

# Nutrition Management of HIV-infected Women of Reproductive Age

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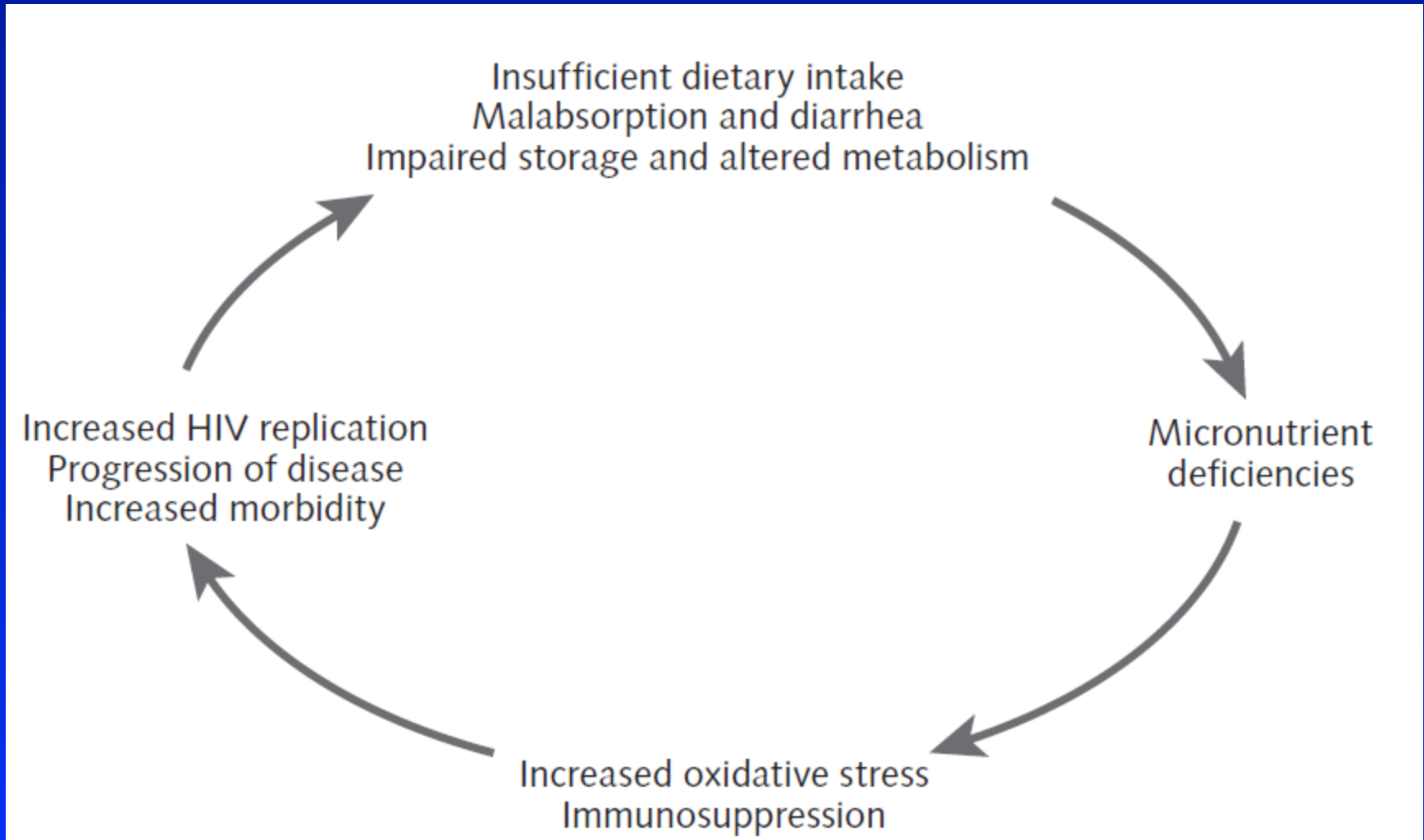
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# Nutrition and HIV infection

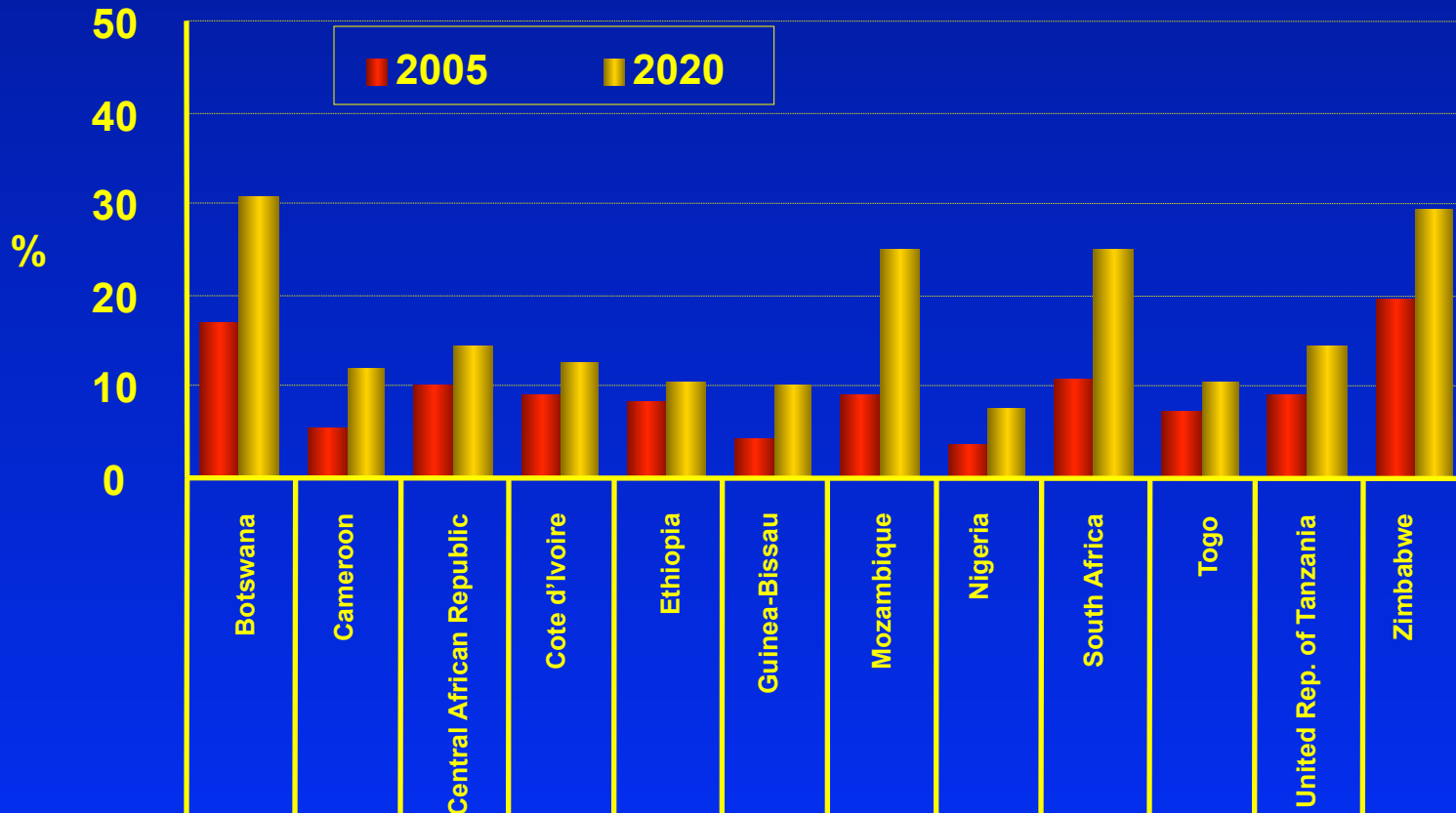
## Vicious cycle of micronutrient deficiencies and HIV pathogenesis



# Interaction of HIV and Nutrition



# Percentage of workforce lost to AIDS by 2005 and 2020 in selected African countries



Sources: ILO (2000) POPILO population and labour force projection; UN Department of Economic and Social Affairs, Population Division (1998) *World Population Prospects: the 1998 Revision*

**Table 2.** Estimated mean values (at age 35 years) of the parameters of energy balance in HIV-seropositive subjects compared with HIV-seronegative controls, from fitting the analysis of covariance model.

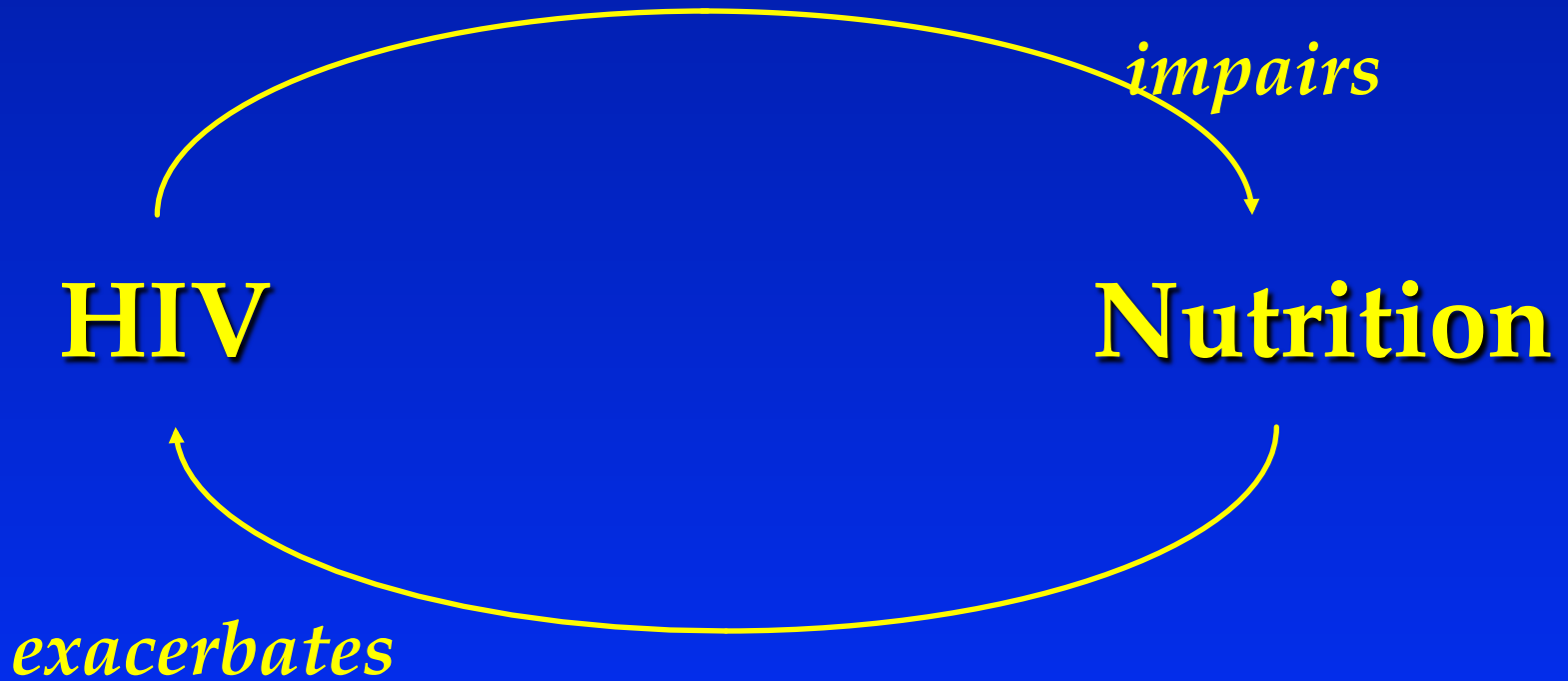
|                                       | HIV+       | HIV-       | <i>P</i> * |
|---------------------------------------|------------|------------|------------|
| Patient characteristics               |            |            |            |
| No. patients                          | 104        | 57         |            |
| Mean (SD) age (years) <sup>†</sup>    | 37.9 (8.2) | 31.3 (7.3) | < 0.00001  |
| Body mass index                       | 22.4       | 23.4       | 0.06       |
| Dietary intake and nitrogen excretion |            |            |            |
| Energy intake (kcal/day)              | 2243       | 1908       | 0.05       |
| Protein intake (g/day)                | 82.8       | 76.5       | 0.32       |
| Nitrogen intake (g/day)               | 13.2       | 12.2       | 0.32       |
| 24 h urine nitrogen (g/day)           | 12.7       | 14.4       | 0.27       |
| REE and substrate oxidation           |            |            |            |
| REE/FFM (kcal/kg/day)                 | 32.7       | 30.7       | < 0.0001   |
| Respiratory quotient                  | 0.84       | 0.84       | 0.91       |
| Carbohydrate oxidation (g/kg FFM/day) | 3.9        | 3.7        | 0.64       |
| Fat oxidation (g/kg FFM/day)          | 1.6        | 1.8        | 0.14       |
| Protein oxidation (g/kg FFM/day)      | 1.4        | 1.6        | 0.16       |
| Sugar probes                          |            |            |            |

Table 2

Body composition, energy, and metabolic parameters in HIV-infected and non-HIV-infected subjects

| Variable                     | HIV <sup>+</sup> <sup>a</sup> (n = 283) | Control <sup>a</sup> (n = 146) | <i>P</i> value <sup>b</sup> | <i>P</i> value adjusted for age and BMI |
|------------------------------|---|--------------------------------|-----------------------------|---|
| Body composition parameters  |   |                                |                             |   |
| Waist (cm)                   | 94.8 ± 0.8                              | 97.2 ± 1.5                     | .13                         | .0003                                   |
| Hip (cm)                     | 100.4 ± 0.7                             | 108.0 ± 1.2                    | <.0001                      | <.0001                                  |
| Waist-to-hip ratio           | 0.94 ± 0.00                             | 0.90 ± 0.01                    | <.0001                      | <.0001                                  |
| CT VAT (cm <sup>2</sup> )    | 121.5 ± 4.1                             | 130.8 ± 7.9                    | .25                         | .020                                    |
| CT SAT (cm <sup>2</sup> )    | 231.3 ± 9.1                             | 319.3 ± 17.3                   | <.0001                      | .64                                     |
| Total body fat (kg)          | 21.1 ± 0.6                              | 26.4 ± 1.2                     | <.0001                      | .011                                    |
| FFM (kg)                     | 54.7 ± 0.7                              | 56.5 ± 1.1                     | .12                         | .85                                     |
| Energy parameters            |   |                                |                             |   |
| REE (kcal/d)                 | 1730 ± 22                               | 1705 ± 40                      | .56                         | .027                                    |
| % Predicted BMR <sup>c</sup> | 108 ± 1                                 | 98 ± 1                         | <.0001                      | <.0001                                  |
| REE/FFM (kcal/[d kg])        | 31.8 ± 0.3                              | 29.8 ± 0.3                     | <.0001                      | <.0001                                  |
| RQ                           | 0.83 ± 0.00                             | 0.85 ± 0.01                    | .005                        | .025                                    |

# Interaction of HIV and Nutrition



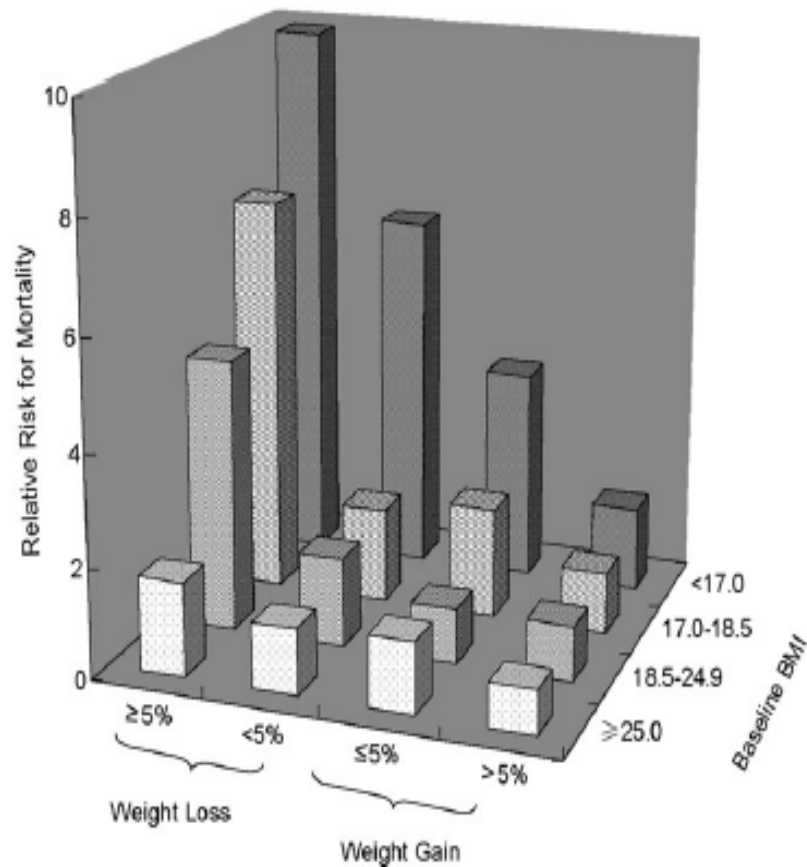
**TABLE 2.** Follow-Up Characteristics of HIV-Infected Patients Aged  $\geq 15$  Years Stratified by BMI (weight/height<sup>2</sup>)

|   | BMI <16       | 16 $\leq$ BMI <18 | 18 $\leq$ BMI <20 | 20 $\leq$ BMI <22 | BMI $\geq 22$ | No BMI        | BMI Late*  |
|---|---------------|-------------------|-------------------|-------------------|---------------|---------------|------------|
| n   | 354           | 320               | 348               | 280               | 355           | 266           | 142        |
| Median follow-up time in months (IQR)                       | 6 (2–18)      | 9 (4–24)          | 19 (7–41)         | 22 (8–52)         | 32 (14–56)    | 3 (0–25)      | 49 (20–82) |
| Number who started on co-trimoxazole prophylaxis (%)        | 102 (29)      | 103 (32)          | 123 (35)          | 109 (39)          | 111 (31)      | 44 (17)       | 45 (32)    |
| Number of deaths during follow-up (%)                       | 268 (76)      | 206 (64)          | 154 (44)          | 104 (37)          | 96 (27)       | 187 (70)      | 47 (33)    |
| Median survival time in years (IQR)                         | 0.8 (0.2–2.0) | 1.2 (0.4–4.2)     | 3.6 (1.0–8.5)     | 5.4 (1.6–?)       | 8.9 (3.5–?)   | 0.3 (0.0–4.5) | ? (3.1–?)  |
| Mortality rate (95% CI) per 100 person-years of observation | 66 (63–69)    | 43 (40–46)        | 19 (16–21)        | 14 (5–16)         | 8 (7–10)      | 52 (47–56)    | 8 (6–10)   |

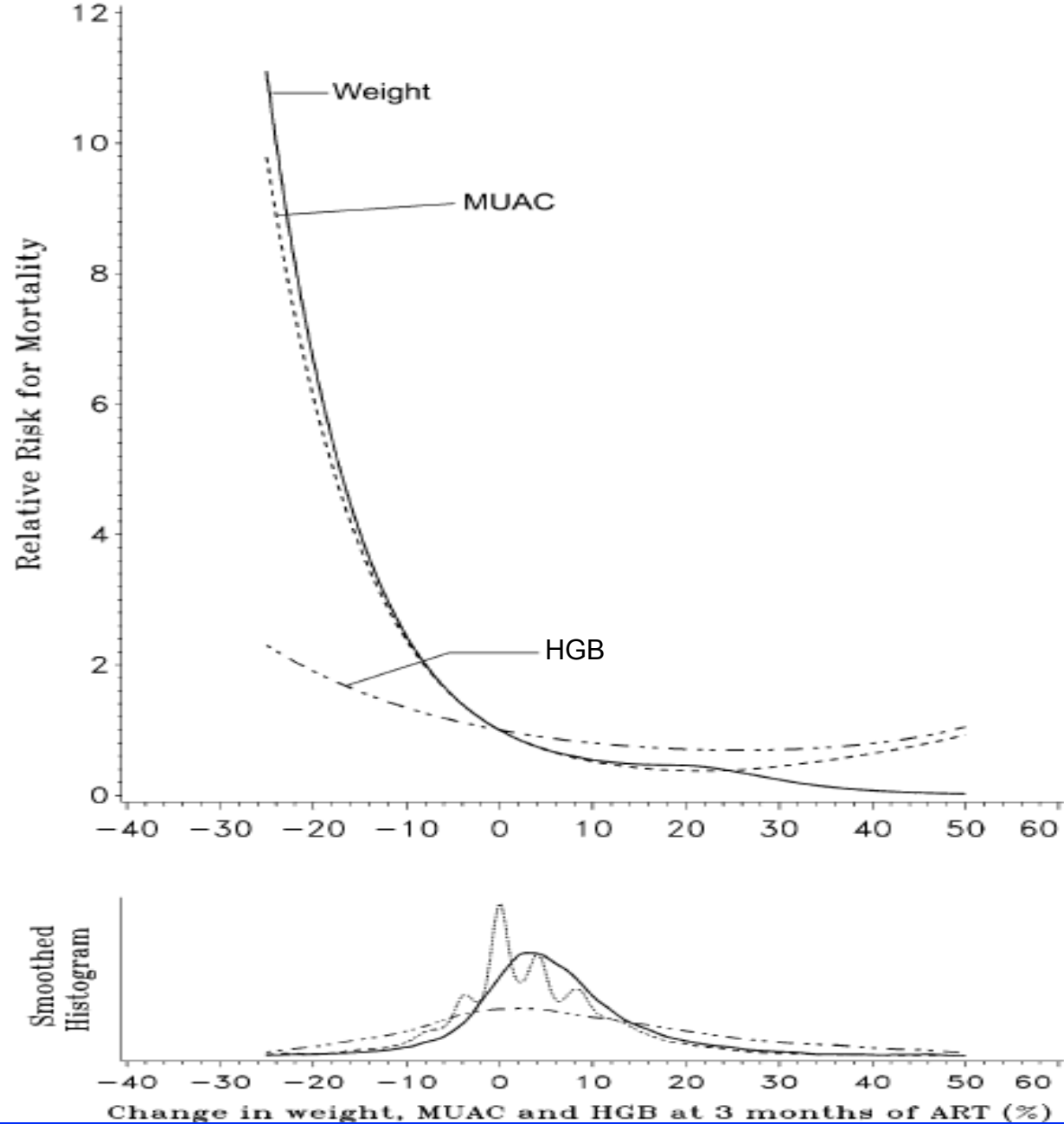
\*First BMI >90 days after diagnosis.

? indicates that the median/upper CI could not be estimated.





**Figure 2.** The combined effect of baseline body mass index (BMI) and weight change after 3 months of ART on the risk of mortality.



## B Vitamins in multiples of RDA may reduce HIV-1 mortality (Tang et al. 1996)

- Vitamin B1 ( $\geq 5 \times$  RDA)
  - RR=0.61, 95% CI: 0.38-0.98
- Vitamin B2 ( $\geq 5 \times$  RDA)
  - RR=0.60, 95% CI: 0.37-0.97
- Vitamin B6 ( $\geq 2 \times$  RDA)
  - RR=0.60, 95% CI: 0.39-0.93

## Supplemental B vitamins (self report) may delay progression to AIDS and death in South African HIV-infected patients

- Matched case-control study, N=175 pairs
- Black HIV + patients in Johannesburg 1985-1997
- Median time to progression 32.0 wk for those without vitamins versus 72.7 wk for those who took B vitamins ( $p=0.004$ )
- Median survival 144.8 wk for patients without vitamins, 264.6 wk for those who took B vitamins ( $p=0.001$ )

# Multiple micronutrients reduce mortality among some HIV-positive Thai patients

- RCT, N=481, duration=48 weeks
- Daily placebo vs. multiple micronutrients
- Overall mortality:  
RR=0.53 (95%CI 0.22-1.25), p=0.10

Mortality Among those with CD4 <200:  
RR=0.37, p=0.05

Mortality Among those with CD4 <100:  
RR=0.26, p=0.03

## Trial of Vitamins, Tanzania

- Factorial design of Vitamin A, and Vitamins B-complex, C, and E
- Women enrolled during pregnancy
- Followed up for median of 6 years
- Monthly assessments of clinical signs
- Regular assessment of CD4+ count, HB concentration, and viral load
- High compliance

DAILY

1. VITAMIN A ALONE (n=272)

- PREFORMED VIT A : 5000 IU
- $\beta$ -CAROTENE : 30 mg

2. MULTIVITAMINS EXCLUDING VIT A (n=271)

- B1 : 20 mg
- B2 : 20 mg
- B6 : 25 mg
- NIACIN : 100 mg
- B12 : 50  $\mu$ g
- C : 500 mg
- E : 30 mg
- FOLATE: 0.8 mg

3. MULTIVITAMINS INCLUDING VIT A (n=268)

4. PLACEBO (n=267)

1. & 3. VITAMIN A 200,000 IU

2. & 4. PLACEBO

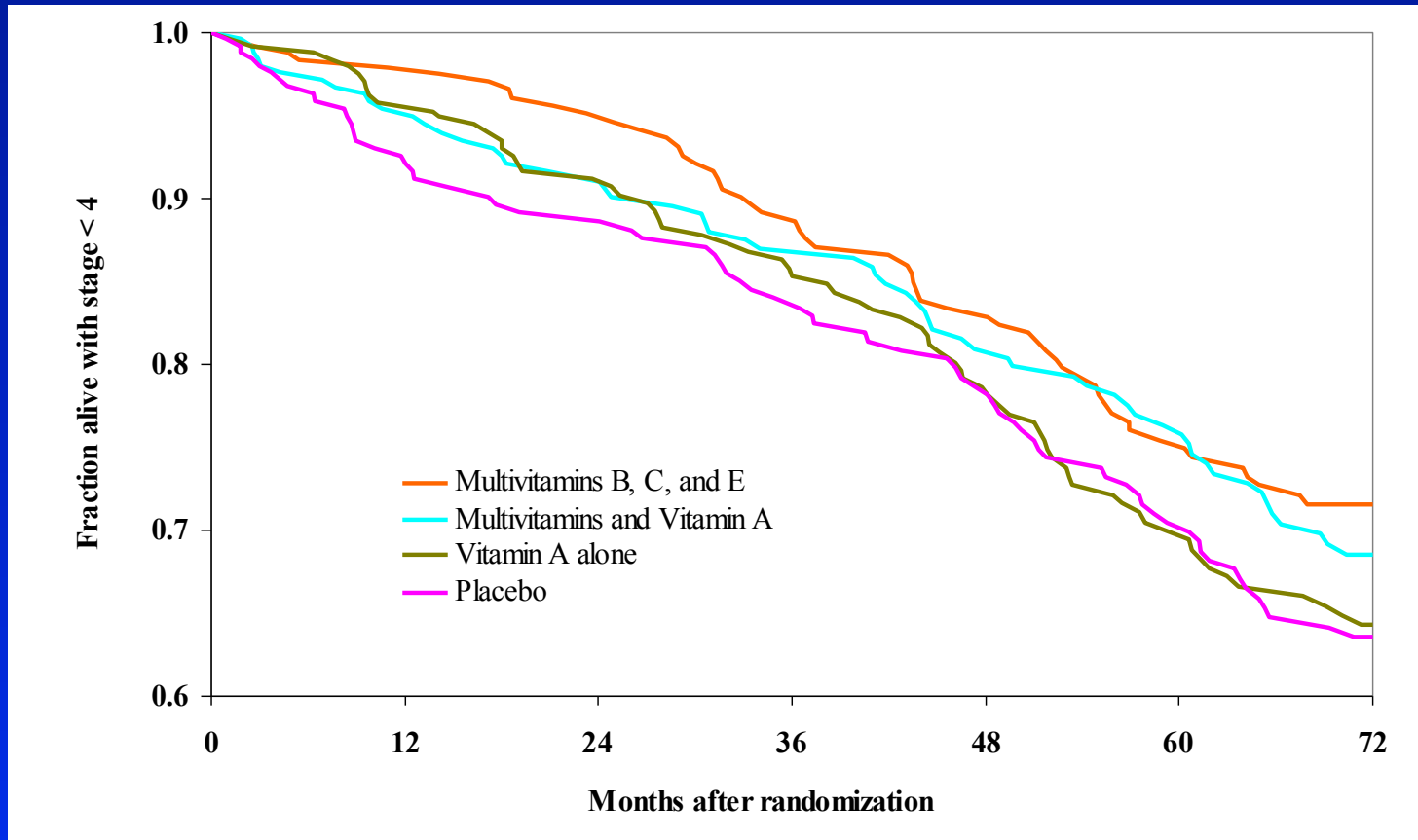
DELIVERY

# Baseline characteristics of mothers in intervention and control groups: *Tanzania Vitamin and HIV Infection Study*

| <b>Characteristic</b>      | <b>Multivitamins<br/>[N=539]</b> | <b>No Multivitamins<br/>[N=539]</b> | <b>Vitamin A<br/>[N= 540]</b> | <b>No Vitamin A<br/>[N=538]</b> |
|----------------------------|----------------------------------|-------------------------------------|-------------------------------|---------------------------------|
| <b>CD4+ cell count</b>     |                                  |                                     |                               |                                 |
| Mean (SD)                  | 444 (249)                        | 453 (289)                           | 438 (255)                     | 459 (284)                       |
| Median                     | 415                              | 407                                 | 404                           | 419                             |
| <b>CD4+ categories (%)</b> |                                  |                                     |                               |                                 |
| <200                       | 11.8                             | 12.2                                | 12.1                          | 11.8                            |
| 200-499                    | 51.0                             | 51.9                                | 53.1                          | 49.7                            |
| 500+                       | 29.7                             | 29.0                                | 27.39                         | 30.7                            |
| Unknown                    | 7.6                              | 7.0                                 | 6.8                           | 7.8                             |



# Kaplan-Meier curves of progression to WHO stage 4 or death, by regimen



| No. at risk                 |     |     |     |     |
|-----------------------------|-----|-----|-----|-----|
| Multivitamins B, C, and E   | 271 | 195 | 157 | 119 |
| Multivitamins and Vitamin A | 267 | 181 | 143 | 102 |
| Vitamin A alone             | 272 | 190 | 147 | 104 |
| Placebo                     | 267 | 173 | 145 | 101 |

# Effect of multivitamins on T cell counts

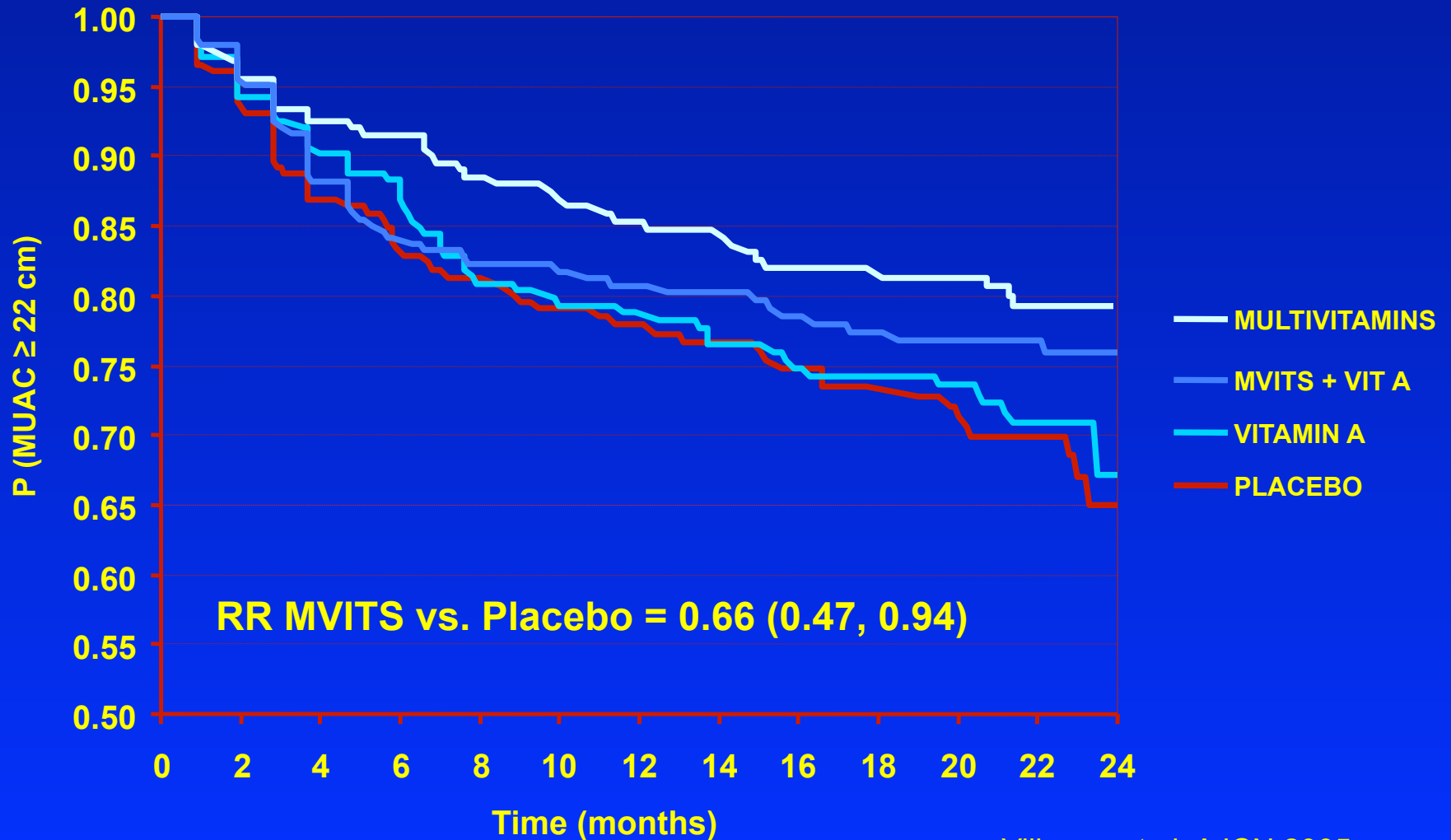
## CD4 count

| End Point                       | Mean Value<br>in Placebo Group <sup>‡</sup> | Multivitamins                |         | Multivitamins + Vitamin A    |         | Vitamin A Alone              |         |
|---------------------------------|---|------------------------------|---------|------------------------------|---------|------------------------------|---------|
|                                 |   | Mean Difference<br>(95% CI)† | P Value | Mean Difference<br>(95% CI)† | P Value | Mean Difference<br>(95% CI)† | P Value |
| <b>Whole period</b>             |   |                              |         |                              |         |                              |         |
| CD4+ cell count/mm <sup>3</sup> | 449±255                                     | 48 (10 to 85)                | 0.01    | 41 (4 to 77)                 | 0.03    | -15 (-45 to 14)              | 0.30    |
| <b>First 2 years</b>            |   |                              |         |                              |         |                              |         |
| CD4+ cell count/mm <sup>3</sup> | 494±257                                     | 48 (18 to 79)                | 0.002   | 21 (-11 to 53)               | 0.20    | -16 (-44 to 13)              | 0.28    |
| <b>First 4 years</b>            |   |                              |         |                              |         |                              |         |
| CD4+ cell count/mm <sup>3</sup> | 470±254                                     | 38 (8 to 68)                 | 0.01    | 19 (-12 to 50)               | 0.22    | -18 (-46 to 11)              | 0.22    |

# Multivitamins and HIV-related complications

| Complication                               | Episodes <sup>†</sup> | Relative Risk<br>in Placebo Group | Multivitamins             |         | Vitamin A Alone           |         |
|--|-----------------------|-----------------------------------|---------------------------|---------|---------------------------|---------|
|  |                       |                                   | Relative Risk<br>(95% CI) | P Value | Relative Risk<br>(95% CI) | P Value |
| Thrush                                     | 0.14±0.48             | 1.0                               | 0.47 (0.30–0.73)          | <0.001  | 0.69 (0.44–1.07)          | 0.10    |
| Gingival erythema                          | 0.02±0.14             | 1.0                               | 0.22 (0.06–0.83)          | 0.02    | 1.00 (0.40–2.46)          | 0.99    |
| Angular cheilitis                          | 0.11±0.48             | 1.0                               | 0.45 (0.25–0.79)          | 0.006   | 1.54 (0.95–2.51)          | 0.08    |
| Oral ulcer                                 | 0.10±0.30             | 1.0                               | 0.44 (0.28–0.68)          | <0.001  | 0.94 (0.59–1.48)          | 0.78    |
| Reported mouth and throat ulcers           | 0.28±0.93             | 1.0                               | 0.47 (0.33–0.66)          | <0.001  | 1.01 (0.74–1.38)          | 0.93    |
| Painful tongue or mouth                    | 0.31±0.98             | 1.0                               | 0.46 (0.33–0.66)          | <0.001  | 1.03 (0.76–1.40)          | 0.85    |
| Difficult or painful swallowing            | 0.16±0.55             | 1.0                               | 0.41 (0.26–0.63)          | <0.001  | 1.25 (0.88–1.77)          | 0.21    |
| Nausea and vomiting                        | 0.38±1.14             | 1.0                               | 0.69 (0.50–0.97)          | 0.03    | 0.98 (0.71–1.35)          | 0.91    |
| Diarrhea                                   | 0.55±1.25             | 1.0                               | 0.83 (0.63–1.09)          | 0.18    | 0.95 (0.72–1.25)          | 0.71    |
| Dysentery                                  | 0.19±0.71             | 1.0                               | 0.66 (0.45–0.95)          | 0.03    | 0.90 (0.62–1.28)          | 0.54    |
| Fatigue                                    | 0.59±1.43             | 1.0                               | 0.64 (0.49–0.86)          | 0.003   | 1.04 (0.79–1.35)          | 0.79    |
| Rash                                       | 0.96±1.76             | 1.0                               | 0.74 (0.57–0.96)          | 0.02    | 0.83 (0.64–1.06)          | 0.13    |
| Acute upper respiratory tract<br>infection | 0.83±1.13             | 1.0                               | 0.79 (0.66–0.96)          | 0.02    | 0.96 (0.80–1.14)          | 0.62    |

# Effect of multivitamins on postpartum wasting



# Effects of multivitamins on hemoglobin concentrations (g/dL)

| Period                   | Placebo<br>(N=219)<br>Mean (SD) | MVits<br>(N = 228)<br>Difference | P     | MVits + A<br>(N = 226)<br>Difference | P     | Vit A Alone<br>(N=233)<br>Difference | P   |
|--------------------------|---------------------------------|----------------------------------|-------|--------------------------------------|-------|--------------------------------------|-----|
| Whole Period             | 10.84 (1.31)                    | 0.20 (0.00,0.40)                 | 0.05  | 0.21 (0.02, 0.40)                    | 0.03  | 0.04 (-0.16,0.23)                    | 0.7 |
| Up to 70 Days Postpartum | 10.16 (1.87)                    | 0.59 (0.22, 0.97)                | 0.002 | 0.53 (0.15, 0.91)                    | 0.006 | 0.32 (-0.06,0.70)                    | 0.1 |
| First 2 Years            | 10.64 (1.49)                    | 0.37 (0.13, 0.62)                | 0.003 | 0.36 (0.12, 0.60)                    | 0.003 | 0.17 (-0.08,0.42)                    | 0.2 |
| First 4 Years            | 10.88 (1.42)                    | 0.27 (0.06, 0.48)                | 0.01  | 0.27 (0.07, 0.48)                    | 0.009 | 0.09 (-0.12,0.30)                    | 0.4 |

# Randomized Trial of High vs. Standard Dose Multivitamins: Effects on HIV Progression and Death

| Outcome   | No. (%) of Patients              |                              | High-Dose Multivitamins, RR (95% CI) | P Value <sup>a</sup> |
|---|----------------------------------|------------------------------|--------------------------------------|----------------------|
|   | Standard-Dose Regimen (n = 1708) | High-Dose Regimen (n = 1710) |                                      |                      |
| HIV disease progression or death from any cause |                                  |                              |                                      |                      |
| All patients                                    | 1229 (72.0)                      | 1231 (72.0)                  | 1.00 (0.96-1.04)                     | .98                  |
| By baseline BMI <sup>b</sup>                    |                                  |                              |                                      |                      |
| ≥16   | 1127 (71.1)                      | 1120 (71.1)                  | 1.00 (0.96-1.05)                     | .99                  |
| <16   | 92 (82.9)                        | 99 (85.3)                    | 1.03 (0.92-1.15)                     | .61                  |
| Death from any cause                            |                                  |                              |                                      |                      |
| All patients                                    | 220 (12.9)                       | 233 (13.6)                   | 1.06 (0.89-1.26)                     | .52                  |
| By baseline BMI <sup>b</sup>                    |                                  |                              |                                      |                      |
| ≥16   | 187 (11.8)                       | 183 (11.6)                   | 0.98 (0.81-1.19)                     | .88                  |
| <16   | 31 (27.9)                        | 44 (37.9)                    | 1.36 (0.93-1.98)                     | .11                  |
| AIDS-related death                              |                                  |                              |                                      |                      |
| All patients                                    | 64 (3.8)                         | 73 (4.3)                     | 1.14 (0.82-1.58)                     | .44                  |
| By baseline BMI <sup>b</sup>                    |                                  |                              |                                      |                      |
| ≥16   | 54 (3.4)                         | 57 (3.6)                     | 1.06 (0.74-1.53)                     | .75                  |
| <16   | 8 (7.2)                          | 14 (12.1)                    | 1.67 (0.73-3.84)                     | .22                  |

Abbreviations: BMI, body mass index, calculated as weight in kilograms divided by height in meters squared; HIV, human immunodeficiency virus; RR, risk ratio.

<sup>a</sup>By  $\chi^2$  test.

<sup>b</sup>P values were calculated by test for interaction from the Wald test for risk-ratio homogeneity. Test for interaction by baseline BMI,  $P = .63$  for HIV disease progression or death from any cause;  $P = .14$  for death from any cause; and  $P = .32$  for AIDS-related death.

# Effect of High-Dose Multivitamins on Clinical and Laboratory Markers of Health Status

| Laboratory Outcomes              | Standard-Dose Regimen<br>(n = 1708) |   | High-Dose Regimen<br>(n = 1710)   |   | Mean Difference<br>(95% CI) <sup>b</sup>      | P<br>Value <sup>c</sup> |
|----------------------------------|-------------------------------------|---|-----------------------------------|---|---|-------------------------|
|                                  | No. of Patients<br>(Measurements)   | Mean (SD)                               | No. of Patients<br>(Measurements) | Mean (SD)                               |   |                         |
| CD4 count/ $\mu$ L               | 1394 (5221)                         | 324 (163)                               | 1374 (5215)                       | 312 (159)                               | -6 (-16 to 4)                                 | .18                     |
| Plasma viral load, log copies/mL | 109 (140)                           | 3.7 (1.2)                               | 127 (166)                         | 3.5 (1.2)                               | -0.1 (-0.4 to 0.3)                            | .66                     |
| BMI                              | 1602 (13 927)                       | 22.4 (5.7)                              | 1593 (13 655)                     | 22.2 (4.3)                              | 0.0 (-0.2 to 0.1)                             | .42                     |
| Hemoglobin, g/dL                 | 1467 (5844)                         | 11.0 (1.9)                              | 1468 (5866)                       | 11.1 (1.9)                              | -0.1 (-0.2 to 0.0)                            | .26                     |
| Clinical Outcomes                | No. of Patients<br>(Measurements)   | Events per<br>Person-Years <sup>d</sup> | No. of Patients<br>(Measurements) | Events per<br>Person-Years <sup>d</sup> | Incidence Rate Ratio<br>(95% CI) <sup>e</sup> | P<br>Value <sup>e</sup> |
| Fatigue                          | 1581 (24 392)                       | 1175 per 1854                           | 1596 (24 196)                     | 1115 per 1835                           | 0.95 (0.85 to 1.07)                           | .43                     |
| Nausea or vomiting               | 1581 (24 392)                       | 744 per 1854                            | 1596 (24 196)                     | 729 per 1853                            | 0.99 (0.87 to 1.14)                           | .90                     |
| Diarrhea                         | 1581 (24 392)                       | 709 per 1854                            | 1596 (24 196)                     | 657 per 1835                            | 0.92 (0.80 to 1.07)                           | .29                     |
| Severe anemia                    | 1530 (6057)                         | 612 per 1616                            | 1544 (6112)                       | 581 per 1615                            | 0.82 (0.60 to 1.12)                           | .22                     |
| Rashes or lesions                | 1581 (24 392)                       | 3529 per 1854                           | 1596 (24 196)                     | 3446 per 1835                           | 1.00 (0.91 to 1.10)                           | .98                     |
| Neuropathy                       | 1255 (19 129)                       | 1365 per 1450                           | 1310 (19 802)                     | 1213 per 1503                           | 0.81 (0.70 to 0.94)                           | .004                    |
| Genital discharge or sores       | 1581 (24 392)                       | 305 per 1854                            | 1596 (24 196)                     | 293 per 1835                            | 0.92 (0.75 to 1.13)                           | .44                     |
| ALT >40 IU/L                     | 1468 (5383)                         | 879 per 1236                            | 1453 (5387)                       | 1239 per 1215                           | 1.44 (1.11 to 1.87)                           | .006                    |
| ALT >200 IU/L                    | 1468 (5383)                         | 25 per 1236                             | 1453 (5387)                       | 41 per 1215                             | 1.12 (0.50 to 2.50)                           | .79                     |

Abbreviations: ALT, alanine aminotransferase; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared).

<sup>a</sup>Venous blood samples were collected for determination of CD4 count and complete blood cell count every 4 months. Anthropometry and the incidence of clinical complications were assessed on a monthly basis. Viral load was to be assessed at enrollment and every 4 months thereafter, subject to the availability of reagents. The number of patients and available measurements contributing to generalized estimating equation (GEE) analysis in parentheses are shown. Data are the means (SDs) of measurements during follow-up. Severe anemia is defined as hemoglobin level of less than 8.5 g/dL.

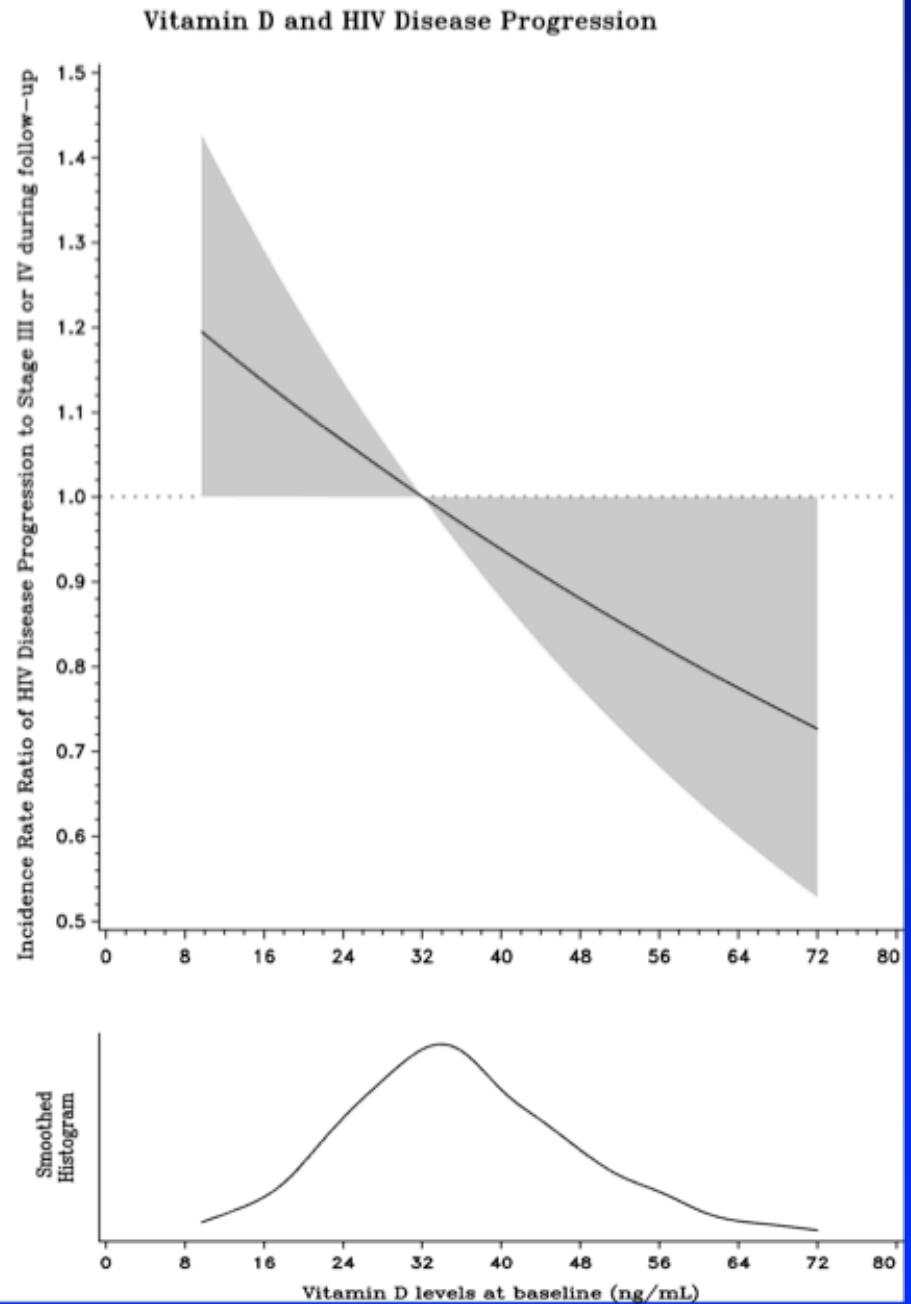
<sup>b</sup>Data are the mean difference between the high-dose group and the standard-dose group. The mean differences (95% CIs) are from GEEs using the identity link and Gaussian variance function with the difference between baseline and postrandomization measures as the outcome and study regimen as the exposure.

<sup>c</sup>From a GEE for parallel-group designs.<sup>30</sup>

<sup>d</sup>Number of events is based on the occurrence of clinical and laboratory complications reported during the month before each study visit or diagnosed at the study visit over follow-up time. Person-years is based on the follow-up time contributed by each patient from enrollment until the last study visit.

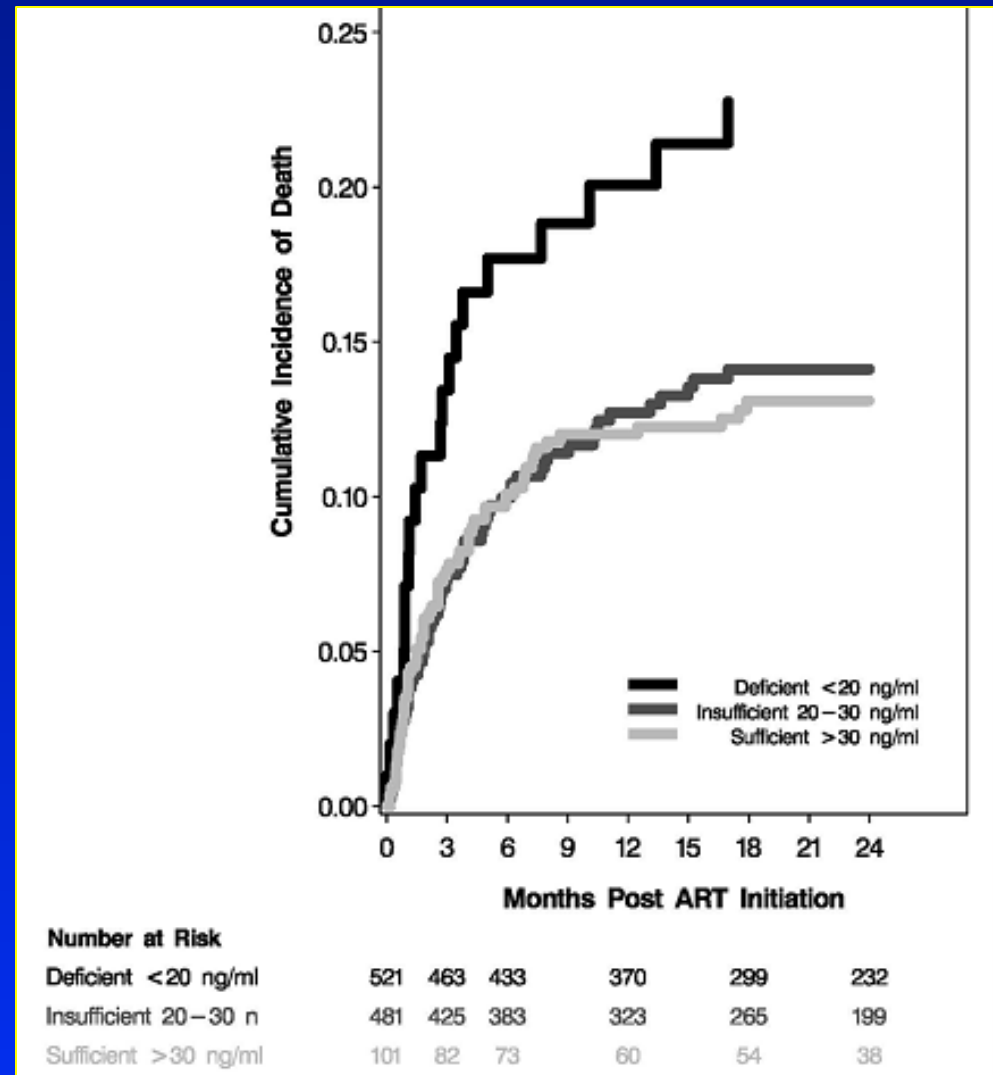
<sup>e</sup>The incidence rate ratios, 95% CIs, and corresponding P values are from GEEs using the log link and Poisson variance function.

# Vitamin D and Disease Progression among Tanzanian Women Pre-HAAART





# Vitamin D status of HIV-infected Adults and All-cause Mortality among Tanzanian Adults Initiating HAART





**TABLE 7**  
**Energy cost of lactation**

| Stage postpartum   | Breast-milk production | Energy content of milk* | Energy cost of lactation† |
|--------------------|------------------------|-------------------------|---------------------------|
| <i>mo</i>          | <i>g/d</i>             | <i>kcal/d</i>           |                           |
| 2 ( <i>n</i> = 40) | 745                    | 520                     | 650                       |
| 1 ( <i>n</i> = 16) | 692                    | 485                     | 605                       |
| 2 ( <i>n</i> = 16) | 718                    | 505                     | 630                       |
| 3 ( <i>n</i> = 16) | 746                    | 520                     | 655                       |
| 6 ( <i>n</i> = 16) | 573                    | 400                     | 500                       |

\* Take as 0.70 kcal/g (1).

† Assumed efficiency of conversion 80% (1).

Figure 2. Maternal MUAC and risk of maternal mortality among HIV-infected pregnant women

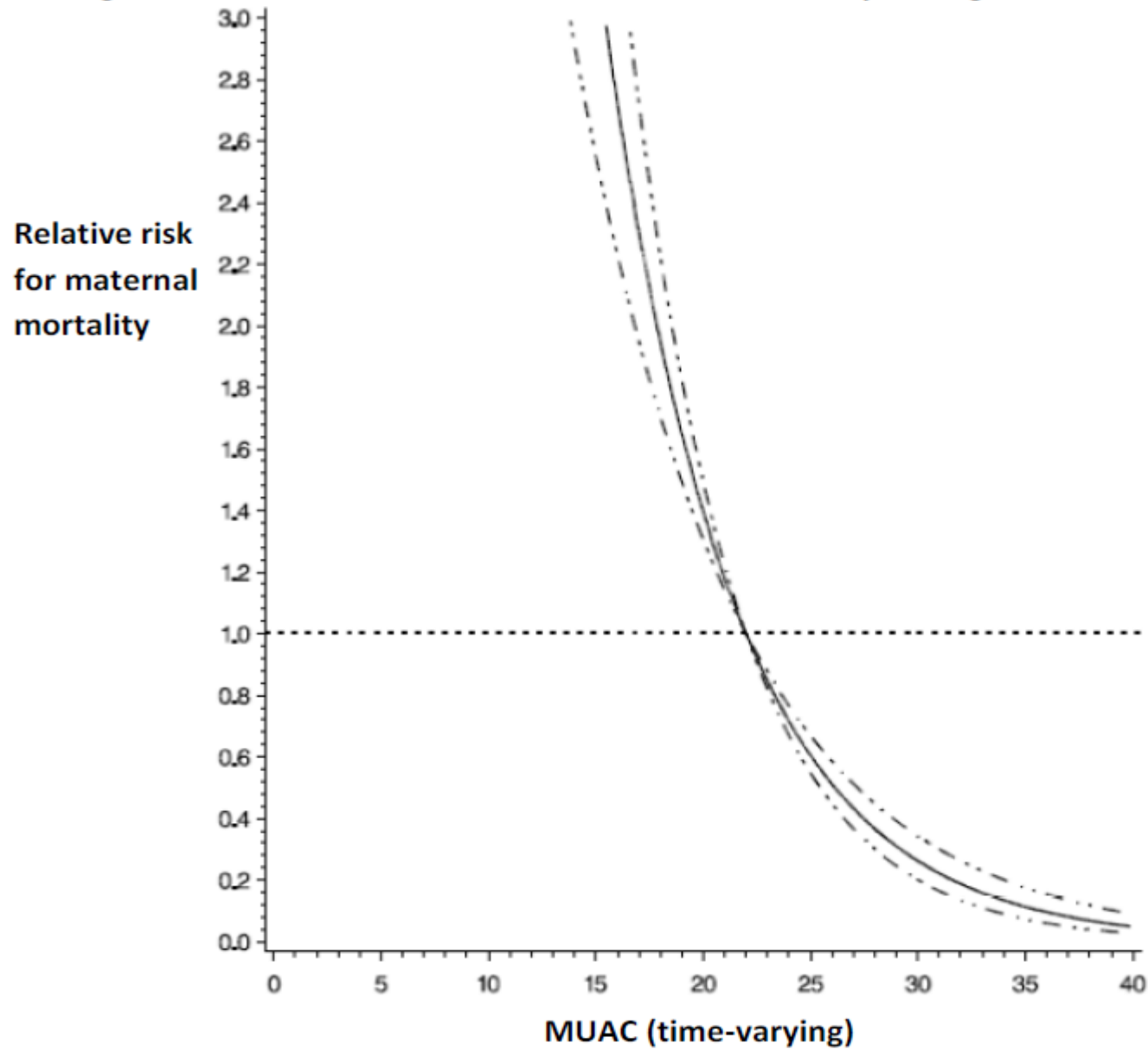




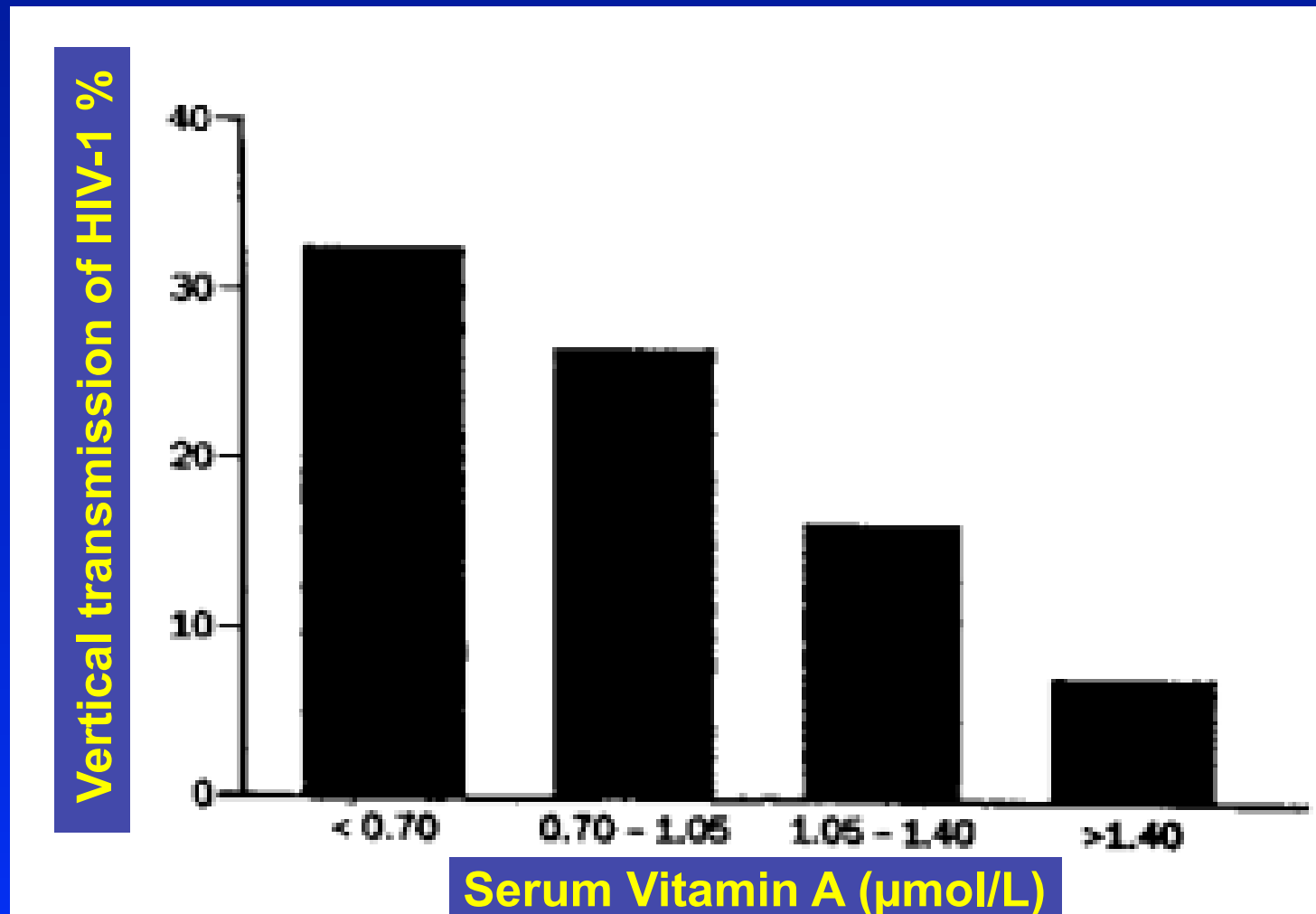
TABLE 3

Mother-to-child transmission of HIV by maternal BMI and hemoglobin at enrollment and weight change during pregnancy<sup>1</sup>

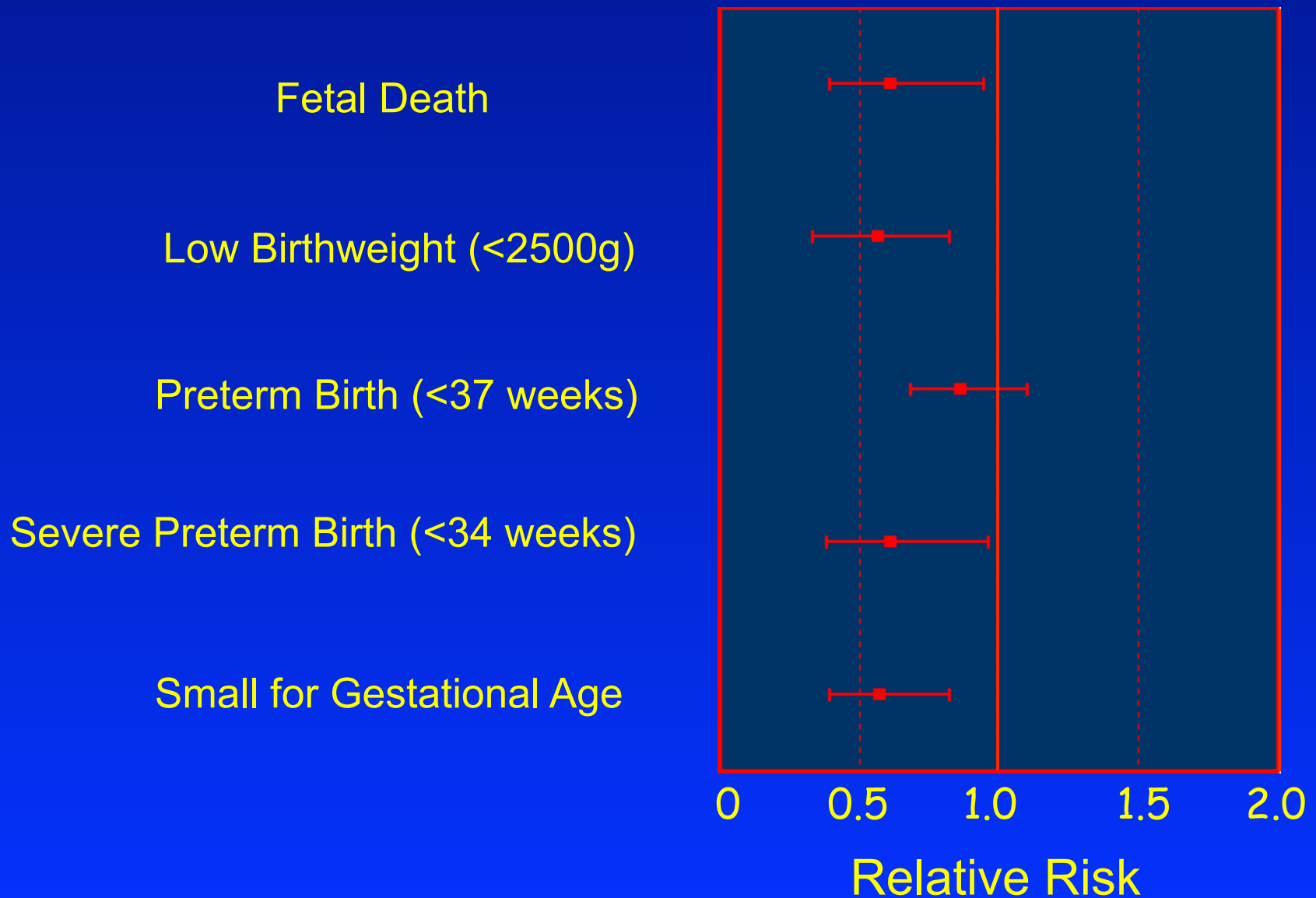
| Time of HIV infection                  | BMI at enrollment (kg/m <sup>2</sup> ) |                        |                    | Hemoglobin at enrollment (g/dL) |                      |                  | Weight change during pregnancy (kg) |                              |                                 |                               |
|--|--|------------------------|--------------------|---------------------------------|----------------------|------------------|-------------------------------------|------------------------------|---------------------------------|-------------------------------|
|  | <21.8<br>(n = 654)                     | 21.8–23.9<br>(n = 652) | ≥24.0<br>(n = 671) | <8.5<br>(n = 230)               | 8.5–11<br>(n = 1191) | ≥11<br>(n = 532) | Weight loss<br>(n = 310)            | Low weight gain<br>(n = 434) | Normal weight gain<br>(n = 806) | High weight gain<br>(n = 367) |
| Birth                                  |  |                        |                    |                                 |                      |                  |                                     |                              |                                 |                               |
| Probability of HIV+                    | 0.08                                   | 0.09                   | 0.06               | 0.13                            | 0.09                 | 0.05             | 0.09                                | 0.08                         | 0.07                            | 0.11                          |
| 95% CI                                 | (0.06, 0.10)                           | (0.08, 0.11)           | (0.04, 0.08)       | (0.09, 0.17)                    | (0.07, 0.10)         | (0.03, 0.07)     | (0.06, 0.12)                        | (0.05, 0.10)                 | (0.05, 0.09)                    | (0.08, 0.15)                  |
| 4–6 wk (among those negative at birth) |  |                        |                    |                                 |                      |                  |                                     |                              |                                 |                               |
| Probability of HIV+                    | 0.10                                   | 0.08                   | 0.06               | 0.17                            | 0.08                 | 0.04             | 0.10                                | 0.06                         | 0.08                            | 0.08                          |
| 95% CI                                 | (0.07, 0.12)                           | (0.07, 0.10)           | (0.04, 0.08)       | (0.12, 0.23)                    | (0.07, 0.10)         | (0.02, 0.06)     | (0.06, 0.14)                        | (0.04, 0.09)                 | (0.06, 0.10)                    | (0.05, 0.11)                  |
| 4–6 wk                                 |  |                        |                    |                                 |                      |                  |                                     |                              |                                 |                               |
| Probability of HIV+                    | 0.17                                   | 0.17                   | 0.12               | 0.28                            | 0.16                 | 0.09             | 0.18                                | 0.14                         | 0.15                            | 0.18                          |
| 95% CI                                 | (0.14, 0.20)                           | (0.15, 0.19)           | (0.09, 0.14)       | (0.22, 0.34)                    | (0.14, 0.18)         | (0.07, 0.12)     | (0.14, 0.22)                        | (0.10, 0.17)                 | (0.12, 0.17)                    | (0.14, 0.22)                  |

<sup>1</sup> Estimates obtained from univariate censored multinomial models for HIV infection.

# Maternal vitamin A levels and mother-to-child transmission of HIV-1



# Effect of Multivitamins on Pregnancy Outcomes



# Effect of Vitamin A on Pregnancy Outcomes

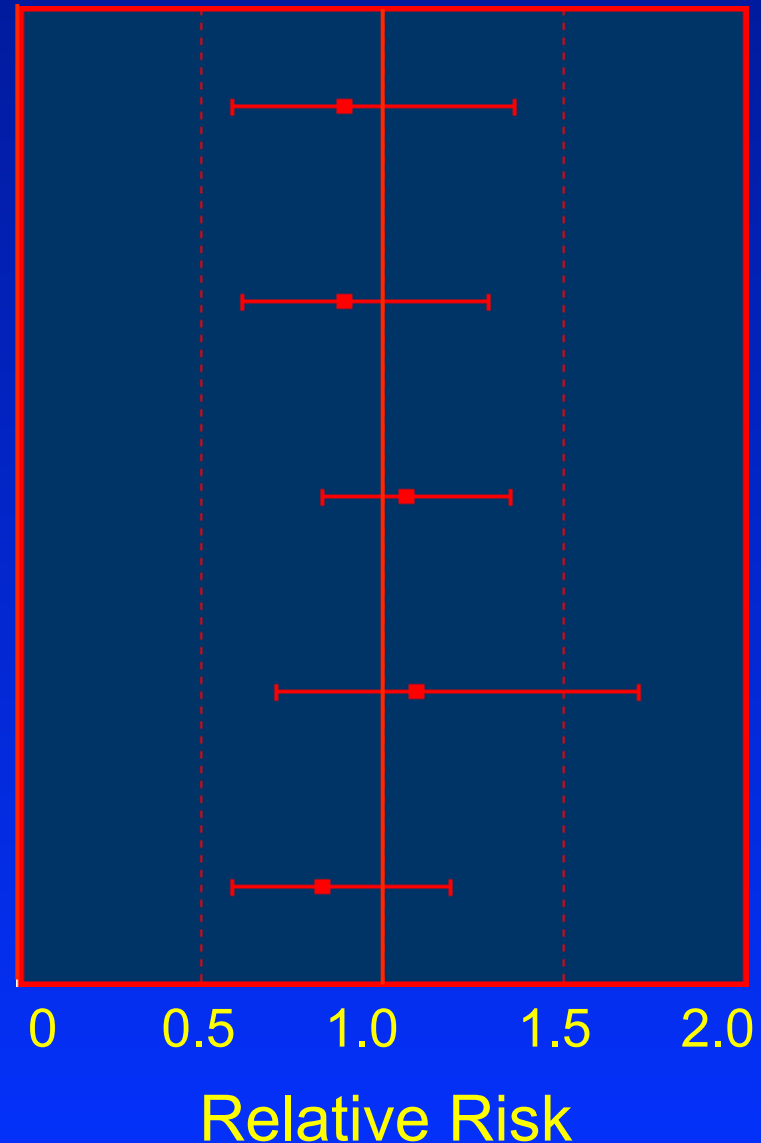
Fetal Death

Low Birthweight (<2500g)

Preterm Birth (<37 weeks)

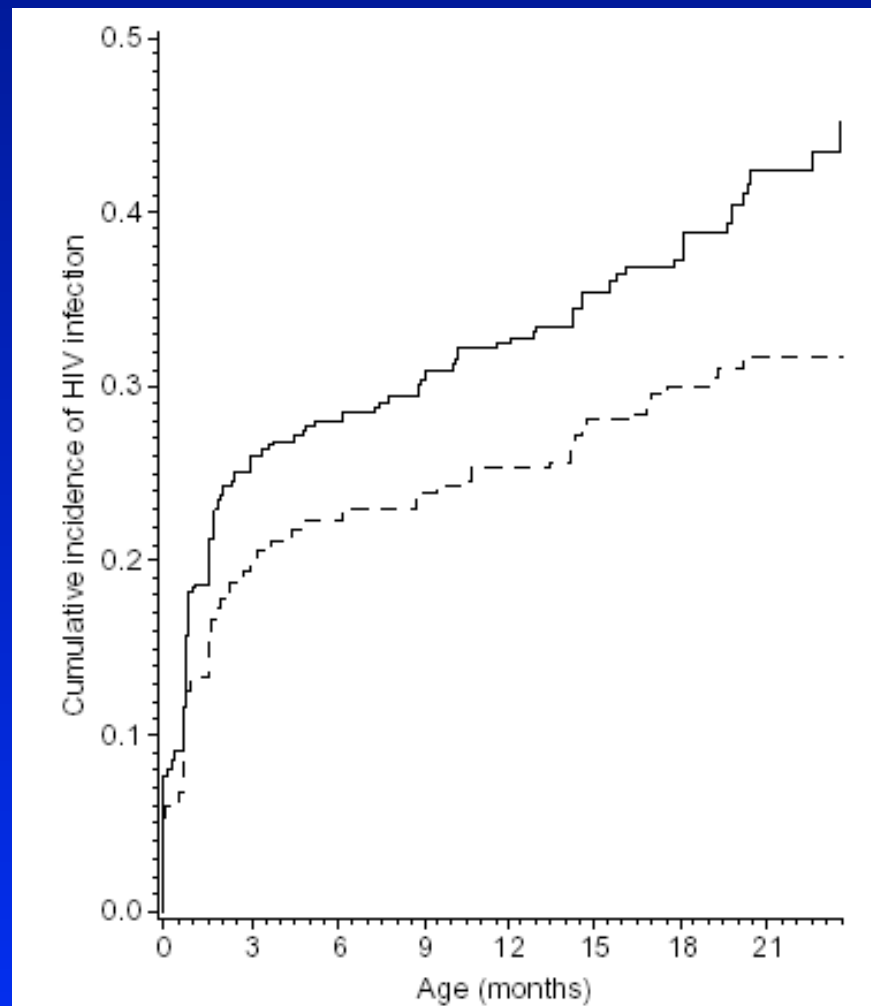
Severe Preterm Birth (<34 weeks)

Small for Gestational Age





# Effect of vitamin A supplementation on HIV infection of offspring



**Fig. 1.** Incidence of HIV infection in children by vitamin A regimen of mother. Regimen of mother: — vitamin A; --- no vitamin A.

# Vitamin A trial among HIV-infected women in Zimbabwe

- Examined efficacy of a single large dose of vitamin A given to women in the early postpartum period (400,000 IU) and/or to neonates (50,000 IU)
- 2 by 2 factorial design
  - Aa (maternal and infant vitamin A supplementation)
  - Ap (maternal vitamin A and infant placebo)
  - Pa (maternal placebo and infant vitamin A)
  - Pp (maternal and infant placebo)

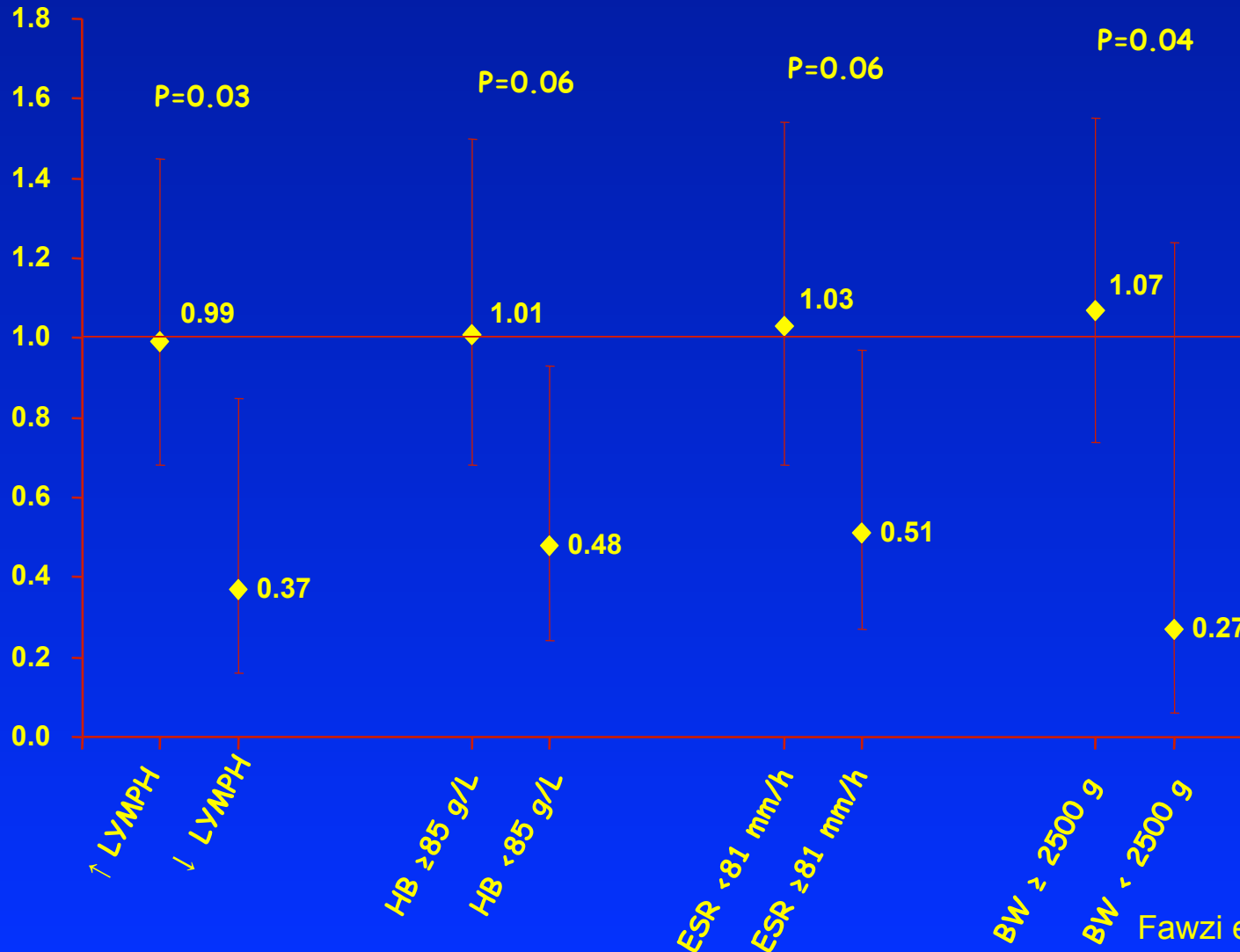
Among the majority of infants, namely those who were PCR negative at 6 weeks, all three vitamin A regimens were significantly associated with an ~2-fold higher mortality

**Table 8. Adjusted child mortality risk, by vitamin A treatment group and infant HIV infection group.**

| Vitamin A treatment group                                      | PCR positive at baseline<br>( <i>n</i> = 381; 228 deaths) |          | PCR negative at baseline<br>and PCR positive<br>at 6 weeks<br>( <i>n</i> = 504; 285 deaths) |          | PCR negative at baseline<br>and at 6 weeks<br>( <i>n</i> = 2876; 115 deaths) |          |
|--|---|----------|---|----------|--|----------|
|  | HR (95% CI)   | <i>P</i> | HR (95% CI)   | <i>P</i> | HR (95% CI)  | <i>P</i> |
| Aa vs. Pp  | 1.04 (0.69–1.56)  | .87      | 0.75 (0.51–1.10)  | .14      | 2.05 (1.14–3.67)   | .02      |
| Ap vs. Pp  | 0.89 (0.60–1.31)  | .55      | 1.08 (0.76–1.53)  | .66      | 1.82 (0.99–3.31)   | .05      |
| Pa vs. Pp  | 0.88 (0.58–1.32)  | .53      | 0.74 (0.52–1.05)  | .09      | 1.89 (1.05–3.40)   | .03      |
| Maternal vitamin A (Aa + Ap)<br>vs. maternal placebo (Pa + Pp) | 1.06 (0.81–1.40)  | .67      | 1.09 (0.85–1.41)  | .49      | 1.33 (0.92–1.92)   | .14      |
| Infant vitamin A (Aa + Pa)<br>vs. infant placebo (Ap + Pp)     | 1.00 (0.76–1.32)  | .99      | 0.72 (0.57–0.92)  | .01      | 1.41 (0.97–2.05)   | .07      |

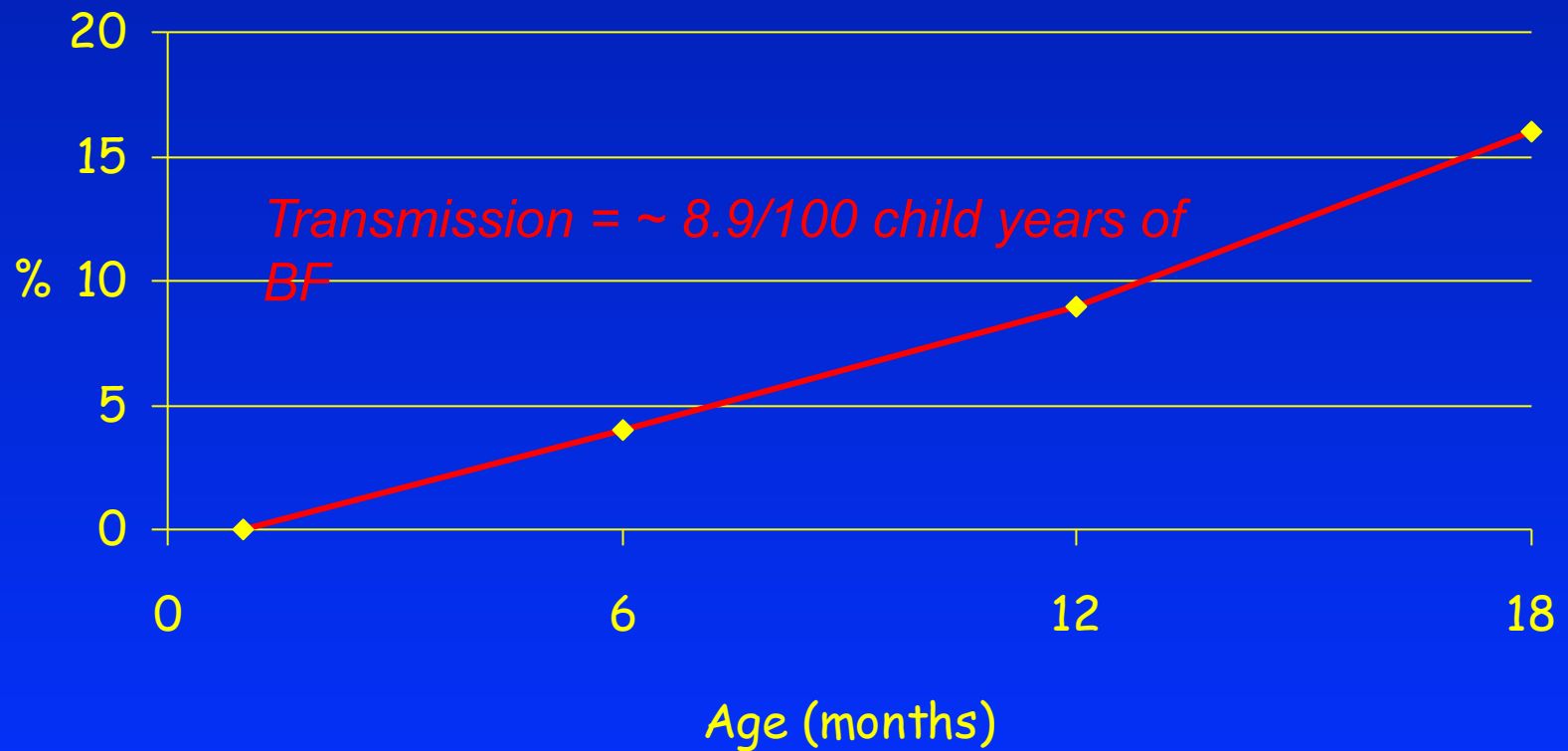
# Multivitamins reduced risk of infection through breastfeeding in population subgroups

RELATIVE RISK



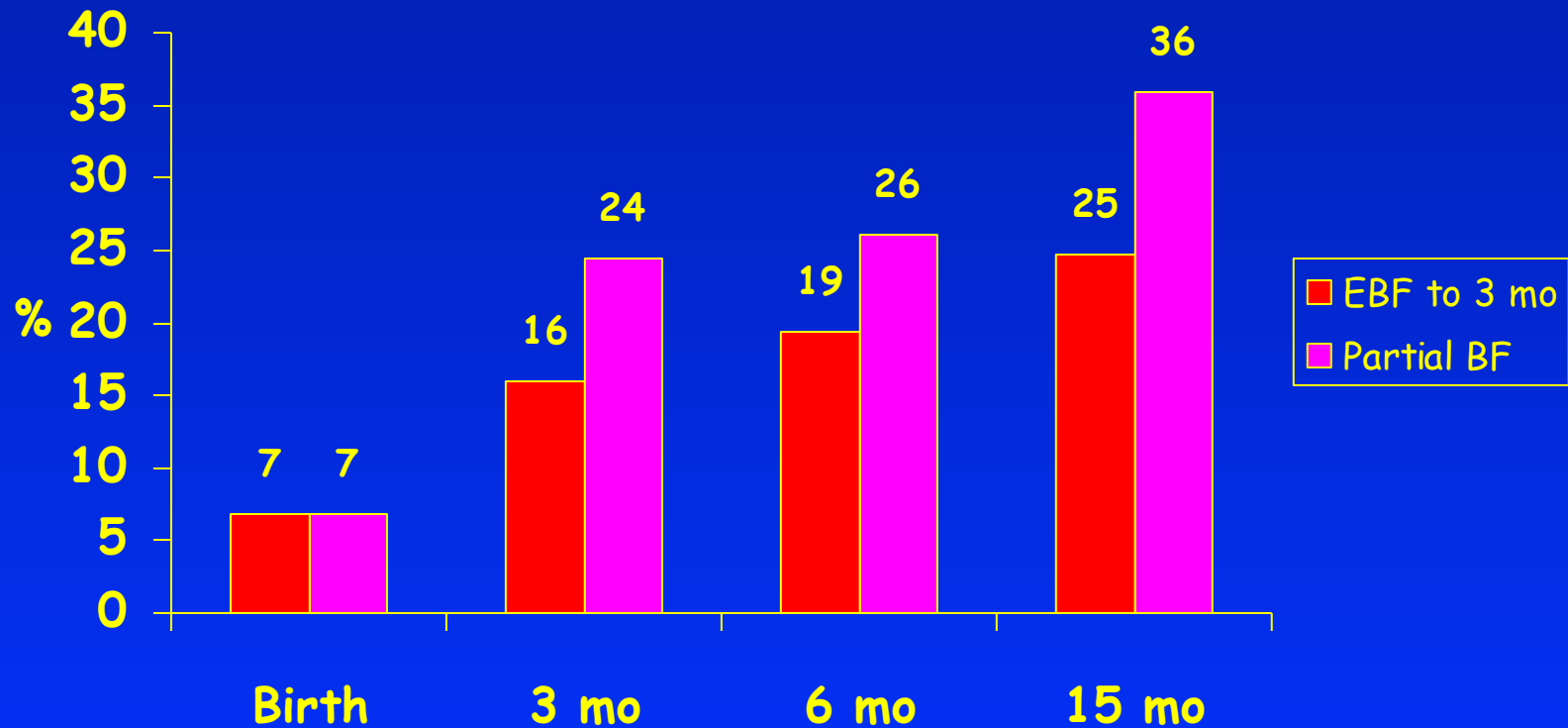
# Duration of breastfeeding BHITS meta-analysis

Risk of PNT is cumulative and relatively constant over time



# Mixed breastfeeding

Cumulative HIV transmission Durban, SA



**Table 6 Effect of maternal supplementation on growth of the breastfed infant**

| Growth and development parameters        |          | Breastfeeding control (n = 63) | Breastfeeding supplemented (n = 66) | p value for the difference between the groups (95% CI of the difference) | *Adjusted p value for the difference between the groups (95% CI of the difference) |
|--|----------|--------------------------------|-------------------------------------|--|--|
| Weight/age z scores Mean (SD)            | 14 weeks | 0.44 (1.03)                    | 0.06 (1.09)                         | 0.058 (-0.01, 0.77)  | 0.455 (-1.52, 0.68)  |
|  | 6 months | 0.61 (1.17)                    | 0.15 (1.13)                         | 0.035 (0.03, 0.88)   |  |
|  | 9 months | 0.65 (1.16)                    | 0.28 (1.15)                         | 0.098 (-0.07, 0.82)  |  |
| Length/age z score Mean (SD)             | 14 weeks | -0.59 (1.08)                   | -0.48 (1.12)                        | 0.613 (-0.51, 0.3)   | 0.891 (-1.29, 1.12)  |
|  | 6 months | -0.35 (1.03)                   | -0.47 (1.24)                        | 0.574 (-0.3, 0.54)   |  |
|  | 9 months | 0.39 (1.14)                    | 0.41 (1.17)                         | 0.899 (-0.42, 0.47)  |  |
| Head circumference/age z score Mean (SD) | 14 weeks | 0.50 (1.07)                    | 0.73 (1.1)                          | 0.249 (-0.63, 0.17)  | 0.247 (-1.45, 0.37)  |
|  | 6 months | 0.42 (1.19)                    | 0.66 (1.03)                         | 0.267 (-0.64, 0.18)  |  |
|  | 9 months | 0.51 (1.02)                    | 0.68 (1.01)                         | 0.368 (-0.57, 0.21)  |  |

Kindra G, Coutsoydis A, Esposito F. Effect of nutritional supplementation of breastfeeding HIV positive mothers on maternal and child health: findings from a randomized controlled clinical trial. *BMC Public Health*. 2011;11:946.

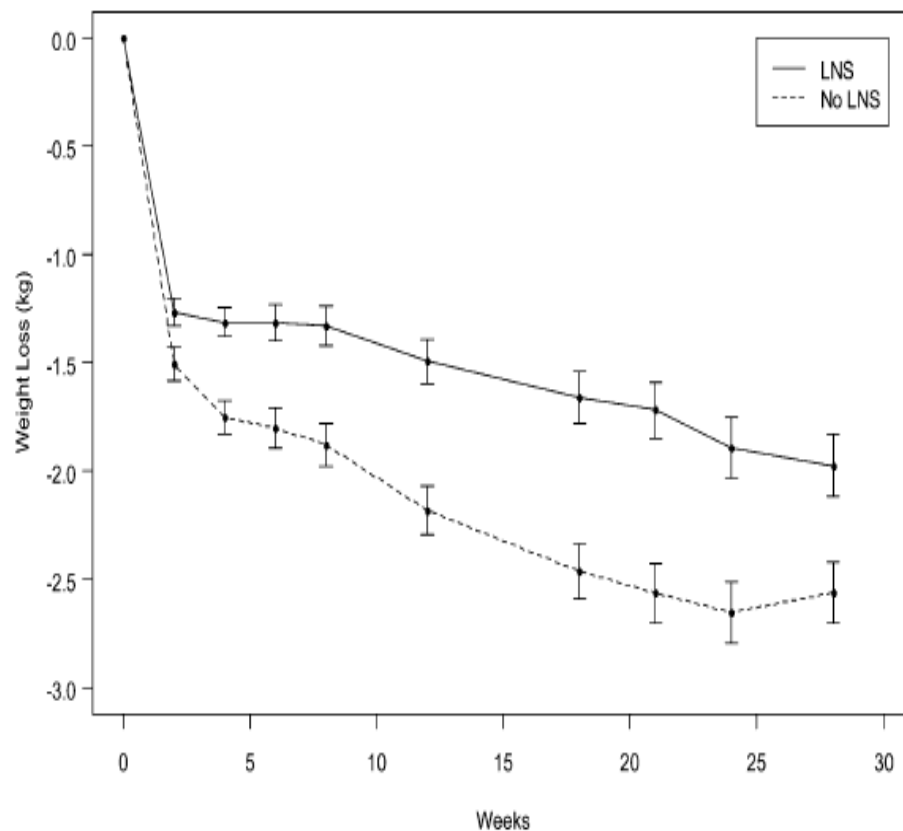


FIGURE 2. Mean ( $\pm$ SE) cumulative maternal weight loss by random assignment to the LNS and weeks since delivery among BAN Study participants. The mean ( $\pm$ SE) weight loss was calculated from delivery cumulatively at each visit and includes data for all women with at least one weight measurement ( $n = 1182$  in the LNS intervention arm,  $n = 1181$  in the control arm). BAN, Breastfeeding, Antiretroviral, and Nutrition; LNS, lipid-based nutrient supplement.

Kayira D, Bentley ME, Wiener J, et al. A lipid-based nutrient supplement mitigates weight loss among HIV-infected women in a factorial randomized trial to prevent mother-to-child transmission during exclusive breastfeeding. *Am J Clin Nutr.* Mar 2012;95(3):759-765



# Nutrition Management of HIV-infected Women of Reproductive Age

An Integrated Approach

# Integrated maternal, newborn, and child health packages

