Impact of quasi-elimination of *Wuchereria bancrofti* on HIV incidence in southwest Tanzania: a 12-year prospective cohort study

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For the Swahili translation of the abstract see Online for appendix 1

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Summary

Background Before introduction of anthelmintic treatment programmes in southwest Tanzania, our group described a 2·3-fold increase in HIV incidence among adults infected with the helminth *Wuchereria bancrofti*. Between 2007 and 2011, HIV incidence was 1·91 cases per 100 person-years in people with a *W bancrofti* infection and 0·80 cases per 100 person-years in those without the infection. We aimed to examine the impact of a reduction in *W bancrofti* infection as a result of mass drug administration on HIV incidence in southwest Tanzania.

Methods The Risk of HIV Infections through Nematode Organism (RHINO) study is a prospective cohort study that used data from participants in one village collected during the Evaluation and Monitoring of the Impact of New Interventions (EMINI) study in 2007–11 and new data from EMINI participants collected in 2019. Study participants were tested for HIV and circulating filarial antigen (an indicator of *W bancrofti* infection), once a year from 2007 to 2011 and once in 2019. From 2009 to 2015, anthelmintics were annually distributed to all villagers through government programmes, followed by transmission assessment surveys. We analysed data from individuals aged 14–65 years with negative HIV test results at enrolment in EMINI in 2007. We did multilevel mixed-effects Poisson regression to describe and compare age-adjusted and sex-adjusted incidence rates.

Findings Of the 1299 previous study participants rescreened in 2019, 1139 had been HIV-negative at the end of the last surveillance period in 2011 and were included in this analysis. 552 (48·5%) participants were female and 587 (51·5%) were male, and the median age was 26.4 years (IQR 19·8–37·8). Of the 1139 participants included, 848 (74·5%) never tested positive for *W bancrofti* infection, 272 (23·9%) previously tested positive but did not have a *W bancrofti* infection in 2019 (cured individuals), 15 (1·3%) tested positive for *W bancrofti* infection both in 2007–11 and 2019, and four (0·4%) had a new *W bancrofti* infection in 2019. Between 2011 and 2019, HIV incidence rate was 0·68 cases (95% CI 0·50–0·93) per 100 person-years in the 848 participants with no *W bancrofti* infection (39 new HIV infections during 5724 person-years) and 0·73 cases (0·45–1·17) per 100 person-years in the 272 cured individuals (17 new HIV cases during 2344 person-years; incidence rate ratio (IRR) after adjusting for age and sex 1·14, 95% CI 0·64–2·04; p=0·65). HIV incidence rate was 1·5 cases (0·39–6·04) per 100 person-years in the 15 individuals who tested positive for *W bancrofti* infection both in 2007–11 and in 2019 (two new HIV infection in 131 person-years; adjusted IRR 3·43, 95% CI 0·8–15; p=0·10).

Interpretation In the group of participants cured of *W bancrofti* infection, the HIV incidence significantly decreased in 2011–19 compared with 2007–11, the period when they tested positive for *W bancrofti* infection. This effect was not observed in the group of individuals who never had a positive *W bancrofti* test, supporting the role of *W bancrofti* in HIV infection.

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Introduction

Chronic helminth infections have been suggested as a factor that could increase susceptibility to HIV.[1–5] The hypothesis is that modulation of the human immune system caused by chronic helminth infections leads to a favourable condition for viruses, thus facilitating HIV acquisition.[1,6–9] Asymptomatic infections with *Wuchereria bancrofti* have been associated with systematic activation of CD4 cells, pronounced regulatory T and B cells, and dominant IgG4 and IL-10 responses that might reduce the antiviral capacity of the human host.[10–12] Most mosquito-borne *W bancrofti* infections are asymptomatic, even though they affect the lymphatic system and can lead to lymphoedema of the limbs (elephantiasis) and scrotal lymphangiectasia and swelling (hydrocele) in a subset of individuals.[13] Lymphatic filariasis, the disease

Research in context

Evidence before this study

Helminth infections have been suggested to be one of the factors driving the HIV/AIDS epidemic in sub-Saharan Africa. For the helminth *Wuchereria bancrofti*, a mosquito-borne filarial nematode, our group reported a 2·3-fold increased HIV incidence among *W bancrofti*-infected individuals in Tanzania in a prospective cohort study published in 2016. An additional evaluation of the same cohort showed that the HIV incidence was highest among individuals with a filarial infection harbouring microfilariae in their blood. We searched PubMed for papers published from database inception to Dec 31, 2024, in English with the terms "Wuchereria bancrofti", "HIV" and "Incidence" and found only the two articles mentioned above. The search for "Wuchereria bancrofti" and "HIV" (without incidence) yielded a larger number of 24 manuscripts. However, all reports from other research groups described cross-sectional evaluations that focused on the interaction of *W bancrofti* and HIV at a time when both infections were already present, rather than on HIV incidence. These reports described no significant effect of *W bancrofti* or its treatment on the HIV clinical course or its surrogate markers.

Added value of this study

The high prevalence of *W bancrofti* infections in Tanzania led to government action against this disease, and the prevalence fell dramatically from 35·1% to 1·7% in our study area. The focus of our follow-up intervention was to assess the impact of the quasi-elimination of filarial infection on HIV incidence by revisiting the previous study participants in one village in southwest Tanzania. The incidence of HIV decreased significantly among villagers who were cured of the filarial infection during the two surveillance periods (2007–11 and 2011–19). By contrast, no decline in HIV incidence was observed among individuals who had never been infected with *W bancrofti*. In our 2016 publication, we demonstrated in a prospective cohort study that mosquito-borne infection with the helminth *W bancrofti* increases susceptibility to HIV. However, the mechanisms responsible for this finding are not fully understood. The decrease in HIV incidence in the subgroup of originally infected but now cured individuals shows that the mechanisms are apparently reversed after successful treatment of *W bancrofti*.

Implications of all the available evidence

Our results are a further argument for placing the control of neglected diseases, in this case filariae, at the centre of global strategies, as these diseases not only cause morbidity but also increase the risk of acquiring HIV. The mechanism of the increased susceptibility should also be explored, as it seems that it can be reversed once the filarial infection has been treated.

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caused by *W bancrofti*, was present in most of the 31 administrative regions of Tanzania before the introduction of countrywide elimination programmes.[14,15] In the southwest of the country, the reported prevalence of lymphatic filariasis in adults was 42% in 2009.[16,17] The Tanzanian National Lymphatic Filariasis Elimination Programme began mass drug administration with ivermectin and albendazole to all individuals older than 2 years in the coastal areas in 2000 and extended coverage to the Mbeya region of Tanzania (southwest) in 2009.[18] All individuals, regardless of whether they had a *W bancrofti* infection or not, received this medication annually between 2009 and 2015. As a result of these measures, the prevalence of *W bancrofti* infection in the Mbeya region fell from 35·1% in 2009 to 1·7% in 2019 in people aged 14 years or older.[19] Population-based Tanzanian HIV/AIDS and Malaria Indicator Surveys showed a countrywide decline of HIV prevalence in people aged 15–49 years from 5·7% in 2007, to 5·1% in 2011, 5·0 % in 2016, and 4·4% in 2022.[20–23] In contrast, HIV prevalence in the Mbeya region remained high during that period (9·2% in 2007, 9·0% in 2011, 9·3% in 2016, and 9·6% in 2022).[20–23]

Before the government programmes for lymphatic filariasis elimination reached the southwest of Tanzania in October, 2009, our group started a prospective cohort study focusing on the impact of *W bancrofti* infection on HIV susceptibility in Kyela, one of the towns in the Mbeya region, which was highly endemic for filarial infection. During this period of high prevalence of *W bancrofti* infection, we were able to show that HIV incidence was higher in people with *W bancrofti* infection than in those with no infection.[24]

In the first observation phase in 2007–11, people living in Kyela were tested annually for HIV and *W bancrofti*. Our previous study included initially HIV-negative participants with at least two test results for *W bancrofti* and HIV.[24] First, we used a conservative definition of *W bancrofti* status, which only included *W bancrofti* test results if they were congruent at the beginning and at the end of the period when HIV acquisition occurred.[24] This evaluation showed an HIV incidence of 1·91 cases per 100 person-years in people with *W bancrofti* infection compared with 0·80 cases per 100 person-years in those without the infection.[24] In a second, more liberal analysis, published in the same manuscript, a positive *W bancrofti* status was defined by at least one positive *W bancrofti* test result over the course of the study (from 2007 to 2011). Using the liberal definition, we obtained similar results, with an HIV incidence of 1·7 cases per 100 person-years in people with *W bancrofti* infection compared with 0·76 cases per 100 person-years in those without the infection.[24] The impact of *W bancrofti* infection on HIV incidence was found to be consistent for both versions of the analysis after adjustment for age, sex, and socioeconomic status, as well as for other

factors that might influence HIV transmission (eg, number of sexual partners, marital status, HIV status of spouse, circumcision, and use of condom).

In 2019, our group did a follow-up study to assess the impact of the government mass drug administration programme against *W bancrofti* on HIV incidence, as a decrease in prevalence of *W bancrofti* infection from 35·1% to 1·7% was observed in the study area for individuals aged 14 years or older.[19] In this study, we aimed to assess the effect of this quasi-elimination of *W bancrofti* infection on HIV incidence in this area, with data spanning 12 years.

See Online for appendix 2

Methods

Study design and participants

The Risk of HIV Infections through Nematode Organism (RHINO) study is a prospective cohort study that used data collected in 2007–11 from the Evaluation and Monitoring of the Impact of New Interventions (EMINI) study and new data collected from the same EMINI participants in one site in 2019. Between 2007 and 2011, the EMINI population-based cohort study was done at the National Institute for Medical Research (NIMR)-Mbeya Medical Research Centre (MMRC) in the Mbeya region of southwest Tanzania.[16,17,25–28] The EMINI study enrolled a geographically stratified random sample of approximately 10% of the households at nine distinct sites. These nine villages surrounded Mbeya but differed in terms of climate, vegetation, and vicinity to the TransAfrican highway. All household inhabitants aged 6 months and older, who were willing to participate and donate a sample or for whom consent to participate had been obtained from a parent or guardian, were included in the EMINI cohort and followed up yearly until 2011.

One of the selected sites for the EMINI study was Kyela, a village bordering Malawi with a humid climate. We previously described a high prevalence of different helminths and arthropod infections in that village.[11,16,17,25–29] Testing of plasma samples for the circulating antigen of the adult form of *W bancrofti* (an indicator of *W bancrofti* infection) had shown a prevalence of *W bancrofti* infection of 24·8% in people aged 6 months and older in 2009.[16,17] With a particular focus on adolescents and adults, we calculated a prevalence of *W bancrofti* infection of 35·1% in the participants older than 14 years and 42·6% in those older than 18 years.[16,17,19] The adult worm of *W bancrofti* infections has a lifespan of 5–7 years during which it produces millions of offspring, the microfilariae, which are responsible for the transmission of the diseases. Since treatment with ivermectin and albendazole mainly kill the microfilariae but only mildly damage adult worms, effectiveness of treatment can only be evaluated after a long treatment period.[16,17]

After reporting the association between *W bancrofti* infection and HIV incidence, we decided to do the RHINO study. This RHINO study focused solely on the Kyela study site and aimed to identify reasons for the increased HIV risk among people with *W bancrofti* infection in that area.

The RHINO study was approved by the Mbeya Medical Research Ethics Committee (GB.152/377/01/194), the Tanzanian National Health Research Ethics Committee (NIMR/HQ/R.8a/Vol IX/2856), and the Ethics Committee of the medical faculty of the University of Munich (Project ID: 18–377). The EMINI study had been approved by both the National Ethical Committee/Medical Research Coordinating Committee of the National Institute for Medical Research, Tanzania, and the Mbeya Medical Research Ethics Committee. More details are given in appendix 2 (p 1).

Between March 13 and Oct 25, 2019, we collected new data from participants living in in Kyela, who were aged 14–65 years, and who had participated in the EMINI study.[19] We used the data of individuals aged 14–65 years with negative HIV test results at EMINI enrolment and who agreed to participate in RHINO to calculate and compare the HIV incidence. During the time of the EMINI study, each household had at least one member with *W bancrofti* infection (one to four members) and one member without *W bancrofti* infection (one to six members). Each study participant signed a written informed consent form in Swahili. Parents consented for their children younger than 18 years, and children who were able to sign their own assent forms were also allowed to do so (appendix 2 p 1).

Procedures

Blood, urine, and stool samples had been collected annually from participants in the Kyela site of the EMINI study from 2007 to 2011, as previously described.[16,17,25–28] Between March 13, and Oct 25, 2019, previous EMINI participants who agreed to participate were visited again.[19] During those visits, a sample of 10 mL of blood was collected for each study participant in the morning and immediately stored at room temperature (18–20°C). Plasma and whole blood cells were separated within 24 h and stored at –20°C and –80°C, respectively. During household visits, each participant was separated from the household to a private spot to undergo HIV counselling and testing in accordance with the national guidelines. The results of the testing were provided immediately. The collected blood specimens were used for further confirmatory tests, HIV viral load testing, *W bancrofti* ELISA, and immunological assays.

The interviewer administered a questionnaire to capture data related to health knowledge and health behaviour using the mobile data collection tool OpenDataKit (2020 Get ODK) on Android smartphones.[30] OpenDataKit is a tool for creating digital forms for data collection that can be used offline. Health data were then downloaded, exported to Microsoft Excel worksheets, and imported into STATA version 17.1 for further analysis. Laboratory data were captured on paper, double entered

into a Microsoft Access database, and compared and checked for discrepancies before they were approved for analysis.

Outcomes

All filarial antigen tests were done at the NIMR-MMRC laboratories in Mbeya, Tanzania. The commercially available ELISA TropBio Og4C3 (Celllabs, Brookvale, NSW, Australia) was used to detect the circulating filarial antigen in the collected serum samples, as described in appendix 2 (pp 1–2) and a previous publication.[19]

Participants with at least one positive *W bancrofti* ELISA result during 2017–11 were classified as having a *W bancrofti* infection during that time. This group was further divided into two subgroups (cured of *W bancrofti* infection or having *W bancrofti* infection) at the RHINO study visit in 2019, based on their *W bancrofti* ELISA result at that timepoint. Participants with negative *W bancrofti* ELISA results in 2007–11 and 2019 were classified as having no *W bancrofti* infection.

Recruitment of participants in 2019 involved voluntary counselling and testing for HIV for every participant. Per the Tanzanian national guidelines, HIV testing was done with a rapid diagnostic test, SD-Bioline HIV-1/2 3·0 (Standard Diagnostics, Kyonggi-do, South Korea). All positive rapid test results were confirmed using the Uni-Gold HIV test (Trinity Biotech, Bray, Ireland). All samples with positive HIV test results were further tested to assess the viral load using Xpert (Cepheid, Solna, Sweden). All participants newly diagnosed as HIV-positive were referred to the nearest HIV care and treatment centre (CTC) for antiretroviral treatment. These CTC clinics were supported by the US President's Emergency Plan for AIDS Relief, where medication and care were given without charge. During the annual visits from 2007 to 2011, plasma samples were tested for HIV-ELISA and western blot at the NIMR-MMRC laboratory in Mbeya using a previously published algorithm (appendix 2 p 2).[25]

To measure HIV incidence and related parameters, we calculated the exposure time as follows: if a participant had a negative HIV test result at the beginning of the study period, we used the first visit at which the participant was aged 14 years or older as the start of the exposure time. For the EMINI study, the exposure time was the time between the first and last documented visit of the EMINI study in which the participant was aged 14 years or older. For the RHINO study, the exposure time was calculated from the last participation in an EMINI visit until the RHINO visit. Only the time after the 14th birthday was used for the person's time calculation. Individuals participating only once during the EMINI study did not contribute any person-time to the observation period and were therefore excluded from exposure time calculations.

Statistical analysis

We did multilevel mixed-effects Poisson regression with cluster for households to describe and compare age-adjusted and sex-adjusted incidence rates, as well as incidence rate ratios (IRRs). Mixed-effects Poisson regression contains both fixed effects and random effects. In longitudinal data, random effects are useful for modelling intracluster correlation; that is, observations in the same cluster are correlated because they share common cluster-level random effects. Furthermore, univariable and multivariable log-link binominal regression analyses were used to adjust for age, sex, and other potentially confounding known risk factors for HIV infection (eg, sex [self-reported], marital status, number of sexual partners). We used Stata/SE software (version 17.1) for all statistical analyses and plots.

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

All households in Kyela that had previously participated in the EMINI study were contacted to enrol in the RHINO study in 2019. Of 2186 potentially eligible individuals from the EMINI study, 1299 (59·4%) agreed to participate in the RHINO study. The primary reasons for not participating in the follow-up study were permanent move of the household (552 [25·3%] participants), death (104 [4·8%] participants), and refusal of follow-up (55 [2·5%] participants). In the previous publication focusing on the prevalence of *W bancrofti* infection, we compared the individuals who participated in 2019 and those lost to follow-up; we did not find differences regarding age, sex, and *W bancrofti* prevalence between these groups.[19]

We used the data of 1164 individuals aged 14–65 years at the time of the RHINO visit, with negative HIV test results at enrolment in the EMINI study, to calculate and compare the HIV incidence. The participating households had on average 2·6 members (range 1–10 participants per household).

Of these 1164 individuals, 25 (2·1%) acquired an HIV infection between 2007 and 2011. To calculate the HIV incidence between 2011 and 2019, we used the data of the remaining 1139 individuals who had a negative HIV test result at the end of the last surveillance period of 2011. 552 (48·5%) of 1139 participants were female and 587 (51·5%) were male. The median age was 26·4 years (IQR 19·8–37·8), and 508 (44·6%) study participants were aged 14 to <25 years, 451 (39·6%) were aged 25 to <45 years, and 180 (15·8%) were aged 45–65 years. 58 (5·1%) of 1139 participants acquired an HIV infection between 2011 and 2019 and were included in this analysis.

Of the 1139 individuals included, 848 (74·5%) never tested positive for *W bancrofti* infection, 272 (23·9%) had tested positive at least at one timepoint between 2007 and 2011 but tested negative for the *W bancrofti* antigen in 2019 (ie, cured individuals), 15 (1·3%) tested positive for

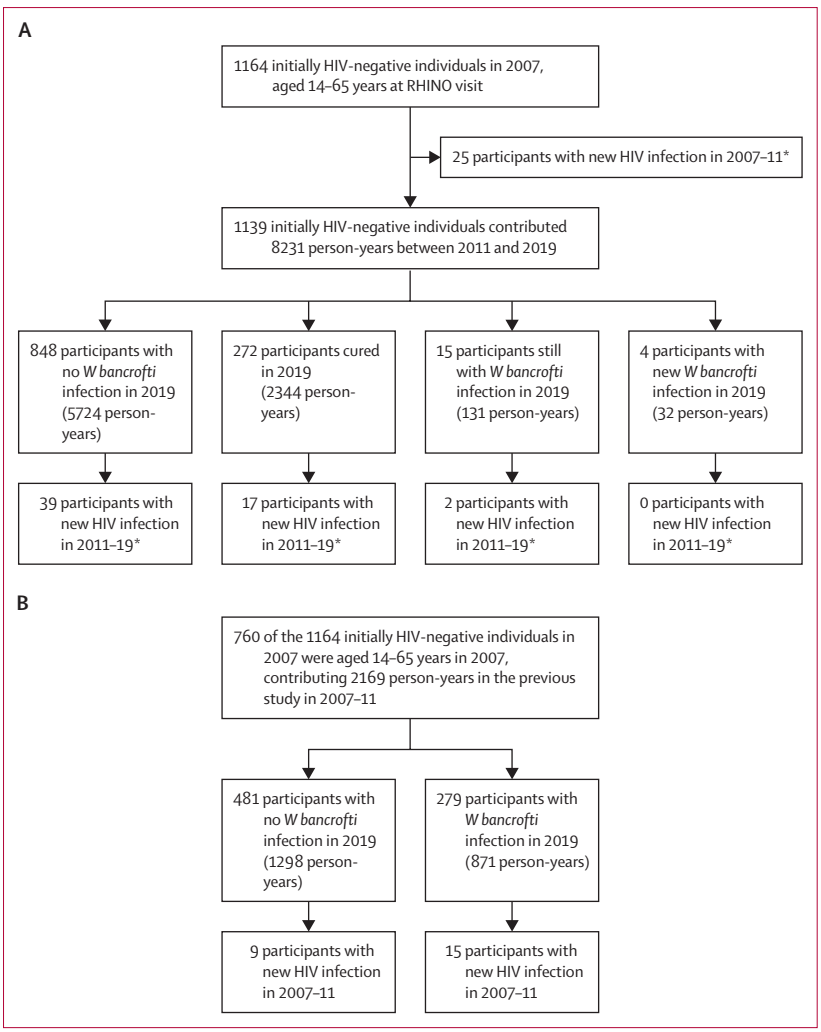


Figure 1: **Study profile showing participants and person-years for 2007–11 and 2011–19**
(A) Overview of 1164 study participants aged 14–65 years, who were HIV uninfected in 2007 and participated in the follow-up study in 2019. 58 HIV seroconversions took place between 2011 and 2019. The seroconversions among different subgroups are shown. (B) 24 HIV seroconversions occurred in the time period 2007–11. Only 760 of the 1164 individuals were aged 14–65 years at that time. The remaining 404 were younger. *W bancrofti=Wuchereria bancrofti.* *One seroconversion occured in this group, outside of the age range of the studied population.

W bancrofti infection both in 2007–11 and 2019, and four (0·4%) had a new *W bancrofti* infection in 2019 (figure 1). The median age was 23·8 years for those without an infection, 34·8 years for those cured, 50·9 years for those still positive for *W bancrofti* infection in 2019, and 24·3 years for those with a new *W bancrofti* infection in 2019.

During the surveillance from 2007 to 2011, our data indicated that sexual transmission of HIV started around the age of 14 years in our study area. Thus, to compare the HIV incidence through sexual transmission of the virus between the two time periods, we focused on the subgroup of individuals who were aged 14–65 years during 2007–11 and compared them with those aged 14–65 years in 2011–19. Of the 1139 HIV-negative individuals included in our analysis, 760 (66·7%) had been aged 14–65 years in 2007–11, contributing 2169 person-years. Of them, 481 (63·3%) participants tested negative for *W bancrofti* infection at all study visits, contributing to a total of 1298 person-years, and 279 (36·7%) tested positive for *W bancrofti* infection at least once, contributing 871 person-years. The median age of the participants with no *W bancrofti* infection was 22·9 years (IQR 17·9–35·2), compared with 28·3 years (IQR 21·3–38·3) for those with a *W bancrofti* infection. During 2007–11, HIV seroconversions occurred in one individual outside of the age range (younger than 14 years) and in 24 participants aged 14–65 years. Of the 24 new HIV infections, 15 (62·5%) occurred in people with a *W bancrofti* infection during 871 person-years (crude HIV incidence rate 1·72 cases [95% CI 1·04–2·84] per 100 person-years) and nine (37·5%) occurred in people with no *W bancrofti* infection during 1298 person-years (0·69 cases [0·36–1·33] per 100 person-years). The age-adjusted and sex-adjusted HIV IRR was 2·52 (95% CI 1·13–5·64, p=0·025) using a multivariable mixed-effect Poisson regression.

Between 2011 and 2019, we recorded 58 HIV seroconversions. These new HIV infections occurred in 39 (4·6%) of 848 participants who never tested positive for *W bancrofti* infection during 5724 person-years (HIV incidence rate 0·68 cases [0·50 to 0·93] per 100 person-years) and in 17 (6·2%) of 272 participants previously infected with *W bancrofti* but cured in 2019 during 2344 person-years (0·73 cases [0·45 to 1·17] per 100 person-years). The difference in HIV incidence between these subgroups was not significant (age-adjusted and sex-adjusted IRR 1·14, 95% CI 0·64–2·04; p=0·65). The remaining HIV seroconversions occurred in two (13·3%) of 15 individuals who tested positive for *W bancrofti* infection both in 2007–11 and in 2019 during 131 person-years (HIV incidence rate 1·5 cases [0·39–6·04] per 100 person-years). The difference in HIV incidence between the group with no *W bancrofti* infection and the group with *W bancrofti* infection at both timepoints was not significant (age-adjusted and sex-adjusted IRR 3·43, 95% CI 0·8–15; p=0·10). Among the four individuals who were newly infected with *W bancrofti*, no HIV seroconversions were recorded during 32 person-years.

For the participants living in Kyela who were cured of their *W bancrofti* infection, the age-adjusted HIV incidence dropped significantly from 1·77 cases per 100 person-years in 2007–11 to 0·6 cases per 100 person-years in 2011–19 (figure 2), with an age-adjusted and sex-adjusted IRR of 0·41 (95% CI 0·2–0·8; p=0·012). In contrast, among the individuals who consistently tested negative, the age-adjusted HIV incidence was 0·8 cases per 100 person-years in 2007–11 and 0·66 cases per 100 person-years in 2011–19 (figure 2), with an age-adjusted and sex-adjusted IRR of 1·07 (0·5–2·2; p=0·85, table 1). A small group of 15 participants tested positive for *W bancrofti* infection

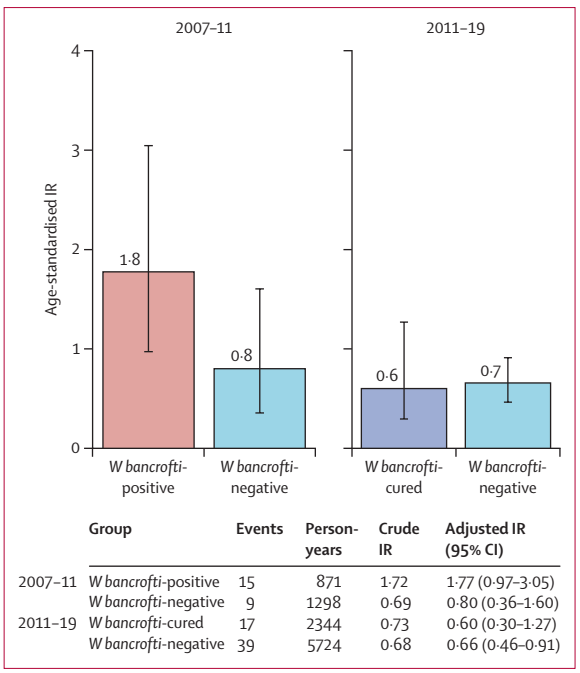
during both study periods, 2007–11 and 2011–19. The HIV incidence rate in that group was 1·5 cases per 100 person-years (95% CI 0·39–6·04), which was very similar to the incidence recorded in *W bancrofti* infected individuals, but with a wider confidence interval.

To adjust for more confounding factors, we estimated the association between HIV incidence and status of *W bancrofti* infection in a multivariable log-link binomial regression model adjusted for sex, age, and additional risk factors for HIV (table 2). No difference was seen between those who had been cured of *W bancrofti* infection and those who never had one. The odds of having a new HIV infection were lower in men than in women. The age group of 25–45 years showed a trend towards having more odds of new HIV infections than other age groups, although differences were not significant. Marital status and number of sexual partners seemed to have an impact on the odds of having a new HIV infection, but differences were not significant.

Discussion

We previously reported a significantly increased HIV incidence among people with *W bancrofti* infection in the Kyela district study population aged 14 years or older.[24] This finding was found true after adjusting for sex and age, as well as known HIV risk factors such as a high number of sexual partners. Here, we describe the impact of the elimination of that helminth, which has led to a significant decrease in HIV incidence among individuals who had a previous *W bancrofti* infection but who were later cured in 2019. In contrast, we did not observe a reduction in HIV incidence among the participants who had never had an *W bancrofti* infection, indicating that the recorded decrease in HIV incidence could indeed be attributable to the cure of the filarial infection. The treatment of *W bancrofti* in the study area led to a quasi-elimination of the parasite in Kyela, as only 15 of 848 individuals still tested positive in the second period of the surveillance. This small group of individuals had a similar HIV incidence to that of the group who tested positive for *W bancrofti* infection in the first study period. However, as this group of people is small, we found a wide confidence interval and therefore no significant difference between this group and the group of people who had no *W bancrofti* infection.

Assessing the link between *W bancrofti* infection and HIV incidence is complex and requires specific conditions. In this instance, several factors made this evaluation possible: (1) the high prevalence of infections with *W bancrofti* and HIV in the study area during the first surveillance period; (2) the longevity of the infection with the adult worm of *W bancrofti* despite medical treatment with WHO-recommended drugs; (3) a carefully selected representative study population; and (4) a high retention rate of the participants (almost 60% of the individuals after 8 years from the last visit) after very effective community engagement activities.[16,17,19]



	Group	Events	Person-years	Crude IR	Adjusted IR (95% CI)
2007–11	*W bancrofti*-positive	15	871	1·72	1·77 (0·97–3·05)
	W bancrofti-negative	9	1298	0·69	0·80 (0·36–1·60)
2011–19	*W bancrofti*-cured	17	2344	0·73	0·60 (0·30–1·27)
	W bancrofti-negative	39	5724	0·68	0·66 (0·46–0·91)

Figure 2: **Age-standardised HIV incidence rate during two surveillance periods (2007–11 and 2011–19)**
Comparison of the age-standardised HIV incidence among individuals who tested positive for *Wuchereria bancrofti* infection, those with previous *W bancrofti* infection and no infection in 2019 (ie, cured), and those with no *W bancrofti* infection. IR=incidence rate.

	Person-years	Incident HIV cases	Incidence rate per 100 person-years	Univariable analysis		Multivariable analysis	
				IRR (95% CI)	p value	IRR (95% CI)	p value
***W bancrofti*-positive or cured**							
2007–11	871	15	1·72	1 (ref)	..	1 (ref)	..
2011–19	2344	17	0·73	0·42 (0·2–0·8)	0·015	0·41 (0·2–0·8)	0·012
***W bancrofti*-negative**							
2007–11	1298	9	0·69	1 (ref)	..	1 (ref)	..
2011–19	5724	39	0·68	0·98 (0·5–2·0)	0·96	1·07 (0·5–2·2)	0·85

Univariable and multivariable mixed-effects Poisson regression results, with random effects for household (HouseID) and adjusted for age and sex, displayed separately for the *W bancrofti*-positive or cured and the *W bancrofti*-negative (who never tested positive) subgroups. IRR=incidence rate ratio.

Table 1: **Change of HIV incidence from 2007–11 to 2011–19, by status of *Wuchereria bancrofti* infection**

We recalculated the HIV incidence from 2007 to 2011 for the group of 760 participants who were revisited in 2019 and were aged 14–65 years in 2007. We found similar values to those we had previously published, reaffirming that during the follow-up visit in 2019, we recruited a representative subgroup of the initial cohort.[24] Here, we describe the findings of three distinct subgroups: (1) study participants who never tested positive for *W bancrofti* infection; (2) study participants who had been infected during at least one visit from 2007 to 2011 but tested negative for *W bancrofti* infection in 2019 (cured individuals); and (3) study participants who tested positive

	Person-years	Incident HIV cases	Incidence rate per 100 person-years	Univariable analysis		Multivariable analysis	
				IRR (95% CI)	p value	IRR (95% CI)	p value
All	8199*	58	0·71				
W bancrofti infection status							
Negative	5724	39	0·68	1 (ref)	..	1 (ref)	..
Cured	2344	17	0·73	1·06 (0·6–1·9)	0·83	0·91 (0·5–1·6)	0·75
Positive*	131	2	1·52	2·23 (0·6–8·4)	0·24	2·68 (0·6–12)	0·20
Gender							
Female	4027	38	0·94	1 (ref)	..	1 (ref)	..
Male	4172	20	0·48	0·51 (0·3–0·9)	0·012	0·44 (0·2–0·8)	0·0086
Age, years							
14 to <25	2556	11	0·43	1 (ref)	..	1 (ref)	..
25 to <45	4064	41	1·01	2·35 (1·2–4·5)	0·011	1·90 (0·9–4·1)	0·11
≥45	1579	6	0·38	0·89 (0·3–2·4)	0·81	0·70 (0·2–2·3)	0·56
Marital status							
Never	2624	12	0·46	1 (ref)	..	1 (ref)	..
Currently married	4511	34	0·75	1·65 (0·9–3·1)	0·13	1·21 (0·6–2.6)	0·63
Divorced	578	9	1·56	3·39 (1·5–7·8)	0·0038	1·82 (0·7–4·8)	0·22
Widowed	486	3	0·62	1·35 (0·4–4·6)	0·64	1·11 (0·2–5·9)	0·90
Number of sexual partners within the past year							
0	780	5	0·64	1 (ref)	..	1 (ref)	..
1	4671	33	0·71	1·10 (0·4–2·8)	0·84	0·92 (0·3–3·3)	0·89
2	1153	9	0·78	1·22 (0·4–3·5)	0·72	1·17 (0·3–4·3)	0·82
≥3	902	9	0·99	1·55 (0·5–4·5)	0·42	1·71 (0·4–6·6)	0·44
No answer	693	2	0·29	0·45 (0·1–2·3)	0·33	0·75 (0·1–4·8)	0·76

Univariable and multivariable log-link binomial regression results. IRR=incidence rate ratio. *32 person-years of four participants who were found to be newly infected with *W bancrofti* were excluded from the analysis, as they had no case of new HIV infection.

Table 2: **Association between status of *Wuchereria bancrofti* infection and HIV incidence according to various covariates, for 2011–19**

for *W bancrofti* infection during both study periods. We found a substantial decrease in the HIV incidence in cured individuals. In contrast, the HIV incidence remained stable in the subgroup of participants who had never tested positive for *W bancrofti* infection. Despite the fact that we restricted our analysis to individuals aged 14–65 years, we noticed that the subgroups we analysed differed in age. Therefore, we adjusted our incidence calculations for age and sex using a multivariable mixed-effect Poisson regression model. In the multivariable logistic analysis, we noticed increased HIV incidence for women. This finding has been described in several publications, including our previous manuscripts from this study area.

There were several limitations to our study. The first limitation is the observational nature of this study. It is not a clinical randomised trial in which conditions can be controlled. Therefore, we looked at risk factors for HIV transmission and adjusted for these using log-link binomial regression. Another limitation is that we could not know whether health interventions took place and whether participants were uniformly exposed to them. The government treatment programmes in the study area included mass drug administration of ivermectin and albendazole for all individuals older than 2 years. In the study village, all individuals, regardless of whether they had a *W bancrofti* infection or not, were offered medication annually for 7 years. During the surveillance period, other Tanzania National Commission for AIDS interventions took place in the area. There were both people with and without *W bancrofti* infection in each of the sampled households, so we relied on the (unsubstantiated) assumption that all villagers, both those with and without *W bancrofti*, were equally affected by the interventions. Another limitation is the age difference between the groups: the group that previously had *W bancrofti* and were later cured was older than the group that never had the infection. However, we took this into account by including age and sex in all incidence calculations.

In conclusion, these data support our previous findings that a chronic *W bancrofti* infection increases the susceptibility to HIV, since we show a great reduction of the HIV incidence in individuals who were previously infected but later cured of the *W bancrofti* infection. We suggest considering the elimination of *W bancrofti* infection as an additional measure, which could be taken to reduce HIV infection in areas with high *W bancrofti* prevalence.

Contributors
MH, ES, and LMab planned and received funding for the EMINI study; IK, MC, CG, MR, and AHo planned and secured funding for the

RHINO study. IK, LMag, PC, BP, ES, and LMab were involved in the conduct and supervision of EMINI; MC, LMag, TFM, NEN, AU, AHa, JMh, JMn, MM, and EN were involved in the conduct and supervision of RHINO. IK, NC, BH, FR, and SH analysed the data and take responsibility for the integrity of the data and the accuracy of the analysis. IK drafted the initial manuscript and received major input from MC, MR, and TFM. All authors were involved in the critical revision of the manuscript. IK, NC, BH, FR, SH, TFM, and MC accessed the data and did statistical calculations. IK, BH, and SH accessed and verified the underlying data. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Declaration of interests

We declare no competing interests.

Data sharing

The raw data supporting the conclusions of this Article will be made available by the authors, on request to the corresponding author (IK), without undue reservation.

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