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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

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| Abstract: | <p>Objective: 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>Methods: A cross-sectional multicenter population-based study was carried out among participants aged ≥ 65 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-<i>T.gondii</i> 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>Results: 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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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 (± 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 (β 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 γ (IFN- γ) 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 β -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 ≥ 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 ≤ 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

| | Total | CAR | ROC | p |
|-----------------------------------|--------------|------------|------------|--------------|
| Sample, n | 1662 | 827 | 835 | |
| Age (years), n (%) | | | | 0.010 |
| 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) | |
| Sex, n (%) | | | | 0.583 |
| Males | 644 (38.8) | 315 (38.1) | 329 (39.4) | |
| Females | 1018 (61.3) | 512 (61.9) | 506 (60.6) | |
| Area, n (%) | | | | 0.085 |
| Urban | 847 (51.0) | 439 (53.1) | 408 (48.9) | |
| Rural | 815 (49.0) | 388 (46.9) | 427 (51.1) | |
| Education, n (%) | | | | 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 | |
| Marital status, n (%) | | | | 0.017 |
| 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 | |
| Previous occupation, n (%) | | | | 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> |
| Age (years) | | | | 0.029 | | 0.003 | | 0.006 |
| 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) | 1.3 (1.0-1.7) | | 1.4 (1.1-1.9) | | 1.4 (1.0-1.8) | |
| 80+ | 96 (15.6) | 204 (19.5) | 1.4 (1.0-1.8) | | 1.5 (1.1-2.1) | | 1.5 (1.1-2.0) | |
| Sex | | | | 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) | | | |
| Country | | | | 0.002 | | 0.002 | | 0.002 |
| CAR | 276 (44.9) | 551 (52.6) | 1 | | 1 | | 1 | |
| ROC | 339 (55.1) | 496 (47.4) | 0.7 (0.6-0.9) | | 0.7 (0.6-0.9) | | 0.7 (0.6-0.9) | |
| Area | | | | 0.001 | | | | 0.001 |
| Rural | 348 (56.6) | 467 (44.6) | 1 | | 1 | | 1 | |
| Urban | 267 (43.4) | 580 (55.4) | 1.6 (1.3-2.0) | | 1.4 (1.1-1.8) | | 1.4 (1.2-1.8) | |
| Education | | | | 0.019 | | 0.288 | | |
| No education | 446 (72.6) | 702 (67.1) | 1 | | 1 | | | |

| | | | | | | |
|-----------------------------------|------------|------------|----------------------|----------------------|----------------------|--------------|
| At least primary school | 168 (27.4) | 344 (32.9) | 1.3 (1.0-1.6) | 1.2 (0.9-1.5) | | |
| Marital status | | | | 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) | - | | |
| Previous occupation | | | | <0.001 | 0.013 | 0.002 |
| Others | 270 (44.0) | 572 (54.7) | 1 | 1 | 1 | |
| Farmer, breeder, fisherman | 344 (56.0) | 473 (45.3) | 0.6 (0.5-0.8) | 0.7 (0.6-0.9) | 0.7 (0.6-0.9) | |

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

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

CAR: Central African Republic; IQR: interquartile range

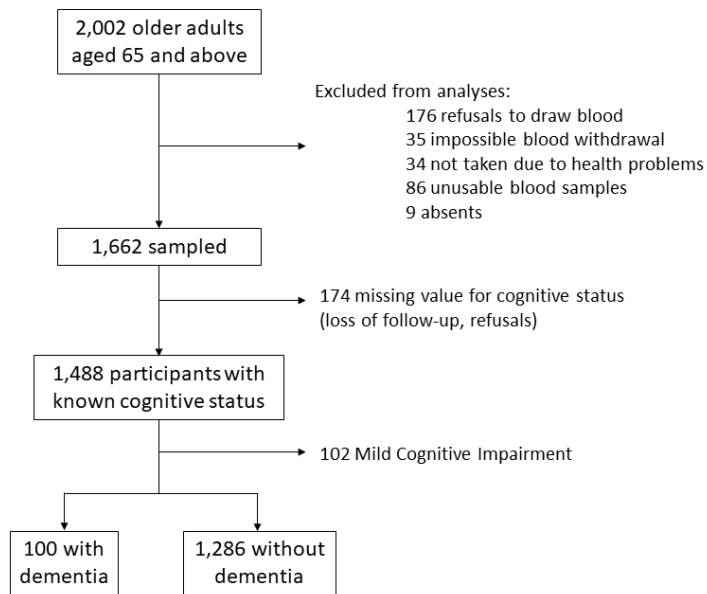
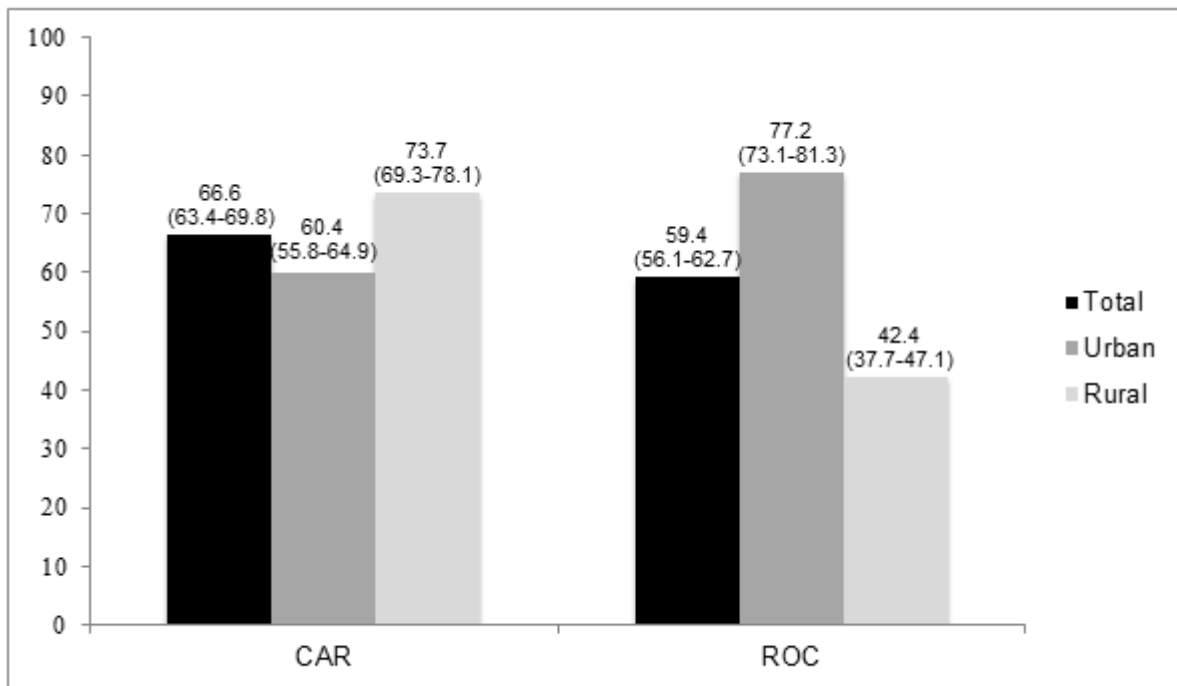


Figure 1: Flow chart of study sample, EPIDEMCA, 2011-2012



CAR Central African Republic; ROC Republic of Congo

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

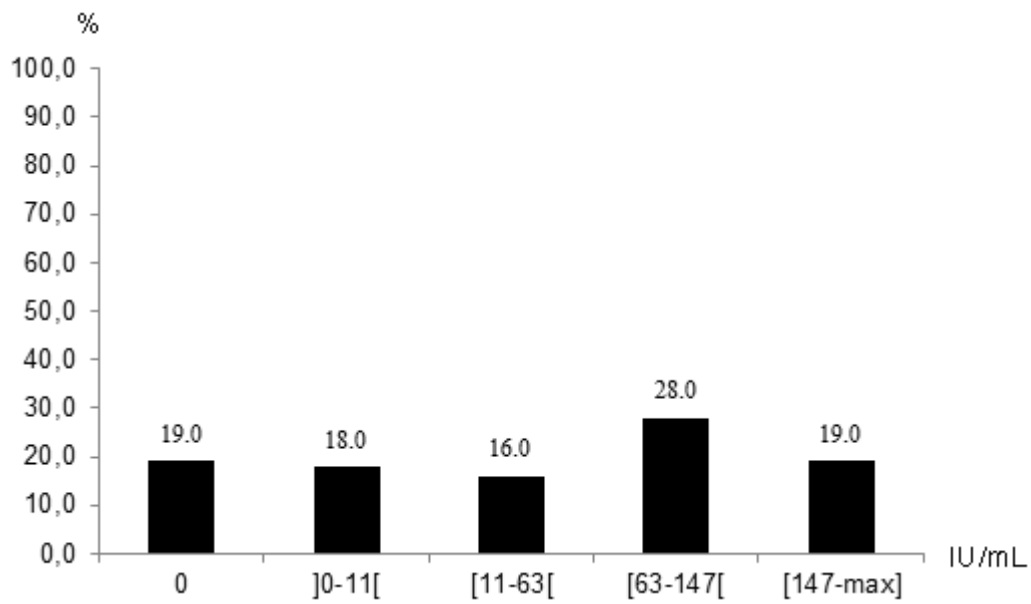


Figure 3: Prevalence of dementia based on quintiles of anti-*Toxoplasma* IgG titres (n=1,386), EPIDEMCA, 2011-2012.