



SDI Review Form 1.6

Journal Name:	International Journal of TROPICAL DISEASE & Health
Manuscript Number:	2014_IJTDH_14182
Title of the Manuscript:	Risk Factors of Human African Trypanosomiasis in Mbuji Mayi, Eastern Kasai Province, Democratic Republic of the Congo
Type of the Article	

General guideline for Peer Review process:

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty**', provided the manuscript is scientifically robust and technically sound.

To know the complete guideline for Peer Review process, reviewers are requested to visit this link:

(<http://www.sciencedomain.org/page.php?id=sdi-general-editorial-policy#Peer-Review-Guideline>)



SDI Review Form 1.6

PART 1: Review Comments

	Reviewer's comment	Author's comment <i>(if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)</i>
<u>Compulsory</u> REVISION comments	INTRODUCTION 1. To be removed to the paragraph: from line 64 to 84. 2. Situation of HAT in DRC as stated from line 87 to 101 should be put directly after line 30. STUDY SETTING 1. To be removed: from line 152 to 165 as there is no link between the acquisition of HAT and political organization of a city. 2. Paragraph titled "Economy and living conditions" should be put together and titled "socio-economic conditions". In that paragraph, socio-economic level of populations should be described.	Thank you for your helpful comments. INTRODUCTION 1. As per your suggestion, we have removed the paragraph from line 64 to 84 in the original submission. 2. Section from line 87 to line 101 was moved directly after line in original submission. However, due to other request to create clear sub-sections under the introduction, there was no way to keep the structure of the introduction as it was before. STUDY SETTING 1. Line 152 to line 165 has been removed 2. We have put together the paragraph titled "Economy and living conditions" and the paragraph on "socio-economic conditions." Since this section is crucial for the understanding of the way the environment affects the spread of the infection, we have further enriched this new combined section with additional data. This new section now takes about 2 pages. It runs from line 148 to line 234. STUDY JUSTIFICATION AND AIMS The purpose has been clarified. Clarification can be



SDI Review Form 1.6

	STUDY JUSTIFICATION AND AIMS The purpose of identifying risk factors of HAT in Mbuji-May I is not well clarified. A discussion section must be included in the paper. Do not repeat results in the interpretation section.	seen in newer version: Line 252-line 264. A discussion section has been included in the paper. It does and it does not repeat results in the interpretation section.
--	---	--



SDI Review Form 1.6

Minor REVISION comments	Name of species and sub species should be written in <i>italic</i>. Reference number should be put before the full stop outstanding the end of the sentence. MATERIAL AND METHODOLOGY: As there is no list of material used, the word Material should be removed.	Name of species and sub species have been thoroughly written in <i>italic</i>. See highlights in the new text. Reference numbers have been put before the full stop outstanding the end of the sentence. MATERIAL AND METHODOLOGY: We do not agree with this request as we consider that our study involves the analysis of the data that have been collected. These data do represent study materials. However, we have preferred to comply with the request as it does not make a major difference to have that title either way.
Optional/General comments	This paper provides good information as regards risk factors of HAT in Mbuji-May I, a sub urban focus. Despite encouraging efforts, sleeping sickness is still endemic in many areas in DRC. Knowledge of transmission modalities could improve disease control. As a matter of accuracy, note that conclusion section in regular articles is made of only few sentences found at the end of the paper. Findings are interpreted in a section called "Discussion". Authors should clarify the study-design process. Were the 60 HAT cases selected only in the basis of their positivity after CATT test or also after parasitological test? Which parasitological test allows the diagnosis of infected patients? It should have been better for authors to provide also data about the presence or not of tsetse flies in areas frequented by populations during their activities. For ethical issues, why do authors not used a written consent and allows parents (adults) for children under 18 to sign it?	Thank you. No further comments! We have created a shorter conclusion after the discussion section. The discussion section runs from line 473 to line 566 in the newer text. The conclusion section runs from line 570 to line 603. We have clarified the study-design process and we have provided two end notes to explain our understanding of the role of the CATT test. We have also briefly explained the parasitological tests in the same end notes. See end of paper after the references section. This study was more focused and it was not designed to determine the presence or not of tsetse flies in areas frequented by populations during their activities. Given needed resources we would be glad to pursue another study on this dimension. We had developed the protocols for data collection under the understanding that the study involved minimal risks for the subjects. These protocols were approved and we proceeded



SDI Review Form 1.6

	Authors should rewrite the discussion section titled "conclusion" by avoiding repetition of data already shown in results section. This manuscript should be given to an English speaking person to correct the English mistakes. Other remarks can be found in the manuscript. A written consent should have been better.	with data collection under that coverage of the approval by the ethics committee. We have provided further details about the approval and the data collection procedures in the newer text of the manuscript. We have asked an English-speaking colleague to correct English mistakes. The new text incorporates the corrections made through the kindness of this colleague. We have identified the other remarks and we have addressed them as requested. Please see below a section of each remark and then a section of the new paper showing what and how corrections were made. In the hindsight, we agree with you and we are prepared to take this suggestion into account for our upcoming research projects.
--	--	--

151 Tshiluba, Lingala, Swahili, Tetela and French. [38]

152  Political Organization: The city of Mbuji-Mayi is made of 5 administrative communes:
153 Bipemba, Dibindi, Diulu, Kanshi and Muya. Politically speaking, the province has endured its
154 share of problems which have impacted its economy and the well-being of its population. At
155 the end of the successive crises up to the culmination of the process of reconciliation with
156 the elections held in 2006, the province has served as a place of great political turmoil where
157 diamond, the natural resource of the province, has made the political leaders to seek and
158 achieve great control of the province by appointing and controlling the leadership of the
159 province and of the most important diamond mining company in the DRC (mining company
160 of Bakwanga or MIBA). [38] Unfortunately most of the resources produced by MIBA during
161 most of the 54 years of the Congolese Independence have been drained out to enrich the



SDI Review Form 1.6

You suggested that we deleted the paragraph running from 151-161 and we did remove it. You can see that it is gone, non-existent in the newer text.

188 **3. STUDY PROBLEM AND OBJECTIVES**
189 **3.1. Situation of HAT in eastern Kasai Province:**
190 HAT due to *Trypanosoma brucei gambiense* is endemo-epidemic in Eastern Kasai-province.
191 In 2009, 869 new HAT cases were declared. Since 2010 to this day, there is stagnation of
192 the annual number of new cases of HAT, with an annual average of 533 cases of patients
193 infected with trypanosoma declared. [27]
194 During 2012, a total of 95 cases of HAT infected patients (source population) has been
195 identified and treated at HAT referral and treatment center of Dipumba (RTC) in Mbuji-Mayi.
196 Among these patients, 60 (63.2 %) were residents of the city of Mbuji-Mayi. These 60 cases
197 constitute our study sample. The other patients (35 or 36.8 per cent) were transferred to the
198 Referral and Treatment Center (DIPUMBA) for intake and management. [27]
199 **3.2. Study Justification and Aims:**
200 This study is needed at this juncture for at least three major reasons. First, it focuses on the
201 DRC, a country that is most affected by HAT. Second, it targets the Congolese province that is
202 ranked as the second worst place in terms of HAT incidence. Third, it looks at a major city at
203 a time where there is not yet a clear understanding of the risk factors that make cities
204 particularly vulnerable to HAT infection. The mechanism through which HAT parasites move
205 in Mbuji-Mayi is poorly known. No study on the social conditions, space occupation and
206

You suggested that we make some corrections in the paragraph running from 190 through line 206 and we made these corrections. You can see this in the paragraphs running from line 242 through line 265 in the new text where we have specifically written the following:

3.1. Situation of HAT in eastern Kasai Province:

HAT due to *Trypanosoma brucei gambiense* is endemo-epidemic in Eastern Kasai-province. In 2009, 869 new HAT cases were declared. Since 2010 to nowadays, there is a stagnation of the annual number of new cases of HAT, with an annual average of 533 cases of HAT- infected patients declared [2].

During 2012, a total of 95 cases of HAT infected patients (source population) has been identified and treated at HAT referral and treatment center of Dipumba (RTC) in Mbuji-Mayi. Among these patients, 60 (63.2 %) were residents of the city of Mbuji-Mayi. These 60 cases constituted our study sample. The other patients (35 or 36.8 per cent) were transferred from other sites outside of Mbuji Mayi to the Referral and Treatment Center (DIPUMBA) for intake and management [2].



SDI Review Form 1.6

3.2. Study Site Justification and Aims of the Study:

This study is needed at this juncture for at least three major reasons. Firstly, it focuses on the DRC, a country that is most affected by HAT. Secondly, it targets a Congolese province that is ranked as the second worst place in terms of HAT incidence. Thirdly, it looks at a major city at a time where there is not yet a clear understanding of the risk factors that make cities particularly vulnerable to HAT infection. Modalities of transmission and disease expansion in Mbuji Mayi are poorly known. Nobody so far has conducted a study on the social conditions, space occupation and human behavior of HAT patients in that area. In the present study, we want to identify the risk factors of HAT infection in Mbuji-Mayi and we particularly emphasize the socio-demographic characteristics and the human factors that contribute to its transmission. Our aim is to provide a better understanding of the epidemiology of HAT and facilitate the formulation of effective interventions for the prevention of HAT infection in Mbuji Mayi and in other African cities.

207 human behavior. HAT patients has been conducted up to this day. In the present study,
208 we want to identify the risk factors of HAT infection in the city of Mbuji-Mayi, with particular
209 emphasis on the socio-demographic characteristics and on the human factors that contribute
210 to its transmission.

211
212

4. MATERIAL AND METHODOLOGY

4.1. Study Design, Population, and Case and Control Identification

215 Study Design: Case-Control Study. The study group consisted of 60 HAT cases and 120
216 healthy controls. The 60 HAT cases were selected on the basis of three criteria: (a) Having
217 during the period going from January to December 2012 a confirmed pathological diagnosis
218 of HAT - - diagnosis based on the results of the card agglutination test for trypanosomiasis
219 (CATT) which is a rapid, simple assay for the detection of specific antibodies in patients with
220 gambiense HAT [40], (b) having one's residence in Mbuji Mayi and (c) being of an age equal
221 to or older than 10 years.



SDI Review Form 1.6

You suggested that we make some corrections in the paragraph running from 207 through line 221 and we made these corrections. You can see this in the paragraphs running from line 267 through line 305 in the new text.

242 During this period of January to December 2012, 95 patients with HAT have been registered
243 including 60 residents of Mbuji-Mayi. Only cases aged 10 years or older were considered.
244 Each case was matched on age (≥ 10 years), sex and place of residence to two controls.
245 These controls were individuals known to be free of THA after clinical examination, and
246 presenting a negative serology test Card Agglutination Test for Trypanosomiasis (CATT-test)
247 [46] in the course of the field survey of May 2012. There was no a single case of
248 trypanosome-infected patient that has declared having changed place of residence. In the
249 recruitment of controls, we have excluded any of the aforementioned patients as well as any
250 persons who live together with the cases. This survey was approved by the local authorities
251 and the provincial ethics committee. The cases and the controls were informed of the
252 purpose and expectations of the study; they have all provided a verbal consent to be
253 participants in the study.

You made some comments/suggestions about the participation of children in the study (line 252). We have revised the paragraph to provide further details. These details can be found in the new text from line 338 through line 355.



SDI Review Form 1.6

333 The proportion of people who know HAT and the tsetse fly as a vector of this diseases is
334 relatively high (86.7% of cases vs 77.5% of the controls) in both groups. The mode of HAT
335 transmission was mentioned by 75% of the cases and 53.3% of the controls (bite by
336 infected/contaminated tsetse). The path of blood transfusion and the vertical transmission
337 (from mother to child during pregnancy/before birth have not been mentioned. Some modes
338 of erroneous transmissions have been cited such as physical contact with HAT patients.

339 The manifestations of HAT that are most known by the cases are, in descending order of
340 importance, sleep disorders (daytime sleepiness and insomnia night) cited by less than half
341 of the cases (31.7%) and controls (40.8 %); slimming (30% vs 22.5 %) and mental disorders
342 (23.3% vs 17.5%). Nobody among HAT cases and their controls has cited cervical
343 adenopathy. The majority of HAT cases are aware that THA reaches the entire world (71.7
344 % vs 68.3 %); they also know that the HAT is curable (83.3% vs 72.5 %). Less than half of
345 the controls (48.3%) are favorable to a close contact (eating and sleeping together) with HAT
346 patients. A non-negligible proportion of the cases (23.3%) and cases (28.3%) believe in the
347 mystical origin of the THA (witchcraft).

348 The majority of cases (76.7% vs 54.2%; $p = .03$) are favorable to HAT screening. A low
349 proportion of cases (33.3% vs 25%) have cited the fixed health structures as a place
350 recommended for HAT screening.

351 Concerning the health care facilities, the majority of HAT patients (83.3% vs 55%; $P = .004$)
352 were aware of and cited the specialized centers of fight, treatment and control of HAT. Less
353 than half of the cases (41.7%) are aware that prevention of the THA is possible. Barely 32%
354 of the cases and 36% of the controls mentioned the trap to tsetse flies as a means
355 of primary prevention of HAT.

You made some comments/suggestions about the terms “diseases” (line 333), “cases” (line 346) and “THA” (line 353). We have revised the paragraph to correct these errors. These details can be found in the new text from line 425 through line 445.



SDI Review Form 1.6

375 Using the logistic regression multivariate analysis, we got the following results (also
376 displayed in Table 2): The supply of water to household and activities carried out in close
377 proximity with a river multiplied by 3.5 the risk of HAT (Adjusted OR = 3.5; 95%CI: 1.2 -10.7,
378 P = .05). The activity of digging diamond multiplied by 4.13 (Adjusted OR = 4.13; 95 %CI:
379 1.89-9.00; P < .0001) the risk of HAT. The proximity of a hog farm multiplied by a factor of
380 2.6 the risk of acquiring HAT (Adjusted OR = 2.6; 95 %CI: 1.3 - 5.2, P = .01). Dish and cloth
381 washing in the water stream multiplied the risk of acquiring HAT by a factor of 1.7 (Adjusted
382 OR = 1.7; 95 %CI, 1.1 - 2.6, P = .05). Engaging in trade activities that involve traveling to
383 rural areas multiplied the risk of acquiring HAT by a factor of 2.32 (Adjusted OR =2.32; 95
384 %CI: 1.07 - 5.02, P = .032).

385

386 **6. CONCLUSION**

387 In the Democratic Republic of the Congo, research published in the medical literature on the
388 risk factors of the HAT has been very limited. Tshimungu et al. (2010) conducted a case-
389 control study in Kinshasa, capital of the DRC, in an endemic area to *Trypanosoma brucei*
390 gambiense. [28] As this was the case in Tshimungu's study, the present study shows that
391 some groups, some activities and some environments increase the risk of acquiring HAT.

You made some comments/suggestions about the terms “traveling” (line 382) and “Conclusion” (line 386). We have revised the text to correct the error. Traveling has been replaced by “travelling”; and a new section called “Discussion” has been added. The details about the change can be found in the new text from line 474 through line 566.



SDI Review Form 1.6

440 The water factor, more precisely, the water supply in the point of natural water significantly
441 increases the risk of HAT infection. According to Meda et al. (1993), the vector of THA
442 (*Glossina palpalis* flies) is particularly abundant near the water points frequented by the
443 human beings from which it gets its food. [51]
444 The data on the dwelling space show that the persons residing close to Savannah are more
445 exposed. The presence of pigs around the habitat appears as a risk factor. Meda and his
446 colleagues (1993) mention that the presence of pigs around the habitat plays two
447 contradictory roles, a protective role by way of diverting the tse-tse flies from the human bait
448 and a role of potential reservoir of the zymodemes which have been isolated in this animal in
449 the Ivory Coast and which are infectious for humans. [51]

We replaced line 444 in first text with what is in line 532 in the new text: “The data on the dwelling space show that the subjects residing close to Savannah are more exposed.”

471 mass screening in the fixed health structures in the city of Mbuji-Mayi. When it is adopted,
472 such integration will be accompanied by the information and the education of the populations
473 as well as the training of health personnel in Mbuji-Mayi who are not seasoned to the
474 principles and practices of HAT screening and eradication. A specific program of active
475 screening in diamond mines along with the establishment of a sustainable and permanent
476 system for safe water supply can significantly reduce the incidence of HAT in Mbuji Mayi.

We replaced “eradication” in line 444 in first text with “elimination” which can be found in line 562 in the new text: “as well as the training of health personnel in Mbuji-Mayi who are not seasoned to the principles and practices of HAT screening and elimination.”