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Multivitamin supplementation in HIV-positive pregnant women: impact on depression and quality of life in a resource-poor setting

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Abstract

Objectives—The primary objective of this study was to examine the effect of vitamin supplementation on health-related quality of life and the risk of elevated depressive symptoms comparable to major depressive disorder (MDD) in HIV-positive pregnant women in Dar es Salaam, Tanzania.

Methods—From April 1995 to July 1997, 1078 HIV-positive pregnant women were enrolled in a randomized controlled trial. We examined the effects of vitamin supplementation on quality of life and the risk of elevated depressive symptoms, assessed longitudinally every 6–12 months.

Results—A substantial prevalence of elevated depressive symptoms (42%) was observed in HIV-positive pregnant women. Multivitamin supplementation (B-complex, C and E) demonstrated a protective effect on depression [relative risk (RR) = 0.78; $P = 0.005$] and quality of life [RR = 0.72 for social functioning ($P = 0.001$) and vitality ($P = 0.0001$); RR = 0.70 for role-physical ($P = 0.002$)]; however, vitamin A showed no effect on these outcomes.

Conclusions—Multivitamin supplementation (B-complex, C and E) resulted in a reduction in risk of elevated depressive symptoms comparable to MDD and improvement in quality of life in HIV-positive pregnant women in Tanzania.

Keywords

depression; HIV; quality of life; Tanzania; vitamin supplementation

Introduction

Of the 38.6 million individuals with HIV infection worldwide, approximately 64% (24.5 million) are from sub-Saharan Africa [1]. Despite the fact that sub-Saharan Africa bears the largest burden of HIV infection, access to antiretroviral (ARV) therapy for HIV remains limited, with only 310 000 patients receiving treatment by the end of 2004 [2]. This has resulted in dramatic decreases in life expectancy in some sub-Saharan African countries [3], largely as a result of premature mortality from untreated HIV infection. Limited access to ARV therapy has also resulted in excess morbidity from opportunistic infections as well as transmission of HIV, including mother-to-child transmission [2].

Given the excess morbidity and mortality related to HIV infection in resource-poor settings, there is a great need to identify strategies to improve the quality of life and related psychosocial outcomes of HIV-infected patients. Major depression has been shown to be highly prevalent among HIV-positive individuals [4–6] and has been associated with significant reductions in quality of life for these patients [7–13]. In addition, levels of depression or depressive symptoms have been shown to be elevated in HIV-positive as well as HIV-negative pregnant women accessing prenatal, prevention of mother-to-child transmission (PMTCT), or other healthcare services [14–17]. Some micronutrients, in particular the B-complex vitamins, have demonstrated a protective effect on depression; however, the studies in which these findings were obtained were largely cross-sectional and performed in HIV-negative populations [18–22].

Multivitamin supplementation (vitamins B-complex, C and E) has shown a protective effect on disease progression and HIV-related mortality in HIV-positive pregnant women in Dar es Salaam, Tanzania [23]. Provision of the multivitamins at the doses described in that trial may delay the need for antiretrovirals (ARVs), prolonging the ‘healthy’ phase of HIV disease. Promoting pre-ARV therapy, such as chemoprophylaxis, multivitamins and early treatment of opportunistic infections, can also increase access to services for HIV-infected individuals, increasing the likelihood that those individuals may later benefit from the mobilization of resources aimed at expanding access to ARVs in resource-poor settings.

If vitamin supplementation can reduce the burden of depression and improve quality of life in HIV-positive patients, it may also serve as an adjunctive therapy when ARVs are indicated. Given the protective effect of vitamin supplementation on HIV disease progression and mortality [23], the goal of the present analysis was to examine in the same study population the effect of these supplements on depression and health-related quality of life outcomes in HIV-positive pregnant women in Tanzania.

Methods

Study population and design

The study design was a double-blind, placebo-controlled trial to examine the effects of daily supplements of vitamin A (preformed vitamin A and beta carotene) and multivitamins (vitamins B-complex, C and E) on HIV-related outcomes, including perinatal transmission,

disease progression, and other health outcomes. Pregnant women were counselled and tested for HIV and informed of their test results at selected health centres in Dar es Salaam. Women who were HIV-positive, resided in Dar es Salaam, were at 12–27 weeks' gestation, and intended to stay in the city until at least 1 year after delivery were invited to enrol in the randomized controlled trial. From April 1995 to July 1997, 1078 HIV-positive pregnant women were enrolled in the trial. Women were randomly assigned to one of four arms based on a 2×2 factorial design: vitamin A alone (30 mg of beta carotene plus 5000 IU of preformed vitamin A); multivitamins excluding vitamin A (20 mg of B₁, 20 mg of B₂, 25 mg of B₆, 100 mg of niacin, 50 mg of B₁₂, 500 mg of C, 30 mg of vitamin E and 0.8 mg of folic acid); multivitamins plus vitamin A in the same doses above; or placebo. Women in the two groups that received vitamin A were given an additional oral dose of 200 000 IU of vitamin A at delivery; a placebo was given to the women at delivery for the other two groups. Study participants were followed monthly, and later quarterly, until August 2003 for an average of 38.7 months (median 44.4 months; standard deviation 24.7 months). T-cell subsets (including CD4) were measured at enrolment and every 6 months using the FACScount and FACSCAN systems (Becton Dickinson, San Jose, CA, USA). HIV disease stage was assessed on a monthly basis according to World Health Organization (WHO) criteria [24]. More detailed description of the study design and recruitment process has been provided elsewhere by Fawzi *et al.* [25,26].

In addition to the HIV-related outcomes described above, a psychosocial assessment was performed throughout the follow-up period, starting with 2 months after enrolment on average (range 0.8–4 months), 2 months after delivery, every 6 months until 2001, and every 12 months thereafter. The mean number of psychosocial assessments was 6 (median 7; standard deviation 3.5). The psychosocial questionnaire assessed depression/anxiety symptoms; health-related quality of life; disability; HIV-related life events; perceived social support; and disclosure of HIV test result. Outcomes analysed for the current study included depression and health-related quality of life as described in more detail below.

Measures

Depressive symptoms—A validated subset of items from the Hopkins Symptom Checklist-25 (HSCL-25) was used to assess depressive symptoms comparable to major depressive disorder (MDD). The original scale included a 10-item anxiety scale and a 15-item depression scale [27]. The HSCL was validated in Tanzania to identify MDD in the study population. Kaaya *et al.* [28] developed a subscale that included eight of the original 25 items. This subscale demonstrated a sensitivity of 88% and a specificity of 89% for detecting MDD according to diagnostic and statistical manual of mental disorders, 4th edition (DSM-IV) criteria and included the following symptoms: feeling sad; feeling trapped or caught; difficulty falling asleep, staying asleep; worrying too much about things; heart pounding or racing; feeling hopeless about the future; faintness, dizziness or weakness; and crying easily. Each symptom was scored by severity, ranging from '1 = not at all' to '4 = extremely', and the overall scale score was based on the total score divided by the number of items. Women who had an average symptom score that was greater than 1.06 on this subscale were classified as having a symptom level comparable to MDD based on results from the validation study by Kaaya *et al.* [28].

Health-related quality of life—The Medical Outcomes Study Short Form-36 (SF-36) was used to assess health-related quality of life. The SF-36 has been used in a wide variety of settings in individuals suffering from a broad range of conditions, such as heart disease, diabetes and depression, as well as other illnesses [29]. The SF-36 has also been validated in a representative urban population in Tanzania [30]. Among adults in Dar es Salaam, Tanzania, individuals who were ‘healthy’ demonstrated significantly higher health-related quality of life scores compared with those who were ill or disabled [30]. This finding was observed for all eight dimensions of health-related quality of life that were included in the current analysis: physical functioning; role-physical; bodily pain; general health; vitality; social functioning; role-emotional; and mental health. We used the 25th percentile of these eight continuous subscales as the cut-off to define ‘poor’ health-related quality of life.

Statistical analysis

We compared characteristics at the time of enrolment for women on different regimens (i.e. multivitamins vs no multivitamins and vitamin A vs no vitamin A), including women’s age, education, HIV disease stage and CD4 count, using the GLM procedure of Statistical Analysis Software (SAS; SAS Institute, Cary, NC, USA) for continuous variables and the χ^2 test for categorical variables ($n = 1013$). The percentages or mean scores of the depressive symptoms and health-related quality of life variables at first psychosocial assessment were calculated for 912 study participants who had this first assessment performed 2 months after enrolment on average. We also calculated the percentages and means for these psychosocial variables, stratifying by regimen status; *P*-values were generated for continuous and categorical variables based on the same procedures described above.

We assessed the effects of vitamin regimens on a level of depressive symptoms comparable to MDD and health-related quality of life by comparing the effect of multivitamins with no multivitamins as well as vitamin A with no vitamin A, given the factorial design of the trial; an ‘intent to treat’ analysis was performed. Generalized estimating equations (GEEs) [31] were employed with the GENMOD procedure of SAS statistical software. Exchangeable working covariance structure and a working binomial distribution were used. These associations were examined longitudinally, allowing for the examination of the incidence of elevated depressive symptom levels as well as ‘poor’ health-related quality of life during the follow-up period. We checked for interactions between multivitamins and vitamin A, and the modifiers of the regimens by baseline characteristics, including CD4 count, CD8 count, HIV disease stage, mid-upper arm circumference, total lymphocyte count, plasma vitamin A and E concentrations, haemoglobin concentration, viral load, social support, and participation in counselling (group and/or individual).

Results

Of 1078 women in the study, a total of 1013 had at least one psychosocial assessment and 912 had their first assessment 2 months after enrolment on average. The mean age of the HIV-positive pregnant women with at least one psychosocial assessment ($n = 1013$) was 25 years at baseline, with minimal variability by the multivitamins or vitamin A regimens (Table 1). In terms of other factors assessed at baseline, there were no statistically significant

differences between the multivitamins and no multivitamins groups or between the vitamin A and no vitamin A groups; these factors included education, WHO disease stage, and CD4 count. The majority of HIV-positive women at baseline were at stage 1 of HIV disease (ranging from 80.1 to 82.2%) and had CD4 counts of 200 cells/ μ L or greater (ranging from 86.5 to 87.9%) (Table 1).

Given that the 1013 women with at least one psychosocial assessment were a subset of the 1078 women, we compared sociodemographic variables and other characteristics at baseline for the 1013 women with those for the remaining 65 who did not have at least one psychosocial assessment. The groups were comparable with respect to level of education. The difference for age was small and marginally significant (24.7 years vs 23.5 years; $P=0.05$), with the 65 women younger on average. Also, the 65 women had a higher mean CD4 count ($P=0.007$), and a greater proportion of these women were at HIV WHO stage 2 or higher ($P=0.03$).

Table 2 shows data for the first psychosocial assessment performed 2 months after enrolment on average ($n=912$). There was a fairly high burden of depressive symptoms comparable to MDD in this population (42.4%). However, mean scores for the eight dimensions of health-related quality of life were fairly good, with the physical functioning subscale demonstrating the highest score (94.2), followed by social functioning (93.1), mental health (90.6), and role-emotional (89.3). General health demonstrated the lowest overall score (80.8) in this population of HIV-positive pregnant women. For depressive symptoms, there were no significant differences at first assessment between the multivitamins and the no multivitamins groups or between the vitamin A and no vitamin A groups. Health-related quality of life scores were higher for the multivitamins group compared with the no multivitamins group; however, no differences in health-related quality of life were observed for the vitamin A vs no vitamin A groups.

In examining the effect of vitamin supplementation on a level of symptoms comparable to MDD and health-related quality of life, it was found that the multivitamin supplement demonstrated a reduced incidence of elevated depressive symptoms [relative risk (RR) 0.78; 95% confidence interval (CI) 0.66, 0.92]. A similar pattern was observed for health-related quality of life, in which the multivitamins had a protective effect with respect to reduced incidence of poor health-related quality of life (Table 3). The strongest protective effects were observed for the role-physical (RR 0.70; 95% CI 0.57, 0.88), vitality (RR 0.72; 95% CI 0.61, 0.84), and social functioning (RR 0.72; 95% CI 0.59, 0.88) dimensions of health-related quality of life. No associations between the vitamin A supplement and depressive symptoms or health-related quality of life were observed and no interactions between the multivitamins and vitamin A were demonstrated. In addition, for the effect of multivitamin supplements, we did not observe any effect modification by baseline characteristics, including CD4 count, HIV disease stage and haemoglobin concentration.

Discussion

The prevalence of a level of depressive symptoms comparable to MDD in our cohort of HIV-positive pregnant women was 42.4% at first psychosocial assessment. This finding is

consistent with those of other studies of HIV-positive women, which have demonstrated rates of major depression from 32 to 62% [4–6]. The level of depressive symptomatology in the present study was also comparable to that found in studies of HIV-positive and HIV-negative women accessing PMTCT services in South Africa (41%) [15] as well as HIV-positive women who had recently given birth in Thailand (43%) [32]. The results from the health-related quality of life subscale scores were either comparable to or higher than scores obtained from a random sample of adults from a large household survey conducted in Dar es Salaam, Tanzania (ranging from 62.9 to 93.8 vs 80.8 to 94.2 for the current study). It is important to note that the women in our study sample were primarily in the earlier stages of HIV disease and were younger on average than the study population included in the Dar es Salaam survey [30]. Asymptomatic HIV-infected patients in Venezuela demonstrated higher health-related quality of life scores compared with those with symptomatic HIV infection or AIDS [33]. The subscale scores of this asymptomatic HIV-positive study population from Venezuela were comparable to or lower than the mean scores presented by the current study population (ranging from 66.7 to 88.6) [33].

A number of studies have demonstrated an association between low levels of B vitamins and depressive symptoms or depression [18,19,21]. Clinical studies have shown systematically low folate levels in depressed patients [34–36]. In middle-aged men in Finland there was nearly a 50% increase in the risk of depression for those who were in the lowest tertile of folate intake compared with those in the highest tertile [18]. Similarly, in a study of the general US population (ages 15–39 years), folate levels were on average significantly lower in those who had major depression compared with those who were not depressed [37]. There is also some indication of an association between vitamin B₁₂ deficiency and depression [19,20]. Tiemeier *et al.* [19] reported that those with vitamin B₁₂ deficiency were nearly 70% more likely to have a depressive disorder compared with those without B₁₂ deficiency. Among HIV-positive and HIV-negative homosexual men, lower vitamin B₁₂ level was associated with depressive symptoms; this association was also observed for major depressive disorder in a multivariate logistic regression model [22]. For other B-complex vitamins (vitamins B₁, B₂ and B₆), Bell *et al.* [21] observed a trend towards a greater reduction in depressive symptoms and a larger increase in serum nortriptyline level for those patients who received the vitamin B complex [21].

Several possible mechanisms may explain the association between vitamin B₁₂, folate levels and depression. Both vitamin B₁₂ and folate are involved in methylation processes that can impact upon neurotransmitter metabolism [38]. The availability of a folate metabolite (5,6,7,8-tetrahydrobiopterin) affects the metabolism of serotonin (5-HT); low central nervous system concentrations of 5-HT have been linked to depressive illness [38]. Cerebral spinal fluid (CSF) 5-hydroxyindole acetic acid (5-HIAA), a metabolite of 5-HT, was lower in a group of depressed patients who were folate deficient compared with control patients with neurological disorders; interestingly, among depressed patients in the same study population, red cell folate was positively correlated with CSF 5-HIAA levels [35].

The association between low vitamin B₁₂ and folate levels and depression may also indicate the role of oxidative stress. Widner *et al.* [39] suggest that the relationship between reduced folate availability and disturbed monoamine metabolism that is found in depression may

manifest as elevated homocysteine levels, which can be linked through enhanced oxidative stress. Bottiglieri *et al.* [40] observed elevated levels of homocysteine in 52% of depressed inpatients studied; depressed patients also demonstrated a higher mean value of total plasma homocysteine compared with normal and neurological control groups. Among those with major depression, oxidative stress in red blood cell membranes and decreased antioxidant defences have also been observed [41,42].

In contrast to the B vitamins, there is limited empirical evidence to support the association between vitamins C and E and depression or depressive symptoms, despite the fact that they are also antioxidants. In a small placebo-controlled crossover trial ($n = 23$) in patients with mood disorders (major depression and bipolar illness), large doses of ascorbic acid (3g) were associated with a reduction in severity of depression compared with placebo [43]. Similarly, in case reports of four patients, provision of intravenous vitamin C resulted in a reduction of depressive symptoms [44]. Maes *et al.* [41] found that vitamin E level was significantly lower in depressed patients compared with healthy controls; however, among those who were depressed there was no association between vitamin E and severity of depressive symptoms [41]. In elderly people in Japan, a reduction of depressive symptoms was associated with an increase in alpha-tocopherol over a 4-year period, but this was observed only in men [45]. No association between vitamin E level and depressive symptoms was observed in a large cohort ($n = 3884$) of adults aged 60 years and older who participated in the population-based Rotterdam Study in the Netherlands [46].

In terms of quality of life, there are relatively few studies that have examined the association between vitamin supplementation and health-related quality of life. A randomized placebo-controlled study of the effects of vitamin B₁₂ was performed in individuals with elevated plasma methylmalonic acid in Denmark [47]. These authors found that only one of eight dimensions of health-related quality of life had improved with administration of vitamin B₁₂ (general health) in this population [47]. Similarly, in a trial of pravastatin and vitamin E, no significant changes on health-related quality of life scores were observed for vitamin E after 12 months of therapy [48]. Among patients with congestive heart failure who received vitamin E as part of a clinical trial, no changes in quality of life were observed after 12 weeks of treatment [49].

In the present study, multivitamin supplementation (vitamins B-complex, C and E) demonstrated a protective effect on the incidence of a level of depressive symptoms comparable to MDD and poor health-related quality of life in HIV-positive pregnant women in Dar es Salaam, Tanzania. There are a number of pathways in which this observation can be explained. First, based on the existing literature, it is possible that the folate and vitamin B₁₂ elements of the multivitamin had a protective effect on depressive symptoms in this population. For folate in particular, this association may have occurred through two possible mechanisms: increases in folate levels may have resulted in an increase in 5-HT/5-HIAA in this population; alternatively, the multivitamins may have resulted in a reduction in oxidative stress (Fig. 1). As indicated in the literature cited above [34,38,39,41,42], both of these mechanisms might account for the reduction in risk of depressive symptoms. Although the multivitamin supplementation may have directly impacted health-related quality of life, there is minimum prior evidence for this type of association. Therefore, it is more likely that

the reduction in depressive symptoms resulted in improvements in quality of life; the association between depression and quality of life has also been reported in a number of studies in HIV-positive individuals [7–13].

In addition, there is evidence that the multivitamin supplements reduced progression of HIV disease [23] and the risk of fetal loss, low birth weight, and severe preterm birth [50] among women in the present study population, which may also have resulted in an improvement in quality of life and a reduction in the risk of depressive symptoms in these HIV-positive pregnant women. Given the potential impact of depression on the immune system [51–53], some researchers have examined the association between depression and the progression of HIV disease. Whereas some studies have demonstrated a link between depression and HIV disease progression [5,54,55], others have not [56–58]. The association between depression and HIV disease progression is currently being analysed in the present study population. If such a relationship exists in the current study population, then a reduction in depression may have had an impact on the rate of progression of HIV disease.

There are a number of limitations in the present study. Firstly, given that the multivitamin supplement included vitamins B-complex, C and E, it is not possible to tease apart the effect of specific vitamins on the level of depressive symptoms and quality of life in this population. Although prior literature provides more support for the association between B-complex vitamins and depression, one cannot infer that association in a definitive manner from this study. Secondly, while we can present different potential mechanisms for the impact of the multivitamins on depression and quality of life, we are not able to provide a definitive interpretation. This is reflected in Fig. 1, where various explanations for this association are delineated. While it is difficult to tease apart depression from HIV-related symptoms, the confluence of the two is minimized in this study as only one of the eight items from the HSCL-revised scale can also serve as a somatic symptom of HIV disease (faintness, dizziness or weakness). Although diagnosis of MDD by a psychiatrist was not feasible for this large study, the validation substudy [28] provided data that allowed us to identify women who demonstrated a level of depressive symptoms comparable to major depression. While elevated levels of depressive symptoms have been documented in HIV-positive as well as HIV-negative pregnant women [14–17], as all of the women in the study were pregnant at the time of enrolment this should not pose a threat to internal validity. However, there are limitations in generalizability of these results to nonpregnant populations, although we anticipate that the results would be relevant for pregnant women in other resource-poor settings. Strengths of the study are the randomized controlled trial design to minimize the effects of confounding and bias and the longitudinal follow up which allowed examination of the direction of the relationship between vitamin supplementation and depression as well as health-related quality of life outcomes.

In conclusion, multivitamin supplementation (vitamins B-complex, C and E) but not supplementation with vitamin A resulted in a reduction in a level of depressive symptoms comparable to MDD and improvement in quality of life in HIV-positive pregnant women in Tanzania. This finding should be explored further, particularly in terms of the potential impact of multivitamin supplementation on depression in HIV-negative populations in Tanzania and other resource-limited settings. For HIV-positive populations, we recommend

providing multivitamin supplementation (vitamins B-complex, C and E) at the doses described in this study, given the observed reduction in risk of depressive symptoms and improvement in quality of life. For patients who require ARVs, multivitamin supplementation may serve as an adjunctive therapy to potentially enhance quality of life. In addition, reducing the risk of depression and improving quality of life among HIV-positive patients may positively impact utilization of ARVs. Cook *et al.* [59] observed that women with high levels of depressive symptoms and poor mental health quality of life were less likely to utilize highly active antiretroviral therapy (HAART) and those who received mental health services had increased probability of accessing HAART. This intervention has the capacity to prevent disease progression and mortality [23] and it has been demonstrated to reduce the burden of depression and improve quality of life in patients with HIV infection.

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Fig. 1.
Potential mechanisms for the effect of multivitamin supplementation on depressive symptoms and health-related quality of life.

Table 1Baseline characteristics of HIV-positive pregnant Tanzanian women (*n* = 1013)

Characteristics	Multivitamins		Vitamin A		<i>P</i> -value	<i>P</i> -value *
	Yes (<i>n</i> = 508)	No (<i>n</i> = 505)	Yes (<i>n</i> = 506)	No (<i>n</i> = 507)		
Age (years)	24.7 (4.7)	24.7 (4.9)	24.8 (4.8)	24.7 (4.7)	0.89	0.74
Education (%)					0.35	0.34
None or adult	8.9	7.5	7.3	9.1		
Primary 1–4 years	5.3	5.2	4.3	6.1		
Primary 5–8 years	74.0	78.4	77.1	75.3		
>8 years	11.8	8.9	11.3	9.5		
WHO disease stage (%)					0.21	0.20
1	81.9	80.4	80.1	82.2		
2	17.5	17.9	18.1	17.2		
3	0.6	1.7	1.8	0.6		
CD4 count (cells/ μ L) (%)					0.52	0.09
0–199	12.1	13.5	12.4	13.2		
200–349	24.0	26.2	28.2	21.9		
350	63.9	60.3	59.4	64.9		
CD4 count (cells/ μ L)	424 (201)	413 (199)	414 (202)	423 (197)	0.40	0.51

Values are given as the percentage or mean (with standard deviation).

* *P*-values were generated using the GLM procedure of SAS for continuous variables and the χ^2 test for categorical variables.

Table 2

Psychosocial characteristics of women at first psychosocial assessment (2 months after randomization on average; $n = 912$)

Outcome	Overall	Multivitamins			Vitamin A		
		Yes ($n = 457$)	No ($n = 455$)	P-value	Yes ($n = 461$)	No ($n = 451$)	P-value*
Elevated level of depressive symptoms (%) [†]	42.4	40.0	44.8	0.14	45.6	39.3	0.05
Physical functioning	94.2 (11.0)	95.0 (10.3)	93.4 (11.6)	0.02	94.4 (10.9)	94.0 (11.1)	0.54
Role-physical	85.8 (31.3)	90.0 (27.0)	81.7 (34.6)	0.0001	85.7 (31.5)	85.9 (31.1)	0.93
Bodily pain	85.2 (20.8)	88.3 (18.2)	82.1 (22.8)	0.0001	85.0 (21.6)	85.5 (20.1)	0.69
General health	80.8 (18.9)	83.2 (17.4)	78.5 (20.0)	0.0002	80.4 (19.1)	81.3 (18.6)	0.49
Vitality	88.1 (18.4)	90.8 (15.9)	85.3 (20.3)	0.0001	88.0 (18.7)	88.2 (18.2)	0.87
Social functioning	93.1 (15.5)	95.1 (12.3)	91.0 (18.0)	0.0001	92.6 (15.9)	93.5 (15.1)	0.39
Role-emotional	89.3 (27.8)	92.1 (24.1)	86.5 (30.8)	0.002	88.0 (29.4)	90.5 (26.0)	0.17
Mental health	90.6 (16.5)	92.2 (15.2)	89.0 (17.5)	0.004	89.8 (17.1)	91.5 (15.8)	0.12

Values are given as the percentage or mean (with standard deviation).

* P-values were generated using the GLM procedure of SAS for continuous variables and the χ^2 test for categorical variables.

[†] An elevated level of depressive symptoms is defined as having a score greater than 1.06 on the validated eight-item Hopkins Symptom Checklist.

Table 3
Effects of vitamin supplementation on psychosocial outcomes in HIV-positive pregnant women ($n = 1013$)

Outcome	Multivitamins compared with no multivitamins			Vitamin A compared with no vitamin A		
	RR* (95% CI)	P-value		RR* (95% CI)	P-value	
Elevated level of depressive symptoms [†]	0.78 (0.66, 0.92)	0.005		1.15 (0.97, 1.38)	0.10	
Physical functioning	0.76 (0.63, 0.90)	0.002		1.00 (0.84, 1.20)	0.98	
Role-physical	0.70 (0.57, 0.88)	0.002		1.01 (0.82, 1.26)	0.91	
Bodily pain	0.81 (0.69, 0.95)	0.008		1.03 (0.88, 1.20)	0.73	
General health	0.77 (0.66, 0.90)	0.0007		1.05 (0.90, 1.22)	0.54	
Vitality	0.72 (0.61, 0.84)	0.0001		1.03 (0.88, 1.20)	0.74	
Social functioning	0.72 (0.59, 0.88)	0.001		1.09 (0.90, 1.32)	0.38	
Role-emotional	0.80 (0.64, 1.01)	0.06		1.13 (0.90, 1.42)	0.31	
Mental health	0.82 (0.70, 0.96)	0.01		0.99 (0.84, 1.16)	0.87	

* Relative risk (RR) of depression and 'poor' health-related quality of life (<25th percentile for each subscale) during follow-up, estimated from generalized estimating equations (GEEs), controlled for the other regimen.

[†] An elevated level of depressive symptoms is defined as having a score greater than 1.06 on the validated eight-item Hopkins Symptom Checklist.
CI, confidence interval.