

The low prevalence of dementia in sub-Saharan Africa: a systematic review and meta-analysis of geographical variations and associations

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Abstract

Background: Conflicting findings from individual epidemiological studies do not allow for valid assumptions about the true prevalence of dementia in sub-Saharan Africa (SSA). We conducted a systematic review and meta-analysis of dementia studies in SSA to arrive at a pooled prevalence estimate and associated factors.

Materials and methods: We searched Medline, EMBASE, PsychINFO, and African Journals Online using index medicus keywords for dementia and the .mp operator for all 54 SSA countries or regions. Further information was retrieved through a manual search of references from relevant articles. We included peer-reviewed original studies with epidemiological or experimental designs, conducted random effect meta-analysis of prevalence estimates and determined associated factors using the inverse of variance method.

Results: A total of 38 studies met criteria for syntheses. The pooled prevalence of clinically diagnosed dementia derived from an overall sample of 6964 older community-dwellers was 4.0% (95% C.I.=3.0%-6.0%). We observed a pattern of distinctly low rates in West Africa (2.0%, 95% C.I.=2.0%-3.0%) and higher rates in East and Central Africa (6.0%, 95% C.I.=5.0%-8.0%). Older age was the dominant factor associated with prevalent dementia. This factor contributed 99.3% of the total variance of all systematically associated factors. Most of the weight of association of older age and dementia was provided by studies conducted in West Africa (the region with the lower estimated prevalence).

Conclusion: There are subsisting evidence gaps precluding robust estimation of age-adjusted prevalence of dementia in SSA. Nevertheless, the findings from the present study provide useful information about the possible mechanisms underlying the observed low prevalence of dementia in SSA and other developing countries.

Keywords: Low and Middle income countries; sub-Saharan Africa; Dementia; prevalence; epidemiology; pooled estimates

Résumé

Contexte: Les résultats contradictoires des études épidémiologiques individuelles ne permettent pas de supposer valides sur la prévalence réelle de la démence en Afrique subsaharienne (ASS). Nous avons effectué une revue systématique et une méta-analyse des études sur la démence en Afrique subsaharienne pour arriver à une estimation de la prévalence regroupée et des facteurs associés.

Matériel et méthodes: Nous avons effectué des recherches dans Medline, EMBASE, PsychINFO et Journaux Africain En Ligne à l'aide d'index mots-clés Médecus pour la démence et l'opérateur mp pour tous les 54 pays ou régions d'Afrique subsaharienne. De plus amples informations ont été obtenues grâce à une recherche manuelle des références des articles pertinents. Nous avons inclus des études originales évaluées par des pairs avec des plans épidémiologiques ou expérimentaux, effectué une méta-analyse à effet aléatoire des estimations de la prévalence et déterminé les facteurs associés en utilisant la méthode de l'inverse de la variance.

Résultats: Au total, 38 études répondaient aux critères de synthèse. La prévalence groupée de démence diagnostiquée cliniquement dérivée d'un échantillon total de 6964 d'habitants plus âgés de la communauté était de 4,0% (IC à 95% = 3,0% à 6,0%). Nous avons observé un schéma de taux nettement bas en Afrique de l'Ouest (2,0%, IC 95% = 2,0% -3,0%) et des taux plus élevés en Afrique de l'Est et Centrale (6,0%, IC 95% = 5,0% - 8,0%). L'âge avancé était le facteur dominant associé à la démence prévalente. Ce facteur a contribué à 99,3% de la variance totale de tous les facteurs systématiquement associés. La majeure partie de la charge de l'association entre l'âge avancé et la démence a été fournie par des études menées en Afrique de l'Ouest (la région avec la prévalence estimée la plus faible).

Conclusion: Il existe des lacunes dans les preuves qui empêchent une estimation robuste de la

prévalence de la démence ajustée selon l'âge en ASS. Néanmoins, les résultats de la présente étude fournissent des informations utiles sur les mécanismes possibles à l'origine de la faible prévalence observée de la démence en Afrique subsaharienne et dans d'autres pays en développement.

Mots-clés: *Pays à revenu faible et intermédiaire ; Afrique Sub-Saharienne ; Démence; prévalence ; épidémiologie; estimationsgroupées*

Introduction

Projections from the global literature [1,2] suggest that by 2040 over 71% of persons with dementia will reside in low- and middle-income countries (LMICs). However, evidence from individual studies conducted in sub-Saharan Africa (SSA) [3-5] suggest a pattern characterised by widely varied but low rates of dementia relative to reports from higher income countries.

Given the widely varying findings from individual studies, it is reasonable to hypothesize that the true prevalence of dementia in SSA is yet unknown. It is also currently difficult to make valid assumptions about the importance of associated factors identified in many individual studies.

One important strategy to generate an integrated understanding of conflicting findings from different studies is the syntheses of data derived from all such studies. Pooled data could generate more precise estimates of prevalence and significance of previously identified factors associated with dementia in SSA. This could, in turn, help in the identification of important targets for the design and trial of tailored preventive interventions for dementia in the sub-region.

The objective of the present study was to conduct a systematic review and meta-analysis of dementia studies in SSA to arrive at a pooled estimate of prevalence and associated factors.

Methods

This review followed conventional recommendations for the methodology and reporting of systematic reviews as described in the guidelines of the National Institute of Health and Care Excellence (NICE) and Preferred Reporting Items for Systematic reviews and Meta-analyses (PRISMA) [6,7].

Search strategy

An initial search of the African Journals Online database was conducted on 15th January 2017. This

was followed by a search of the Medline, PsychINFO, and Embase databases using the following keywords with the 'explode' operator: dementia or 'Alzheimer's disease', AND epidemiology OR frequency OR prevalence OR incidence OR factors OR 'risk factors' OR 'associated factors' OR outcome OR mortality. We next searched each of the 54 sub-Saharan African countries or regions by name using the .mp. operator.

A second stage consisting of hand searching of the reference list of relevant articles retrieved from the databases was also implemented. An additional search of the pubmed was conducted on the 2nd of February 2018 to retrieve ahead of print citations using the same keywords as for the other databases. Limits on language and publication dates were not imposed in conducting the searches.

Inclusion criteria

Studies were included if; 1) they investigated epidemiological phenomena such as frequencies, prevalence, incidence, risk or associated factors, and outcome, 2) they included participants with any type of dementia regardless of method of diagnoses or ascertainment, 3) conducted among community-dwelling participants, those in hospitals, rehabilitation settings, nursing homes or other such institutions, 4) they used epidemiological or experimental study designs such as descriptive and analytical cross-sectional studies, prospective and retrospective cohort studies, case control studies, randomized controlled trials, non-randomized controlled trials, quasi-experimental, as well as before and after studies.

Exclusion criteria

We excluded the following types of studies, 1) review papers, case series, individual case reports, other textual materials such as expert opinions, discussion papers, and position papers; and 2) studies focusing solely on qualitative data.

Study assessments and data extraction

Study assessment for inclusion and exclusion criteria as well as subsequent data extraction was conducted by two independent assessors based on the descriptions in the original article. It was agreed a priori that in cases of disagreement, a consensus will be reached based on the decision of an experienced colleague.

Ascertainment of risk of bias in studies exploring associations

A standard framework [6,8] was used for judgments about the risk of bias in studies describing

associations. All 5 steps in the modified Graphical Appraisal Tool for Epidemiologic Studies (GATE) [6,8] were used for the determination of the risk of bias. We determined external validity by assessing key characteristics of the eligible sample in the relevant studies and made judgments about the level of representativeness of the source population. We made judgment about internal validity by assessing the method of identification of outcome measurements, and analytical strategies. These steps were undertaken to ensure that the associations identified by the respective studies are valid and are not due to unidentified factors that may be related to both exposure and outcome.

Risk of bias was classified as low, unclear/unknown, and high [6]. Points were allocated to each component of the study as follows: 2 points when the risk of bias was low, 1 point when this was unclear /unknown and no points when the risk of bias was clearly high. Judgment about overall risk of bias in the selected studies was made by averaging risk of bias for a particular study, calculated by summing up the total points accrued by that study and dividing the result by the total number of components assessed. Finally, we classified the overall risk of bias for a particular study as high (when the average risk of bias scores for that study is less than 1), moderate (when this is between 1 and 1.5), and low (when the score is greater than 1.5).

Statistical methods

Meta-analysis was conducted using prevalence estimates of dementia reported in the original articles meeting the review protocol criteria for quantitative synthesis. We centred the display of prevalence estimates on the point of zero for better illustration.

The 95% percent confidence intervals (C.I) of each prevalence estimate together with their quantitative summary are also presented. Greater weights are given to studies with narrower C.I.

As heterogeneity was expected due to differences in the type of dementia assessments (clinical diagnostic criteria or rating scales), as well as setting of studies, a random effect meta-analysis model was chosen. To reduce the extent of methodological heterogeneity, we combined studies with similar diagnostic procedures in the same meta-analysis model. To determine the extent of statistical heterogeneity, we estimated the percentage of total variation in estimates reported across studies that is due to heterogeneity, rather than chance. This was computed using the I^2 test. In the present study, values of $I^2 > 50\%$ were chosen as evidence of statistical heterogeneity [9].

For the objective of investigating the most important factors associated with dementia by rank, we used the log of odds ratios (O.R) and the corresponding standard errors (S.E) of the associations. The inverse of variance method was used for weighting in all quantitative estimations.

All quantitative analyses were conducted using the Cochrane review manager (Revman) version 5.3 software [10].

Results

The combined database and hand searches identified a total of 2848 records. After removing duplicates in the databases (N=1647 articles), the titles and abstract of 1208 articles were screened. From these, 42 articles that might have contained information relevant to the review were retrieved and their full text evaluated. After reading through the texts, 4 articles were further excluded because they examined broadly defined cognitive impairment/disorders and did not provide information about participants with dementia (Figure 1). Of the four excluded articles, one each was from Senegal [11] and Rwanda [12], while the remaining two were from Nigeria [13,14].

Qualitative appraisal of identified studies

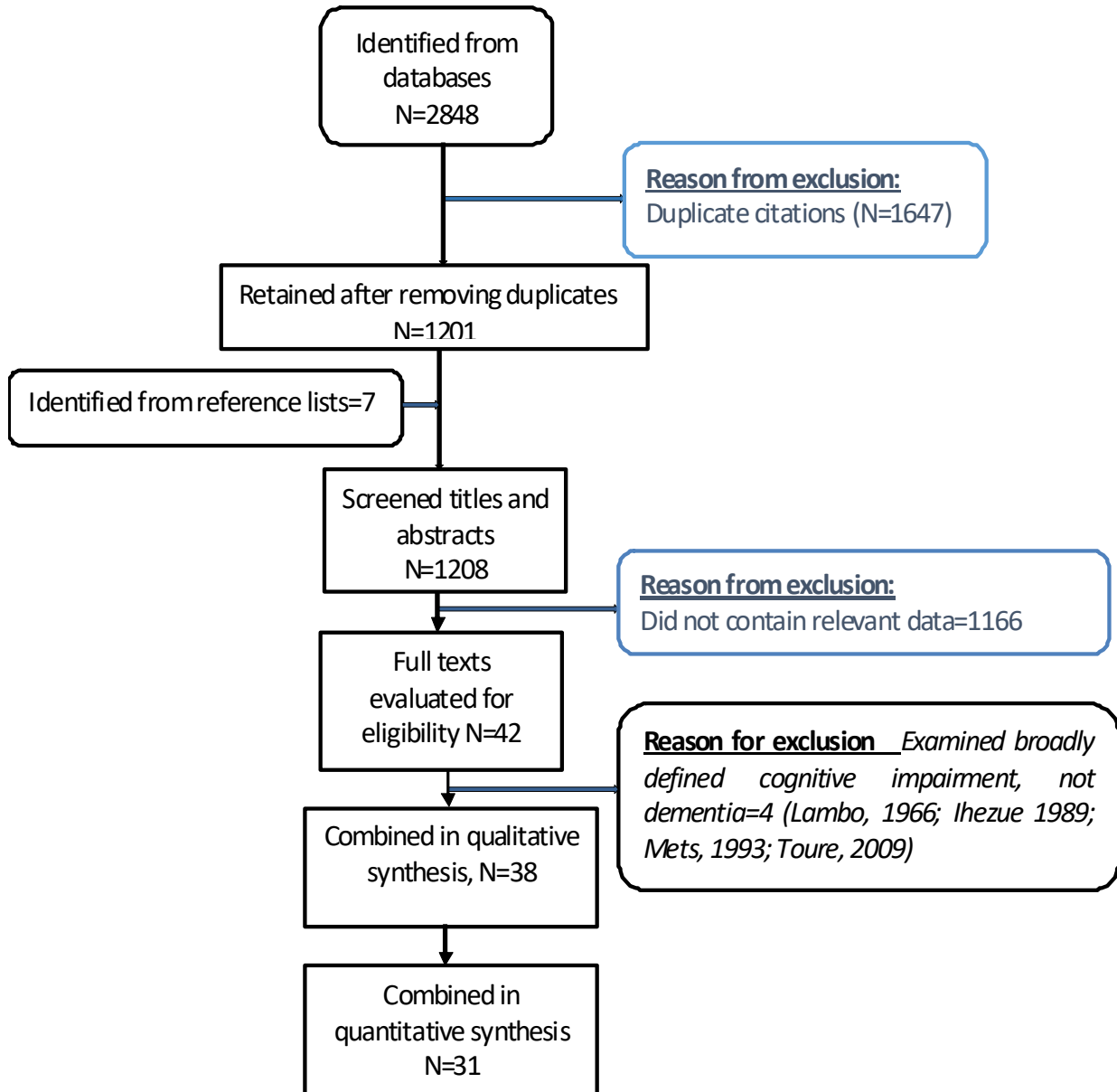
Studies included were published between February 1992 and May 2016. Over 60% of identified studies were publications of data from 6 major research programs (Indianapolis Ibadan Dementia Project, Epidemiology of Dementia in Central Africa-EDAC-, Epidemiology of Dementia in Central Africa-EPIDEMCA-, EPIDEMCA Follow-up, Ibadan Study of Ageing, Kilimajaro cohort from the Hai District of rural Tanzania).

Geographical location of studies

All included studies came from primarily three regions in sub-Saharan Africa: West, East, and Central Africa. However, about 50% of identified studies were from one country, Nigeria. We did not identify any studies from Southern Africa meeting our review criteria.

Types of study design and methods

Six studies^[15-20] relied on hospital records (Table 1). One report of cognitive examination conducted on nursing home residents in Lagos, Nigeria [21] is also included in the same table. However, 81.6% of identified studies were community based, including reports of ten prospective longitudinal observations of between two and ten years duration [3,5,22-29]. As the objective of the present systematic review was to examine dementia prevalence and associated

Figure 1: Flow chart showing details of included and excluded studies

factors, only the baseline observations of the prospective longitudinal studies are included in qualitative and quantitative syntheses.

Ascertainment of dementia

The majority of included studies used a two staged procedure and made formal clinical diagnoses of dementia according to codified criteria [30,31]. Two hospital based studies [17,18] relied on clinicians' best judgement of dementia while three community based cross-sectional surveys used rating scales in ascertaining dementia [32-34] (Table 2).

Quantitative syntheses

Extensive variability in types of setting (i.e., in-patients, outpatients, nursing homes and autopsy),

definition of dementia and ascertainment procedures meant that we could not combine the hospital-based studies in a meaningful meta-analysis model.

The community-based studies provided useful data for quantitative syntheses. They included sufficient sample sizes and appropriate analytical techniques in establishing their findings. The combined risk of bias, as assessed using the modified GATE criteria was moderate.

Prevalence of dementia

Apart from a frequency of 12.4% reported in one study of 912 older attendees at a neurology clinic in the Cameroun [19], there was a pattern of mostly low frequency of dementia in hospital-based studies (0.5%-4%). The autopsy study of the brains of 198

Table 1: Hospital or Nursing home studies

Reference	Country	Setting	Definition of dementia	Sample size	Female %	Age (years) Mean (SD)	Frequency %
<i>Ogunniyi et al. 1993</i>	Nigeria	General hospital medical In-patients	ICD 9 criteria	37	24.3	67 (9.0)	0.6
<i>Osuntokun et al. 1995</i>	Nigeria	Autopsy	Histological hallmarks	198	46.0	40-85	0
<i>Baiyewu et al. 1997</i>	Nigeria	Nursing homes	DSM III-R criteria	23	47.8	78.7 (8.6)	48
<i>Napon et al., 2009</i>	Burkina Faso In- and outpatient	General hospital	DSM IV	15817	33.3	62.2 ^a	0.5
<i>Siddiqi et al., 2010</i> Out/Inpatient	Zambia	General hospital	2396 In-patients Clinician best judgment	811	52.2	39/15-80	2.9/4.0
<i>Ouango, et al. 2014</i>	Burkina Faso	General hospital In- and outpatients	Clinician best judgment	7974	40.2	49-90 ^b	Out/Inpatient 1.9
<i>Calliste et al., 2015</i>	Cameroun	Neurology Outpatient	ICD 10 criteria	912	50.8	68.8 (7.2)	12.4

Notes: SD=Standard deviation, DSM=Diagnostic and Statistical Manual of Mental disorders, III-R=Text revision of 3rd edition, IV=4th Edition, ICD= International Classification of Diseases

^aMedian

^bRange

Table 2: Community based cross-sectional surveys

Reference	Country/Location	Definition of dementia	Sample size	Female (%)	Age (Years) Mean (SD)	Prevalence (%)
Clinically diagnosed						
<i>Osuntokun et al, 1992</i>	Nigeria (Idikan)	DSM III-R	930	61.2	40-85	0
<i>IIDP^a</i>	Nigeria (Idikan)	ICD 10/DSM III-R	2494	71.4	81.0 (9.9)	2.3
<i>Guerchet et al, 2009</i>	Benin (Djidja)	DSM-IV	502	57.0	76.1 (9.4)	2.6
<i>Yusuf et al 2010</i>	Nigeria (Zaria)	ICD 10/DSM IV	322	60.2	75.5 (9.4)	2.8
<i>Ogunniyi et al, 2016</i>	Nigeria (Lalupon)	DSM IV/ Alzheimer's Association	613	69.7	72.9 (8.9)	2.9
<i>EDAC Survey^b</i>	CAR (Bangui)	DSM IV/Alzheimer's Association	496	55.6	77.4 (7.3)	8.1
<i>EDAC Survey^b</i>	Congo (Brazzaville)	DSM IV/Alzheimer's Association	520	40.9	74.7 (6.7)	6.7
<i>Kilimajaro cohort^c</i>	Tanzania (Hai)	DSM IV	1198	56.2	≥70 ^e	6.4
<i>EPIDEMCA^d</i>	CAR (Nola)	DSM IV	359	91.4	75.6 (7.1)	6.5
<i>EPIDEMCA^d</i>	Congo (Gamboma)	DSM IV	460	69.7	72.9 (8.9)	3.4
Rating scales defined						
<i>Ochayi et al 2006</i>	Nigeria (Jos)	CSID	280	89.0	77.2 (9.7)	6.4
<i>Gureje et al, 2006</i>	Nigeria (West/Central regions)	10 Words list learning/Delayed recall test	2152	53.8	74.5 (8.4)	10.1
<i>Paraiso et al 2011</i>	Benin	CSID/Five word test	1139	54.1	73.4 (7.2)	3.7

Notes: SD=Standard deviation, DSM=Diagnostic and Statistical Manual of Mental disorders, III-R=Text revision of 3rd edition, IV=4th Edition, IIDP=Indianapolis Ibadan Dementia Project, ICD 10=10th Revision of the International Classification of Diseases, EDAC= Epidemiology of Dementia in Central Africa, CAR=Central African Republic, EPIDEMCA= Epidemiology of Dementia in Central Africa, CSID=Community Screening Instrument for Dementia.

^aReported in three studies with 21.6% also meeting 10/66 dementia research group criteria.

^bReported in five studies

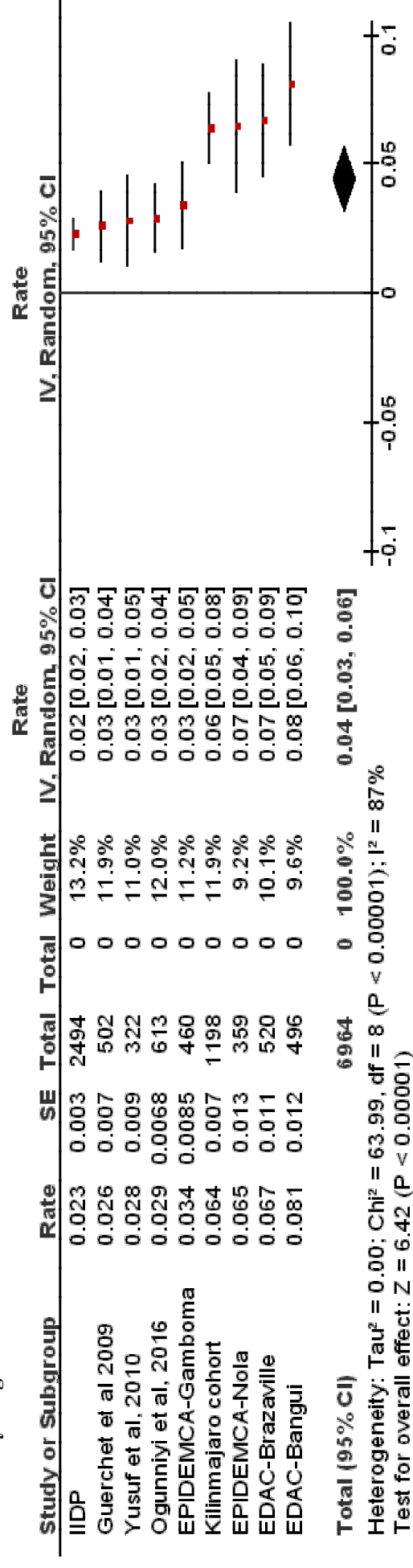
^cReported in three studies

^dReported in four studies

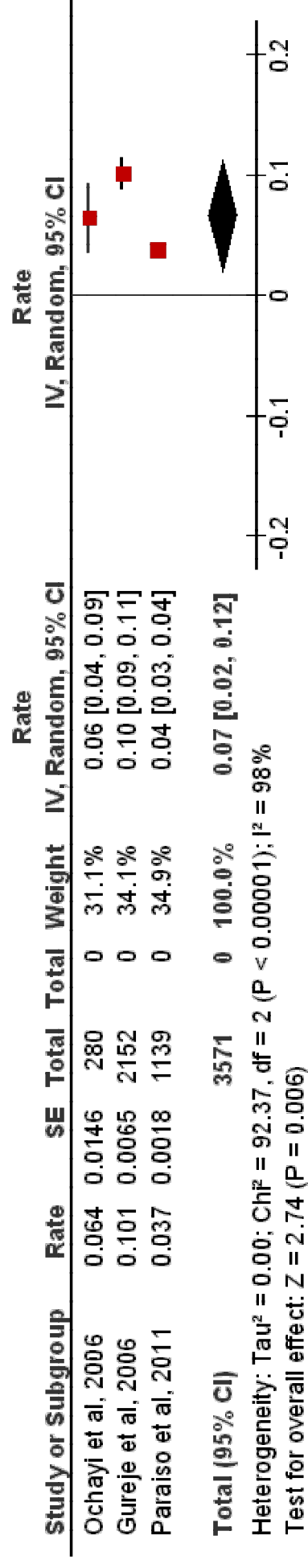
^eAll participants were 70 years or older.

Fig. 2: Forest plots showing the prevalence of clinically diagnosed and rating scale defined dementias in sub-Saharan Africa.

A. Clinically diagnosed dementia

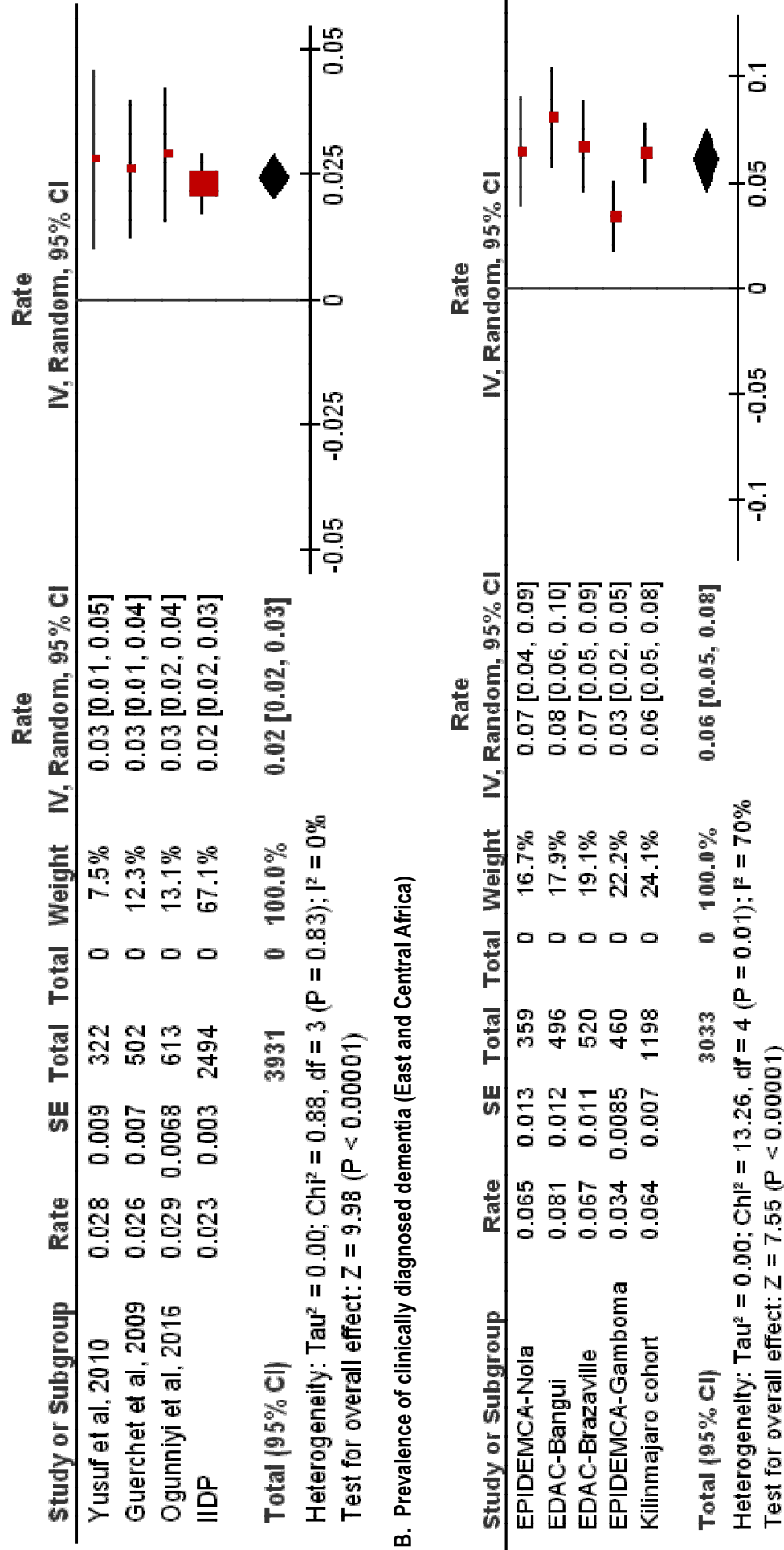


B. Rating scales defined dementia



Key: IIDP= Indianapolis Ibadan Dementia Project, EDAC= Epidemiology in Central Africa, EPIDEMCA= Epidemiology of Dementia in Centra Africa

Figure 3: Prevalence of clinically diagnosed dementia by geographical distribution showing distinctly low rates in West Africa and Higher rates in East/Central Africa.



Key: IIDP= Indianapolis Ibadan Dementia Project, EDAC= Epidemiology in Central Africa, EPIDEMCA= Epidemiology of Dementia in Centra Africa

adult Nigerians did not find the histological hallmarks of Alzheimer's disease [16]. However, 48% of nursing home residents in Lagos Nigeria met clinical diagnostic criteria for dementia [21].

Figure 2 presents forest plots showing the prevalence of dementia in community based cross-sectional surveys. A higher pooled prevalence estimate of 7.0% (95% C.I.=2.0%-12.0%) was reported among 3571 participants in studies using various rating scales in defining dementia. The pooled prevalence of clinically diagnosed dementia among 6964 participants was 4.0% (95% C.I.=3.0%-6.0%). There was an indication of statistical heterogeneity in these estimates (Rating scale: $I^2=98\%$, $p<0.001$; Diagnostic assessment: $I^2=87.0\%$, $p<0.001$). Heterogeneity was investigated and found to be due to rate-ratio outliers in one study of rating-scale-defined dementia [33] and four studies of clinically diagnosed dementia[35-39]. We also observed important geographical variations in the prevalence estimates of clinically diagnosed dementia.

was 6.0% (5.0%-6.0%). Notably, the estimates determined for the two regions showed distinct non-overlapping confidence intervals.

Systematic associations with prevalent dementia

Older age was the most cited associated factor with prevalent dementia [32-35,39-43]. Older age also had the most precise systematic association (by weight) with prevalent dementia (Table 3). Three studies [32,40,42] from West Africa provided 99.8% of the weight of association of age with prevalent dementia.

All other identified factors contributed less than 1.0% to the total variance of all associations with prevalent dementia. Female gender [32-34,40,43] and undernutrition[32,44,45] were the other frequently cited associated factors.

Discussion

In the present systematic review and meta-analyses we found that the pooled prevalence of clinically diagnosed dementia in SSA is 4.0%. We observed a pattern of distinctly low prevalence estimates in West

Table 3: Independently associated factors with prevalent dementia in Sub-Saharan Africa (ranked by the inverse of variance method)

Associated factors	S.E	Weight (%)
Older age ^a	0.02	99.3
Systemic hypertension ^b	0.49	0.1
Loss of a parent before age 16 years ^b	0.49	0.1
Recent change in residence ^b	0.51	0.1
Female gender ^c	0.64	0.1
No formal education ^b	0.66	0.1
Undernutrition ^d	0.74	0.1
Peripheral artery disease ^b	0.74	0.1
Diet low in oleagenous acid ^b	1.71	<0.1
Dependent personality disorder ^b	2.42	<0.1
Depression ^e	3.33	<0.1
Change in financial status ^b	5.28	<0.1

NOTE: S.E is the estimated Standard error of the association as reported by the original study or determined by meta-analysis (if reported in more than one study)

^aNine studies,

^bOne study

^cFive studies

^dThree studies

^eTwo studies

In adjusted analyses to correct for heterogeneity (Figure 3), the pooled prevalence reported in studies from West Africa was 2.0% (95% C.I.=2.0%-3.0%), with results indicating absence of heterogeneity ($I^2=0.0\%$, $p=0.84$). In contrast, the pooled prevalence of dementia in East/Central Africa

Africa and higher proportions in East and Central Africa. Older age was the dominant factor associated with prevalent dementia in SSA. Other commonly cited factors in individual studies contributed less than 1.0% to the total variance of associations with prevalent dementia.

Our results overlap within 95% C.I of age adjusted prevalence (3.9%-6.5%) of dementia in persons who are 65 years or older living in developing countries^[4]. Also, the finding in the present study suggesting varying estimates of dementia within SSA is similar to reports from other developing regions of the world [4,46-48]. This variation in pooled prevalence estimates has been observed to reflect the use of different dementia-ascertainment procedures [49,50], genetic predispositions to the disease, lifestyle factors [51], urban versus rural distribution of study participants [52], literacy levels [48], and age structure of the studied population [53]. In the present systematic review, we have combined data comprising similar diagnostic procedures in the same meta-analysis model in order to reduce the effect of methodological differences in identified studies on our results.

Clinical and epidemiological implications of the key findings

We found in the present study that older age was the pre-eminent factor associated with prevalent dementia in SSA, with most of the weight of association of age and prevalent dementia provided by studies conducted in West Africa (the region with a distinctly low estimated prevalence of the disease). This pattern of stronger association of older age with dementia in regions with the lowest reported prevalence would suggest the operation of a possible 'natural selection phenomenon' within samples of older persons from those regions. Given the prevailing low life expectancy at birth in most of SSA [54], individuals surviving to old age in locations with lower life expectancy may include a comparatively healthier section of the population who may have a lower latent risk of dementia, while those with higher cumulative morbidity may be more likely to die at a younger age [55]. In a country like Nigeria, as an example, it is projected that despite an average life expectancy at birth of about 52 years [56], the population surviving to the age of 65 years may have the prospect of an additional 15 years of life [57,58]. It is important to note that Nigeria also provided about 50% of the studies included in the present review.

Low and varying estimates of dementia in SSA may also be the result of differences in sociocultural practices and knowledge about the disease. For example, multigenerational living is common in most of SSA. In this scenario, older people are more likely to be supported by family members in the performance of activities of daily life. As such, milder functional deficits (which may

nonetheless reach the threshold for the diagnosis of dementia) may become unobservable. In many cases of apparent functional deficits, family members simply take over social-functional roles of the affected individual. The above observation is reflected in the results of the present systematic review suggesting a higher prevalence of dementia in studies [32-34] relying on ascertainment procedures that precluded physical functioning assessments.

Beyond SSA, variations in socio-cultural practices within the same country or region have also been shown to result in disparities of reported estimates of dementia in other developing contexts [51]. The low frequency of dementia found in hospital-based studies included in the present systematic review may reflect a possible low healthcare utilization which may also result from prevailing sociocultural practices and pathways to care [59]. These and other factors such as stigma and cost [60] may in turn lead to a higher risk of mortality from dementia in developing countries compared with more developed parts of the World. Pooled estimates of differential mortality from dementia and its effect on reported prevalence of the disease is yet to be determined in developing countries, and could be the basis of a future meta-analytic study.

Strength and limitations

The search strategies were designed to be meaningfully sensitive. In this regard, the searches were focused on some of the largest repositories of biomedical literature. We included additional search strategies to cover references of fully appraised articles. Nevertheless, our results might not be completely representative of all regions in SSA since we did not find studies from southern Africa meeting our review criteria.

Conclusion

The pooled prevalence of clinically diagnosed dementia in SSA is 4.0%. It varies between 2.0% in West Africa and 6.0% in East and Central Africa. Older age is the dominant associated factor. While there are subsisting evidence gaps precluding robust estimation of age-adjusted prevalence across studies, the findings in the present systematic review provides useful information about the possible mechanisms driving variations in the prevalence of dementia in SSA and other developing contexts.

Implication for future research

It is feasible that there is a higher risk of mortality from dementia in developing countries compared with more developed parts of the World. This difference may be hypothesized as another important

mechanism (apart from natural selection) underlying the observed low prevalence of dementia in SSA. Future systematic reviews of observational studies from SSA should quantify the substantive effect of differential mortality from dementia in sustaining the prevailing low rates of the disease in the region.

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