

## Prevalence and Factors Associated with Tb-HIV Co-Infection among Tuberculosis Patients Treated at Specialist Hospital, Sokoto State, Nigeria 2014- 2017

Article by Nuruddeen Aliyu<sup>1</sup>, Bello Arkilla Magaji<sup>2</sup>

<sup>1</sup>African Field Epidemiology Network, Abuja, Nigeria

<sup>2</sup>Department of Community Health, Faculty of Clinical Sciences, College of Health Sciences, Usmanu Danfodiyo University PMB 2346, Sokoto, Nigeria

E-mail: annurzawiyya@yahoo.co.uk

### Abstract

**Background:** Tuberculosis (TB) control remains a global public health challenge especially in resource-limited settings, Nigeria inclusive. In 2017, TB was the leading cause of preventable deaths worldwide with an estimated 1.6 million deaths. We conducted this study to determine the prevalence and predictors of HIV co-infection among tuberculosis patients treated at Specialist Hospital, Sokoto, Nigeria.

**Materials and Methods:** This is part of a large retrospective cohort study conducted to determine the predictors of treatment outcomes among TB patients treated at specialist hospital, Sokoto from January 2014 to December 2017. Data was analyzed using Epi-info version 7. Bivariate and multivariate analysis was conducted to identify predictors of TB-HIV co-infection. Odds ratio (OR) and 95% confidence interval (CI) was calculated. P-value of 0.05 was considered as statistically significant.

**Results:** A total of 1,501 TB cases were reviewed. HIV co-infection was found in 174 (11.6%) of cases and is more prevalent among males 125 (71.8%). Majority were males (71.2%), The mean age was 36.5 ±14.9 years. Pulmonary TB accounts for 1143 (76.2%). Of all the TB cases, 89 (5.9%) were previously treated. TB-HIV co-infection was found in 174 (11.6%) cases. Formal education, Pulmonary Tb and unsuccessful treatment outcome were independent predictors of TB-HIV co-infection.

**Conclusion:** Prevalence of TB HIV co-infection found in this study is within the range of other studies in the region. We recommend that all newly diagnosed TB patients be tested for HIV after counselling and targeted interventions of high-risk patients for TB-HIV co-infection is recommended.

**Keywords:** Tuberculosis, TB/HIV co-infection, prevalence, retrospective, Sokoto.

### Introduction

Tuberculosis (TB) remains the leading cause of death in people living with HIV (PLHIV) and a major cause of antimicrobial resistance related deaths worldwide (Tuberculosis 2018). Globally in 2017, there were an estimated 10.0 million incident cases of TB (range, 9.0–11.1 million), equivalent to 133 cases (range, 120–148) per 100 000 populations. HIV status averaged 66% of TB patients in the 30 high TB/HIV burden countries, but varied considerably, from 13% in Congo to above 80% in 16 high TB/HIV burden countries in the WHO African Region. In the WHO African Region, which accounted for 72% of the global burden of HIV-associated TB in 2017 (global 2018). Globally, 464 633 cases of TB among people living with HIV were notified in 2017, equivalent to 12% of TB patients with an HIV test result. The number notified was only 51% of the estimated number of incident cases among people living with HIV, but an increase from 49% in 2016 (global 2018).

The duo of TB and HIV taken together are responsible for the deaths of over 2.9 million people annually (Tuberculosis 2018). TB is one of the most common infections that threaten people living with HIV in the developing world (Gray, Jacob M., and David L. Cohn. 2013 2010). TB/HIV co-infection poses a major threat to the international community's effort to achieve the health-related United Nations Millennium Development Goals for TB and HIV infection (Getahun et al. 2010). It constitutes a serious diagnostic and therapeutic challenge and, especially in resource limited settings, weighs heavily on already strained health care budgets. It has recently been realized that the epidemiology, clinical presentations, and management of both HIV and TB are different and far more complex in co-infected compared to mono-infected patients (Gao, Zheng, and Fu 2013). TB is a well-established opportunistic

infection and a leading cause of accelerated disease progression to AIDS in HIV-infected individuals due to significantly enhanced destruction of active CD4 helper T-cells and a rapid breakdown of immune functions (Kolade et al. 2016; Tavares et al. 2017), on the other hand HIV infection accelerates progression of latent TB infection into active TB disease (Adejumo et al. 2017; Alau et al. 2016).

There have been several studies of the prevalence of TB/HIV co-infection in different parts of Nigeria, with prevalences ranging from 9.6% in Jos (Agbaji et al. 2013), 10.5% in Kano (Iliyasu and Babashani 2009) and 21.6% in Lagos (Adejumo et al. 2017). However, higher prevalences were reported in some African countries including Ethiopia; 27.7% and 57.1% by (Mitku et al. 2016) and (Belay, Bjune, and Abebe 2015a) as well as Tanzania; 43.6% by (Range et al. 2007). There has been no report of TB/HIV co-infection prevalence and associated risk factors in Sokoto north western Nigeria. We conducted this study to determine the prevalence and associated factors of TB/HIV co-infection in Specialist hospital, Sokoto State, Nigeria.

## Methods

The methodology applied was the same as contained in a larger study on predictors of treatment outcomes among TB patients treated at Specialist hospital, Sokoto, Nigeria. The article was accepted for publication in Texila international Journal of Public Health.

The method applied is summarised thus;

### Study design, setting and target population

Hospital based retrospective study was conducted the study included all TB patients who were registered and commenced TB treatment for the past four years (January 1<sup>st</sup>, 2014 – December 31<sup>st</sup>, 2017)

at the directly observed treatment short course (DOTS) clinic of Specialist hospital Sokoto, Nigeria. Sokoto State is located in the north-western part of Nigeria and has a population of about 5.4 million people. There are 23 local government areas (LGAs) in the state. The Specialist hospital is a tertiary hospital in Sokoto State which also serves as a referral centre for health facilities in other LGAs of the state.

### Sources of data and method of data collection

The TB treatment register and hospital patient folders were the primary sources of data in this study. Data was collected retrospectively by trained health professionals using structured checklist. Data collected included; patients' socio-demographic characteristics, TB history (new or previous history of TB), TB type, HIV status, drug resistance, treatment outcome of the patient and HIV status of patients.

We trained the data collectors and pretested the questionnaires to ensure quality in the data collection. Also, the data collectors were closely supervised to further ensure quality in the data.

### Ethical considerations

Ethical clearance was obtained from ethics and research committee of Specialist Hospital, Sokoto, Nigeria.

### Statistical analysis

Data was analyzed using Epi info version 7 for windows. Categorical (such as sex, tribe) and numeric (such as age) variables were summarized using frequencies, percentages, means and standard deviations accordingly. Univariate and multivariate logistic regression analyses with a confidence level of 95% was performed. Additionally, adjusted odds ratios with their 95% confidence intervals and independent variables with p-value of 0.05 were considered to be independent risk factor for development of TB/HIV co-infection in this study.

## Results

Of the 1,501 records of patients reviewed, the majority 410 (27.3%) were between 20 – 29 years. Mean age was 36.5±14.9 years. The majority were males (72.2%). Seven hundred and ninety- three (52.8%) of the study population were married, while 93 (6.2%) had no formal education. And 358

(23.9%) account for extra-pulmonary TB cases while 89 (5.9%) were previously treated. The TB/HIV co-infection was found in 174 (11.6%) of cases.

The highest proportion of TB/HIV co-infection was in the age group 20 – 29 years, accounting for 12.2% of the cases. There was statistical difference in the HIV co-infection rate among the age groups ( $P < 0.001$ ). Of the 1069 males, 125 (11.7%) were HIV positive. There was no evidence of a difference in sex of the cases in relation to their HIV status ( $p = 0.85$ ). There is no statistically significant difference an association between HIV status and marital status ( $p = 0.15$ ), and level of education ( $P = 0.14$ ). However, there was statistically significant association between HIV status and tuberculosis type ( $p < 0.001$ ) and treatment category ( $p < 0.001$ ) as shown in Table 1.

**Table 1.** Sociodemographic and clinical characteristics of TB patients treated at Specialist Hospital, Sokoto, Nigeria

Characteristics	HIV positive	HIV negative	Total	P- value
	N (%)	N (%)		
<b>Age group (years)</b>				
<20	9 (6.7)	126 (93.3)	135	<0.01
20-29	50 (12.2)	360 (87.8)	410	
30-39	48 (12.3)	341 (87.7)	389	
40-49	41 (16.7)	205 (83.3)	246	
50-59	16 (9.5)	153 (90.5)	169	
60+yrs	10 (6.6)	142 (93.4)	152	
<b>Sex</b>				
Male	125 (11.7)	944 (88.3)	1069	0.85
Female	49 (11.3)	383 (88.7)	432	
<b>Marital status</b>				
Single	67 (9.9)	613 (90.1)	680	0.15
Married	104 (13.1)	689 (86.9)	793	
Divorced/separated	3 (10.7)	25 (89.3)	28	
<b>Educational level</b>				
No formal education	9 (9.7)	84 (90.3)	93	0.14
Primary	24 (21.2)	89 (78.8)	113	
Secondary	70 (16.9)	343 (83.1)	413	
Tertiary	33 (14.8)	190 (85.2)	223	
<b>Tuberculosis Type</b>				
Extra pulmonary	28 (7.8)	330 (92.2)	358	<0.01
Smear-negative	14 (7.6)	171 (92.4)	185	
Smear-positive	132 (13.8)	826 (86.2)	958	
<b>Treatment category</b>				
New	139 (9.8)	1273 (90.2)	1412	<0.01
Previously-treated	35 (39.3)	54 (60.7)	89	

Table 2 shows TB treatment outcomes by HIV status. The table also shows a significantly higher proportion of TB patients were cured than TB/HIV co-infected patients (29.5% vs 11.5%). However, more TB/HIV co-infected patients died than TB patients (15.5.1% vs 1.3%). Similarly, treatment failure was more in TB.HIV co-infected patient that in mono infection (4.0% vs 0.1%). There was statistical

difference in the HIV co-infection rate among the treatment outcomes ( $P < 0.01$ ) as shown in Table 2 below:

**Table 2.** Treatment outcomes in TB/HIV co- infected and TB patients

Treatment outcomes	TB/HIV	TB	Total number of TB cases	P value
	n = 174 (%)	n = 1327 (%)		
Cured	20 (11.5)	392 (29.5)	412	< 0.001
Death	27 (15.5)	17 (1.3)	44	
Default	63 (36.2)	116 (8.7)	179	
Transferred-out	24 (13.8)	17 (1.3)	41	
Treatment-completed	33 (19.0)	784 (59.1)	817	
Treatment-failure	7 (4.0)	1 (0.1)	8	

In bivariate analysis, pulmonary TB, previously treated and unsuccessful treatment outcomes were all significantly associated with TB-HIV co- infection (OR: 1.70, 5.9, and 19.74 respectively). The odds of having TB-HIV co-infection was 5.9 times more in those with previously treated cases than new cases, likewise, the odds of having TB-HIV co-infection was 19.7 times more in those with unsuccessful treatment outcomes than those with successful outcomes. However, no association was observed between Age group, sex, educational level and cavity on radiography and TB-HIV co-infection (Table 3).

**Table 3.** Bivariate analysis of factors that are associated with TB/HIV co-infection at Specialist Hospital, Sokoto, Nigeria

Variable	TB/HIV	TB	OR (95% C.I)	P value
<b>Age group (yrs):</b>				
< 40	107 (61.5)	826 (62.3)	0.97 (0.70 – 1.34)	0.838
≥ 40	67 (38.5)	500 (37.7)		
<b>Sex:</b>				
Female	49 (28.2)	382 (28.9)	0.97 (0.68 – 1.37)	0.845
Male	125 (71.8)	941 (71.1)		
<b>Educational level</b>				
No formal education	9 (6.6)	84 (11.9)	0.52 (0.3 – 1.1)	0.071
Formal education	127 (93.4)	621 (88.1)		
<b>TB Location</b>				
Pulmonary	146 (83.9)	997 (75.2)	1.70 (1.1 – 2.6)	<0.001
Extra-pulmonary	28 (16.1)	329 (24.8)		
<b>Treatment category</b>				
Previously-treated	35 (20.1)	54 (4.1)	5.9 (3.7 – 9.4)	<0.001
New	139 (79.9)	1272 (95.1)		
<b>Cavity on radiography</b>				
Yes	5 (3.3)	25 (4.0)	0.81 (0.31 – 2.2)	0.678
No	148 (96.7)	602 (96.0)		
<b>Treatment outcome Status</b>				
Unsuccessful treatment outcome	124 (71.3)	148 (11.2)	19.74 (13.6 – 28.6)	<0.001
Successful treatment outcome	50 (28.7)	1178 (88.8)		

Findings from logistic regression analysis shows no association between previously treated cases and TB-HIV co-infection as was seen in the bivariate analyses. Formal education (aOR 0.51, 95% C.I 0.36 – 0.71, P<0.001), pulmonary TB (aOR 0.34, 95% C.I 0.20 – 0.59, P<0.001) and unsuccessful treatment outcome (aOR 9.8, 95% C.I 6.37 – 14.99, P<0.001) remained the only independent predictors for TB-HIV co-infection (P<0.001) as shown in table 4 below:

**Table 4.** Logistic regression of factors that are associated with TB/HIV co-infection at Specialist Hospital, Sokoto, Nigeria

Variable	Adjusted OR	95% C. I	P-Value
No formal education	0		
Formal education	0.51	0.36 – 0.71	<0.001
Extra pulmonary TB	0		
Pulmonary TB	0.34	0.20 – 0.59	<0.001
New TB case	0		
Previously treated	1.50	0.80 – 2.81	0.2081
Successful treatment	0		
Unsuccessful treatment outcome	9.8	6.37 – 14.99	<0.001

## Discussion

The prevalence of TB – HIV co-infection reported in this study was 11.6%. Co-infection was associated with formal education, pulmonary TB and unsuccessful treatment outcomes. The co-infection rate reported in this study is much lower than 40.0%, 21.6% and 14.2% reported in a similar studies in Nigerian cities of Ilorin (AK Salami et al. 2006), Lagos (Adejumo et al. 2017) and Oyo (Oladimeji et al. 2013). The reported prevalence is also lower than what was reported in some African countries; 27.7% in Ethiopia, and 43.6% in Tanzania (Mitku et al. 2016) and (Range et al. 2007) respectively. High prevalence rate of 57.1% was also reported in Ethiopia (Belay, Bjune, and Abebe 2015). However, the prevalence observed in this study is higher than that reported in Jos; 9.6% (Agbaji et al. 2013) and in Kano; 10.5% (Iliyasu and Babashani 2009) respectively. The differences observed in the TB-HIV co-infection rate might be partly due to diagnostic capacity and procedures available, service utilization, under reporting and the overall burden of TB and HIV in different countries and methodology used.

In this study, we observed a higher HIV prevalence among males than females, this is consistent with the findings from a recent study by (Daniel and Alausa n.d.) and (Zwang et al. 2007). However, this is contrary to the findings reported in Port Harcourt, Nigeria by (Erhabor et al. 2010) where females have higher HIV prevalence than males.

TB-HIV co-infected patients were 1.7 times more likely to have pulmonary TB than extra-pulmonary TB in this study. This finding is consistent with a study conducted in North-eastern Ethiopia which reported 2.8 and 1.7 times odds of co-infection among smear positive and smear negative patients with pulmonary TB respectively (Mekonnen, Derby, and Desalegn 2015). However, this is contrary to the findings of (Adejumo et al. 2017) where extra-pulmonary TB cases are more likely to have TB-HIV co-infection.

Treatment default and treatment of recurrent TB infection has serious public health consequences especially continuous infectivity, drug resistance and development of MDR-TB (Unis et al. 2014). In our study, there was significant association between the previously treated TB cases and TB-HIV co-infection, this finding is similar to what was reported by (Nahid et al. 2007; do Prado et al. 2014). TB/HIV co-infection was significantly associated with unsuccessful TB treatment outcome in the present study. This might due to presence of TB and HIV drug interaction that sometimes results in poor adherence to anti-TB drugs. A similar result was found in other studies conducted in Nigeria, Brazil and Ethiopia by (Mekonnen, Derby, and Desalegn 2015; Ofoegbu and Odume 2015; do Prado et al. 2014) indicating that co-infected patients were more likely to have unsuccessful treatment

outcomes. This is incongruent to a study from Sagamu, Nigeria and India that reported association between unsuccessful TB treatment and TB-HIV co-infection by (Daniel and Alausa n.d.; Shastri et al. 2013) respectively.

Our study had limitations; firstly, incomplete records and therefore not captured in data analyses. Nevertheless, our large sample size still allowed us to maintain high statistical power for all analyses, but not accounting for potential biases. Secondly, we did not have access to information about antiretroviral therapy (ART) history or CD4 count among HIV co-infected patients. Therefore, we did not know if the patients were diagnosed with HIV prior to, concomitant with, or after the diagnosis of TB. Thirdly, our study is retrospective facility-based, and therefore, the prevalence observed may not accurately reflect the prevalence of the entire population in the study area and being it retrospective, the number of variables available to determine predictors is limited and therefore prospective study is recommended to explore other factors that may be associated with TB-HIV co-infection.

## Conclusion

TB-HIV co-infection was moderately high in this study and it was associated with no formal education, previously treated TB cases and unsuccessful treatment outcome. We recommend that there should be strict compliance to centers for disease prevention and control center (CDC) that all newly diagnosed TB patients be tested for HIV after counselling. Communication and integration of services between the HIV/AIDS and TB programs should be strengthened.

## References

- [1]. Adejumo, Olusola A. et al. 2017. "Factors Associated with TB/HIV Co-Infection among Drug Sensitive Tuberculosis Patients Managed in a Secondary Health Facility in Lagos, Nigeria." *African Journal of Infectious Diseases* 11(2): 75–82.
- [2]. Agbaji, Citation et al. 2013. "Factors Associated with Pulmonary Tuberculosis-HIV Co-Infection in Treatment-Naive Adults in Jos." *North Central Nigeria. J AIDS Clin Res* 4: 222. <http://dx.doi.org/10.4172/2155-6113.1000222> (October 16, 2018).
- [3]. Alau, K K et al. 2016. 4 International Research on Medical Sciences Prevalence of Tuberculosis and HIV/AIDS Co-Infection among HIV Clients at Global Fund Supported Comprehensive Facilities in Nigeria. <http://www.apexjournal.org> (October 16, 2018).
- [4]. Belay, Mulugeta, Gunnar Bjune, and Fekadu Abebe. 2015a. "Prevalence of Tuberculosis, HIV, and TB-HIV Co-Infection among Pulmonary Tuberculosis Suspects in a Predominantly Pastoralist Area, Northeast Ethiopia." *Global Health Action* 8.
- [5]. ———. 2015b. "Prevalence of Tuberculosis, HIV, and TB-HIV Co-Infection among Pulmonary Tuberculosis Suspects in a Predominantly Pastoralist Area, Northeast Ethiopia." *Global Health Action* 8(5): 1–7.
- [6]. Daniel, O J, and O K Alausa. "Treatment Outcome of TB/HIV Positive and TB/HIV Negative Patients on Directly Observed Treatment, Short Course (DOTS) in Sagamu, Nigeria." *Nigerian journal of medicine: journal of the National Association of Resident Doctors of Nigeria* 15(3): 222–26. <http://www.ncbi.nlm.nih.gov/pubmed/17111747> (October 16, 2018).
- [7]. Erhabor, O, Z A Jeremiah, T C Adias, and Ce Okere. 2010. "The Prevalence of Human Immunodeficiency Virus Infection among TB Patients in Port Harcourt Nigeria." *HIV/AIDS (Auckland, N.Z.)* 2: 1–5. <http://www.ncbi.nlm.nih.gov/pubmed/22096379> (October 16, 2018).
- [8]. Gao, Junling, Pinpin Zheng, and Hua Fu. 2013. "Prevalence of TB/HIV Co-Infection in Countries Except China: A Systematic Review and Meta-Analysis." *PLoS ONE* 8(5).
- [9]. Getahun, Haileyesus, Christian Gunneberg, Reuben Granich, and Paul Nunn. 2010. "HIV Infection–Associated Tuberculosis: The Epidemiology and the Response." *Clinical Infectious Diseases* 50(s3): S201–7. <https://academic.oup.com/cid/article-lookup/doi/10.1086/651492>.
- [10]. Global. 2018.
- [11]. "Human Immunodeficiency Virus Associated Tuberculosis: Pattern and Trend in the University of Ilorin Teaching Hospital | AK Salami | Request PDF." [https://www.researchgate.net/publication/6117161\\_Human\\_immunodeficiency\\_virus\\_associated\\_tuberculosis\\_Pattern\\_and\\_trend\\_in\\_the\\_University\\_of\\_Ilorin\\_Teaching\\_Hospital](https://www.researchgate.net/publication/6117161_Human_immunodeficiency_virus_associated_tuberculosis_Pattern_and_trend_in_the_University_of_Ilorin_Teaching_Hospital) (July 31, 2019).

- [12]. Iliyasu, Zubairu, and Musa Babashani. 2009. "Prevalence and Predictors of Tuberculosis Coinfection among HIV-Seropositive Patients Attending the Aminu Kano Teaching Hospital, Northern Nigeria." *Journal of epidemiology* 19(2): 81–87. <http://www.ncbi.nlm.nih.gov/pubmed/19265273> (October 16, 2018).
- [13]. Kolade, E. Ranti, O. Glory Atilola, T. Victoria Babalola, and O. Isaac Komolafe. 2016. "HIV-TB Co-Infection and Associated Risk Factors among HIV Positive Patients at Olabisi Onabanjo University Teaching Hospital, Ogun State, South-West Nigeria." *HIV and AIDS Review*.
- [14]. Mekonnen, Daniel, Awoke Derbie, and Endalkachew Desalegn. 2015. "TB/HIV Co-Infections and Associated Factors among Patients on Directly Observed Treatment Short Course in Northeastern Ethiopia: A 4 Years Retrospective Study." *BMC Research Notes* 8(1): 666. <http://www.biomedcentral.com/1756-0500/8/666> (July 5, 2019).
- [15]. Mitku, Aweke Abebaw, Zelalem Getahun Dessie, Essey Kebede Muluneh, and Demeke Lakew Workie. 2016. "Prevalence and Associated Factors of TB/HIV Co-Infection among HIV Infected Patients in Amhara Region, Ethiopia." *African Health Sciences* 16(2): 588–95.
- [16]. Nahid, Payam et al. 2007. "Treatment Outcomes of Patients with HIV and Tuberculosis." *American Journal of Respiratory and Critical Care Medicine* 175(11): 1199–1206.
- [17]. Ofoegbu, Onyebuchi Stephanie, and Bethrand Brian Odume. 2015. "Treatment Outcome of Tuberculosis Patients at National Hospital Abuja Nigeria: A Five-Year Retrospective Study." *South African Family Practice* 57(1): 50–56. <https://www.tandfonline.com/doi/full/10.1080/20786190.2014.995913>.
- [18]. Oladimeji, Olanrewaju et al. 2013. "Factors Associated with Treatment Success among Pulmonary Tuberculosis and HIV Co-Infected Patients in Oyo State, South West-Nigeria." *the Nigerian Health Journal* 13(2).
- [19]. do Prado, Thiago N. et al. 2014. "Factors Associated with Tuberculosis by HIV Status in the Brazilian National Surveillance System: A Cross Sectional Study." *BMC Infectious Diseases* 14(1): 1–8.
- [20]. Range, N. et al. 2007. "HIV and Parasitic Co-Infections in Tuberculosis Patients: A Cross-Sectional Study in Mwanza, Tanzania." *Annals of Tropical Medicine & Parasitology* 101(4): 343–51. <http://www.tandfonline.com/doi/full/10.1179/136485907X176373> (July 25, 2019).
- [21]. Shastri, Suresh et al. 2013. "TB Treatment Outcomes among TB-HIV Co-Infections in Karnataka, India: How Do These Compare with Non-HIV Tuberculosis Outcomes in the Province?" *BMC Public Health* 13(1): 5–10.
- [22]. Tavares, Ana Maria et al. 2017. "HIV and Tuberculosis Co-Infection among Migrants in Europe: A Systematic Review on the Prevalence, Incidence and Mortality." *PloS one* 12(9): e0185526. <http://www.ncbi.nlm.nih.gov/pubmed/28957400> (July 5, 2019).
- [23]. TB/HIV Co-Infection. 2010. [www.icad-cisd.com](http://www.icad-cisd.com) (October 16, 2018).
- [24]. Tuberculosis, Global. 2018. "Report 2018."
- [25]. Unis, Gisela et al. 2014. "Tuberculosis Recurrence in a High Incidence Setting for HIV and Tuberculosis in Brazil." *BMC Infectious Diseases* 14(1): 1–6.
- [26]. Zwang, Julien et al. 2007. "Trends in Mortality from Pulmonary Tuberculosis and HIV/AIDS Co-Infection in Rural South Africa (Agincourt)." *Transactions of the Royal Society of Tropical Medicine and Hygiene* 101(9): 893–98. <https://academic.oup.com/trstmh/article-lookup/doi/10.1016/j.trstmh.2007.04.023> (July 31, 2019).