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## **Prevalence of toxoplasmosis and its association with dementia in older adults in central Africa: A result from the EPIDEMCA programme**

Nathalie Bouscaren, Sophie Pilleron, Pascal Mbelesso, Bébène Ndamba-Bandzouzi, Jean-François Dartigues, Jean-Pierre Clément, Pierre-Marie Preux, Marie-Laure Dardé, Maëlen Guerchet

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# Tropical Medicine & International Health

## PREVALENCE OF TOXOPLASMOSIS AND ITS ASSOCIATION WITH DEMENTIA IN OLDER ADULTS IN CENTRAL AFRICA: A RESULT FROM THE EPIDEMCA PROGRAMME

--Manuscript Draft--

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<b>Abstract:</b>	<p><b>Objective:</b> This study aimed at estimating the seroprevalence of <i>Toxoplasma gondii</i> infection in older adults living in Central Africa and at investigating its association with dementia using data from the Epidemiology of Dementia in Central Africa programme, a population-based study.</p> <p><b>Methods:</b> A cross-sectional multicenter population-based study was carried out among participants aged <math>\geq 65</math> years living in rural and urban areas of the Central African Republic and the Republic of Congo. Blood samples were collected from each consenting participant. The detection of anti-T.gondii immunoglobulin G antibodies was done in France using a commercially available ELISA kit. Participants were interviewed using a standardized questionnaire including sociodemographic characteristics. DSM-IV criteria were required for a diagnosis of dementia. Multivariate binary logistic regression models were used to estimate the association between toxoplasmosis infection and dementia.</p> <p><b>Results:</b> Among 1,662 participants, the seroprevalence of toxoplasmosis was 63.0% (95% confidence interval (CI): 60.7-65.3) overall, 66.6% (95%CI: 63.4-69.8) in Central African Republic and 59.4% (95%CI: 56.1-62.7) in the Republic of Congo. In multivariate analyses, toxoplasmosis status was significantly associated with</p>

increasing age ( $p=0.006$ ), Republic of Congo ( $p=0.002$ ), urban area ( $p=0.001$ ) and previous occupation ( $p=0.002$ ). No associations between dementia and toxoplasmosis status or anti- *T gondii* IgG titres were found.

Conclusion: Being infected with *T. gondii* was not associated with dementia among older adults in Central Africa. Our findings are consistent with some previous studies and add to the knowledge on the relationship between *T. gondii* infection and neurological disorders.

1 PREVALENCE OF TOXOPLASMOSIS AND ITS ASSOCIATION WITH DEMENTIA IN OLDER  
2 ADULTS IN CENTRAL AFRICA: A RESULT FROM THE EPIDEMCA PROGRAMME

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4 François Dartigues<sup>5</sup>, Jean-Pierre Clément<sup>1,2,6</sup>, Pierre-Marie Preux<sup>1,2,7</sup>, Marie-Laure Dardé<sup>1,2,8</sup>,  
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30

31 Running title: Toxoplasmosis and dementia in Central

32

33 **ABSTRACT (241 words)**

34 Objective: We aimed at estimating the seroprevalence of *Toxoplasma gondii* infection in older adults  
35 living in Central Africa and investigating its association with dementia using data from the  
36 Epidemiology of Dementia in Central Africa (EPIDEMCA) programme.

37 Methods: A cross-sectional multicentre population-based study was carried out among participants  
38 aged 73 ( $\pm 7$ ) years on average, living in rural and urban areas of the Central African Republic and the  
39 Republic of Congo between November 2011 and December 2012. Blood samples were collected from  
40 each consenting participant. The detection of anti-*T.gondii* immunoglobulin G antibodies was  
41 performed in 2014 in France using a commercially available ELISA kit. Participants were interviewed  
42 using a standardized questionnaire including sociodemographic characteristics. DSM-IV criteria were  
43 required for a diagnosis of dementia. Multivariate binary logistic regression models were used to  
44 estimate the association between toxoplasmosis infection and dementia.

45 Results: Among 1,662 participants, the seroprevalence of toxoplasmosis was 63.0% (95% confidence  
46 interval (CI): 60.7-65.3) overall, 66.6% (95%CI: 63.4-69.8) in Central African Republic and 59.4%  
47 (95%CI: 56.1-62.7) in the Republic of Congo. In multivariate analyses, toxoplasmosis status was  
48 significantly associated with increasing age ( $p=0.006$ ), Republic of Congo ( $p=0.002$ ), urban area  
49 ( $p=0.001$ ) and previous occupation ( $p=0.002$ ). No associations between dementia and toxoplasmosis  
50 status or anti- *T.gondii* IgG titres were found.

51 Conclusion: *T.gondii* infection was not associated with dementia among older adults in Central Africa.  
52 Our findings are consistent with previous studies and add to the knowledge on the relationship  
53 between *T.gondii* infection and neurological disorders.

54

55

56 Keywords: Dementia, Alzheimer's Disease, *Toxoplasma gondii*, seroprevalence, older adults, sub-  
57 Saharan Africa



58 **INTRODUCTION (3,103 words)**

59 Globally, 25-30% of individuals are infected with *Toxoplasma gondii* (*T.gondii*) (1;2) with disparities  
60 across regions, depending on geographical and socio-economic conditions (1;2). Previous studies  
61 estimated at around 40% the prevalence of *T.gondii* infection in general population in the Republic of  
62 Congo (ROC) and in the Central African Republic (CAR) (3;4;4). *T.gondii* infection seroprevalence is  
63 primarily studied in population at risk for developing acute toxoplasmosis such as women of  
64 childbearing age and immuno-compromised patients. Although the risk of being infected with *T.gondii*  
65 increases with age (5), its prevalence among older adults and the effect of age on anti-*T.gondii*  
66 antibody titre evolution remain largely unknown.

67 During a primary *T.gondii* infection, the invasive tachyzoite stages circulate in the blood, invade the  
68 various organs, cross the blood-brain barrier and establish themselves in the brain cells probably as  
69 soon as the end of the first week of infection. This acute toxoplasmosis phase lasts a few weeks. It is  
70 usually asymptomatic, but can also present as a benign disease with lymphadenopathies, fever and  
71 asthenia. Beyond this acute phase, the invasive tachyzoite stages are no longer present, and the chronic  
72 stage of infection is characterized by the presence of latent toxoplasmic cysts in the tissues, and more  
73 particularly the central nervous system. This chronic stage is assumed to persist throughout life  
74 without inducing any symptoms in immunocompetent patients (1).

75 Dementia is a neurodegenerative disease characterized by progressive decline in cognitive functions,  
76 progressive functional impairment, and behavioural and psychological symptoms (6). Alzheimer's  
77 disease, characterized by two core cerebral lesions ( $\beta$  amyloid plaques and neurofibrillary tangles), is  
78 the most common cause of dementia among older people. Lewy Body disease, frontotemporal lobar  
79 degeneration, and vascular disease, are other common causes of dementia, differing in  
80 pathophysiology (7). However, mixed pathologies are much more common than 'pure' forms of  
81 dementia (8). Dementia has a significant impact on those affected, their families and society, with  
82 considerable costs worldwide (9). Demographic ageing worldwide is expected to lead to a dramatic  
83 increase in the number of cases, and African countries are not spared by this phenomenon (10). The

84 prevalence of dementia in adults aged 65 years and older was recently estimated between 6.4% and  
85 8.5% in CAR and between 5.7% and 6.7% in ROC (11;12).

86 Literature studying the association between latent *T.gondii* infection and neurological or psychiatric  
87 disorders is growing (13-17). Chronic infection compromised goal-directed behaviour (18), affected  
88 several aspects of memory (19;20), led to a decline in visual motor coordination, coding ability and  
89 short term memory (21), and to a more rapid decline in executive function and cognitive decline  
90 among older adults (21). Cognitive dysfunctions were attributed to cysts' location in the brain (22;23),  
91 to the immune response in chronically infected patients (24), or to a change in cerebral metabolism  
92 (23;25). A chronic infection accompanied by an increase in interferon  $\gamma$  (IFN- $\gamma$ ) production decreases  
93 the tryptophan pool affecting kynurenic acid and serotonin levels. Moreover, *T.gondii* infection  
94 increases the activity of the tyrosine hydrolase that in turn releases dopamine. The increase in  
95 kynurenic acid and dopamine levels along with the decrease in serotonin level were associated with  
96 cognitive dysfunctions in rodents (23;26;27) and in humans (28). *T.gondii* infection was however  
97 shown to decrease  $\beta$ -amyloid plaque deposition in the cortex and hippocampus suggesting positive  
98 effects of *T.gondii* infection on the pathogenesis and progression of Alzheimer's disease (AD) in mice  
99 (29-31). In humans, case-control studies dedicated to *T.gondii* infection and dementia reported  
100 contradictory results (32-35). Most studies focused on the Alzheimer's subtype (32;33;35). Two  
101 studies found no association between AD and toxoplasmosis infection in the USA (33) and in Iran (32)  
102 whilst the third one in Turkey suggested that toxoplasma infection may be involved in the  
103 pathogenetic mechanisms of AD (35). The only study investigating dementia (all subtypes combined),  
104 in Egypt, showed that toxoplasma positive participants had an increased likelihood of having  
105 dementia, regardless of their ApoE genotype (34). To our knowledge, no study has been conducted in  
106 sub-Saharan African countries yet, where both dementia and *T. gondii* epidemiology may present  
107 particular aspects.

108 We aimed first at estimating the seroprevalence of *T.gondii* infection among older adults in Central  
109 Africa; secondly, at investigating the association between *T.gondii* infection and dementia, within the

110 Epidemiology of Dementia in Central Africa (EPIDEMCA) programme, a large population-based  
111 study.

112

## 113 **METHODS**

### 114 *Participants*

115 Our study population consisted of participants included in the EPIDEMCA programme, a multicentre  
116 cross-sectional population-based study conducted in CAR and ROC between November 2011 and  
117 December 2012. The detailed methodology is described in an open access publication (36). In essence,  
118 participants aged 65 years and older who had lived in the study area for at least six months were  
119 included. The study areas included the capitals of CAR (Bangui) and ROC (Brazzaville), and two rural  
120 areas (Nola in CAR and Gamboma in ROC). The sample size was calculated *a priori* with the aim of  
121 estimating dementia prevalence, and was then rounded at 500 in each study site. In absence of detailed  
122 census, the participants' selection in urban areas was carried out using a proportional random sampling  
123 (to represent Bangui and Brazzaville's diverse populations) while a door-to-door approach was  
124 preferred due to logistic and financial constraints in rural areas. Response rates varied between 93 and  
125 97% across sites, with the only exclusion criteria being refusal or the presence of severe disease with  
126 short-term high risk of death.

127 Approvals were obtained from the ethical committee supervised by the Ministry of Public Health in  
128 CAR, the Comité d'Éthique de la Recherche en Sciences de Santé in ROC, and an ethical review  
129 board from the Comité de Protection des Personnes du Sud-Ouest et d'Outre-Mer 4 in France. All  
130 participants and/or their families gave informed consent prior to inclusion in the study. Written  
131 consent was obtained when feasible. Consent was obtained by thumbprint for illiterate people.

### 132 *Serological analysis*

133 Each consenting participant had 20 mL of blood collected into two polypropylene EDTA tubes by a  
134 dedicated nurse. Whole fresh blood samples were centrifuged and aliquoted within few hours to avoid  
135 degradation due to high temperatures and then frozen at -20°C or -80°C in the nearest laboratory.  
136 Plasma aliquots were stored at the Pasteur Institute of Bangui in CAR and the National Laboratory of

137 Public Health in Brazzaville in ROC before dry-ice shipping to the University of Limoges where  
138 plasma samples were kept stored at -80°C until analysed. In 2014, the detection of anti-*T.gondii*  
139 immunoglobulin G (IgG) was done using the VIDAS TOXO IgG II test (Biomérieux, France),  
140 according to the manufacturer's instructions. This test is validated for detection of anti-*T.gondii* IgG in  
141 plasma. Results were reported in International Units per millilitre (IU/mL). Samples with anti-*T.gondii*  
142 IgG <4 IU/mL were considered as seronegative. A sample was considered as positive when the titre  
143 was equal or greater than 8 IU/mL. Samples with titres  $\geq 300$  UI/mL were diluted in the negative  
144 control included with the VIDAS TOXO IgG II test until titres could be determined. Titres comprised  
145 between 4 IU/mL and 8 IU/mL were considered as equivocal and further analysed by VIDAS TOXO  
146 competition (Biomérieux, France), which better correlated with low titres of the usual reference test,  
147 namely dye-test. Samples with indexes below 1.6 were considered as seropositive according to the  
148 manufacturer's instructions. The *T.gondii* positive group included all participants that were positive  
149 either with VIDAS Toxo IgG II or with VIDAS Toxo Competition assay.

#### 150 *Dementia assessment*

151 Dementia was assessed following a two-stage process. First, cognitive screening was performed using  
152 the Community Screening Interview for Dementia (CSI-D) (37) adapted, back-translated and pretested  
153 in the local languages (Sango in CAR, Lari, Lingala, and Kituba in ROC). Every participant obtaining  
154 a poor performance on the CSI-D cognitive tests (COGSCORE  $\leq 24.5$ ) was suspected of having  
155 cognitive impairment and referred for neurological assessment. During the second phase which was  
156 conducted at the hospital 3-14 weeks later, further psychometric tests were conducted, including the  
157 Free and Cued Selective Reminding Test (38), Zazzo's cancellation task (39) and Isaac's Set Test of  
158 verbal fluency (40). Neurologists performed clinical examination, recorded history of stroke and  
159 presence of depressive disorders, and assessed orientation skills and daily activities. Dementia was  
160 diagnosed according to the DSM-IV criteria (6). An experienced neurologist (JFD) reviewed all  
161 medical records and cognitive test performances in order to reach a consensus.

#### 162 *Statistical analysis*

163 Sociodemographic data included age, sex, marital status (married, never  
164 married/widowed/divorced/separated), education (no education, at least primary school), occupation  
165 (farmer/breeder/fisher *vs.* other), country (CAR, ROC) and area (urban, rural). Age was ascertained  
166 from official documents, using historical events or from an informant if previous methods were  
167 unsuccessful. All variables were collected during the first phase in all participants.

168 Study population characteristics were described in terms of means with corresponding standard  
169 deviations for age, median with its inter-quartiles range (IQR) for antibody titres and cognitive scores,  
170 and percentages for all categorical variables. Prevalence of toxoplasmosis was presented with its 95%  
171 confidence interval (CI). Comparisons were carried out between countries using the Chi-square test  
172 and Kruskal-Wallis test when appropriate. The correlation between the anti-IgG titre and age was  
173 tested using the Spearman test.

174 Factors associated with *T.gondii* infection were examined using logistic regression models. All factors  
175 associated with *T.gondii* infection and dementia at  $p < 0.20$  in univariate analysis were included in  
176 multivariate logistic regression model. The variable selection was carried out using a backward  
177 stepwise approach in which variables considered to be a confounder (odds ratio's variation above  
178 15%) were kept in the model. The association between toxoplasmosis and dementia was first analysed  
179 in unadjusted logistic regression model and then in a model adjusted for age, sex, country, area and  
180 education.

181 In a sensitivity analysis, we ran the fully-adjusted logistic regression model with quintiles of anti-IgG  
182 titres as dependent variable instead of toxoplasmosis status.

183 The level of significance was fixed at 0.05 for all analyses. Statistical analyses were carried-out using  
184 Stata version 10.1 for Windows (StataCorp, College Station, TX).

185

## 186 **RESULTS**

### 187 *Characteristics of the EPIDEMCA participants*

188 Among 2,002 participants included in the EPIDEMCA study, 340 participants were excluded because  
189 they did not have blood samples due to refusals (n=176), impossible blood withdrawal (n=35), poor

190 health conditions (n=34), absence on the day of blood collections (n=9), and non-exploitable samples  
191 (n=86). A total of 1,662 participants were therefore analysed (Figure 1).

192 General socio-demographic characteristics are shown in Table 1. Participants were 73.1 ( $\pm$ 6.6) years  
193 on average and ROC participants were older and less likely living as a couple than those from CAR.

#### 194 *Seroprevalence of Toxoplasma infection*

195 Of the 1,662 individuals, 1,047 were found to be positive for anti-*T.gondii* IgG antibodies, *i.e.* a  
196 seroprevalence of 63.0% (95%CI: 60.7-65.3). The seroprevalence was lower in ROC than in CAR  
197 ( $p=0.002$ ) and as a whole, lower in rural areas than urban areas (57.3% [95%CI: 53.9-60.7] vs. 68.5%  
198 [95%CI:65.4-71.6];  $p<0.001$ ) (Figure 2). In both country, the seroprevalence was significantly  
199 associated with areas ( $p<0.001$ ) but the urban-rural gradient was inversed.

200 In bivariate analyses, *T.gondii* infection was significantly associated with increasing age in 5-year  
201 bands, country, rural areas, no education, and previous occupation. In multivariate analysis, *T.gondii*  
202 infection remained significantly associated with country, area and previous occupation (Table 2).

203 Median anti-*T.gondii* IgG titre was 32 (IQR 120) IU/mL (min-max: 0-15 000), 22 (105) IU/mL in  
204 ROC and 47 (128) IU/mL in CAR ( $p<0.001$ ). A total of 99 participants (6.0%) had anti-*T.gondii* IgG  
205 titre>300 IU/mL, 44 (5.3%) in CAR and 55 (6.0%) in ROC ( $p=0.28$ ), and 48 (2.9%) had a titre above  
206 1000 IU/mL, 21 (2.5%) in CAR and 27 (3.2%) in ROC ( $p=0.40$ ). No correlation between the anti-IgG  
207 titre and age was found ( $r=0.044$ ;  $p=0.07$ ).

#### 208 *Association between T.gondii infection and dementia*

209 A total of 379 participants were excluded because cognitive status could not be determined for 276 of  
210 them (including 174 lost of follow up or missing) and 102 participants were diagnosed with MCI,  
211 resulting in an analytical sample size of 1,386 participants (Figure 1). Among them, 100 (7.2%) had  
212 dementia. Table 3 presents the socio-economic and clinical characteristics of participants with and  
213 without dementia. The *T.gondii* infection seroprevalence did not differ significantly based on the  
214 cognitive status: 64.0% (95%CI: 54.6-73.4) in participants with dementia *versus* 63.4% (95%CI: 60.7-  
215 66.0) in those without dementia ( $p=0.94$ ). In the unadjusted and adjusted models, no association was

216 shown between *T.gondii* seroprevalence and dementia (respectively OR=1.0 (95%CI: 0.7-1.6) and  
217 adjusted OR=1.0 (95%CI: 0.6-1.6)).

218 In a sensitivity analysis, we replaced the *Toxoplasma* infection status by quintiles of anti-IgG titre  
219 (Figure 3). No association was observed in both unadjusted (p=0.13) or adjusted models (p=0.36).

220

## 221 **DISCUSSION**

222 To our knowledge, this large population-based study is the first study to investigate the prevalence of  
223 *T.gondii* infection in older native African adults and the first study to examine its relationship with  
224 dementia in the Central African context. We found a high prevalence of *T.gondii* infection in older  
225 people regardless of areas (urban or rural) and countries. However we did not find any association  
226 between *T.gondii* and dementia.

227 In African tropical countries, such as CAR and ROC, a high prevalence of toxoplasmosis is usually  
228 observed due to the low sanitary conditions, with poor or inexistent water treatment (1;2). In these  
229 conditions, soil, food and water contaminated with oocysts increase the risk of *T.gondii* infection.

230 The higher seroprevalence observed in CAR may be partly explained by the lower socioeconomic  
231 status in CAR compared to ROC (41). *T.gondii* infection was described as associated with poverty in  
232 different countries due to poor hygienic and sanitary conditions (42-44).

233 In our study, the seroprevalence was significantly higher in urban areas than in rural areas as a whole,  
234 but differences were observed at the country level. In CAR, the seroprevalence was higher in rural  
235 area than in urban area while, in ROC, an inverse rural-urban gradient was observed. In ROC, a more  
236 westernised lifestyle of Brazzaville inhabitants could lead to a more frequent meat intake than in  
237 Gamboma where meat is more expensive. Seroprevalence was also lower in people who worked or are  
238 working in farms, fisheries or with livestock. People performing better paid occupations may thus  
239 have access to a diet richer in fruits, vegetables and meat that may be contaminated with parasite.  
240 Unfortunately, soil exposure was not collected and data about food consumption were limited.

241 Heterogeneity in populations (women of childbearing age vs. older people) and design (case-control  
242 vs. cross-sectional survey) limits the comparison of our findings with other studies.

243 Surprisingly, we found a relatively large number of older adults with high antibody titres. Although  
244 studies on the evolution of the *T.gondii* serology in older populations are scarce (45), it is generally  
245 accepted that antibody titre decreases with age and are maintained at a low level over lifetime after an  
246 initial primary infection (46). Lifetime persistence of anti-*T.gondii* IgG results from continuous  
247 immune system stimulation by long-lasting tissue cysts. The usual decrease in antibody titres in older  
248 adults is hypothesized to be linked to the development of immunosenescence (47). Several hypotheses  
249 may explain the relatively high proportion of elevated titres in older people in our study: i) a primary  
250 infection during the sample collection. The detection of IgM antibodies could have confirmed this  
251 hypothesis, but it was not tested here due to financial constraints; ii) a reinfection by a different  
252 *Toxoplasma* strain that would have resulted in an increase in IgG titres. Indeed, clinical observations  
253 have shown that an immune response against a chronic infection does not prevent reinfection of  
254 immunocompetent individuals with a strain different that the one responsible for the primary infection  
255 (48). This hypothesis cannot be ruled out in our study since different genotypes have been identified in  
256 Central Africa (49-51). The immunosenescence or a T-cell exhaustion during a chronic infection (52)  
257 could facilitate the process of re-infection. iii) a non-specific and chronic immune stimulation due to  
258 different infectious agents (malaria, and other parasitic and viral diseases); iv) a genetic background  
259 leading to a higher humoral immune response in African population. Indeed, a high proportion  
260 (40.8%) of high levels of anti-*T.gondii* IgG (>400 IU/mL) was also reported in CAR in younger  
261 people (53).

262 Previous studies that examined the association between *T.gondii* chronic infection and Alzheimer's  
263 disease (AD) or dementia reported conflicting results (32-35). Our findings are contradictory with the  
264 ones of the only study assessing *T.gondii* infection as a correlate of dementia, carried out in a much  
265 younger population in Egypt (34). Different methodologies, including participant recruitment and  
266 statistical analyses, may explain these discrepancies. Another explanation may be the influence of the  
267 *T.gondii* strain on chronic brain infection in immunocompetent patients. In *in-vitro* cell culture  
268 systems, different immune responses or neurotransmitter expression were observed in human nervous  
269 cell infected by diverse *T.gondii* strains (54-56). In humans, a serotyping study suggested that



270 serological pattern consistent with Type I strain in mothers was more susceptible to be associated with  
271 psychosis in offspring (57). More recently, in a murine model of AD, only mice infected with a type II  
272 strain of *T.gondii*, a major lineage that predominates in Europe and North America, were protected  
273 against deposition of amyloid beta, a marker of AD, despite both type II and type III strains  
274 establishing a chronic CNS infection and inflammatory response (29). Mice infected with an  
275 attenuated type I strain that does not persist in mouse brain were not protected against amyloid beta  
276 deposition. Transposing data from animal models to human populations is particularly delicate as not  
277 all dementia subtypes share the same pathophysiological process and knowledge of the strains  
278 circulating in different countries is still incomplete (51;58;59). We however can reasonably think that  
279 our participants were infected by African strains, which share some genetic similarities with type I  
280 strains. Our results suggest that strains circulating in sub-Saharan Africa have no association with  
281 dementia.

282 The main strengths of our study are the use of a large, multicentre population-based design, the high  
283 number of participants with blood sample and a rigorous methodological method for establishing  
284 dementia diagnosis. However, a few limitations must be acknowledged. We were not able to analyse  
285 dementia sub-types, notably Alzheimer's disease, due to low frequencies. Additionally, we lack data  
286 that might influence our results such as timing of initial infection, interactions with other infectious  
287 diseases, and host genetic factors, as well as wealth or income which are potential confounders. Due to  
288 the study design, we are not able to rule out that earlier deaths due to *T.gondii* seropositivity obscured  
289 the association with dementia.

290 This large multicentre population-based study showed a high prevalence of *T.gondii* infection in older  
291 adults in Central Africa, with disparities in two neighbouring but different countries and areas related  
292 to socioeconomic and sanitary conditions. We failed to show any association between *T.gondii* chronic  
293 infection and dementia but future investigations should consider the association with Alzheimer's  
294 disease and Mild Cognitive Impairment. Another perspective would be to evaluate associated  
295 infectious agents as done for other neurological conditions (60).

296

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313

314 **Declaration of interest**

315 We declare that we have no conflict of interest.

316

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472 Table 1: Sociodemographic characteristics of participants based on country (n=1,662), EPIDEMCA,  
 473 2011-2012  
 474

	<b>Total</b>	<b>CAR</b>	<b>ROC</b>	<b>p</b>
<b>Sample, n</b>	1662	827	835	
<b>Age (years), n (%)</b>				<b>0.010</b>
65-69	608 (36.6)	329 (39.8)	279 (33.4)	
70-74	427 (25.7)	216 (26.1)	211 (25.3)	
75-79	327 (19.7)	153 (18.5)	174 (20.8)	
80 +	300 (18.1)	129 (15.6)	171 (20.5)	
<b>Sex, n (%)</b>				0.583
Males	644 (38.8)	315 (38.1)	329 (39.4)	
Females	1018 (61.3)	512 (61.9)	506 (60.6)	
<b>Area, n (%)</b>				0.085
Urban	847 (51.0)	439 (53.1)	408 (48.9)	
Rural	815 (49.0)	388 (46.9)	427 (51.1)	
<b>Education, n (%)</b>				0.812
No education	1148 (69.2)	569 (68.9)	579 (69.4)	
At least primary school	512 (30.8)	257 (31.1)	255 (30.6)	
<i>Missing values</i>	2	1	1	
<b>Marital status, n (%)</b>				<b>0.017</b>
Living as a couple	616 (37.1)	283 (45.9)	333 (39.9)	
Single, widow, separated/divorced	1044 (62.9)	543 (65.7)	501 (60.1)	
<i>Missing values</i>	2	1	1	
<b>Previous occupation, n (%)</b>				0.790
Farmer, breeder, fisherman	817 (49.3)	409 (49.6)	408 (48.9)	
Others	842 (50.8)	416 (50.4)	426 (51.1)	
<i>Missing values</i>	3	2	1	

Table 2: Factors associated with Toxoplasma seroprevalence (n=1662), EPIDEMCA, 2011-2012

	Not infected n(%)	Infected n(%)	Univariate analysis		Initial multivariate model		Final multivariate model	
			OR (95%CI)	<i>p</i>	OR (95%CI)	<i>p</i>	OR (95%CI)	<i>p</i>
<b>Age (years)</b>				<b>0.029</b>		<b>0.003</b>		<b>0.006</b>
65-69	237 (38.5)	371 (35.4)	1		1		1	
70-74	174 (28.3)	253 (24.2)	0.9 (0.7-1.2)		1.0 (0.7-1.2)		0.9 (0.7-1.2)	
75-79	108 (17.6)	219 (20.9)	<b>1.3 (1.0-1.7)</b>		<b>1.4 (1.1-1.9)</b>		<b>1.4 (1.0-1.8)</b>	
80+	96 (15.6)	204 (19.5)	<b>1.4 (1.0-1.8)</b>		<b>1.5 (1.1-2.1)</b>		<b>1.5 (1.1-2.0)</b>	
<b>Sex</b>				0.111		0.631		
Males	223 (36.3)	421 (40.2)	1		1			
Females	392 (63.7)	626 (59.8)	0.8 (0.7-1.0)		0.9 (0.7-1.2)			
<b>Country</b>				<b>0.002</b>		<b>0.002</b>		<b>0.002</b>
CAR	276 (44.9)	551 (52.6)	1		1		1	
ROC	339 (55.1)	496 (47.4)	<b>0.7 (0.6-0.9)</b>		<b>0.7 (0.6-0.9)</b>		<b>0.7 (0.6-0.9)</b>	
<b>Area</b>				<b>0.001</b>				<b>0.001</b>
Rural	348 (56.6)	467 (44.6)	1		1		1	
Urban	267 (43.4)	580 (55.4)	<b>1.6 (1.3-2.0)</b>		<b>1.4 (1.1-1.8)</b>		<b>1.4 (1.2-1.8)</b>	
<b>Education</b>				<b>0.019</b>		0.288		
No education	446 (72.6)	702 (67.1)	1		1			



At least primary school	168 (27.4)	344 (32.9)	<b>1.3 (1.0-1.6)</b>	1.2 (0.9-1.5)		
<b>Marital status</b>				0.587		
Single, widow, separated/divorced	381 (62.1)	663 (63.4)	1	-		
Living as a couple	233 (38.0)	383 (36.6)	0.9 (0.8-1.2)	-		
<b>Previous occupation</b>				<b>&lt;0.001</b>	<b>0.013</b>	<b>0.002</b>
Others	270 (44.0)	572 (54.7)	1	1	1	
Farmer, breeder, fisherman	344 (56.0)	473 (45.3)	<b>0.6 (0.5-0.8)</b>	<b>0.7 (0.6-0.9)</b>	<b>0.7 (0.6-0.9)</b>	

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CAR, Central African Republic; CI, Confidence Interval; OR, Odds ratio; ROC, Republic of Congo

Table 3. Characteristics of participants according to dementia diagnosis, EPIDEMCA, 2011-2012

	<b>No dementia (n=1286)</b>	<b>Dementia (n=100)</b>	<b>p</b>
<b>Age (years)</b>			<0.001
65-69	528 (41.1)	13 (13.0)	
70-74	343 (26.7)	16 (16.0)	
75-79	226 (17.6)	20 (20.0)	
80+	189 (14.7)	51 (51.0)	
<b>Females</b>	713 (55.4)	80 (80.0)	<0.001
<b>CAR</b>	627 (48.8)	57 (57.0)	0.112
<b>ROC</b>	659 (51.2)	43 (43.0)	
<b>Rural</b>	592 (46.0)	51 (51.0)	0.337
<b>No education</b>	814 (63.3)	88 (88.9)	<0.001
<i>missing data</i>		0	1
<b>Living as a couple</b>	539 (41.9)	22 (22.2)	<0.001
<i>missing data</i>		0	1
<b>Farmer, breeder, fisherman</b>	575 (44.8)	61 (61.6)	0.001
<i>missing data</i>		0	1
<b>Cognitive score (median, IQR)</b>	28.5 (25.4-30.4)	19.1 (15.3-21.9)	<0.001
<b><i>T.gondii</i> infection (positive)</b>	815 (63.4)	64 (64.0)	0.900
<b>Anti-IgG titers (median, IQR)</b>	32 (0.0-120.0)	40.5 (1.0-11.5)	0.421

CAR: Central African Republic; IQR: interquartile range

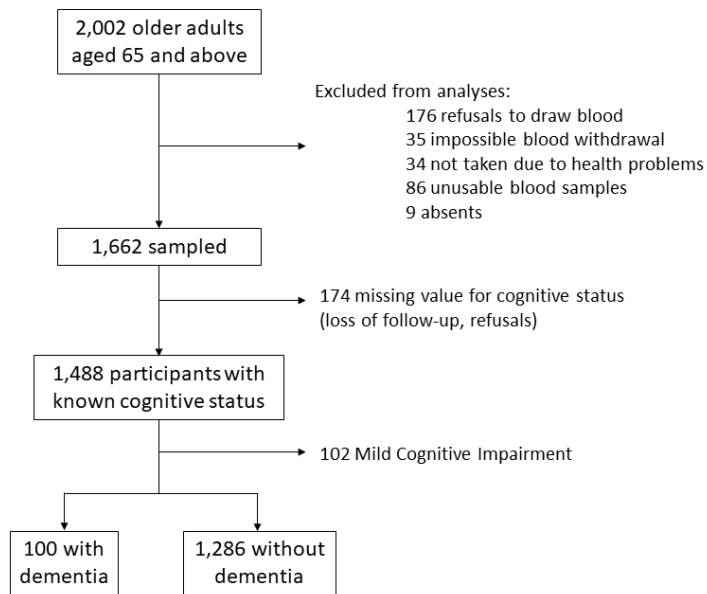
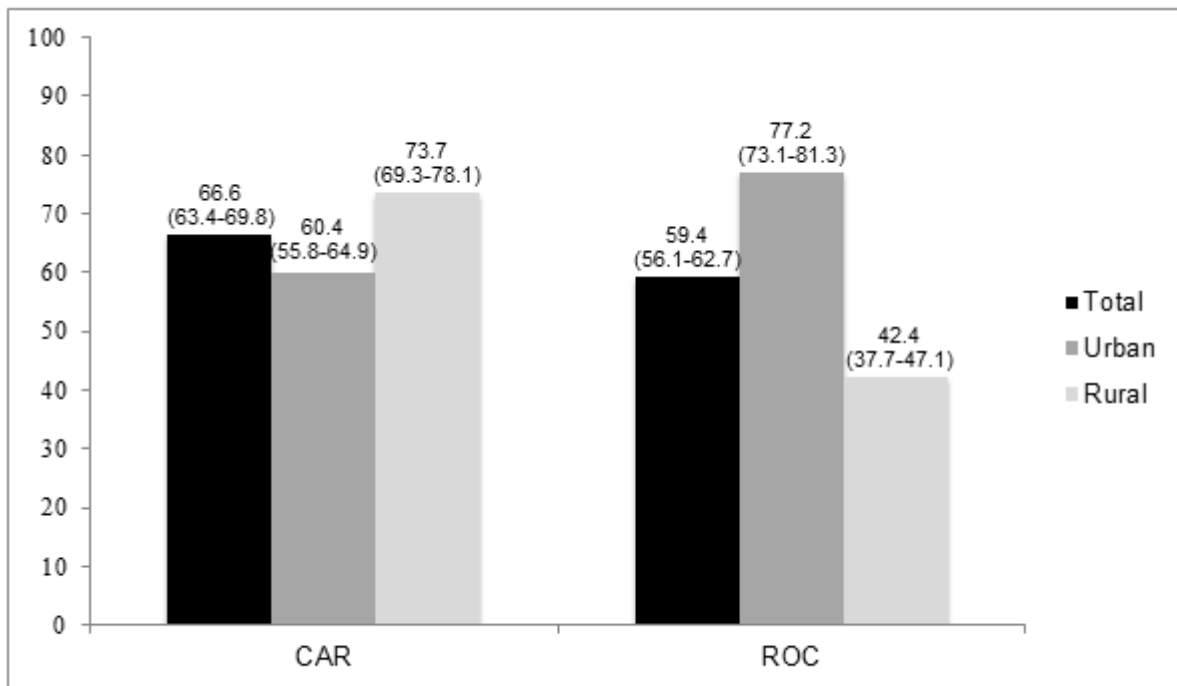


Figure 1: Flow chart of study sample, EPIDEMCA, 2011-2012



CAR Central African Republic; ROC Republic of Congo

Figure 2: Seroprevalence of *Toxoplasma* infection based on country and area, EPIDEMCA, 2011-2012.

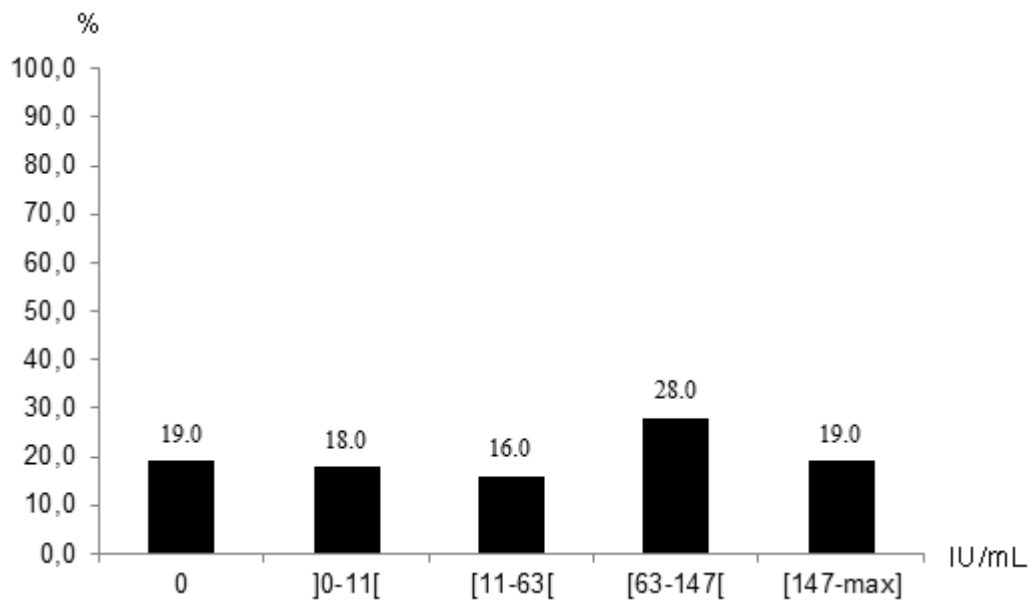


Figure 3: Prevalence of dementia based on quintiles of anti-*Toxoplasma* IgG titres (n=1,386), EPIDEMCA, 2011-2012.