Title:

Neuropsychiatric symptoms among older adults living in two countries in Central Africa (EPIDEMCA study).

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Acknowledgements

- French National Agency (ANR) for funding this study through the ANR-09-MNPS-009-01 grant
- Universities of Bangui (CAR) and Marien Ngouabi in Brazzaville (ROC)
- Institut Pasteur in Bangui and Laboratoire National de Santé Publique in Brazzaville
- Health ministries of the Central African Republic and the Republic of Congo, for their moral support
- University of Limoges, Doctoral School of Limoges University
- Limousin Regional Council

All the participants to this survey, the investigators, and staffs of Bangui and Brazzaville hospitals for their assistance.

Description of author's roles:

All authors worked collectively to design the EPIDEMCA protocol.

I. Yoro-Zohoun conducted data analysis and wrote the first draft.

M. Guerchet, P. Nubukpo, P-M Preux were involved in data analysis and interpretation.

J-P Clément, D. Houinato have participated in critical revision of the manuscript for important intellectual content

B. Ndamba-Bandzouzi, P. Mbelesso and M. Guerchet supervised data collection.

J-F. Dartigues, B. Ndamba-Bandzouzi, and P. Mbelesso were responsible for diagnosing cognitive disorders.

All authors reviewed the manuscript, provided further contributions and suggestions, and approved the final manuscript.

Abstract: 250 words

Objectives: Our study aimed at estimating the prevalence of neuropsychiatric symptoms and investigating associated factors among older adults living in two countries in Central Africa (Central African Republic (CAR) and Republic of Congo (ROC)).

Methods: The EPIDEMCA multicentre population-based study was carried out in rural and urban areas of CAR and ROC between 2011 and 2012 among people aged 65 and over. After cognitive screening using the Community Screening Interview for Dementia, participants with low performances underwent neurological examination including the brief version of the NeuroPsychiatric Inventory (NPI-Q). Multivariate logistic regression analyses were performed to identify factors independently associated with neuropsychiatric symptoms in this population.

Results: NPI-Q data were available for 532 participants. Overall, 333 elderly people (63.7%) reported at least one neuropsychiatric symptom. The prevalence of neuropsychiatric symptoms was 89.9% (95% CI: 84.6-95.1) in participants with dementia, 73.4% (95% CI: 65.1-81.7) in participants with Mild Cognitive Impairment (MCI), and 48.7% (95% CI: 42.9-54.6) in participants with no MCI nor dementia after neurological examination" ($p<0.0001$). The most common symptoms were depression, anxiety and irritability. Participants living in Gamboma, with normal hearing and with friends in the community were less likely to present neuropsychiatric symptoms. Physical disability, difficulties in eating, female sex and dementia were significantly associated with neuropsychiatric symptoms.

Conclusion: Neuropsychiatric symptoms are common among older people with neurocognitive disorders in CAR and ROC. Our results confirm those from previous studies in Nigeria and Tanzania. Nevertheless, knowledge of these symptoms remains limited in sub-Saharan Africa, hampering their appropriate management.

Keywords: Neuropsychiatric symptoms, neuropsychiatric inventory, older adults, neurocognitive disorders, dementia, sub-Saharan Africa, Republic of Congo, Central African Republic.

Key points:

- Prevalence of neuropsychiatric symptoms among older people with neurocognitive disorders is high in CAR and ROC.
- Both presence of neuropsychiatric symptoms and their number increased with the severity of the cognitive impairment.
- The most frequent symptoms reported were depression, anxiety, irritability, sleep and night time behaviour disorders, delusions and apathy.
- Difficulties in eating, physical disability, female sex and dementia were significantly associated with neuropsychiatric symptoms.

Main text (introduction, materials and methods, results, discussion)

Introduction

Neuropsychiatric symptoms, also called behavioural and psychological symptoms of dementia (BPSD), are often associated with neurocognitive disorders. Prevalence of BPSD between 50.0 and 100.0% were reported worldwide among people with dementia, with the most common symptoms being apathy, agitation and depression [1–3]. Only a few studies focussing on BSPD were conducted in low-and middle-income countries (LMIC). In a multicentre study performed across 17 LMIC, at least one BPSD was reported in 70.9% of the 555 participants with dementia [4]. In sub-Saharan Africa (SSA), neuropsychiatric symptoms were investigated in community-based studies. These symptoms were present in 61.9% of older participants with normal cognition, 90.6% of Mild Cognitive Impairment (MCI) participants and 79.4% of participants with dementia in Nigeria [5] . In Tanzania, the prevalence of neuropsychiatric symptoms was estimated at 64.0% in controls and 88.4% in people with dementia[6].

According to the World Health Organization, neuropsychiatric disorders are responsible for 6.6% of Disability-Adjusted Life Years (DALYs) among people aged 60 and over [7]. BPSD increase the burden in people with dementia and their caregivers [8]. They are leading to poorer quality of life, mood disorders and psychological distress among caregivers [9]. In SSA, people with dementia are mainly cared for by family members and live in the community [10], while healthcare systems are not yet equipped to cope with increasing health issues of ageing populations [11], adding to the burden experienced.

To date, there are no studies on neuropsychiatric symptoms among older adults in Central Africa. The present study aimed at estimating the prevalence of neuropsychiatric symptoms and investigating associated factors in older people living in two Central Africa countries, the Central African Republic (CAR) and the Republic of Congo (ROC). This study is part of the Epidemiology of Dementia in Central Africa (EPIDEMCA) programme, which main objectives were to estimate the prevalence of dementia and cognitive disorders and to evaluate associated factors among older people from rural and urban areas of Central Africa.

Materials and Methods

- **Design and Participants**

The EPIDEMCA multicentre population-based survey included 2002 adults aged 65 years and over, living in the capitals of CAR (Bangui) and ROC (Brazzaville), and rural areas (Nola in CAR and Gamboma in ROC) between November 2011 and December 2012. The detailed methodology has been described elsewhere [12]. Sample size was estimated at 500 in each study site, based on an expected dementia

prevalence of 5% with a precision of 2% (EpiInfo 6.04, Epiconcept). A random sampling proportional to the size of each main subdivision of the city, and a door-to-door approach were used respectively in urban sites and rural areas to select participants.

A two-phase design was performed. In the first phase, all subjects had a physical examination while socio-demographic and vascular risk factors were assessed with a structured questionnaire. Cognitive screening was based on the Community Screening Interview for Dementia (CSI-D) [13] and mental state was evaluated through the Geriatric Mental State (GMS) [14]. Assessments were performed in local languages (Sango in CAR, Lari, Kituba and Lingala in ROC) after a translation and back translation process, followed by a consensus with clinicians and study investigators to ensure conceptual equivalence.

Participants with a low cognitive performance at the CSI-D (≤24.5) were suspected of cognitive impairment/dementia. In the second phase, those participants were invited to a clinical examination by a neurologist. Further psychometric tests for the diagnosis of dementia were performed including the Free and Cued Selective Reminding Test [15], Zazzo's cancellation task [16] and Isaac's Set Test of verbal fluency [17]. A functional assessment was also conducted. It included the activities of daily living scale and the instrumental activities of daily living scale that were adapted to the African context, in order to evaluate dependence through the Central Africa - Daily Functioning Interference scale (CA-DFI) [18]. Neuropsychiatric symptoms were then assessed through the brief version of the Neuropsychiatric Inventory (NPI-Q) [19] in the second stage.

The research was ethically approved by the Ministry of Public Health in CAR, the CERSSA (Comité d'Ethique de la Recherche en Sciences de Santé) in ROC and the Comité de Protection des Personnes du Sud-Ouest et d'Outre-Mer 4 (CPP-SOOM4) in France. All participants and/or their families gave informed consent prior inclusion in the study.

- **Assessment of Neuropsychiatric symptoms**

The Neuropsychiatric Inventory (NPI) is one of the most commonly used instruments to assess BPSD [20] and has previously been used and validated in African populations [6,10], underlining its transcultural value. The NPI-Q (validated French version translated into local languages) was performed by trained clinicians with experience of neurological and psychiatric assessments, ensuring an accurate description of the symptoms.

Based on interviews with the informant, the NPI-Q measures the frequency, severity, and stress of neuropsychiatric symptoms over the last 30 days. It was originally developed for the assessment of 10 neuropsychiatric symptoms in community-dwelling dementia patients [21]. Two other neuropsychiatric symptoms have subsequently been added and a distress score was developed to assess the emotional

or psychological impact of individual symptoms [22,23]. The NPI-Q was developed and cross validated with the standard NPI to provide a brief assessment of neuropsychiatric symptomatology in routine clinical practice settings. It assesses 12 neuropsychiatric symptoms in older people such as delusions, hallucinations, agitation, depression, anxiety, euphoria, apathy, disinhibition, irritability, aberrant motor behaviour, sleep and night-time behaviour disorders and appetite and eating disorders. The NPI-Q only evaluates severity and distress ratings for each symptom, hence total severity and distress scores reflect the sum of individual domain scores.

- **Cognitive status**

After the neurological examination and additional psychometric tests, diagnosis of MCI and dementia were respectively made according to Petersen's [24] and DSM-IV-TR criteria [25]. Diagnoses of dementia subtypes were based on medical history and clinical features. Clinical criteria proposed by the NINCDS-ADRDA (National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association) were used to diagnose Alzheimer's disease (AD) [26]. Experienced neurologists reviewed all medical records and performances to tests, and consensus on the diagnosis was obtained. Severity of dementia was evaluated by the Clinical Dementia Rating (CDR) Scale [27].

- **Other assessments**

All covariates were collected during the first phase. Sociodemographic data included age, sex, marital status, education, site (Nola, Bangui, Gamboma, Brazzaville), and self-reported friendships in the community. Age was ascertained either from official documents, an informant report or estimated using the historical events [28]. In this study, marital status was dichotomised into "married / living as a couple" and "not married" (including single, widowed & divorced participants), as were education ("no formal education" and "some formal education" (i.e. attended primary school)) and friendships in the community (yes or no).

Lifestyle and vascular risk factors such as the frequency of alcohol consumption (any, sometimes, regularly), smoking status (current smokers and non-smoker), and history of stroke (yes/no), hypertension (yes/no) and diabetes (yes/no) were also assessed. Hypertension was defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg in a physical assessment and/or self-reported antihypertensive treatment. Diabetes was defined according to self-reported antidiabetic treatment or glycaemia ≥126 mg/dl if the fasting period > 2 hours or ≥200 mg/dl in non-fasting participants. Body mass index (BMI) was categorised in four categories: undernutrition (BMI<18.5 kg/m^2), normal nutritional status (18.5 ≤ BMI ≤ 24.9 kg/m^2), overweight (25.0 ≤ BMI ≤ 29.9

kg/m^2) and obesity (BMI≥30.0). Dietary factors like difficulties in eating an individual's fill were included. Presence of dependent personality disorder using the Personality Diagnostic Questionnaire-4+ [29] and other factors such as hearing (normal or not), vision (normal or not), physical disability (yes/no) were also collected. Indication on happiness was collected using the Center for Epidemiologic Studies Depression scale [30]. Stressful life events according to Persson & Skoog's questionnaire [31] and psychoactive drug abuse (opioids, hallucinogens, barbiturates, hypnotics and tranquilizers as explored in the GMS) were also investigated.

- **Statistical analysis**

All data were computerized directly on the field using an interface created with Epidata (version 3.1). Data analyses were performed using Stata Software version 12 for Windows (StataCorp LP, College Station, TEXAS).

Frequencies and percentages were calculated for all categorical variables. The Chi² or Fisher's exact tests were used to compare percentages depending on numbers. Median values (with their interquartile range - IQR) or means values (with their standard deviation) were used to describe quantitative variables, depending on the normality of their distribution. Analyses of variance or Kruskall-Wallis tests were also used to compare differences among the groups.

To investigate independent factors associated with neuropsychiatric symptoms, a univariate analysis using logistic regression models was performed with neuropsychiatric symptoms (at least one/none) as the dependent variable. Variables that had a p-value lower than 0.2 in the univariate analysis were included in a multivariate logistic regression model. Backward stepwise elimination procedure was realized, confounders and interactions were examined, leading to a final model with a level of statistical significance of 0.05.

Results

- **Characteristics of the Study Sample**

Among the 2,002 participants, 775 had a low CSI-D cognitive score (≤24.5) and were invited to the clinical interview of the second phase. Of them, 556 were assessed, due to 111 lost to follow-up, 14 deaths, 35 recurrent absences, 10 moving and 50 refusals. Out of the 556 participants assessed, 532 participants with complete NPI-Q data were included in the current study (figure 1). Characteristics, including age, sex, marital status and education, were similar for participants included in the study (n=532) and the ones excluded from the study (n=243) (supplementary table 1).

Median age in this sample was 75.0 years [IQR: 70.0-81.0]. Overall 130 (24.4%) participants were diagnosed with dementia, 113 (21.2%) participants were diagnosed with MCI, and 284 (53.4%) had no cognitive impairment and were considered as a group with neither MCI nor dementia after neurological examination, while five (1.0%) remained without cognitive diagnosis. Among the 130 people with dementia, 98 had Alzheimer's disease (AD) and 15 had vascular dementia (VaD). Participants were mainly females (79.0%) and most had no formal education (88.8%).

Regarding countries, the proportion of female participants seemed greater, although not significantly, in CAR than ROC (p=0.4). More participants were cognitively impaired in CAR than in ROC (p=0.001). Similarly, the proportion of participants with physical disability was significantly lower in ROC than CAR (p<0.0001). Participants were more hypertensive (p<0.0001) and had more history of stroke in both urban than rural areas (p=0.03). Demographic and clinical characteristics of participants by site are shown in table 1.

Participants with dementia had significantly more physical disability (54.6%) than participants with MCI (45.1%) and participants with no MCI nor dementia (32.0%) (p=0.001). Participants with dementia were also less likely to have friends in the community (p=0.0001) and normal hearing (p=0.003). They were older (p<0.0001) and had less formal education (p=0.3) than participants with no MCI nor dementia. Characteristics of participants according their cognitive status are summarized in supplementary table 2.

- **Neuropsychiatric symptoms**

Overall, at least one neuropsychiatric symptom was reported by 63.7% (95% CI: 59.5-67.8) of older people, 31.5% (95% CI: 27.5-35.4) reported one or two symptoms and 32.2% (95% CI: 28.3-36.2) reported three or more. The most frequent symptoms were depression, anxiety and irritability (table 2).

The prevalence of neuropsychiatric symptoms was greater in urban than rural areas (p<0.0001), and in CAR than ROC (p<0.0001): 84.8% (95% CI: 76.8-90.9) of participants in Nola and 91.9% (95% CI: 85.2-96.2) in Bangui presented at least one symptom while the prevalence of neuropsychiatric symptoms was 34.2% (95% CI: 27.3-41.6) in Gamboma and 62.4% (95% CI: 53.2-70.9) in Brazzaville. Among the participants with neuropsychiatric symptoms, 46.4% presented one or two symptoms and 38.4% reported three or more in Nola. Those proportions were respectively: 40.1% and 51.8% in Bangui, 16.5% and 17.7% in Gamboma, and 32.0% and 30.4% in Brazzaville.

In CAR, the most frequent symptoms were depression and anxiety. In ROC, it was irritability and depression (supplementary table 3).

- **Influence of cognitive status**

The prevalence of neuropsychiatric symptoms increased with cognitive impairment. In participants with no MCI nor dementia, 48.7% (95% CI: 42.9-54.6) reported at least one symptom. The prevalence of neuropsychiatric symptoms was 73.4% (95% CI: 65.1-81.7) in participants with MCI and 89.9% (95% CI: 84.6-95.1) in people with dementia (p<0.0001). The number of neuropsychiatric symptoms also significantly increased with cognitive impairment (figure 2): participants who had experienced three or more symptoms were 75.1% among people with dementia, 53.1% among participants with MCI and 32.5% among participants with no MCI nor dementia (p<0.0001).

Table 2 shows the prevalence of each symptom according to cognitive status. Regardless of sites, the most common symptoms were depression, anxiety and irritability. Apart from sleep, night-time behaviour, appetite and eating disorders, the prevalence of all symptoms was significantly higher in people with dementia than those with MCI and those with no MCI nor dementia (table 2). Likewise, aberrant motor behaviour was present almost exclusively in people with dementia (17.6% vs 1.2% in MCI, p<0.0001).

Prevalence of neuropsychiatric symptoms did not significantly vary with the severity of dementia: 89.3% (95% CI: 80.0-95.2) among the participants with very mild to mild dementia, 89.2% (95% CI: 71.7-97.7) among the participants with moderate dementia and 92.3% (95% CI: 74.8-99.0) among participants with severe dementia (p=0.9). The number of neuropsychiatric symptoms tended to increase non-significantly with the severity of dementia (p=0.6), with 72.0% of participants with very mild to mild dementia who had at least three symptoms compared with 75.0% of participants with moderate dementia and 84.6% of participants with severe dementia.

Participants with AD had significantly more symptoms than VaD participants (p<0.0001). Among the 98 AD cases, 91.7% (95% CI: 84.3-96.3) had at least one neuropsychiatric symptom compared to 73.3% (95% CI: 44.8-92.2) of the subjects with VaD. While among AD participants, 38.1% reported one or two symptoms and 53.6% reported three or more, 20.0% of VaD participants had one or two symptoms and 53.3% had three symptoms or more.

There were no significant differences in symptom patterns between dementia subtypes compared to the rest of the participants. The most frequent symptoms remained depression, anxiety and irritability (supplementary table 4).

- **Associated factors**

After adjustment on age and education, participants living in Gamboma (OR=0.12, 95% CI=0.05-0.24), with normal hearing (OR=0.48, 95% CI=0.26-0.86) and with friends in the community (OR=0.46, 95% CI=0.28-0.75) were less likely to present neuropsychiatric symptoms. Difficulties in eating (OR=1.89,

95% CI=1.14-3.12), physical disability (OR=2.00, 95% CI=1.22-3.26), female sex (OR=2.29, 95% CI=1.19-4.42) and dementia (OR=8.13, 95% CI=3.70-17.86) were significantly associated with the presence of neuropsychiatric symptoms (table 3).

Discussion

Our study shows that neuropsychiatric symptoms are common in CAR and ROC among older people with neurocognitive disorders. The prevalence of symptoms was significantly higher in participants with dementia than in those with MCI or those with no MCI nor dementia; the number of symptoms also increased with cognitive impairment.

Our results are similar to those reported in community-based studies from other SSA countries. Indeed, in both Nigeria [5] and Tanzania [6] the prevalence of neuropsychiatric symptoms was significantly higher in the MCI group than in the normal group, respectively 90.6% vs 61.9% and 88.4% vs 64.0% . Likewise, in Tanzania, the number of symptoms reported was higher in dementia than in MCI and control participants. Overall, the high prevalence of symptoms in dementia estimated in our study (89.9%) is in the same range as those reported in Nigeria and Tanzania (79.4% in Nigeria, 88.4% in Tanzania).

The most frequent symptoms were depression, anxiety and irritability. The pattern of neuropsychiatric symptoms observed was relatively similar to those reported in other SSA countries [5,6]. In these community-based studies, depression was also the most frequent symptom in MCI and dementia however its prevalence was lower than what we observed. Indeed, in Nigeria, depression was reported by 45.3% of participants with MCI and 44.1% of participants with dementia [5] and in Tanzania depression was present in 32.6% of MCI and 33.3% of dementia participants [6]. Alongside depression, apathy and aberrant motor behaviour were also reported in MCI and dementia, and night time behaviour among people cognitively normal in Nigeria [5]. Anxiety and irritability were the next commonest symptoms after depression in Tanzania [6]. In our study, no difference in symptoms pattern was found between AD and VaD. This result may be explained by the small number of VaD included thus limiting statistical power. Differences in symptom patterns between the two subtypes of dementia were found in Tanzania where anxiety, depression and irritability were common among participants with AD whilst agitation, anxiety and sleep and night-time behaviour disorders were the most reported in people with VaD. Despite being smaller, a more balanced distribution between AD and VaD (38 AD and 32 VaD) was observed in that study [6].

Prevalence of neuropsychiatric symptoms was significantly higher in urban than in rural area, and also in CAR than in ROC. These findings might reflect cultural differences in understanding and reporting of neuropsychiatric symptoms between CAR and ROC and/or between the rural and urban areas. There

might also be differences between sociodemographic and clinical characteristics of the countries contributing to those results. Indeed, difficulties in eating and physical disability were more frequent in CAR than in ROC as was dementia. These factors, identified as associated with the presence of neuropsychiatric symptoms here, may partly explain the higher prevalence of symptoms in CAR. A higher prevalence of symptoms observed in urban areas could have several potential origins. People living in urban areas could be more exposed to some risk factors such as stress. Neuropsychiatric symptoms could also be less reported in rural areas because older people were better integrated in the community, as social network (participating in religious activities, having friends in the community and playing board games) was greater in these areas. Having friends is a socializing factor that may be protective of dementia [32] and thus neuropsychiatric symptoms. However, it is also possible that the absence of neuropsychiatric symptoms allow individuals to have friends and a better social network as neuropsychiatric symptoms can be stigmatizing [33]. Unfortunately, the design of our study and the data available do not allow us to draw any definitive conclusion.

Normal hearing was another factor identified as potentially protective against neuropsychiatric symptoms. Although we cannot totally rule out the potential impact of hearing difficulties on the measurement of cognitive impairment and neuropsychiatric symptoms, recent evidence supports the association between sensory loss and neuropsychiatric symptoms among people with neurocognitive disorders. Vision and hearing loss are two conditions that may participate to the expression of neuropsychiatric symptoms [34]. Sensory loss leads to communication issues and reduced social engagement as well as social isolation [35–37]. While hearing loss has been linked to single neuropsychiatric symptoms (psychosis) [38] and agitation [39], poor vision and self-reported hearing difficulties were associated with a greater number of neuropsychiatric symptoms in a community based study in Australia [34].

Physical disability was associated with a 2-fold increase in the likelihood of neuropsychiatric symptoms in our sample. Our findings are consistent with previous reports. A greater risk of general anxiety and depression among adults (18-75 years) with disability was reported in the Lagos State Mental Health Survey [40] whilst neuropsychiatric symptoms were associated with increased disability in a community sample of cognitively impaired older Latinos (Sacramento Area Latino Study on Aging) [41]. Neuropsychiatric symptoms may influence everyday function and lead to increased disability but some symptoms, such as depression and anxiety, may also be the result of physical impairment. The cross-sectional design of our study limits our interpretation.

Female participants showed a significantly higher risk of having neuropsychiatric symptoms in our study. The association between sex and neuropsychiatric symptoms was not explored in the study

from Tanzania while it was not significant in both Nigeria and the 10/66 Dementia Research Group study in LMICs [4].

Education was not associated with the presence of neuropsychiatric symptoms in our sample. However, considering the high proportion of females in our sample and their low education levels, we cannot rule out that we lacked statistical power to detect a significant effect in our study or a possible cultural factor, with women reporting more symptoms than men. As this association remained significant even after adjustment in this study, it deserves to be further investigated in future studies to understand its mechanisms.

As could be expected, the strongest association identified was the one between dementia and neuropsychiatric symptoms, with a 7-fold increase in risk. There is strong evidence worldwide supporting the link between dementia and neurocognitive disorders in the occurrence of neuropsychiatric symptoms among older people [42]. Unfortunately, differences in study designs prevent us to do direct comparisons of its effect size with studies carried out in SSA or other LMIC.

A major strength of our study lies in the fact that it is one of the very few studies on neuropsychiatric symptoms among older people carried out in SSA and the first in Central Africa. Apart from being population-based, another asset of the present study is the high quality of the cognitive diagnosis relying on a comprehensive assessment including psychometric testing and informant interview, conducted by trained neurologists, ruling out any alternative psychiatric diagnosis, and validated by a consensus of experts. Neuropsychiatric symptoms were also assessed using the NPI-Q which is to date one of the most commonly used instruments [20] to assess behavioural and psychological symptoms of dementia. Although not specifically validated in this context, it has previously been used and validated in other African settings [6,10].

However, we acknowledge some limitations. The sample of participants assessed by the NPI-Q, derived from participants with suspected cognitive impairment (second stage of EPIDEMCA), may have led to an overestimation of the prevalence of neuropsychiatric symptoms in our study. We also acknowledge that the use of translation versions of NPI-Q in local languages, although unavoidable, could be a limitation in our study due to the lack of formal validation. However, questionnaires used in the EPIDEMCA study were translated from French to local languages, then from local languages to French in order to observe translation consistency following the WHO guidelines. These translations were performed by a group of independent linguistic professionals, which then received the input of bilingual clinicians and study investigators in order to reach a consensus on the translations aiming at conceptual equivalence rather than literal translations. Moreover, the NPI-Q was filled by the

interviewers (all fluent in the relevant languages) during the examination. We therefore believe we were able to limit the possible issues related to the meaning of the symptoms.

Over 200 participants selected for the second stage were not assessed because of loss of follow-up, death or refusals. However, the absence of significant difference between their characteristics (sex, age, education and marital status) and the ones of the participants included, rules out the possibility of a major selection bias at that stage. We therefore believe that only the generalizability of those results to all older people living in settings of CAR and ROC is limited as those results cannot be generalized to elderly with normal cognition.

In conclusion, the prevalence and number of neuropsychiatric symptoms increased with cognitive impairment in our study. The burden caused by neuropsychiatric symptoms on patients and their caregivers is important. Due to the essential role of informal caregivers in Africa, it is necessary to inform and improve the knowledge of caregivers about these symptoms as well as to include them in the development of interventions aiming at reducing the impact of neuropsychiatric symptoms among older people. Nevertheless, knowledge of these symptoms remains limited in SSA, hampering their appropriate management. Conducting further research to better characterize neuropsychiatric symptoms among sub-Saharan populations appears to be essential.

Conflict of Interest: None

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Table 1. Characteristics of included participants according to their country, EPIDEMCA, 2011-2012

Characteristics	Nola, rural CAR (n=113) n (%)	Bangui, urban CAR (n=112) n (%)	Gamboma, rural ROC (n=181) n (%)	Brazzaville, urban ROC (n=126) n (%)	p-value	Test statistic	df
Age (years), median [IQR]	75.0 [63.0-87.0]	74.0 [63.5-84.5]	76.0 [66.0-86.0]	76.0 [64.0-88.0]	0.17 A	1.65	3
Sex, Females	93 (82.3)	91 (81.2)	136 (75.1)	100 (79.3)	0.43 C2	2.71	3
No formal education	99 (87.6)	101 (90.6)	173 (95.5)	98 (77.7)	<0.0001 FE	33.64	15
Married or in a couple	22 (19.4)	23 (20.5)	48 (26.5)	30 (23.8)	0.62 C2	4.35	6
Friendships in the community (yes)	50 (44.6)	30 (27.0)	127 (70.5)	70 (55.5)	<0.0001 C2	55.63	3
History of stroke (present)	5 (4.4)	7 (6.3)	3 (1.6)	13 (10.3)	0.03 C2	13.35	6
BMI <18.5 kg/m²	60 (53.1)	34 (30.3)	89 (49.1)	30 (23.8)	<0.0001 FE	57.37	12
Hypertension (present)	52 (46.0)	69 (61.6)	112 (61.8)	96 (76.1)	<0.0001 C2	24.46	6
Diabetes (present)	7 (6.1)	3 (2.6)	20 (11.0)	13 (10.3)	0.18 C2	8.83	6
Difficulties in eating	69 (61.1)	72 (64.2)	52 (28.7)	30 (23.8)	<0.0001 C2	72.60	6
No alcohol consumption	80 (70.8)	87 (77.6)	160 (88.4)	105 (83.3)	<0.0001 FE	28.74	9
Current smoker	50 (44.2)	35 (31.2)	25 (13.8)	14 (11.1)	<0.0001 C2	69.91	9
Normal hearing	83 (73.4)	81 (72.3)	136 (75.1)	98 (77.7)	0.02 FE	17.07	9
Normal vision	40 (35.4)	32 (28.5)	53 (29.2)	32 (25.4)	0.06 C2	16.28	9
Physical disability	62 (54.8)	56 (50.0)	45 (24.8)	52 (41.2)	<0.0001 C2	62.06	6
Dependant personality disorder (present)	13 (11.5)	31 (27.6)	36 (19.8)	33 (26.1)	0.07 C2	11.59	6
Happiness, median [IQR]	7.0 [1.0-13.0]	8.0 [5.0-11.0]	9.0 [6.0-12.0]	8.0 [6.0-10.0]	0.0001 KW	35.12	3
Psychoactive drug abuse (present)	2 (1.8)	1 (0.9)	1 (0.5)	1 (0.8)	0.17 C2	4.37	3
Number of stressful psychosocial factors (mean ± sd)	7.3 (± 3.2)	7.8 (± 3.1)	6.1 (±2.4)	4.9 (±2.1)	<0.0001 A	25.90	3
Cognitive status							
No MCI nor dementia	49 (43.3)	46 (41.1)	120 (67.0)	69 (55.6)			
MCI	27 (23.8)	34 (30.6)	30 (16.7)	22 (17.7)	0.001 C2	27.49	6
Dementia	37 (32.7)	31 (27.9)	31 (21.9)	33 (26.6)			
Severity of dementia (n=130)							
Normal to mild	25 (67.6)	17 (54.8)	15 (51.7)	18 (54.5)			
Moderate	10 (27.0)	10 (32.3)	5 (17.3)	3 (9.1)	0.013 C2	16.16	6
Severe	2 (5.4)	4 (12.9)	9 (31.0)	12 (36.4)			

C2=chi square, FE=fisher exact, A= Analysis of variance, KW= kruskall wallis, CAR=Central African Republic, ROC=Republic of Congo, IQR= interquartile range, sd=standard deviation, n= number, p= p-value

Table 2. Overall prevalence of each neuropsychiatric symptom and their prevalence according to cognitive status, EPIDEMCA, 2011-2012

Neuropsychiatric symptoms	Overall prevalence		No MCI nor dementia (n=284)		MCI (n=113)		Dementia (n=130)		p-value	Test statistic	df
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)			
Delusions	71	13.4 (10.6-16.6)	17	5.9 (3.5-9.4)	14	12.3 (6.9-19.9)	40	30.7 (23.5-40.3)	<0.0001 C2	53.14	6
Hallucinations	63	11.9 (9.3-15.0)	18	6.3 (3.8-9.9)	11	9.7 (4.9-16.7)	34	26.1 (19.3-35.3)	<0.0001 C2	39.58	6
Agitation	55	10.9 (8.0-13.4)	13	4.5 (2.5-7.8)	14	12.3 (6.9-19.9)	28	21.5 (15.3-30.9)	<0.0001 C2	32.81	6
Depression	**237**	**45.3 (**40.9-49.6)	**95**	**33.4 (27.9-39.2)**	**62**	**54.8 (47.0-66.3)**	**79**	**60.7 (54.1-71.6)**	**<0.0001** C2	50.20	6
Anxiety	**148**	**28.1 (**24.3-32.2)	**57**	**20.0 (15.5-25.2)**	**37**	**32.7 (24.6-42.9)**	**54**	**41.5 (34.3-52.3)**	**<0.0001** C2	36.80	6
Euphoria	21	3.9 (2.4-6.0)	4	1.4 (0.3-3.5)	5	4.4 (1.4-10.1)	12	9.2 (4.9-15.9)	0.006 C2	17.11	6
Apathy	71	13.4 (10.6-16.6)	11	3.8 (1.9-6.8)	15	13.2 (7.6-20.9)	44	33.8 (26.4-43.5)	<0.0001 C2	80.29	6
Disinhibition	36	6.8 (4.8-9.3)	3	1.0 (0.2-3.0)	2	1.2 (0.2-6.2)	31	23.8 (17.3-33.0)	<0.0001 C2	87.15	6
Aberrant motor behaviour	25	4.7 (3.0-6.9)	0	-	2	1.2 (0.2-6.2)	23	17.6 (11.8-25.9)	<0.0001 C2	69.98	6
Irritability	**125**	**23.7 (**20.1-27.6)	**45**	**15.8 (11.8-20.6)**	**31**	**27.4 (19.8-37.2)**	**49**	**37.6 (30.0-47.6)**	**<0.0001** C2	31.20	6
Sleep and night-time behaviour disorders	82	15.4 (12.4-18.8)	31	10.9 (0.7-15.1)	20	17.7 (11.2-26.2)	31	23.8 (16.9-32.3)	0.016 C2	15.53	6
Appetite and eating disorders	59	11.4 (8.5-14.1)	32	11.2 (7.8-15.5)	10	8.8 (4.3-15.6)	16	(12.3)7.2-19.3	0.90 C2	2.20	6

Abbreviations: C2= chi square, CI=confidence interval, n= number, MCI= Mild Cognitive Impairment

Symptoms in bold are the three most frequently reported.

Table 3. Factors associated with the presence of neuropsychiatric symptom, EPIDEMCA, 2011-2012

	Univariate analysis			Final model of multivariate analysis		
Variables	**OR**	**95% CI**	**p-value**	**ORa**	**95% CI**	**p-value**
Site						
Bangui (urban CAR) vs Nola (rural CAR)	2.04	0.87-4.81	0.10	2.24	0.88-5.71	0.08
Gamboma (rural ROC) vs Nola (rural CAR)	0.09	0.05-0.16	<0.0001	**0.12**	**0.05-0.24**	**<0.0001**
Brazzaville (urban ROC) vs Nola (rural CAR)	0.29	0.15-0.55	<0.0001	0.48	0.22-1.03	0.06
Age	1.00	0.97-1.00	0.825	0.97	0.94-1.00	0.134
Education	1.12	0.63-1.99	0.82	1.44	0.67-3.10	0.340
Sex (female vs male)	1.97	1.29-3.02	0.002	**2.29**	**1.19-4.42**	**0.01**
Friendships in the community	0.34	0.23-0.50	<0.0001	**0.46**	**0.28-0.75**	**0.002**
Hearing (normal vs impaired)	0.43	0.27-0.68	<0.0001	**0.48**	**0.26-0.86**	**0.01**
Diabetes	0.41	0.21-0.77	0.006			
Vision (normal vs impaired)	0.65	0.47-0.88	0.006			
Happiness	0.81	0.75-0.87	<0.0001			
Stressful psychosocial factors	1.13	1.06-1.21	<0.0001			
Smoking status	1.26	1.01-1.56	0.03			
Marital status	1.57	1.14-2.16	0.006			
Dependent personality disorder	1.82	1.15-2.90	0.01			
Physical disability	2.54	1.69-3.80	<0.0001	**2.00**	**1.22-3.26**	**0.005**
Cognitive status						
MCI/No MCI nor dementia	2.90	1.80-4.68	<0.0001	**1.93**	**1.0-3.6**	**0.05**
Dementia/No MCI nor dementia	9.37	5.04-17.40	<0.0001	**8.13**	**3.70-17.86**	**<0.0001**
Difficulties in eating	2.82	1.92-4.14	<0.0001	**1.89**	**1.14-3.12**	**0.013**

OR= Odds Ratio, ORa = Odds Ratio Adjusted on age and education level, CAR=Central African Republic, ROC=Republic of Congo, CI=confidence Interval, MCI= Mild Cognitive Impairment

Figure legends

- **Figure 1**: Flow chart of the EPIDEMCA study including selection of the study sample, 2011-2012

CAR= Central African Republic, ROC= Republic of Congo, NPI=Neuropsychiatric Inventory, R=rural, U=urban, CSI-D= Community Screening Interview for Dementia

- **Figure 2**. Number of neuropsychiatric symptoms according to cognitive status, EPIDEMCA, 2011-2012

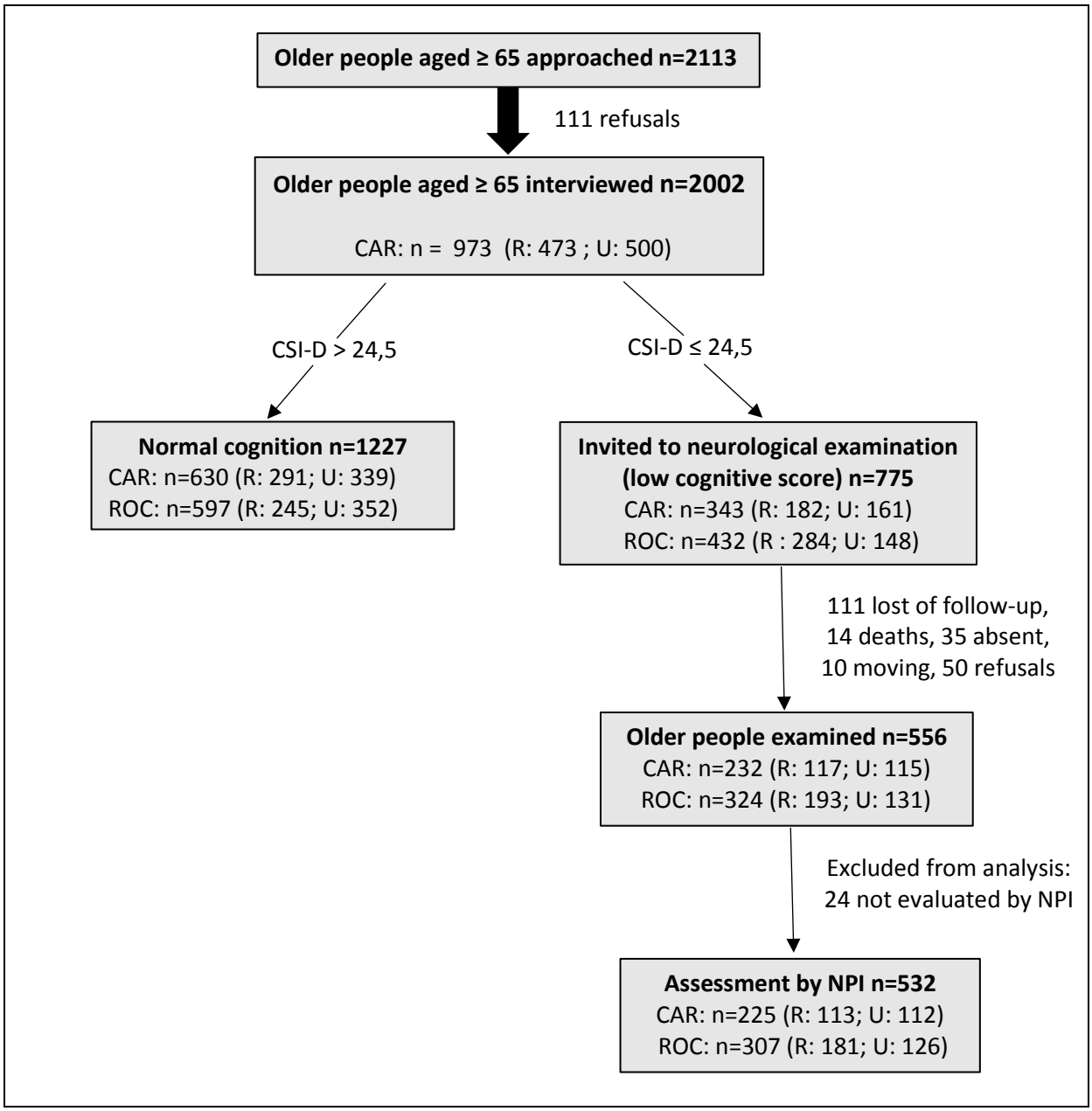

Figure 1: Flow chart of the EPIDEMCA study including selection of the study sample, EPIDEMCA 2011-2012

CAR= Central African Republic, ROC= Republic of Congo, NPI=Neuropsychiatric Inventory, R=rural, U=urban, CSI-D= Community Screening Interview for Dementia

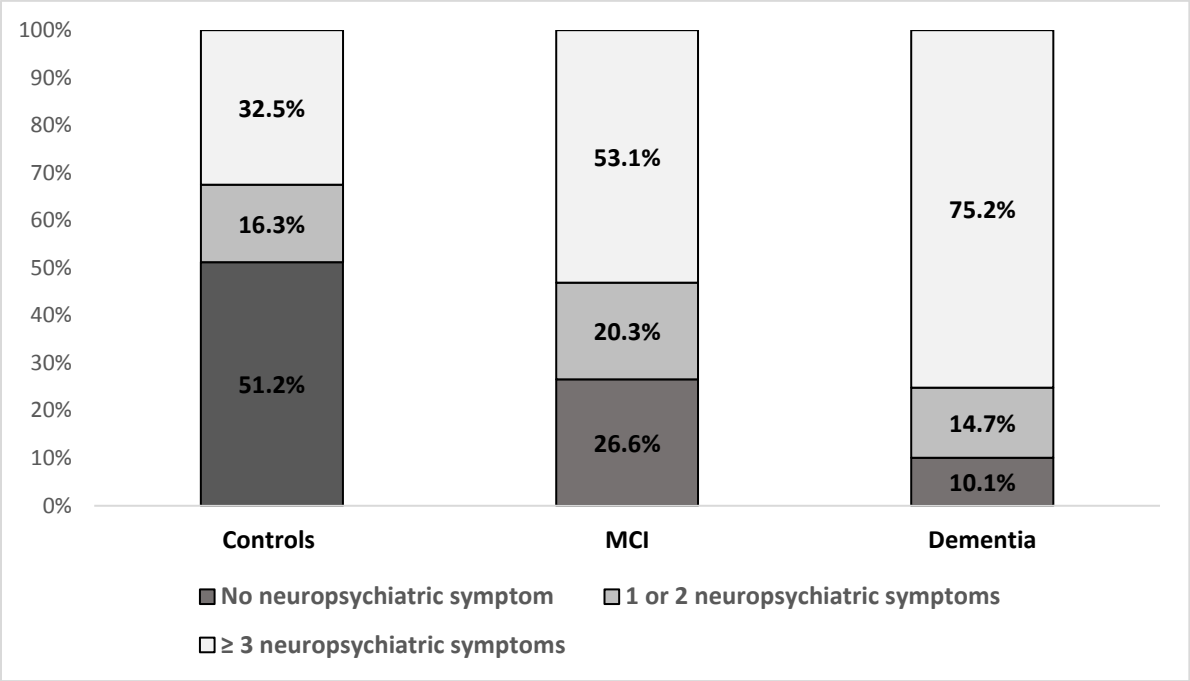

Figure 2. Number of neuropsychiatric symptoms according to cognitive status, EPIDEMCA, 2011-2012

Supplementary Table 1:

Sociodemographic characteristics of participants selected for the second stage, included in the study and the ones excluded from the study, EPIDEMCA, 2011-2012

Characteristics	Excluded from the study (n = 243) n (%) or median [IQR]	Included in the study (n = 532) n (%) or median [IQR]	p-value
Age (years), median [IQR]	74 [69-79]	75 [70-81]	0.10
Sex, Females	196 (80.7)	420 (78.9)	0.58
No formal education	213 (87.7)	471 (88.5)	0.80
Married or in a couple	46 (18.9)	123 (23.1)	0.61

IQR= interquartile range

Supplementary Table 2. Characteristics of included participants according to cognitive disorders, EPIDEMCA, 2011-2012

Characteristics	No MCI nor dementia (n=284) n (%)	MCI (n=113) n (%)	Dementia (n=130) n (%)	p-value
Site				
Nola (rural CAR)	49 (17.2)	27 (23.9)	37 (28.5)	
Bangui (urban CAR)	46 (16.2)	34 (30.1)	31 (23.8)	<0.001
Gamboma (rural ROC)	120 (42.2)	30 (26.5)	29 (22.3)	
Brazzaville (urban ROC)	69 (24.3)	22 (19.5)	33 (25.4)	
Age (years), median [IQR]	73.0 [63.0-83.0]	75.0 [66.0-84.0]	80.0 [69.0-91.0]	<0.00001
Sex, Females	224 (78.9)	93 (82.3)	101 (77.7)	0.142
No formal education	253 (89.1)	102 (90.3)	112 (86.1)	0.03
Married or in couple	213 (75.0)	89 (79.5)	102 (79.1)	0.513
Friendships in the community (yes)	169 (59.5)	58 (51.8)	46 (35.9)	0.0001
History of stroke (present)	14 (4.9)	6 (5.3)	8 (6.1)	0.812
BMI <18.5 kg/m²	111 (39.1)	39 (34.5)	62 (47.7)	<0.0001
Hypertension (present)	99 (34.9)	49 (43.4)	49 (37.7)	0.212
Diabetes (present)	248 (87.3)	107 (94.7)	117 (90.0)	0.057
Difficulties in eating	102 (35.9)	57 (50.4)	61 (46.9)	0.003
No alcohol consumption	228 (80.8)	89 (78.7)	110 (90.2)	0.133
Current smoker	60 (21.2)	34 (30.4)	29 (22.7)	0.162
Normal hearing	230 (81.0)	85 (75.2)	79 (60.8)	0.003
Normal vision	94 (33.1)	34 (30.1)	27 (20.8)	0.07
Physical disability	91 (32.0)	51 (45.1)	71 (54.6)	0.001
Dependent personality disorder (present)	51 (18.0)	30 (26.5)	30 (23.1)	<0.0001
Happiness, median [IQR]	8.0[6.0-10.0]	8.0 [6.0-10.0]	7.0 [2.0-12.0]	0.0001
Number of stressful psychosocial factors (mean ± sd)	6.1 (± 2.7)	7.1 (± 3.0)	6.6 (± 3.2)	0.007

CAR=Central African Republic, ROC=Republic of Congo, IQR= interquartile range, sd=standard deviation

Supplementary Table 3. Prevalence of each neuropsychiatric symptom according to their country, EPIDEMCA, 2011-2012

Neuropsychiatric symptoms	Nola, rural CAR (n=113)		Bangui, urban CAR (n=112)		Gamboma, rural ROC (n=181)		Brazzaville, urban ROC (n=126)		p-value
	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	n	% (95% CI)	
Delusions	**26**	**23.2 (**15.7-32.1)	**30**	**26.7 (**18.8-35.9)	6	3.3 (1.2-7.1)	9	7.2 (2.3-13.3)	<0.0001
Hallucinations	17	15.1 (9.0-23.1)	26	23.2 (15.7-32.1)	7	3.9 (1.5-7.8)	13	10.4 (5.7-17.2)	<0.0001
Agitation	10	9.1 (4.4-16.2)	17	15.3 (9.1-23.3)	**18**	**10.0 (6.0-15.4)**	10	10.0 (3.9-14.3)	0.32
Depression	**88**	**77.8 (69.0-85.1)**	**81**	**75.7 (66.4-83.4)**	**27**	**15.0 (10.1-21.1)**	**41**	**33.0 (24.8-42.0)**	<0.0001
Anxiety	**59**	**52.2 (42.6-61.6)**	**52**	**47.2 (37.6-57.0)**	11	6.1 (3.1-10.7)	26	21.1 (14.2-29.4)	<0.0001
Euphoria	4	3.6 (0.9-8.9)	7	6.3 (2.5-12.5)	3	1.6 (0.3-4.8)	7	5.6 (2.2-11.1)	0.36
Apathy	17	15.0 (9.0-22.9)	22	19.8 (12.8-28.4)	14	7.7 (4.3-12.7)	18	14.4 (8.7-21.8)	0.11
Disinhibition	4	3.5 (0.9-8.8)	12	11.0 (5.8-18.4)	10	5.6 (2.7-10.0)	10	7.9 (3.8-14.1)	0.08
Aberrant motor behaviour	0	-	6	5.4 (2.0-11.3)	13	7.3 (3.9-12.1)	6	4.8 (1.7-10.1)	0.10
Irritability	25	22.7 (15.2-31.6)	28	25.2 (17.4-34.3)	**34**	**18.9 (**13.5-25.5)	**38**	**30.1 (**22.3-38.9)	0.16
Sleep and night-time behaviour	12	10.6 (5.6-17.8)	28	25.2 (14.4-34.3)	11	6.0 (3.0-10.6)	**31**	**24.8 (**17.5-33.3)	<0.0001
Appetite and eating disorders	17	15.1 (9.0-23.1)	10	9.0 (4.4-15.9)	14	7.7 (4.2-12.6)	18	14.2 (8.6-21.6)	0.20

CAR=Central African Republic, ROC=Republic of Congo, CI=confidence interval, MCI= Mild Cognitive Impairment

Supplementary Table 4. Prevalence of each neuropsychiatric symptom in Alzheimer's Disease and in vascular dementia, EPIDEMCA, 2011-2012

	Alzheimer's disease (n=98)		Vascular dementia (n=15)	
Neuropsychiatric symptoms	**n**	**% (95% CI)**	**n**	**% (95% CI)**
Delusions	31	31.6 (23.1-42.6)	2	13.3 (1.7-42.8)
Hallucinations	27	27.5 (19.4-38.2)	2	13.3 (1.7-42.8)
Agitation	21	21.4 (14.3-32.0)	3	20.0 (4.3-48.0)
Depression	**61**	**62.2 (**54.3-74.4)	**9**	**60.0 (**35.1-87.2)
Anxiety	**41**	**41.8 (**33.4-54.2)	**7**	**46.6 (**23.0-76.9)
Euphoria	9	9.1 (4.4-17.2)	1	6.6 (0.1-31.9)
Apathy	33	33.6 (25.2-45.1)	4	26.6 (7.7-55.1)
Disinhibition	19	19.3 (12.4-29.4)	4	26.6 (8.3-58.1)
Aberrant motor behaviour	17	17.3 (10.7-27.0)	3	20.0 (4.3-48.0)
Irritability	**36**	**36.7 (**28.1-48.4)	**5**	**33.3 (**11.18-61.6)
Sleep and night time behaviour	20	20.4 (13.0-30.0)	4	26.6 (7.7-55.1)
Appetite and eating disorders	13	13.4 (7.3-21.8)	1	6.6 (0.1-31.9)

CI=confidence interval