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The effect of anthelminthic treatment during pregnancy on HIV plasma viral load; results from a randomised, double blinded, placebo-controlled trial in Uganda

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Abstract

Background—To investigate the effect of helminth infections and their treatment during pregnancy on HIV load, we conducted a 2×2 factorial randomised controlled trial of albendazole versus placebo and praziquantel versus placebo in pregnant women in Entebbe, Uganda

Methods—Two hundred and sixty-four HIV-infected women from the Entebbe Mother and Baby Study (ISRCTN32849447) were included in this analysis. Women were tested for helminth infections at enrolment and mean HIV load was compared between infected and uninfected groups. The effect of anthelminthic treatment on HIV load was evaluated at six weeks post-treatment and at delivery using linear regression and adjusting for enrolment viral load.

Results—Hookworm and *Trichuris* infections were associated with higher mean viral load at enrolment (adjusted mean difference $0.24\log_{10}$ copies/ml, 95% confidence interval (CI): 0.01 to 0.47, p=0.03 and $0.37\log_{10}$ copies/ml, 95%CI: 0.00 to 0.74, p=0.05, respectively). There were no associations between viral load and other helminth species. There was some evidence that albendazole reduced viral load at six weeks post-treatment (adjusted mean difference −0.17, 95% CI: −0.36 to 0.01, p=0.07), however this effect did not differ according to mother's hookworm infection status and had diminished at delivery (adjusted mean difference −0.11, 95% CI: −0.28 to 0.07, p=0.23). There was no effect of praziquantel treatment on HIV load at any time point.

Conclusions—Infection with some soil-transmitted helminth species is associated with increased HIV load in pregnancy. Treatment with albendazole causes a small decrease in HIV load, however this may not represent a direct effect of worm removal.

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Conflicts of Interest The authors declare no conflicts of interest.

Keywords

HIV; viral load; helminths; anthelminthic treatment; clinical trial

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Introduction

In 2010, 34 million people worldwide were estimated to be living with HIV, with 7000 new infections daily [1]. Antiretroviral therapy (ART) slows disease progression in people living with HIV (PLHIV) by suppressing viral replication, and may prevent both horizontal and vertical transmission of the disease [2,3]. Current WHO guidelines are that ART be initiated in all PLHIV with a CD4 count ≤350 cells/mm3 [4]. In addition, the provision of ART for the prevention of mother-to-child transmission is recommended in all pregnant women with HIV, regardless of their symptoms [5]. Although there have been dramatic improvements in treatment access over the last decade, 9 million individuals who are eligible to receive ART are still estimated not to do so [1]. In parallel with continued efforts to improve ART coverage, other interventions that may impact on HIV disease progression and transmission should be considered.

Sub-Saharan Africa bears a disproportionate burden of the HIV epidemic, with approximately 68% of infected individuals estimated to live in the region [6]. Co-infection with other pathogens including helminths is common [7,8], and it has been suggested that persistent co-infections may have a detrimental impact on PLHIV. Helminths have profound effects on the host immune system, and these effects may spill over to impact on immune responses to other pathogens [9]. Specifically, helminth infection induces a prominent type 2 response profile which inhibits the type 1 response profile needed to combat and control viral antigens such as HIV. It is hypothesised that removal of helminth infections, which can be achieved with cheap and widely available anthelminthic treatments, would reverse these associations.

Observational studies of the relationship between helminths and HIV have found conflicting results [10-13] but a recent systematic review [14], pooled data from three randomised controlled trials [15-17] and concluded there was evidence of a beneficial effect of anthelminthic treatment on markers of HIV disease progression. Level of HIV load during pregnancy is a key determinant of vertical transmission risk and there is some observational evidence for a positive association between helminth infection and increased risk of mother-to-child transmission of HIV [18], however we have previously reported finding no benefit of anthelminthic treatment during pregnancy for vertical HIV transmission in a randomised controlled trial [19]. To further elucidate the relationship between helminth co-infection and HIV, we report results from the same trial, investigating the impact of helminths and their treatment during pregnancy on viral load in HIV infected women six weeks post-treatment and after delivery.

Methods

Study area and participants

Participants were HIV infected pregnant women enrolled in the Entebbe Mother and Baby Study (EMaBS; ISRCTN32849447) [20], a randomised controlled trial of anthelminthic treatment during pregnancy conducted in Entebbe Municipality and Katabi subcounty, a peninsula in Lake Victoria, Uganda, with a high burden of parasitic infections [21]. Pregnant women presenting at the government-funded antenatal clinic at Entebbe General Hospital, who were resident in the study area, planning to deliver in the hospital, willing to know their HIV status, and in the second or third trimester of pregnancy, were eligible for inclusion in

EMaBS. Exclusion criteria were evidence of possible helminth-induced pathology (haemoglobin <8g/dl, clinically apparent severe liver disease, diarrhoea with blood in stool), history of adverse reaction to anthelminthics, prior enrolment in an earlier pregnancy or abnormal pregnancy as assessed by the midwife.

The primary outcomes for EMaBS were response to immunisation and incidence of infectious diseases in the offspring, and vertical transmission of HIV; results for these have been reported elsewhere [19]. In this analysis, we examine the effect of anthelminthic treatment on HIV load in the HIV-1 positive mothers in the cohort. The primary outcome for this analysis is viral load during pregnancy, measured at six weeks post treatment, with secondary outcome viral load at delivery. Women were eligible for inclusion in this analysis if they were HIV-1 positive and had viral load measured at enrolment and were excluded if known to be taking ART.

Study design and procedures

After obtaining written, informed consent, demographic and clinical details were recorded, blood samples obtained and women requested to return with a stool sample. Women were then randomised in a 1:1:1:1 ratio to single-dose albendazole 400 mg or matching placebo and praziquantel 40 mg/kg or matching placebo in a 2×2 factorial design. The randomisation code was generated by the trial statistician in blocks of 100. Sealed envelopes containing the study intervention were prepared by colleagues at the Medical Research Council Unit in Entebbe with no other involvement in the trial. Treatments were allocated in numerical order by trained interviewer-counsellors and taken under observation. All participants and staff were blinded to treatment allocation. After enrolment, women continued to receive standard antenatal care, including haematinics, tetanus immunization, and intermittent presumptive treatment for malaria (with sulfadoxine-pyrimethamine) after the first trimester.

Prior to the start of the project, a programme for prevention of mother-to-child HIV transmission was established at Entebbe Hospital. In accordance with guidelines current at the time, HIV positive women were counselled and given intrapartum and neonatal single-dose nevirapine for prevention of mother-to-child HIV transmission [22]. From March 2005 onwards, when ART provision became available, HIV infected women were offered a repeat full blood count and CD4 T cell count and referred to the Entebbe Hospital ART services if indicated. Those for whom ART was not yet indicated at enrolment had repeat CD4 counts performed annually (or earlier if clinically indicated), to allow referral when necessary.

Blood samples were collected six weeks after enrolment from mothers who had not yet delivered . Blood samples were also collected from the mother after delivery, and from cord blood. Blood samples were taken from offspring of HIV infected women at six weeks and 18 months of age to assess their HIV-1 status.

Stool samples were collected approximately six weeks after delivery to assess effectiveness of anthelminthic treatment; thereafter all mothers were treated with both praziquantel and albendazole.

Parasitology and virology

Stool samples were examined for helminth ova using the Kato-Katz method [23] and by charcoal culture for Strongyloides [24]; two Kato-Katz slides were prepared from each sample and examined within 30 minutes for hookworm ova, the following day for other species. Urine examination for *S. haematobium* was not conducted due to the low prevalence of this species in the study area. Hookworm and *Schistosoma mansoni* infections were classified into low, medium and high intensities according to WHO guidelines [25,26]. Blood samples were examined by a modified Knott's method for *Mansonella perstans* [27] and by thick film

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for malaria parasites. Quality control for Kato-Katz analyses was provided by the Vector Control Programme of the Ministry of Health, Uganda, and for malaria parasitology through the United Kingdom National External Quality Assessment Schemes.

HIV serology was performed for mothers by rapid test algorithm [28]. For viral load assessment, plasma and whole blood cell pellet were separated by centrifugation and stored at −80°C until assays were performed. Plasma HIV load was measured using either Bayer Versant branched DNA assay version 3.0 (Bayer HealthCare, Germany) or Roche Amplicor HIV-1 RNA Monitor test Version 1.5 (Roche Molecular Systems Inc., USA). Methods used to detect HIV-1 proviral DNA in infants at six weeks are described elsewhere [19]. Eighteen month samples were tested for HIV using rapid test algorithm.

Ethical approval

Ethical approval was given by the Uganda Virus Research Institute, Uganda National Council for Science and Technology, and the London School of Hygiene & Tropical Medicine.

Statistical analysis

The sample size for EMaBS was determined for the primary outcomes of the full trial [20]. Data were double entered into Microsoft Access (Redmond, WA, USA) and analysed using Stata version 11 (College Station, TX, USA). Viral load data were $\log_{10}$ transformed for analysis. Baseline characteristics of the mothers included in this study were summarised overall and by randomisation arm.

An observational analysis of the association between infection with each helminth and HIV load was conducted by comparing $\log_{10}$ viral load enrolment samples from mothers with and without infection, using linear regression with adjustment for potential confounders (CD4 count, age, asymptomatic malaria infection at enrolment) to calculate mean differences with 95% confidence intervals. Likelihood ratio tests were used to calculate p-values.

Trial analysis was done by intention-to-treat. The effects of albendazole treatment and of praziquantel treatment on HIV load in mothers at six weeks post-treatment and at delivery were examined separately using linear regression, including treatment group as a covariate and adjusting for baseline (enrolment) viral load, and any factors that showed imbalance between treatment arms and that were thought, *a priori*, likely to impact on viral load. Since the study was designed as a factorial trial, we checked for interaction between albendazole and praziquantel treatments on the two viral load outcomes by fitting interaction terms in regression models.

Since not all women were infected with all helminths at enrolment, a planned subgroup analysis was conducted, comparing the effect of albendazole treatment versus placebo in women who had hookworm (the most prevalent helminth treated by albendazole) at enrolment, and the effect of praziquantel treatment versus placebo in women who had *S. mansoni* at enrolment, using linear regression models adjusted for baseline HIV-1 load and any factors that showed imbalance between treatment arms. Differences between subgroups were examined by fitting interaction terms in regression models. All p-values are two-sided with no adjustment made for multiple comparisons.

Results

Between April 2003 and November 2005, 2507 women were enrolled in EMaBS. Of these, 299 (12%) tested positive for HIV. Five women on HAART and 30 women for whom no

viral load measurement was available at enrolment were excluded from the analysis, leaving 264 women suitable for inclusion (Figure 1). Women who were HIV infected were on average older, less educated, more likely to be widowed or divorced, to already have children, and to be infected with asymptomatic malaria, and less likely to be infected with hookworm, compared to HIV negative women. At enrolment, 67% of the 264 women were infected with at least one helminth species, with individual prevalences: hookworm 39%, *Mansonella perstans* 23%, *Schistosoma mansoni* 18%, *Strongyloides stercoralis* 11%, *Trichuris trichiura* 9%, *Ascaris lumbricoides* 2%. The prevalences of all helminth species other than hookworm were comparable between HIV infected and uninfected women [21]. Helminth infections were generally mild amongst HIV infected women: of hookworm infections, 92% were classified as light (<1000 eggs per gram of stool (epg); of *S. mansoni* infections, 65% were light (<100 epg). Characteristics of the 264 women at enrolment were broadly similar between the four randomisation arms (Table 1), with the exception that women allocated to albendazole had lower mean HIV load, and were less likely to have malaria parasitaemia. In addition, women allocated to albendazole were more likely to have viral load quantified by the Bayer assay at six weeks post-treatment. These chance imbalances were taken into account in the analysis. Numbers of serious adverse events are reported elsewhere [29] and were distributed evenly between treatment groups.

Associations between helminth infections and HIV-1 load at enrolment

The mean (standard deviation, SD) viral load at baseline was 4.09 (0.93) $\log_{10}$ copies/mL. The mean viral load in women infected with hookworm was 0.22 $\log_{10}$ higher than in uninfected women (Table 2). After adjustment for age, CD4 count, and asymptomatic malaria infection, the difference in viral load was 0.24 $\log_{10}$ (95% confidence interval [CI]: 0.01, 0.47; p=0.03). There was some evidence that women infected with *T. trichiura* had higher mean viral loads than those who were uninfected (adjusted mean difference (95% CI): 0.37 $\log_{10}$ (0.00, 0.74); p=0.05). There was no evidence of a difference in $\log_{10}$ viral load for any other helminth infection (Table 2). For hookworm and *S. mansoni*, we found no evidence of an association between infection intensity and viral load.

Effect of anthelminthic treatment on HIV-1 load during pregnancy and post-delivery

At six weeks post-enrolment, 41 women had given birth and one had miscarried. Of the remaining 222 women, HIV-1 load measurements were obtained for 166 (75%) at a median (IQR) of 42 (41-45) days after treatment; mean (SD) viral load was 4.06 (0.91) $\log_{10}$. Based on the single stool samples after delivery, single-dose albendazole and praziquantel treatments were estimated to be 81% and 63% effective in removing hookworm and *S. mansoni*, respectively.

There was no evidence of interaction between albendazole and praziquantel treatments, therefore the effects of each treatment were examined independently. At six weeks post-treatment women who had received albendazole had lower mean viral load than those who received placebo (mean difference −0.40 $\log_{10}$, 95% CI: −0.68, −0.13), however after adjusting for baseline viral load, asymptomatic malaria and assay used for viral load quantification at six weeks post-treatment, this difference was reduced to −0.17 $\log_{10}$ (95% CI: −0.36, 0.01), p=0.07 (Table 3). The effect of albendazole treatment was similar in women with hookworm infection at enrolment compared to those uninfected (interaction p=0.44).

HIV load was measured in 234 (89%) women post-delivery, at a median (IQR) time of 105 (67-133) days post-treatment; this figure was comparable between treatment groups. Adjusting for viral load and malaria parasitaemia at enrolment, the effect of albendazole treatment on viral load had diminished compared to that observed at six weeks post-

treatment during pregnancy (adjusted mean difference −0.11 $\log_{10}$ (95% CI: −0.28, 0.07; p=0.23). There weres no effects of praziquantel treatment on viral load at either time point, nor any evidence of a differential effect of either anthelminthic treatment by susceptible helminth infection (Table 3).

Effect of anthelminthic treatment on HIV vertical transmission and viral load in cord blood

Amongst the 294 HAART-naïve women included in this analysis, 16 were lost to follow-up before delivery, five had miscarriages and nine had stillbirths, leaving information available on 264 live deliveries. We have previously reported that six-week blood samples were available from 211 infants of whom 39 (18%) were diagnosed with HIV infection, and that there were no effects of treatment with albendazole or praziquantel on vertical HIV transmission [19]. Two further HIV transmissions were detected in blood samples taken from children at 18 months, inclusion of these transmissions in the analysis had no impact on results.

Discussion

There are limited data on the relationship between HIV load and helminth infection during pregnancy. We have previously shown, and confirmed in this analysis, that anthelminthic treatment during pregnancy does not significantly reduce the risk of vertical transmission, however this finding is in the context of three quarters of women taking nevirapine at delivery, and power to detect small to moderate sized reductions in risk of vertical transmission was limited. Therefore by analysing the effect of anthelminthic treatment on viral load during pregnancy and at delivery, we sought to further understand the relationship between helminths during pregnancy and factors that could lead to vertical transmission of HIV.

We have shown that infection with the soil-transmitted intestinal helminths, hookworm and *T. trichiura*, during pregnancy is associated with higher HIV load. However, although there was some evidence that albendazole treatment led to a small reduction in viral load six weeks after treatment, this was not sustained to delivery. There was no evidence for a role of other helminth species in HIV load modulation, although power to detect associations for species which were rare in our study population, such as *A. lumbricoides*, was limited, therefore we cannot discount a role for this species in viral load modulation.

The size of the effect of albendazole treatment was modest, conferring a reduction of 0.17 $\log_{10}$ in viral load. However, modelling studies have shown that even small reductions in HIV load at the population level could translate to reductions in disease incidence; for example a decrease in viral load of $0.3\log_{10}$ has been estimated to decrease HIV transmission by 20% and HIV progression by 25% [30].

We found no differential effect of albendazole treatment on HIV load amongst mothers who were diagnosed with hookworm infection at enrolment compared to mothers with no detectable hookworm, raising questions about the mechanism of the effect of albendazole. If the effect was mediated by hookworm removal, we would expect the benefit to be greatest in the hookworm-infected women and to persist to delivery (since stool samples at delivery showed a reduction in hookworm prevalence from 45 to 5% amongst women treated with albendazole [29]). One possible explanation is the low sensitivity of a single Kato Katz stool sample[31,32]: women in the hookworm “uninfected” group may have had low intensity hookworm infection, or infections with other albendazole-susceptible helminth species. However data available from a subgroup of women in the study who provided three stool samples indicate that sensitivity was high for hookworm. Albendazole treatment was not effective in the treatment of *T. trichiura*, therefore the effect of albendazole treatment cannot

be mediated through removal of this worm. Another possible explanation relates to the fact that albendazole has a broad spectrum of action and may clear other infections such as malaria [33,34] which may themselves impact on HIV load [35], thus an effect of anthelminthic treatment is seen in both the helminth "infected" and "uninfected" mothers; in this case weakening of the effect by the time of delivery could be accounted for by the provision of intermittent presumptive treatment for malaria to all women in the latter part of pregnancy.

We found no evidence for a role of *S. mansoni* or *M. perstans* in HIV load modification, in contrast to previous randomised trials that have shown a reduction in viral load after treatment of schistosomiasis [15] and filariasis [16], and our own observational study which showed a transient increase in viral load after treatment of schistosomiasis [13]. For *M. perstans*, this was not unexpected since the single-dose anthelminthic treatments administered in this trial were not effective in its treatment, however praziquantel treatment was 63% effective in treating *S. mansoni* thus we would have expected to see any important effects of the removal of this worm.

An association between *S. haematobium* infection and HIV prevalence has been documented [36,37], suggesting a role for this helminth species in HIV transmission dynamics [38]. We could not examine this possibility since *S. haematobium* was not prevalent in the study area; similar studies conducted in regions where *S. haematobium* infection is endemic are required to elucidate this relationship.

In conclusion, soil-transmitted helminth co-infections may play a role in HIV load modulation during pregnancy, but we found no evidence for involvement of other helminth species. Treatment with albendazole caused a small decrease in HIV load, however the observation that this decrease occurred regardless of whether the mother had an albendazole-susceptible worm taken together with the diminution of the effect of albendazole treatment by delivery indicate that any impact of albendazole treatment on HIV load may not be directly mediated through worm removal.

Acknowledgments

A. Elliott conceived, designed and led the study. J. Kysoiimire-Lugemwa conducted the virological investigations, with contributions from P. Nkurunziza. E. Webb conducted the statistical analysis and drafted the report, with contributions from A. Elliott. D Kizito participated in the collection and curation of samples. S. Lule contributed to recruitment and follow up of participants and to clinical care. L. Muhangi contributed to data management and analysis. M. Muwanga contributed to the design and conduct of the study. P. Kaleebu was in charge of the virology, and contributed to the manuscript. All authors reviewed the final paper.

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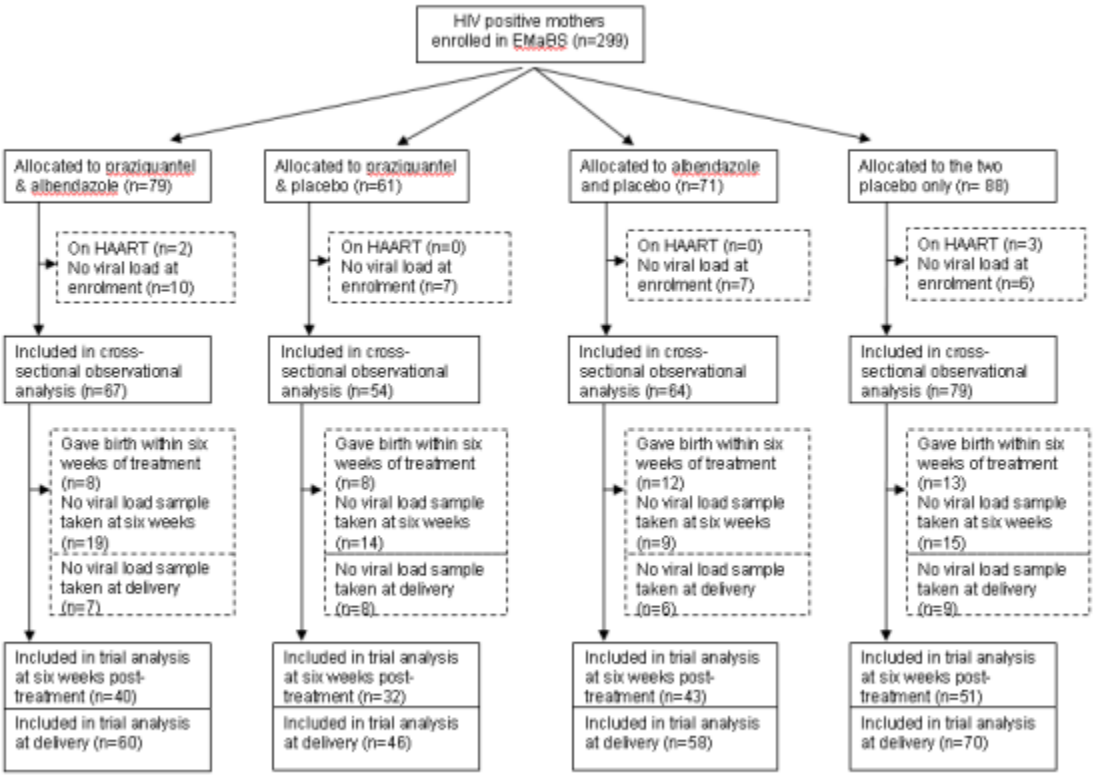

Figure 1.
Flowchart of participants through the study

Table 1

Characteristics of 264 HIV-1 infected women by treatment arm

	Albendazole + praziquantel	Praziquantel only	Albendazole only	Placebo
Number HIV infected women enrolled	67	54	64	79
Age in years				
<20	9 (13%)	8 (15%)	9 (14%)	10 (13%)
20-24	23 (34%)	21 (39%)	18 (28%)	29 (37%)
25-29	18 (27%)	15 (28%)	23 (36%)	22 (28%)
≥30	17 (25%)	10 (19%)	15 (22%)	18 (23%)
Education				
None	9 (13%)	1 (2%)	3 (5%)	5 (6%)
Primary	39 (58%)	33 (61%)	36 (56%)	45 (57%)
Secondary	12 (18%)	16 (30%)	22 (34%)	26 (33%)
Tertiary	7 (10%)	4 (7%)	3 (5%)	3 (4%)
Marital status				
Married	49 (73%)	46 (85%)	52 (81%)	63 (80%)
Single	12 (18%)	5 (9%)	8 (13%)	9 (11%)
Widowed/divorced/separated	6 (9%)	3 (6%)	5 (6%)	7 (9%)
Gravidity				
1	9 (13%)	10 (19%)	14 (22%)	11 (14%)
2-4	41 (61%)	30 (56%)	33 (52%)	50 (63%)
≥5	17 (25%)	14 (26%)	17 (27%)	18 (23%)
Helminth infections				
Hookworm	20 (30%)	24 (44%)	25 (39%)	33 (42%)
S. mansoni	13 (19%)	8 (15%)	14 (22%)	13 (16%)
M. perstans	13 (19%)	14 (26%)	15 (23%)	20 (25%)
S. stercoralis (1mv)	10 (15%)	8 (15%)	4 (6%)	6 (8%)
T. trichiura	6 (9%)	4 (8%)	7 (11%)	7 (9%)
A. lumbricoides	1 (1%)	0 (0%)	3 (5%)	2 (3%)
Any helminth	42 (63%)	35 (65%)	44 (69%)	54 (69%)
Malaria parasitaemia (3 mv) [a]				
Positive	7 (11%)	8 (15%)	8 (13%)	22 (28%)
CD4 count				
<300	13 (19%)	10 (19%)	9 (14%)	14 (18%)
300-499	25 (37%)	11 (20%)	16 (25%)	19 (24%)
>=500	18 (27%)	19 (35%)	26 (41%)	30 (38%)
Not done	11 (16%)	14 (26%)	13 (20%)	16 (20%)
HIV-1 $\log_{10}$ load at enrolment				
Mean (SD)	4.00 (0.91)	4.11 (0.96)	3.96 (0.85)	4.27 (0.96)
Assay used to measure HIV load at baseline				

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	Albendazole + praziquantel	Praziquantel only	Albendazole only	Placebo
Bayer	60 (90%)	49 (91%)	60 (94%)	68 (86%)
Roche	7 (10%)	5 (9%)	4 (6%)	11 (14%)
Assay used to measure HIV load at six weeks post-treatment (166 samples tested)				
Bayer	16 (40%)	11 (34%)	19 (44%)	14 (27%)
Roche	24 (60%)	21 (66%)	24 (56%)	37 (73%)
Assay used to measure HIV load at delivery (234 samples tested)				
Bayer	59 (98%)	46 (100%)	56 (97%)	66 (94%)
Roche	1 (2%)	0 (0%)	2 (3%)	4 (6%)

[a] mv=missing values

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Table 2

Association between helminth infections and HIV-1 load at enrolment

Exposure	Mean (SD) log HIV load	Crude mean difference (95% CI)	p	Adjusted mean difference (95% CI)[a]	p
Hookworm					
Uninfected (n=162)	4.01 (0.93)				
Infected (n=102)	4.23 (0.91)	0.22 (−0.01, 0.45)	0.06	0.24 (0.01, 0.47)	0.03
S. mansoni					
Uninfected (n=216)	4.11 (0.94)				
Infected (n=48)	4.01 (0.87)	−0.11 (−0.40, 0.18)	0.53	−0.05 (−0.33, 0.24)	0.75
M. perstans					
Uninfected (n=202)	4.10 (0.92)				
Infected (n=62)	4.06 (0.96)	−0.04 (−0.31, 0.22)	0.74	−0.01 (−0.27, 0.26)	0.95
S. stercoralis					
Uninfected (n=235)	4.11 (0.91)				
Infected (n=28)	3.95 (1.05)	−0.16 (−0.53, 0.20)	0.38	−0.12 (−0.48, 0.24)	0.51
T. trichiura					
Uninfected (n=240)	4.07 (0.94)				
Infected (n=24)	4.34 (0.76)	0.27 (−0.12, 0.66)	0.17	0.37 (0.00, 0.74)	0.05
A. lumbricoides					
Uninfected (n=258)	4.08 (0.93)				
Infected (n=6)	4.55 (0.84)	0.47 (−0.29, 1.22)	0.22	0.39 (−0.34, 1.11)	0.29

[a]Adjusted for CD4 count, age, concurrent malaria parasitaemia;

SD=standard deviation; CI=confidence interval

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Table 3A

Effect of anthelminthic treatment on HIV-1 load

A. Six weeks post-treatment

Group	Mean (SE) $\log_{10}$ HIV load at baseline[a]		Mean (SE) $\log_{10}$ HIV load at six weeks post-treatment		Crude mean difference (95% CI)	Adjusted mean difference (95% CI)[b]	p
	Placebo	Albendazole	Placebo	Albendazole			
All women	4.21 (0.11)	3.92 (0.10)	4.26 (0.10)	3.85 (0.09)	−0.40 (−0.68, −0.13)	−0.17 (−0.36, 0.01)	0.07
Hookworm infected	4.32 (0.18)	3.99 (0.18)	4.18 (0.16)	3.85 (0.16)	−0.33 (−0.77, 0.11)	−0.12 (−0.46, 0.22)	0.44[c]
Hookworm uninfected	4.13 (0.13)	3.88 (0.13)	4.31 (0.13)	3.85 (0.12)	−0.46 (−0.81, −0.10)	−0.22 (−0.44, −0.01)	
	Placebo	Praziquantel	Placebo	Praziquantel			
All women	4.08 (0.10)	4.05 (0.11)	4.06 (0.09)	4.05 (0.11)	−0.01 (−0.29, 0.27)	0.01 (−0.18, 0.20)	0.94
***S. mansoni* infected**	3.89 (0.22)	4.17 (0.27)	3.80 (0.22)	4.12 (0.27)	0.32 (−0.38, 1.02)	0.07 (−0.27, 0.41)	0.56[c]
***S. mansoni* uninfected**	4.11 (0.11)	4.02 (0.12)	4.11 (0.10)	4.03 (0.12)	−0.08 (−0.39, 0.23)	−0.02 (−0.24, 0.20)	

[a] For those with viral load measured at six weeks post-treatment

[b] For effect of albendazole treatment, results were adjusted for baseline viral load, baseline malaria parasitaemia and viral load assay used at six weeks; for effect of praziquantel treatment, results were adjusted for baseline viral load

[c] Interaction p-value

SE=standard error;CI=confidence interval

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Table 3B

B. At delivery

Group	Mean (SE) $\log_{10}$ HIV load at baseline[a]		Mean (SE) $\log_{10}$ HIV load at delivery		Crude mean difference (95% CI)	Adjusted mean difference (95% CI)[b]	p
	Placebo	**Albendazole**	**Placebo**	**Albendazole**			
All women	4.16 (0.09)	4.05 (0.08)	4.10 (0.09)	3.83 (0.08)	−0.27 (−0.51, −0.03)	−0.11 (−0.28, 0.07)	0.23
Hookworm infected	4.27 (0.13)	4.12 (0.14)	4.10 (0.14)	3.87 (0.14)	−0.24 (−0.63, 0.16)	−0.00 (−0.25, 0.25)	0.43[c]
Hookworm uninfected	4.09 (0.12)	4.03 (0.10)	4.10 (0.12)	3.81 (0.10)	−0.29 (−0.60, 0.03)	−0.17 (−0.42, 0.07)	
	Placebo	**Praziquantel**	**Placebo**	**Praziquantel**			
All women	4.04 (0.08)	4.05 (0.09)	3.94 (0.08)	3.99 (0.09)	0.05 (−0.20, 0.29)	0.04 (−0.13, 0.21)	0.64
***S. mansoni* infected**	3.86 (0.17)	4.12 (0.21)	3.69 (0.20)	4.04 (0.24)	0.35 (−0.27, 0.97)	0.10 (−0.22, 0.42)	0.50[c]
***S. mansoni* uninfected**	4.09 (0.09)	4.03 (0.10)	4.00 (0.09)	3.98 (0.10)	0.02 (−0.25, 0.29)	0.01 (−0.19, 0.21)	

[a] For those with viral load measured at delivery

[b] For effect of albendazole treatment, results were adjusted for baseline viral load and baseline malaria parasitaemia; for effect of praziquantel treatment, results were adjusted for baseline viral load

[c] Interaction p-value

SE=standard error; CI=confidence interval