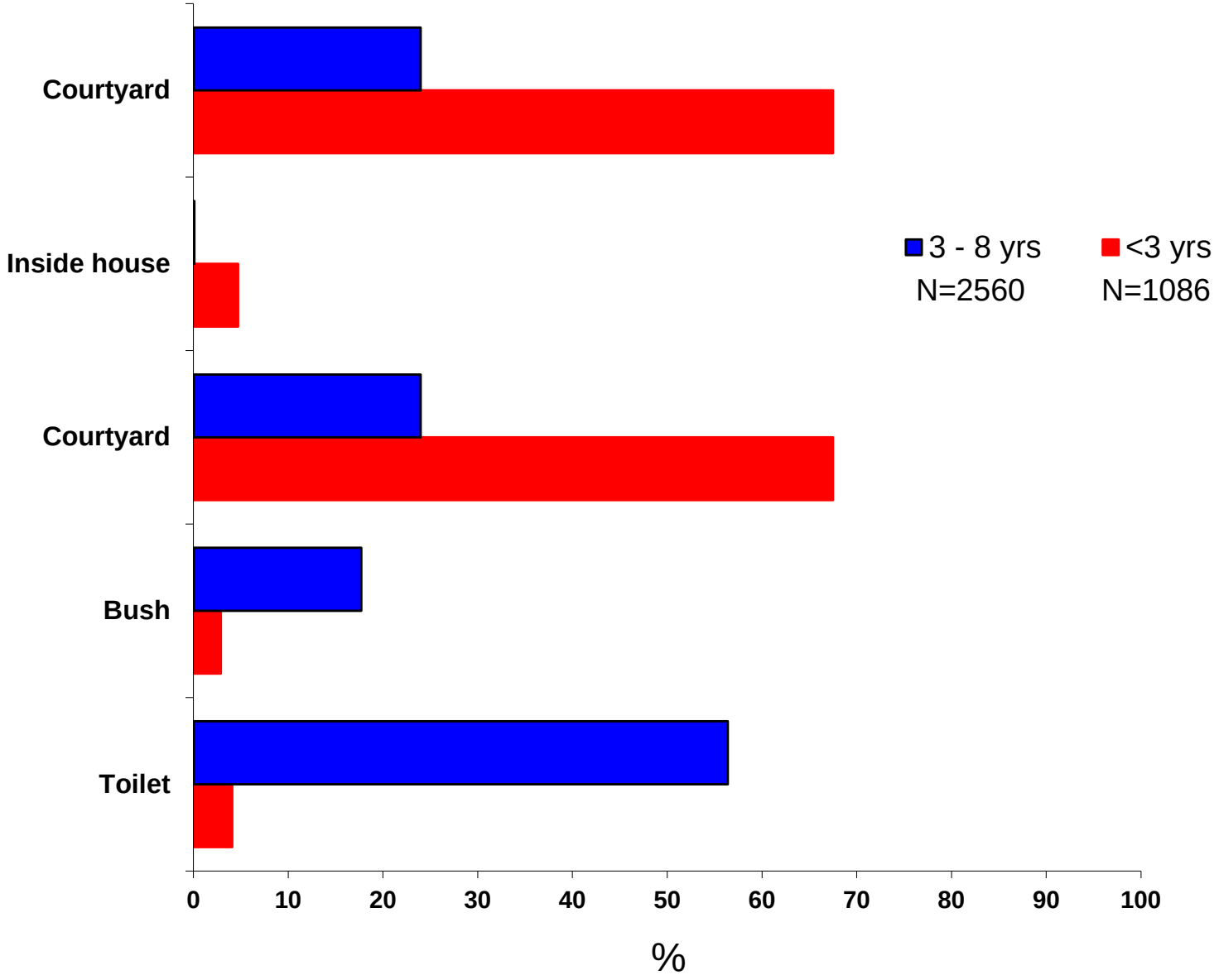


WASH Benefits

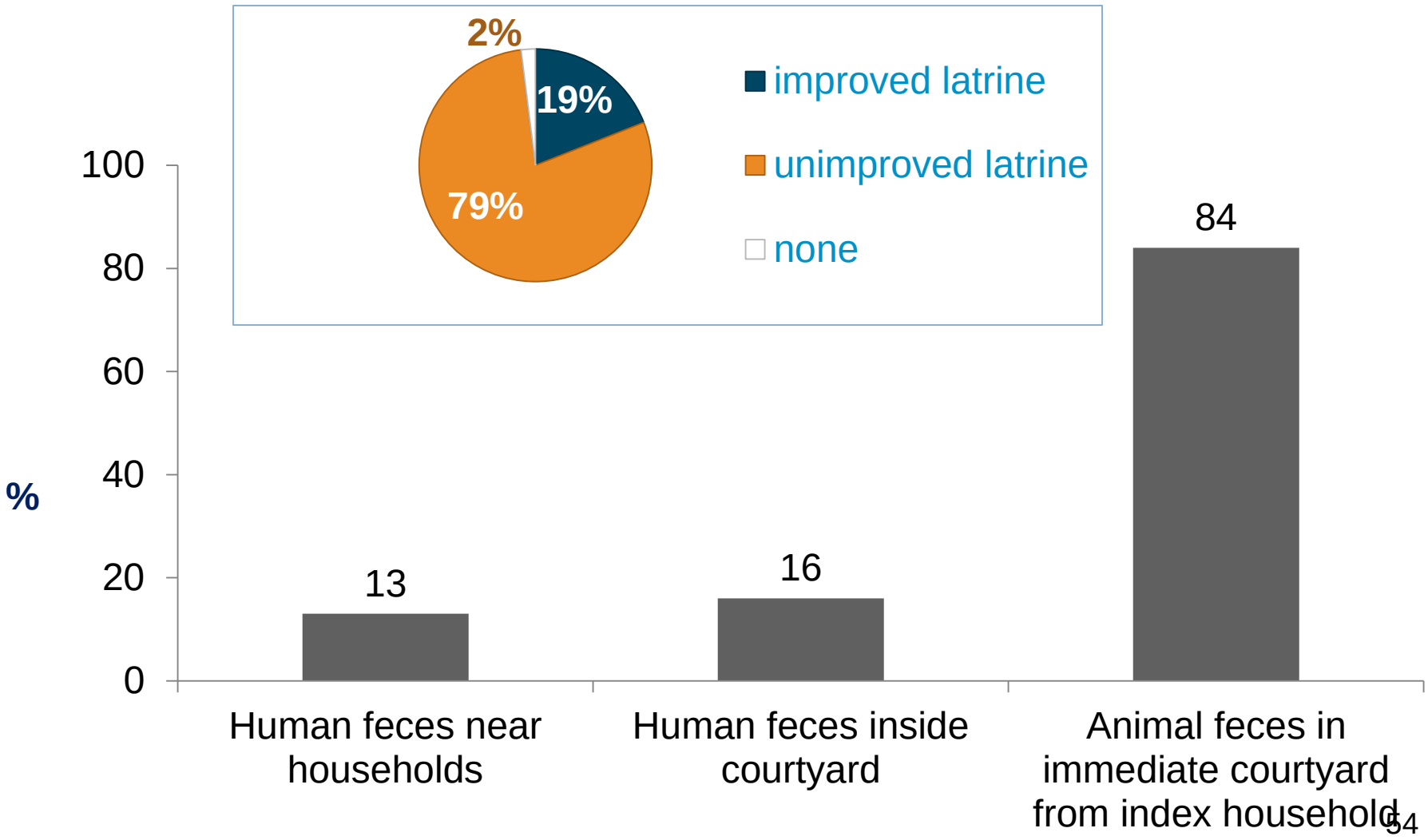
- Large ambitious trial
- High uptake of interventions
- Results available
  - Bangladesh : Mid 2016
  - Kenya : Mid 2017

Reported location of last defecation

WASH Benefits Baseline, Rural Bangladesh



Baseline observations of open feces in study compounds Kishoreganj, 2010



One year old Zimbabwe child on a typical day

	quantity	*E. coli**
chicken feces	1 gm	13,800,000
laundry area soil	20 gm	2,340
contaminated water	400 mL	800

*mid points of 95% confidence intervals

Ngure et. al. *Am J Trop Med Hyg*. 2013 Oct;89(4):709-16.

Food hygiene may be a particularly important area for attention

- Weaning is a critical nutritional transition
- Exponential bacterial growth
- May contribute importantly to intestinal microbiome
- Fermented foods?

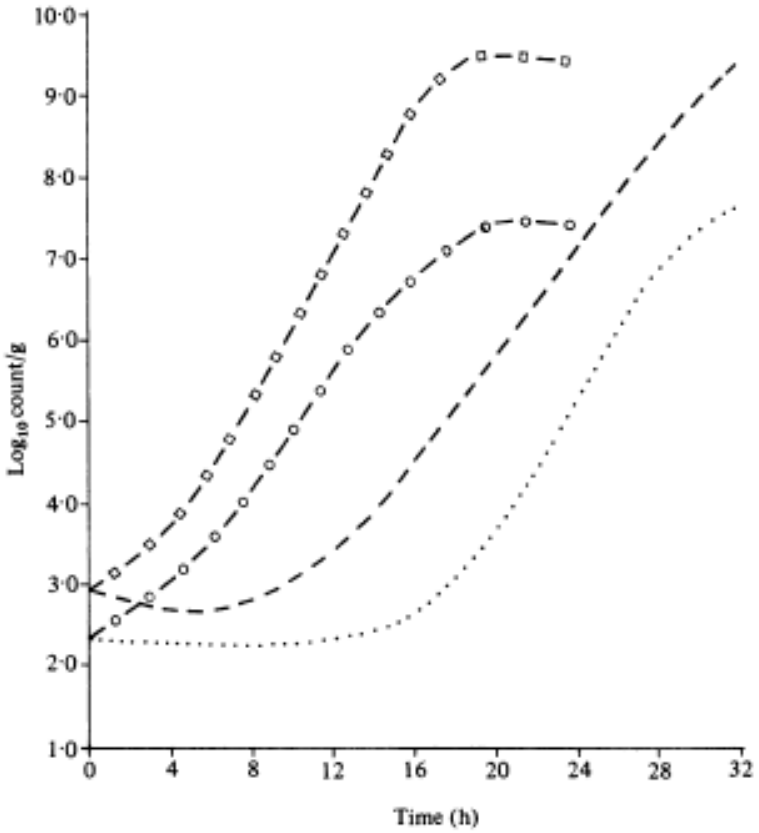


Fig. 2. Growth of *V. cholerae* in cooked rice. F4290 (classical) at 22 °C (·····) and 30 °C (○——○); F4292 (eltor) at 22 °C (– – – –) and 30 °C (□——□).

Colvin JL, Roberts D, J Hyg (Lond). 1982 Oct;89(2):243-52.

Conclusion

- Increasing evidence of linkages between contaminated environment of children and growth faltering
  - A dynamic area of active research
  - Programmatic implications are less worked out.

Acknowledgments

ICDDR,B
Leanne Unicomb
Sania Ashraf
Faruqe Hussain
Fosiul Nizame
Shaila Arman
Farzana Begum
Abu Naser
Mahbubur Rahman
Sarker Masud Parvez
Solaiman Doza
Rashidul Haque
Tahmeed Ahmed
Rubhana Raqib
Mahfuza Sheuli

UC Berkeley
Jack Colford
Ben Arnold
Audrie Lin
Christine Stewart
Ayse Ercumen
Jade Benjamin-Chung
Lia Fernald
Patricia Kariger

Johns Hopkins
Peter Winch
Elli Leontsini

Stanford
Amy Pickering
Jessica Grembi

US Davis
Christine Stewart
Kay Dewey