

Legumes and growth

- Complementary feeding clinical trials were conducted in Machinga and Chikwawa Districts in Malawi with common bean and cowpea.
- These legumes were chosen for their availability, nutrient and fiber content; nutrients to provide protein and indigestible carbohydrate to alter the microbiota.
- Goal was to improve gut health and reduce stunting.

Cowpeas and Common Beans used in the clinical trial

Nutrient	Control				Common bean				Cowpea			
	6	9	12	24	6	9	12	24	6	9	12	24
Age (months)	6	9	12	24	6	9	12	24	6	9	12	24
Macronutrients												
Calories (kcal/day)	78	117	156	196	79	118	158	197	79	118	157	196
Protein (g/day)	3	4	5	7	5	7	10	12	5	8	11	14
Dietary Fiber												
Total fiber (g/day)	1.7	2.5	3.4	4.2	6.0	9.0	12.0	15.0	4.3	6.5	8.6	10.8
Micronutrients												
Calcium (mg/day)	45	67	89	112	43	64	85	107	22	33	44	55
Zinc (mg/day)	0.8	1.2	1.5	1.9	0.6	0.9	1.1	1.4	0.7	1.0	1.3	1.6

Unique metabolites which can potentially used to quantitate intake

Metabolic pathways	Traditional Diet	Common Bean	Cowpea
Amino acid	putrescine argininosuccinate	3-methoxytyramine serotonin tryptophan betaine dimethylglycine	Ophthalmate, S-methylglutathione 2-methylbutyrylcarnitine (C5) 3-hydroxy-2-ethylpropionate 3-hydroxyisobutyrate, 3-methyl-2-oxovalerate, hypotaurine, N-acetyltaurine
Carbohydrate	N-acetylglucosamine/N-acetylgalactosamine *arabinose,	-	N-acetyl-glucosamine 1-phosphate
Cofactors & Vitamins	dehydroascorbate alpha-tocopherol acetate alpha-tocotrienol gamma-tocotrienol	-	flavin mononucleotide (FMN)
Energy	succinylcarnitine	-	-
Lipid	caproate (6:0) glycerophosphoserine valerate	diacylglycerol (12:0/18:1, 14:0/16:1, 16:0/14:1) [2] propionylcarnitine (C3) 1-pentadecanoylglycerol (15:0)	palmitoyl-oleoyl-glycerol, Adipate, nervonate 1-myristoylglycerol 1-palmitoyl-2-arachidonoyl-GPE Docosadienoate, N-palmitoyl-sphingosine stearoyl sphingomyelin
Peptide	-	leucylalanine phenylalanylalanine	Alanylleucine, glycy lleucine Lysylleucine, valylglutamine Valylleucine, gamma-glutamyl-alpha-lysine gamma-glutamylglycine
Xenobiotics	1,1-kestotetraose 2-oxindole-3-acetate chlorogenate coumaroylquininate 2, 3, 4, & 5, feruloylputrescine	*oleanolic acid ⁽³⁹⁾	Benzoate, Taxifolin-ericiotrin Eriodictyol, galacturonate, quercetin 3-galactoside quercetin 3-glucoside, quercetin secoisolariciresinol

Study design

- **Design**
 - Randomized, single blind, controlled clinical trial in 2 rural communities in southern Malawi.
- **Interventions**
 - Milled, roasted, whole common bean or cowpea vs. control (corn-soy blend)
 - Beans provide 40% and 20% of non breast milk energy for <1 year and >1 year olds respectively.

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STUDY PROTOCOL

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Common beans and cowpeas as complementary foods to reduce environmental enteric dysfunction and stunting in Malawian children: study protocol for two randomized controlled trials

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Study outcomes

- **Primary Outcomes**

- Change in length-for-age Z-scores (LAZ)
- Change in lactulose excretion, a biomarker of EED

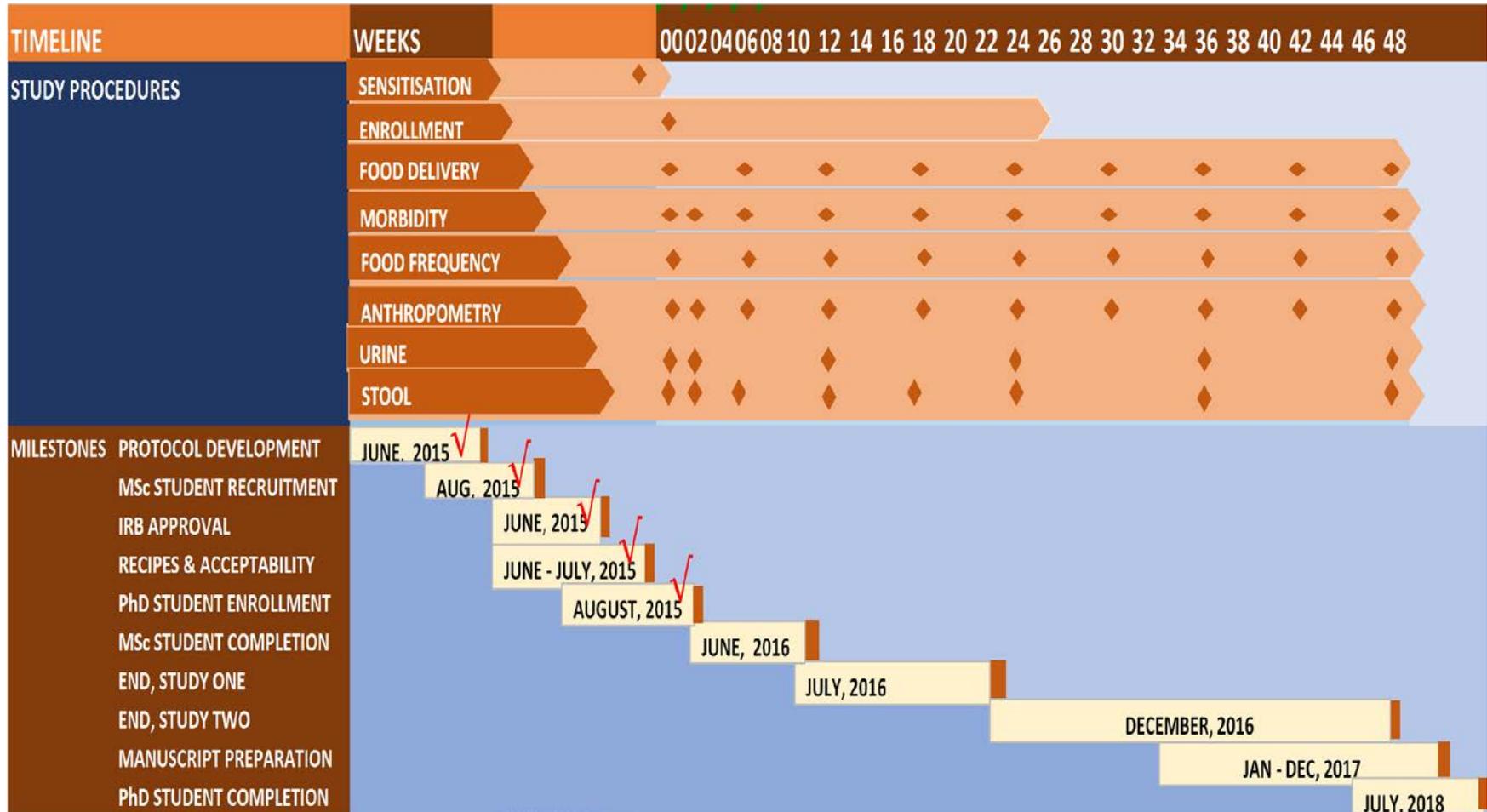
- **Secondary Outcomes**

- Change in novel biomarkers of EED
- Changes in intestinal microbiota and metabolites
 - Sequencing of bacterial genomic DNA from fecal samples to determine changes in population taxonomy and their collective metabolic capacity, and the metabolites present in stool in the study children.

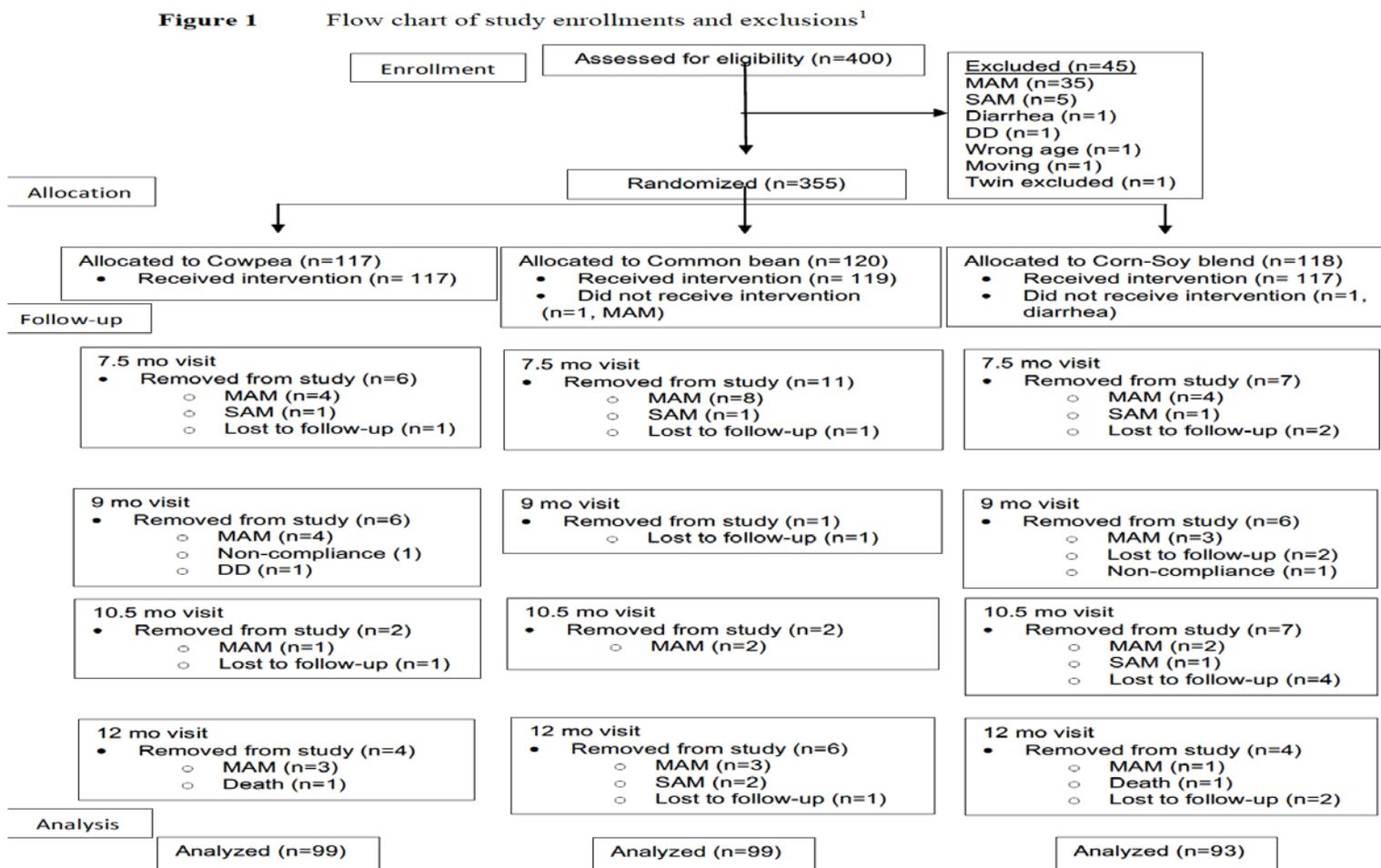
Two studies - younger and older kids

- Younger kids enrolled as they became 5.5-6.5 mo of age and given a legume supplement for the following 6 months.
- Older kids, aged 12-24 mo, enrolled and given legume supplement for next 12 months.

Project profile

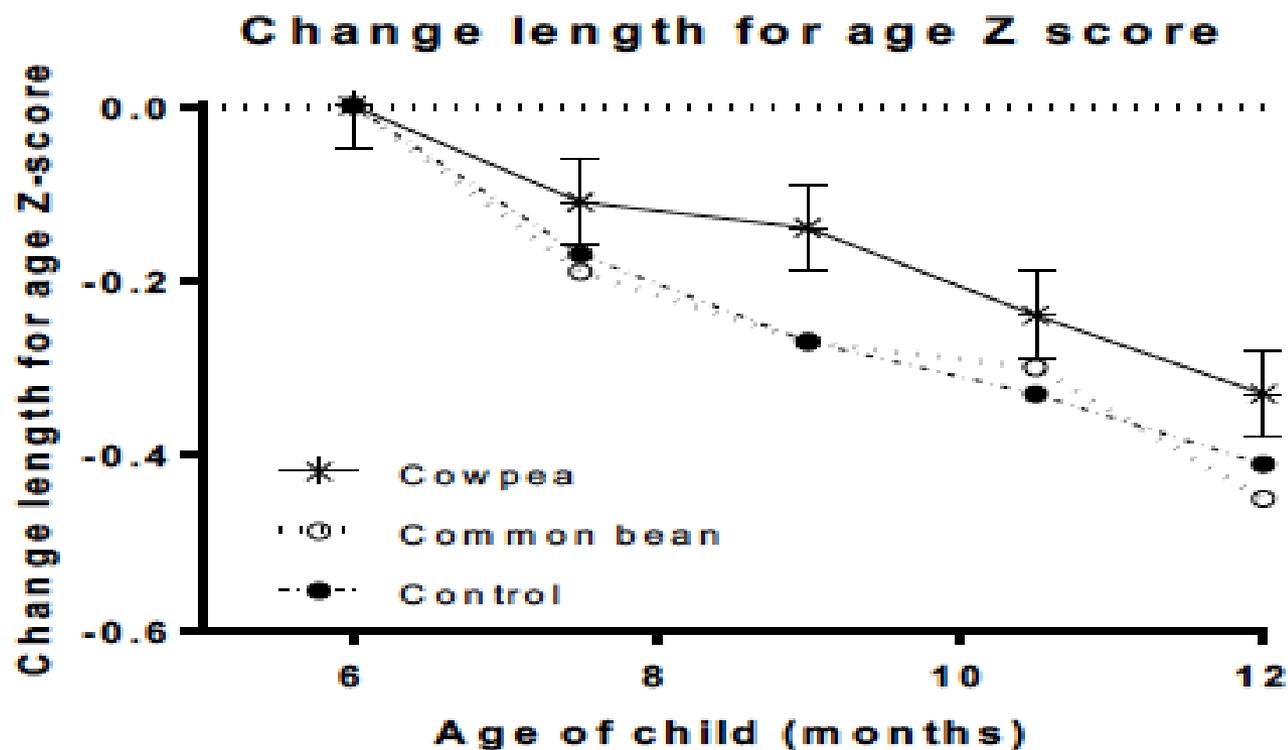


Intervention in 6-12 mo children

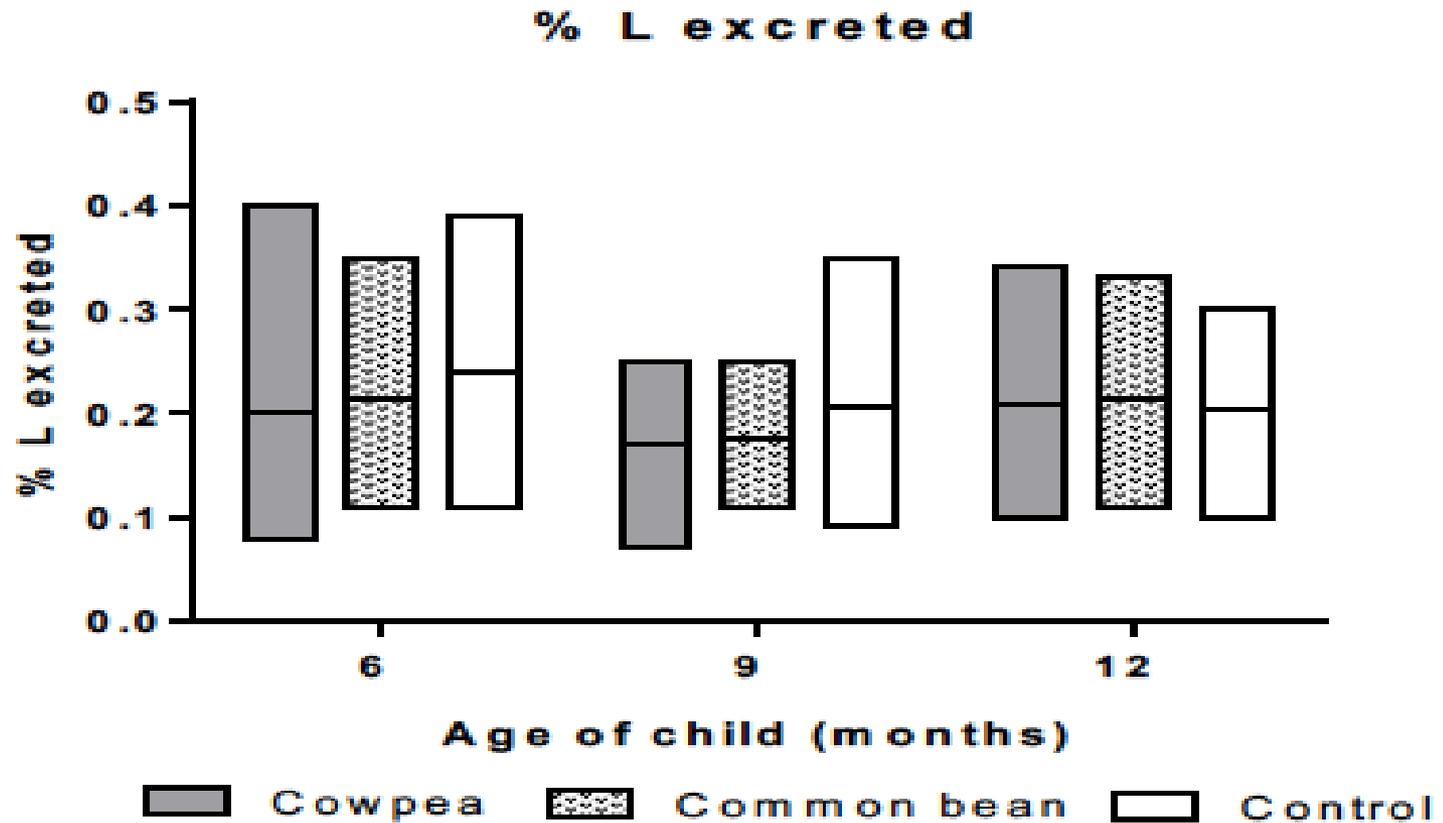


DD- Developmental delay; MAM – moderate acute malnutrition; SAM – severe acute malnutrition

Linear growth in 6-12 mo

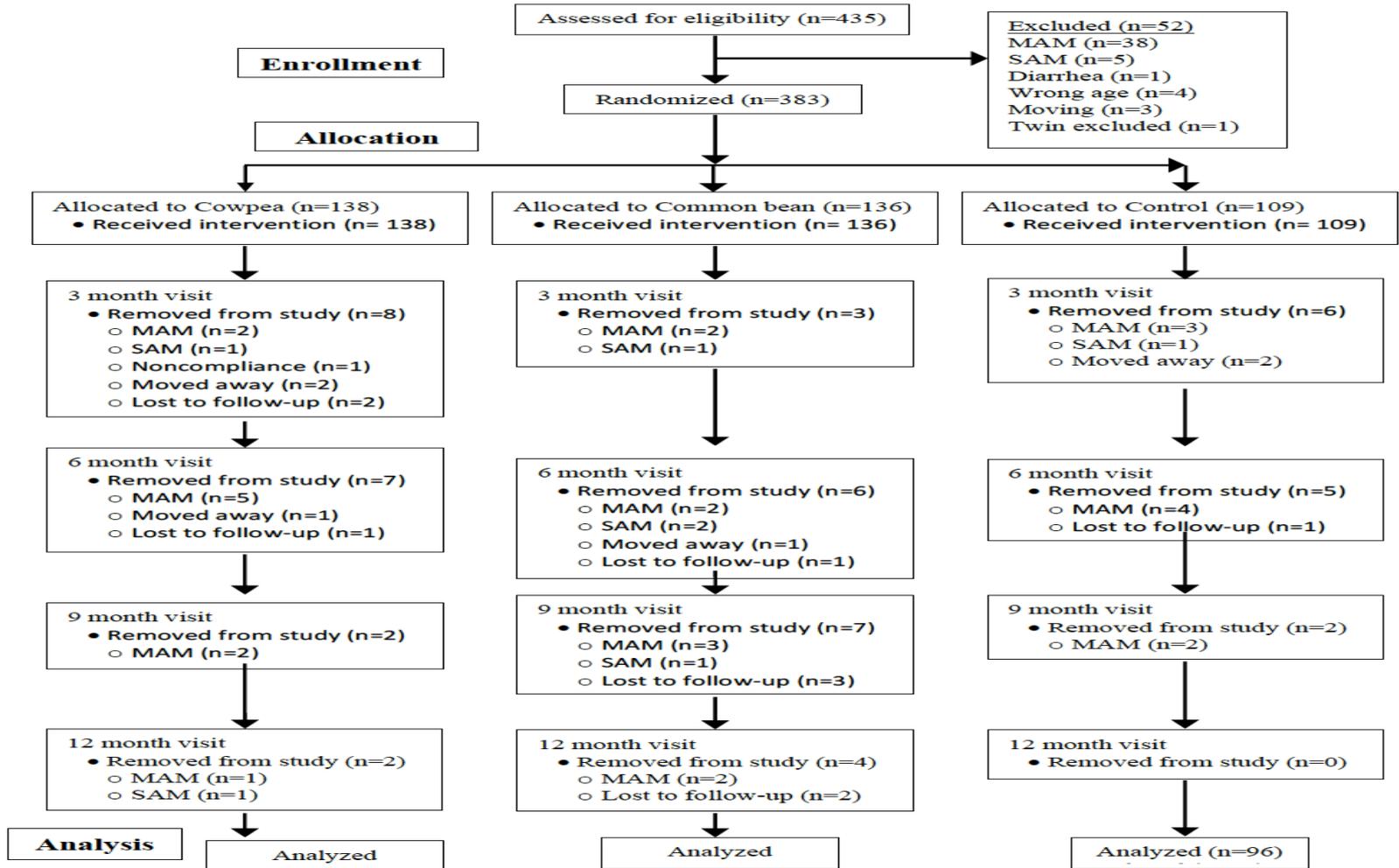


Gut permeability in 6-12 mo old



Intervention in 12-36 mo olds

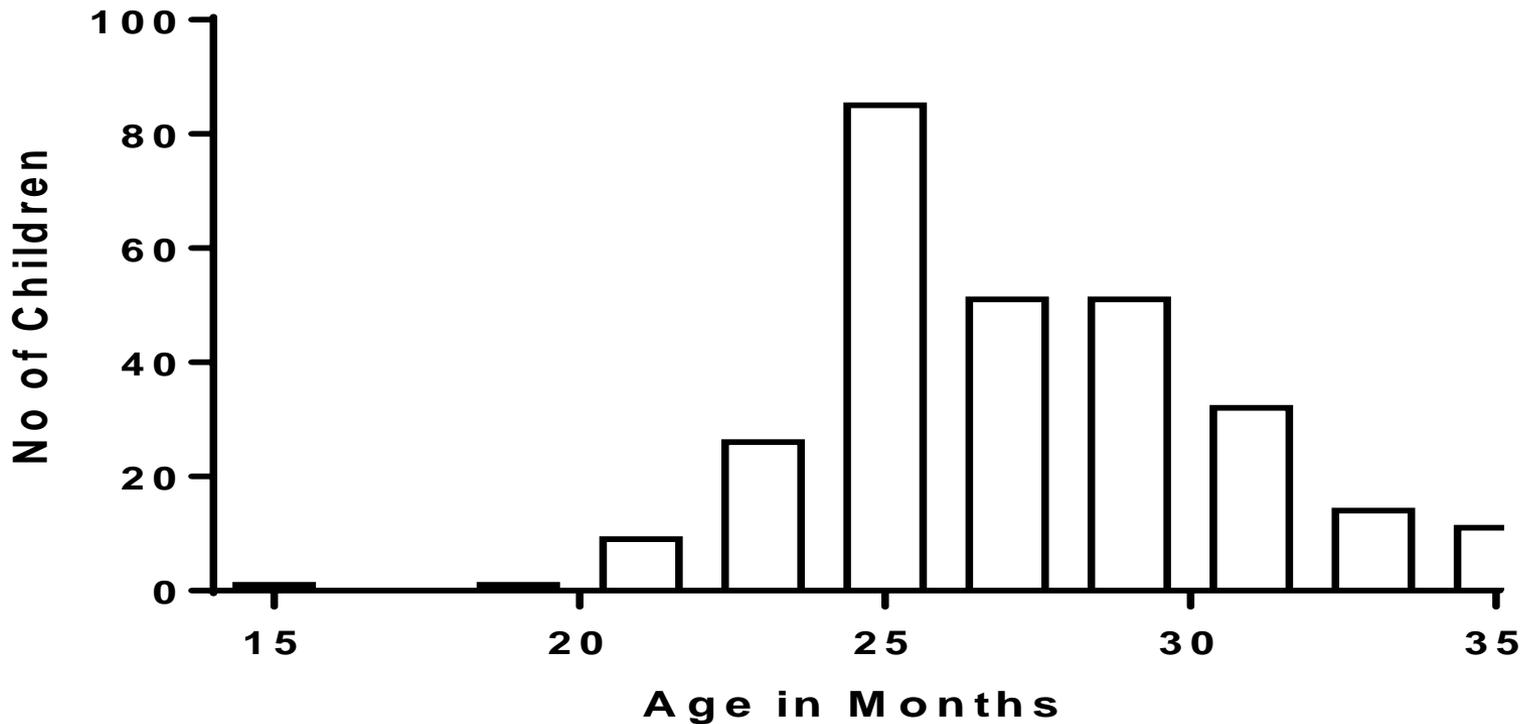
Figure 1 Flow chart of study enrollments and exclusions¹



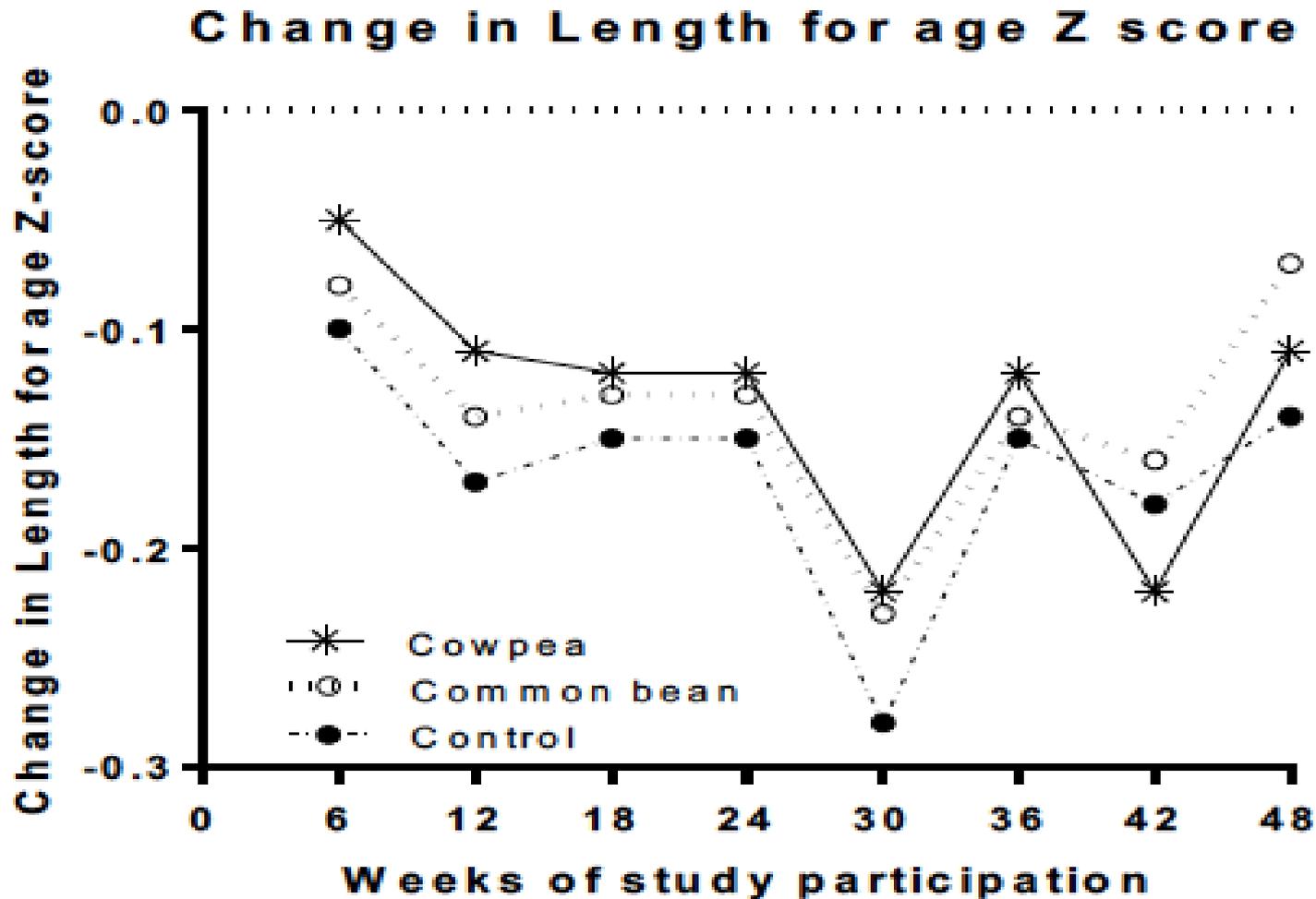
MAM – moderate acute malnutrition; SAM – severe acute malnutrition

Breast feeding in 12-36 mo children

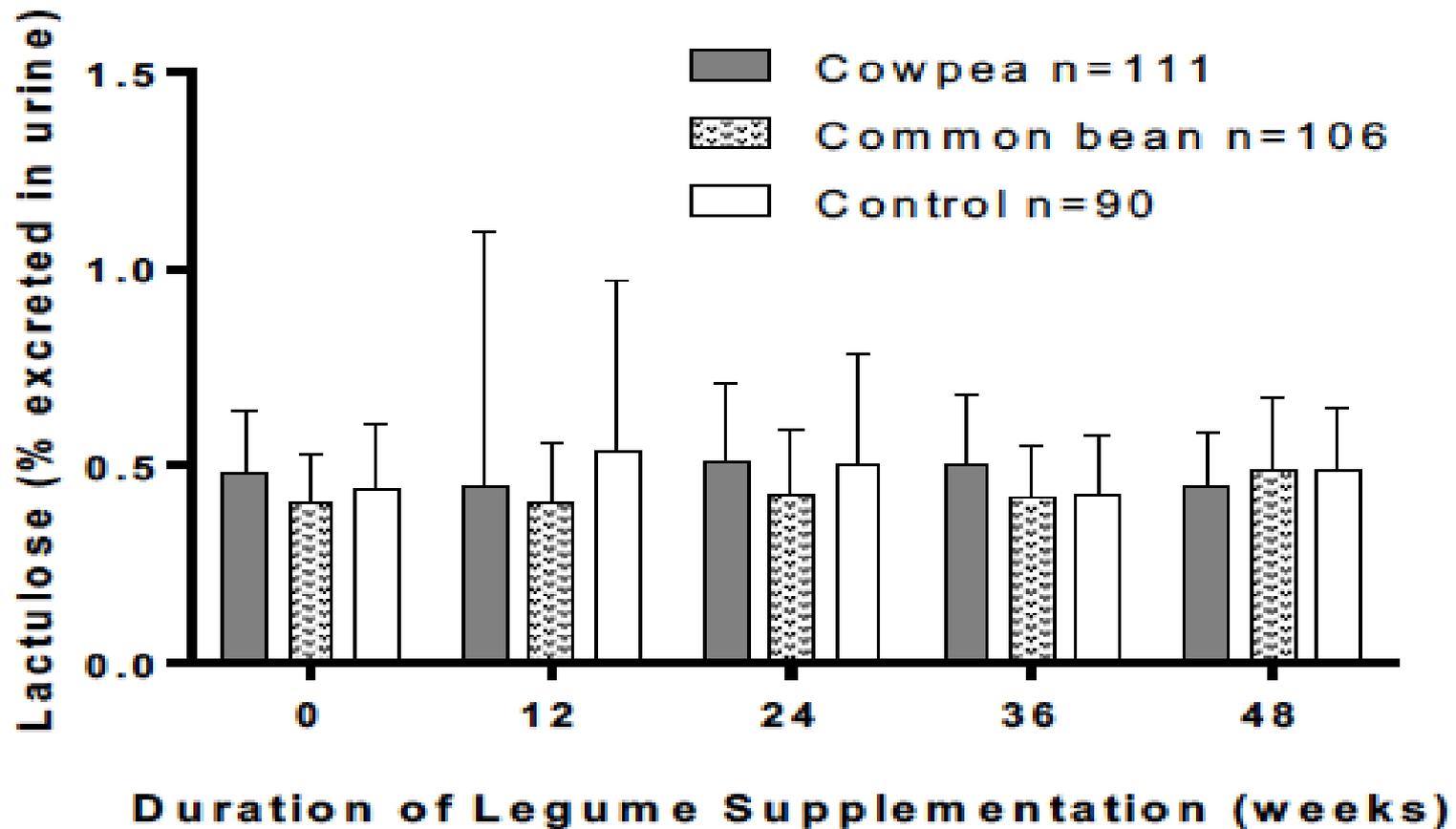
Age at Cessation of Breastfeeding



Linear growth in 12-36 mo old children



Gut permeability in 12-36 mo old



Conclusions

- **Complementary feeding with cowpea flour reduces growth faltering from 6-12 mo old rural African children by 0.13 z-scores.**
- **Complementary feeding with common bean flour reduces EED, effect size is 0.12 %lactulose in 12-36 mo rural African children.**

Strengths of the studies

- There was no reluctance on the part of children or mothers to consume the legumes, no unwanted side effects identified.
- Compliance was very high, mothers gave the foods as directed > 95% of the days, the effects seen can be assumed to be a consequence of foods, not caretaking.
- Intervention legumes were locally available, locally processed without added micronutrients nor efforts to remove antinutrients.
- This is an 'off-the-shelf' solution.
- Outcomes were measured using rigorous, using strictly adhered to protocols by well-trained field workers

Limitations

- The study population consumes primarily corn as a staple and has very high rates of breastfeeding, other populations consuming rice or where breastfeeding patterns differ might or might not benefit from legume supplementation.
- Patterns of growth faltering are different in south Asia when compared to sub-Saharan Africa and therefore are likely due to a different cause

Next steps

- **Develop biomarkers for legume intakes, so the effectiveness of efforts to promote consumption can be measured.**
- **Implement uncontrolled, community-wide interventions in rural Africa that incorporate these dietary interventions with additional efforts to strengthen the ‘3 legs of the stool’ (clean water, reduced exposure to infectious agents) to reduce stunting.**

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