Online supplemental material

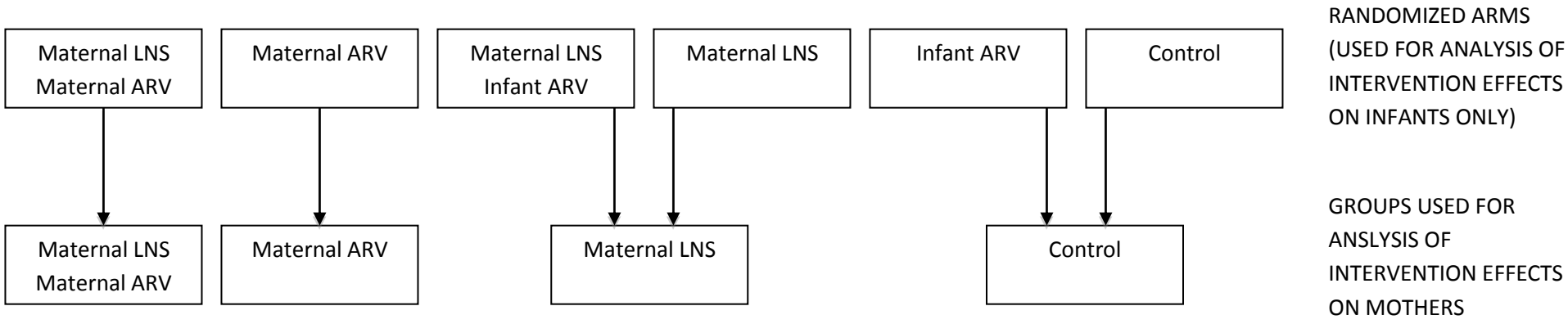
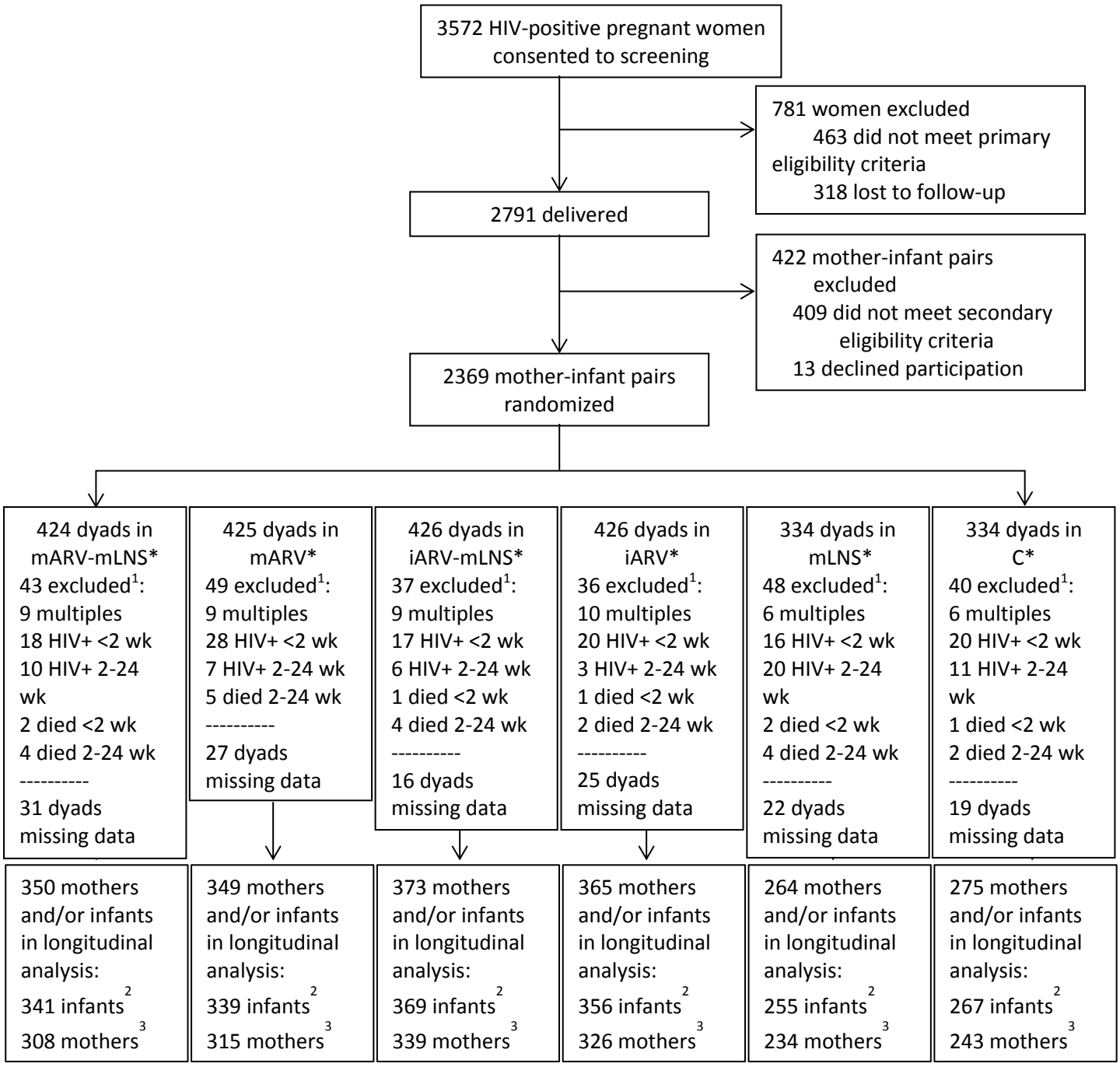


Figure S1. Randomized BAN Study arms and groups used in this analysis. ARV, antiretroviral; LNS, lipid-based nutrient supplements



[1]Exclusions not mutually exclusive

[2]Infants missing data but mothers included (n): mARV-mLNS(9); mARV(10); iARV-mLNS(4); iARV(9); mLNS(9); C(8)

[3]Mothers missing data but infants included (n): mARV-mLNS(42); mARV(33); iARV-mLNS(34); iARV(39); mLNS(30); C(32)

Figure S2.Malawian mothers and infants included in the longitudinal Hb analysis from 2 to 24 weeks by study arm, BAN Study, Malawi, 2004-2010 (mARVLNS, maternal LNS/maternal ARV; mLNS, maternal LNS; mARV, maternal ARV; C, control; BAN, Breastfeeding, Antiretroviral and Nutrition; LNS, lipid-based nutrient supplement; ARV, antiretroviral drug).

*Groups of uneven size due to the data safety and monitoring board recommended change in study design on March 26,

2008. Subsample dyads (n=537) were selected with equal representation from the LNS and no-LNS groups, prioritizing those with anthropometry and dietary data and excluding multiple births and HIV-positive infants.

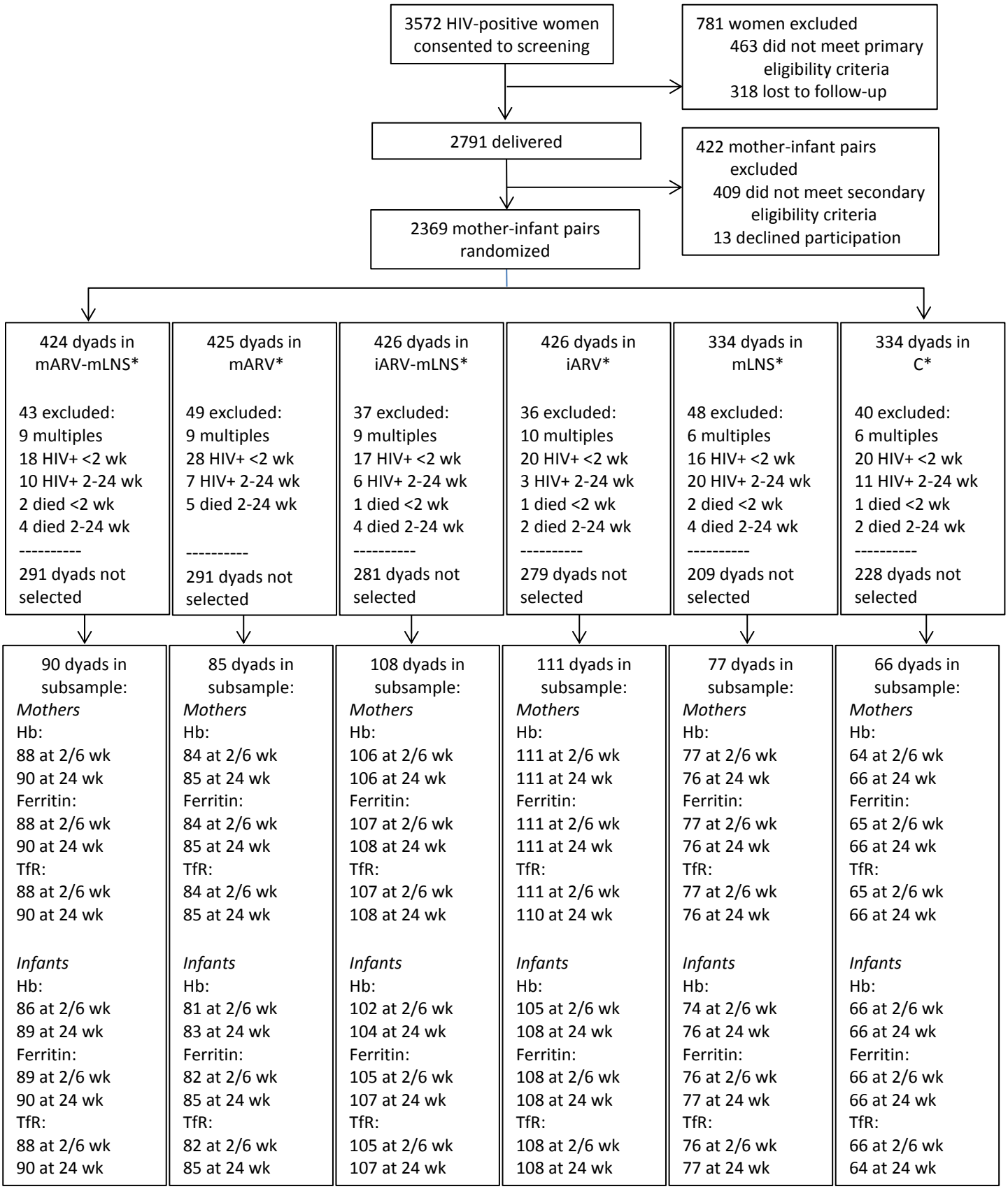


Figure S3. Malawian mothers and infants in the BAN subsample at 2/6 and 24 weeks by study arm. BAN Study, Malawi, 2004-2010 (mARVLNS, maternal LNS/maternal ARV; mLNS, maternal LNS; mARV, maternal ARV; C, control; BAN, Breastfeeding, Antiretroviral and Nutrition; LNS, lipid-based nutrient supplement; ARV, antiretroviral drug)

*Groups of uneven size due to the data safety and monitoring board recommended change in study design on March 26, 2008. Subsample dyads (n=537) were selected with equal representation from the LNS and no-LNS groups, prioritizing those with anthropometry and dietary data and excluding multiple births and HIV-positive infants.

Table S1. Composition of daily ration (140 g) of lipid-based nutrient supplements given to HIV-infected Malawian mothers in the BAN Study, Malawi, 2004-2010.[1]

Component	Provides
Energy	746 kcal
Protein	20.8 g
Lipids	49.6 g
Iron (non-encapsulated ferrous sulfate)	15 mg elemental
Zinc	19 mg
Phosphorus	1200 mg
Selenium	75 µg
B_1 (thiamin)	1.6 mg
B_2 (riboflavin)	1.8 mg
B_3 (niacin)	20 mg equiv
B_6 (pyridoxine)	2.2 mg
B_{12} (cyanocobalamine)	2.6 µg
C (ascorbic acid)	100 mg
E (α-tocopherol)	12 mg
Folic acid	300 µg
Iodine	400 µg
Potassium	1144 mg
Magnesium	124 mg
Copper	0.30 mg
Calcium	588 mg

[1]The supplement was produced by Nutriset in Malaunay, France (www.nutriset.com) from peanut butter, vegetable fat, dried skimmed milk, dry whey, dextrinmaltose sugar and a mineral and vitamin complex. BAN, Breastfeeding Antiretroviral, and Nutrition

Table S2. Associations between the study interventions and maternal and infant Hb, TfR and ferritin outcomes in BAN Study subsample, Malawi, 2004-2010[1]

	Initial measurement						24 weeks		
	2 weeks			6 weeks					
	Coef.	95% CI	p-value	Coef.	95% CI	p-value	Coef.	95% CI	p-value
Maternal									
Hb (g/L)		n=360			n=170			n=534	
mLNS-mARV	-1.29	[-6.53, 3.95]	0.63	-6.95	[-12.5, -1.43]	0.01	0.01	[-2.92, 2.92]	1.00
mARV	2.15	[-3,16, 7.45]	0.43	-9.46	[-15.1, -3.83]	0.001	-1.03	[-4.02, 1.95]	0.50
mLNS	0.97	[-3.03, 4.98]	0.63	-2.14	[-7.21, 2.93]	0.41	-0.61	[-3.00, 1.78]	0.61
Intercept	125.0	[122.0, 127.9]	<0.001	125.8	[122.5, 129.1]	<0.001	125.9	[124.2, 127.6]	<0.001
Log Ferritin (ng/mL)		n=362			n=170			n=536	
mLNS-mARV	0.10	[-0.19, 0.40)	0.49	-0.13	[-0.53, 0.27]	0.51	-0.03	[-0.24, 0.18]	0.81
mARV	0.20	[-0.10, 0.50]	0.19	-0.37	[-0.78, 0.03]	0.07	-0.02	[-0.23, 0.20]	0.88
mLNS	-0.04	[-0.27, 0.18]	0.70	-0.01	[-0.38, 0.36]	0.95	0.07	[-0.10, 0.24]	0.42
Intercept	2.93	[2.76, 3.09]	<0.001	3.36	[3.12, 3.60]	<0.001	3.06	[2.94, 3.19]	<0.001
Log TfR (mg/L)		n=362			n=170			n=535	
mLNS-mARV	-0.05	[-0.20, 0.09]	0.48	0.24	[0.03, 0.45]	0.02	0.16	[0.06, 0.26]	0.002
mARV	-0.11	[-0.25, 0.04]	0.15	0.36	[0.15, 0.57]	0.001	0.25	[0.15, 0.35]	<0.001
mLNS	0.03	[-0.08, 0.14]	0.61	0.15	[-0.04, 0.35]	0.11	0.02	[-0.06, 0.10]	0.64
Intercept	1.65	[1.57, 1.73]	<0.001	1.44	[1.32, 1.57]	<0.001	1.42	[1.36, 1.48]	<0.001
Infant									
Hb (g/L)		n=351			n=163			n=526	
Female sex	3.53	[-0.27, 7.34]	0.07	3.08	[-1.00, 7.17]	0.14	1.80	[-0.07, 3.67]	0.06
Birth weight	2.34	[-2.58, 7.27]	0.35	6.10	[1.06, 11.14]	0.02	5.97	[3.56, 8.38]	<0.001
mLNS-mARV	-6.77	[-13.64, 0.09]	0.05	-2.50	[-10.16, 5.15]	0.52	-1.79	[-5.22, 1.63]	0.31
mARV	-4.99	[-11.94, 1.97]	0.16	-2.76	[-10.44, 4.92]	0.48	-2.44	[-5.92, 1.05]	0.17
mLNS-iARV	-9.98	[-16.44, -3.52]	0.003	-5.29	[-12.94, 2.37]	0.18	-4.77	[-8.09, -1.45]	0.01
iARV	-6.93	[-13.50, -0.37]	0.04	-5.59	[-12.94, 1.76]	0.14	-4.01	[-7.31, -0.71]	0.02
mLNS	-2.39	[-9.07, 4.29]	0.48	-4.27	[-13.56, 5.02]	0.37	-4.29	[-7.84, -0.74]	0.02
Intercept	136.07	[118.50, 153.65]	<0.001	92.08	[74.54, 109.62]	<0.001	86.87	[78.34, 95.41]	<0.001
Log Ferritin (ng/mL)		n=359			n=167			n=533	
Female sex	0.17	[-0.02, 0.35]	0.08	0.24	[-0.10, 0.57]	0.17	0.47	[0.31, 0.64]	<0.001
Birth weight	0.20	[-0.04, 0.44]	0.10	0.17	[-0.24, 0.59]	0.41	0.37	[0.16, 0.58]	0.001
mLNS-mARV	-0.09	[-0.42, 0.24]	0.61	-0.17	[-0.80, 0.47]	0.60	-0.16	[-0.46, 0.14]	0.30
mARV	-0.12	[-0.45, 0.22]	0.50	0.26	[-0.38, 0.89]	0.43	0.17	[-0.14, 0.47]	0.29
mLNS-iARV	-0.23	[-0.54, 0.08]	0.14	0.07	[-0.56, 0.71]	0.82	-0.27	[-0.56, 0.02]	0.07
iARV	-0.10	[-0.42, 0.21]	0.52	0.24	[-0.37, 0.85]	0.44	-0.23	[-0.53, 0.06]	0.12
mLNS	-0.24	[-0.57, 0.08]	0.14	-0.20	[-0.96, 0.55]	0.60	-0.33	[-0.64, -0.01]	0.04
Intercept	5.14	[4.29, 5.99]	<0.001	4.44	[3.00, 5.89]	<0.001	1.35	[0.59, 2.10]	<0.001
Log TfR (mg/L)		n=360			n=165			n=531	
Female sex	-0.17	[-0.31, -0.03]	0.01	-0.12	[-0.27, 0.03]	0.12	-0.26	[-0.34, -0.18]	<0.001

Birth weight	0.02	[-0.15, 0.20]	0.78	-0.14	[-0.33, 0.05]	0.15	-0.26	[-0.36, -0.15]	<0.001
mLNS-mARV	0.26	[0.02, 0.51]	0.04	0.11	[-0.17, 0.40]	0.44	0.06	[-0.09, 0.21]	0.43
mARV	0.23	[-0.02, 0.48]	0.08	0.03	[-0.26, 0.32]	0.83	0.06	[-0.09, 0.22]	0.44
mLNS-iARV	0.17	[-0.06, 0.40]	0.15	0.00	[-0.29, 0.29]	1.00	0.04	[-0.10, 0.19]	0.57
iARV	0.23	[-0.002, 0.47]	0.05	-0.01	[-0.28, 0.27]	0.96	0.07	[-0.08, 0.22]	0.35
mLNS	0.35	[0.11, 0.59]	0.004	0.07	[-0.28, 0.41]	0.71	0.02	[-0.14, 0.17]	0.84
Intercept	1.08	[0.45, 1.72]	0.001	1.65	[1.00, 2.30]	<0.001	2.90	[2.53, 3.28]	<0.001

[1]Linear regression models tested for intervention associations with maternal and infant Hb and iron status outcomes. All indicators were adjusted for inflammation by using group specific correction factors estimated from ratios of medians for the various iron indicators.[34,35]Hb, hemoglobin; TfR, transferrin receptors; BAN, Breastfeeding Antiretroviral and Nutrition; MaMi, Malawi Mothers and Infants; mLNS, maternal LNS; mARV, maternal ARV; iARV, infant ARV.

Table S3. Longitudinal random effects model with first order autoregressive disturbance terms showing the associations between the study interventions and infant Hb (g/L) outcomes in 1927 infants, BAN Study, Malawi, 2004-2010[1]

	Coef.	95% CI	p-value
Infant birth Hb	0.72	[0.68,0.77]	<0.001
Birth weight	4.98	[3.40,6.57]	<0.001
Female	2.54	[1.28,3.80]	<0.001
Rate of weight gain/month	-2.58	[-3.84,-1.32]	<0.001
Age	7.13	[6.05,8.22]	<0.001
Age spline	-8.57	[-9.95,-7.20]	<0.001
Rate*Age spline	3.51	[3.15,3.87]	<0.001
Rate*Age	-1.54	[-1.79,-1.29]	<0.001
Birth Hb*Age spline	-0.07	[-0.07,-0.06]	<0.001
Birth Hb*Age	0.07	[0.06,0.08]	<0.001
mLNS-mARV	-0.81	[-4.05,2.42]	0.62
mARV	-0.94	[-4.15,2.28]	0.57
mLNS-iARV	-1.78	[-4.93,1.38]	0.27
iARV	-1.96	[-5.14,1.23]	0.23
mLNS	-2.36	[-5.83,1.10]	0.18
mLNS-mARV*Age	0.12	[-0.30,0.54]	0.57
mARV*Age	0.10	[-0.31,0.52]	0.62
mLNS-iARV*Age	-0.17	[-0.57,0.24]	0.42
iARV*Age	-0.07	[-0.48,0.34]	0.76
mLNS*Age	0.22	[-0.23,0.66]	0.34
mLNS-mARV*Age spline	-0.11	[-0.63,0.42]	0.69
mARV*Age spline	-0.09	[-0.62,0.43]	0.73
mLNS-iARV*Age spline	0.42	[-0.09,0.93]	0.10
iARV*Age spline	0.23	[-0.29,0.75]	0.38
mLNS*Age spline	-0.29	[-0.86,0.27]	0.31
Intercept	14.51	[4.49,24.53]	0.01

[1]The longitudinal model contained a spline with a knot at 9 weeks to capture the shape of infant Hb over time. A Wald test for the study intervention interactions with age and age spline indicated a significant effect of the interventions over time ($\chi^2(10) = 17.45$, p=0.07). Data from HIV-negative BAN infants with at least one Hb measurement after birth were included until 24 weeks or cessation of exclusive breastfeeding: n=341 in the mLNS-mARV arm; n=338 in the mARV arm; n=369 in the mLNS-iARV arm; n=356 in the iARV arm; n=255 in the mLNS arm; n=267 in the control arm. BAN, Breastfeeding, Antiretroviral and Nutrition; mLNS-mARV, maternal LNS/maternal ARV; mARV, maternal ARV; mLNS-iARV, maternal LNS/infant ARV; iARV, infant ARV; mLNS, maternal LNS; C, control. Hb, Hemoglobin; BAN, Breastfeeding Antiretrovirals and Nutrition; LNS, lipid-based nutrient supplement; ARV, antiretroviral intervention.

Comparisons between samples:

Compared to other randomized infants, included infants were heavier (Longitudinal: 3.02 vs. 2.95 kg, p=0.001; Subsample: 3.04 vs. 3.01 kg, p=0.06), a larger proportion were in the ARV arm (Longitudinal: 37.6% vs. 28.7%, p<0.001; Subsample: 41% vs 35%, p=0.01), and infants in the longitudinal sample infants were longer at birth (48.2 vs. 47.8 cm, p<0.001). Included mothers were older (Longitudinal: 26 vs. 25 y, p<0.001; Subsample (27 vs. 26 y, p=0.01), mothers in the longitudinal sample had higher pregnancy Hb (109 vs. 106 g/L, p<0.001) and a higher proportion were educated beyond primary school (36% vs. 31%, p=0.02). Moreover, subsample mothers had lower BMI at delivery (23.3 vs. 23.7 kg/m^2, p=0.02).

These tests were also conducted to compare characteristics of dyads in the longitudinal sample, but not in the subsample, to those in the subsample to asses for similarity. Most characteristics were similar between the subsample and longitudinal samples; however, more infants in the subsample were in the ARV arm (36 vs. 42%, p=0.02) and subsample mothers were lighter at delivery (23.2 vs. 23.7 kg/m^2, p=0.003) compared to those only included in the longitudinal sample.