**Online supplemental material**

RANDOMIZED ARMS (USED FOR ANALYSIS OF INTERVENTION EFFECTS ON INFANTS ONLY)

GROUPS USED FOR ANSLYSIS OF INTERVENTION EFFECTS ON MOTHERS

Maternal LNS
Maternal ARV

Maternal ARV

Maternal LNS

Control

Maternal LNS
Maternal ARV

Control

Maternal ARV

Maternal LNS

Maternal LNS
Infant ARV

Infant ARV

Supplemental figure 1. Randomized BAN Study arms and groups used in this analysis. ARV, antiretroviral; LNS, lipid-based nutrient supplements

781 women excluded

 463 did not meet primary eligibility criteria

 318 lost to follow-up

422 mother-infant pairs

 excluded

 409 did not meet secondary

 eligibility criteria

 13 declined participation

3572 HIV-positive pregnant women

consented to screening

2791 delivered

2369 mother-infant pairs randomized

424 dyads in

mARV-mLNS\*

43 excluded1:

9 multiples

18 HIV+ <2 wk

10 HIV+ 2-24 wk

2 died <2 wk

4 died 2-24 wk

----------

31 dyads missing data

425 dyads in

 mARV\*

49 excluded1:

9 multiples

28 HIV+ <2 wk

7 HIV+ 2-24 wk

5 died 2-24 wk

----------

27 dyads missing data

426 dyads in
iARV-mLNS\*

37 excluded1:

9 multiples

17 HIV+ <2 wk

6 HIV+ 2-24 wk

1 died <2 wk

4 died 2-24 wk

----------

16 dyads missing data

426 dyads in

iARV\*

36 excluded1:

10 multiples

20 HIV+ <2 wk

3 HIV+ 2-24 wk

1 died <2 wk

2 died 2-24 wk

----------

25 dyads missing data

334 dyads in

 mLNS\*

48 excluded1:

6 multiples

16 HIV+ <2 wk

20 HIV+ 2-24 wk

2 died <2 wk

4 died 2-24 wk

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22 dyads missing data

334 dyads in

C\*

40 excluded1:

6 multiples

20 HIV+ <2 wk

11 HIV+ 2-24 wk

1 died <2 wk

2 died 2-24 wk

----------

19 dyads missing data

350 mothers and/or infants in longitudinal analysis:

341 infants2

308 mothers3

349 mothers and/or infants in longitudinal analysis:

339 infants2

315 mothers3

373 mothers and/or infants in longitudinal analysis:

369 infants2

339 mothers3

365 mothers and/or infants in longitudinal analysis:

356 infants2

326 mothers3

264 mothers and/or infants in longitudinal analysis:

255 infants2

234 mothers3

275 mothers and/or infants in longitudinal analysis:

267 infants2

243 mothers3

1Exclusions not mutually exclusive

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

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

Supplemental figure 2.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.

781 women excluded

 463 did not meet primary

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291 dyads not selected

425 dyads in

 mARV\*

49 excluded:

9 multiples

28 HIV+ <2 wk

7 HIV+ 2-24 wk

5 died 2-24 wk

----------

291 dyads not selected

426 dyads in
iARV-mLNS\*

37 excluded:

9 multiples

17 HIV+ <2 wk

6 HIV+ 2-24 wk

1 died <2 wk

4 died 2-24 wk

----------

281 dyads not selected

426 dyads in

iARV\*

36 excluded:

10 multiples

20 HIV+ <2 wk

3 HIV+ 2-24 wk

1 died <2 wk

2 died 2-24 wk

----------

279 dyads not selected

334 dyads in

 mLNS\*

48 excluded:

6 multiples

16 HIV+ <2 wk

20 HIV+ 2-24 wk

2 died <2 wk

4 died 2-24 wk

----------

209 dyads not selected

334 dyads in

C\*

40 excluded:

6 multiples

20 HIV+ <2 wk

11 HIV+ 2-24 wk

1 died <2 wk

2 died 2-24 wk

----------

228 dyads not selected

90 dyads in subsample:

*Mothers*

Hb:

88 at 2/6 wk

90 at 24 wk

Ferritin:

88 at 2/6 wk

90 at 24 wk

TfR:

88 at 2/6 wk

90 at 24 wk

*Infants*

Hb:

86 at 2/6 wk

89 at 24 wk

Ferritin:

89 at 2/6 wk

90 at 24 wk

TfR:

88 at 2/6 wk

90 at 24 wk

85 dyads in subsample:

*Mothers*

Hb:

84 at 2/6 wk

85 at 24 wk

Ferritin:

84 at 2/6 wk

85 at 24 wk

TfR:

84 at 2/6 wk

85 at 24 wk

*Infants*

Hb:

81 at 2/6 wk

83 at 24 wk

Ferritin:

82 at 2/6 wk

85 at 24 wk

TfR:

82 at 2/6 wk

85 at 24 wk

108 dyads in subsample:

*Mothers*

Hb:

106 at 2/6 wk

106 at 24 wk

Ferritin:

107 at 2/6 wk

108 at 24 wk

TfR:

107 at 2/6 wk

108 at 24 wk

*Infants*

Hb:

102 at 2/6 wk

104 at 24 wk

Ferritin:

105 at 2/6 wk

107 at 24 wk

TfR:

105 at 2/6 wk

107 at 24 wk

111 dyads in subsample:

*Mothers*

Hb:

111 at 2/6 wk

111 at 24 wk

Ferritin:

111 at 2/6 wk

111 at 24 wk

TfR:

111 at 2/6 wk

110 at 24 wk

*Infants*

Hb:

105 at 2/6 wk

108 at 24 wk

Ferritin:

108 at 2/6 wk

108 at 24 wk

TfR:

108 at 2/6 wk

108 at 24 wk

77 dyads in subsample:

*Mothers*

Hb:

77 at 2/6 wk

76 at 24 wk

Ferritin:

77 at 2/6 wk

76 at 24 wk

TfR:

77 at 2/6 wk

76 at 24 wk

*Infants*

Hb:

74 at 2/6 wk

76 at 24 wk

Ferritin:

76 at 2/6 wk

77 at 24 wk

TfR:

76 at 2/6 wk

77 at 24 wk

66 dyads in subsample:

*Mothers*

Hb:

64 at 2/6 wk

66 at 24 wk

Ferritin:

65 at 2/6 wk

66 at 24 wk

TfR:

65 at 2/6 wk

66 at 24 wk

*Infants*

Hb:

66 at 2/6 wk

66 at 24 wk

Ferritin:

66 at 2/6 wk

66 at 24 wk

TfR:

66 at 2/6 wk

64 at 24 wk

Supplemental figure 3. 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.

Supplemental table 1. 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 |
| B1 (thiamin) | 1.6 mg |
| B2 (riboflavin) | 1.8 mg |
| B3 (niacin) | 20 mg equiv |
| B6 (pyridoxine) | 2.2 mg |
| B12 (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 |

1The supplement was produced by Nutriset in Malaunay, France ([www.nutriset.com](http://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

|  |  |
| --- | --- |
| Supplemental table 2. Associations between the study interventions and maternal and infant Hb, TfR and ferritin outcomes in BAN Study subsample, Malawi, 2004-20101 |  |
|   | 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 |
| 1Linear 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.34,35Hb, hemoglobin; TfR, transferrin receptors; BAN, Breastfeeding Antiretroviral and Nutrition; MaMi, Malawi Mothers and Infants; mLNS, maternal LNS; mARV, maternal ARV; iARV, infant ARV. |

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| Supplemental table 3. 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, 2004-20101 |
|  | 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 |
| 1The 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 (χ2(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/m2, 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/m2, p=0.003) compared to those only included in the longitudinal sample.