Cognitive screening for dementia and delirium in sub-Saharan Africa

Development and validation of cognitive screening tools for identification of dementia and delirium in older adults by non-specialist health workers in sub-Saharan Africa

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List of abbreviations

5WT	Five-Word Test
ADD	Alzheimer's Disease Dementia
ADL	Activities of Daily Living
APOE4	Apolipoprotein E4
AUC	Area under the receiver operating curve
CAM	Confusion Assessment Method
CERAD	Consortium for Establishing a Registry for Alzheimer's Disease
CSI-D	Community Screening Instrument for Dementia
DLB	Dementia with Lewy Bodies
DSM	Diagnostic and Statistical Manual
DSS	Demographic Surveillance Site
GMS	Geriatric Mental State
HIC	High Income Country
IADL	Instrumental Activities of Daily Living
ICD	International Classification of Diseases
LMIC	Low-middle income country
KCMC	Kilimanjaro Christian Medical Centre
KCMCo	Kilimanjaro Christian Medical College
MMSE	Mini-Mental State Examination
MRRH	Mawenzi Regional Referral Hospital
NCDDS-AIREN	National Institute of Neurological Disorders and Stroke/Association Internationale pour la Recherché et l' Enseignement en Neurosciences
NHCFT	Northumbria Healthcare NHS Foundation Trust
NINCDS-ADRDA	National Institute of Neurological and Communicative Diseases and Stroke/Alzheimer's Disease and Related Disorders Association
PDD	Parkinson's Disease Dementia
SSA	Sub-Saharan Africa
SIDSA	Six-item cognitive screen for Africa (original name of IDEA cognitive screen)
VAD	Vascular Dementia

1. Summary

This work summarises and contextualises a series of published papers which develop methods of cognitive screening for identification of dementia and delirium in sub-Saharan Africa. The key research question was how best to screen for dementia in older adults in sub-Saharan Africa, where levels of illiteracy are high, particularly in rural areas. Due to the specialist human resource shortages evident in this setting, these studies aim to produce tools suitable for non-specialists to use with a high degree of accuracy. Two inter-related aims which have been achieved were to develop a combined cognitive and functional assessment tool for identification of dementia by rural primary healthcare workers in community settings, and to develop a brief but accurate method of identifying delirium in hospital settings. The validation studies presented were carried out in the Kilimanjaro region of Northern Tanzania, as part of the IDEA (Identification and Interventions for Dementia in Elderly Africans) study. The study settings included rural agriculture-based communities as well as urban secondary and tertiary healthcare facilities. These studies are informed by a systematic review of delirium in SSA, and a meta-analysis of cognitive screening tools in illiterate and low-literate populations. Ongoing work and further directions are summarised.

2. Abstract

Dementia and delirium are recognised to be common inter-related disorders affecting older people worldwide, the majority of whom live in low and middle income countries (LMICs). In sub-Saharan Africa (SSA), research data on dementia and delirium in older adults are currently very few, despite evidence of a growing older population. A major factor limiting research is the lack of appropriately validated cognitive screening instruments. Existing instruments appear educationally biased in SSA, where illiteracy amongst older people remains high. Specialist clinicians are few, and human resources generally limited, resulting in a need for brief tools suitable for use by non-specialists with limited time.

The IDEA six-item screen was developed from cognitive screening data collected during a community based door-to-door prevalence study of dementia conducted in Tanzania in 2010. This work aimed to formally validate the IDEA screen for identification of dementia and delirium in older adults in a variety of clinical settings in Tanzania. Additional aims were to identify potential educational bias, consider feasibility of use of the IDEA screen by non-specialist clinicians and consider utility and effectiveness of additional screening items to improve diagnostic accuracy in some settings.

Validation studies were conducted in the Kilimanjaro region of Tanzania as follows. 1) Consecutive admissions to medical wards of a Government hospital aged 60 and over (n=97); 2) A randomised sample of individuals aged 60 and over attending a free-of-charge Government outpatient clinic (n=108); 3) A randomised rural community sample aged 60 and over presenting for dementia screening (n=466), and 4) A consecutive sample of 507 individuals aged 60 and over admitted to medical wards of a tertiary referral hospital, supported by detailed informant interview and follow-up where necessary (against blinded consensus DSM-IV dementia and DSM-5 delirium criteria).

A culturally appropriate assessment of Instrumental Activities of Daily Living (IDEA-IADL) was developed at a workshop for primary healthcare workers. Validation against DSM-IV dementia criteria took place in a community sample (n=417) of adults aged 60 and over presenting for dementia screening, used alone and in addition to the IDEA six-item screen.

Screening was conducted by trained research nurses, occupational therapists and clinical officers in hospital settings, and by nurses and primary health care workers in rural settings.

Diagnostic accuracy of the IDEA six-item screen for major cognitive impairment was high in the pilot hospital settings (IP AUC 0.917, OPD AUC 0.919). Accuracy in the lower prevalence community setting was lower (AUC 0.846), but improved by the addition of the IDEA-IADL (AUC 0.896). In the tertiary referral hospital sample AUC was 0.874 for major cognitive impairment (DSM-IV delirium or

DSM-IV dementia) and 0.866 for delirium, but a substantial number of participants were unable to complete the screen (83/507) and the IDEA did not differentiate dementia and delirium. A combined tool developed through modelling outperformed the IDEA (AUC 0.94 95% CI 0.92-0.97) and had the advantage of being much shorter, and being possible in most individuals regardless of illness severity.

These studies conclude that the IDEA six-item screen is a brief and culturally appropriate cognitive screening tool with a high degree of diagnostic accuracy for identification of dementia in clinical and community settings in Tanzania. Use of the screen by non-specialist health workers is feasible, and the screen does not appear educationally biased.

Diagnostic accuracy is improved by additional use of a functional assessment tool, the IDEA-IADL in the community. In hospital settings with a relatively high prevalence of delirium, the IDEA six item screen is accurate in identification of major cognitive impairment (dementia or delirium) but cannot differentiate these conditions. An alternative screening method for identification of delirium in this setting is presented. Further validation work in other settings in sub-Saharan Africa is needed.

Since the proportion of individuals aged 50 and over living with HIV in SSA is projected to increase from one in seven to one in four by 2030, assessment of clinical utility in HIV-associated neurocognitive impairment is also needed, and this is the focus of ongoing work.

3. Acknowledgements

These studies would not have been possible without the help and assistance of a great many people, and there really are too many to name.

Those who I need to acknowledge most include my PhD supervisors (Richard Walker, Catherine Dotchin and Raj Kalaria) for allowing me the opportunity to work in Tanzania by employing me as a research doctor, believing in me, and allowing me freedom to develop my ideas and extend the original focus of the project. Keith Gray at Northumbria Healthcare gave patient statistical advice and informal teaching on statistics and research methods which allowed me to progress from having almost no skills in data analysis to independently conducting statistical analysis for published papers.

In Tanzania, the work in the rural Hai district would be impossible without the goodwill, commitment and enthusiasm of a large team of village enumerators, and the support of the district medical office and village committees. The hospital managers of Kilimanjaro Christian Medical Centre (KCMC) (Dr Sarah Urasa) and Mawenzi Regional Referral Hospital (MRRH) (Dr Bingileki Lwezuala) made me welcome in their hospitals and offered support. KCMC neurologists Dr William Howlett, Dr Marieke Dekker and Dr Sarah Urasa gave excellent and much needed clinical advice in Tanzania.

The practicalities of undertaking this type of study in Hai, particularly in upland areas in the rainy season, involves extensive local knowledge and the need to manage very difficult weather and transport conditions with limited resources. I was very fortunate to work with Dr John Kissima and Jane Rogathi who shared their extensive experience of rural Hai, were always available for advice and support, and helped me avoid many potential disasters. Mr Lema (Mudio village enumerator) was unfailingly cheerful and enthusiastic even in the worst driving and weather conditions, and always managed to get our car fixed when we broke down, which was often.

Two excellent Newcastle University MRes students (Celia Collingwood (2014) and Jessica Banks (2015)) helped with clinical workload in Tanzania far in excess of the requirements of their Masters programme, meaning that we were able to complete much larger studies than would have been possible if I were working alone.

I would like to give special thanks to Aloyce Kisoli, my study nurse throughout (and before) this work and whose kind and gentle manner with patients and families was invaluable for this project.

In the UK, Dr Elizabeta Mukaetova-Ladinska, although not my academic supervisor offered a great deal of invaluable academic advice, support and mentoring as well as a means of maintaining clinical skills by working under her supervision in Liaison Psychiatry during my time out of clinical training.

Without her supervision I would not have had the confidence to design and implement the delirium study described in this thesis, or to move forward with ongoing work in HIV.

I would also like to thank my Academic Progress Panel members Dr Louise Allan and Dr John-Paul Taylor for excellent and impartial advice. Their advice to switch from an MD to PhD degree programme at my first annual review, was at the time unexpected, but absolutely the right thing to do.

I am grateful most of all to the participants and their family members who agreed to take part in these studies and who shared their concerns about potentially stigmatising conditions with us.

4. Guide to this presented work

The published work submitted for examination as part of this doctoral thesis is outlined in Figure 1. The work submitted consists of two background review papers, discussed in the introduction to this work, and four key papers, forming the main body of this work. Similarly, the work presented is in two parts. Part one consists of an introductory and background section, contextualising the work later presented in the key papers. Part two consists of the four key papers, and accompanying commentary and discussion. Key data related to each cohort are outlined in Figure 2.

Additional supplementary papers, informing the work presented in this thesis are included for context within the Appendix to this thesis. These do not form part of the main body of work presented, but are referred to where appropriate.

5. List of submitted and supplementary papers

The submitted papers, including supplementary papers which inform the study, are listed below. A flow diagram demonstrating the links between the papers is shown in Figure 1. The cohorts and settings in which studies took place are detailed in Figure 2 for clarity.

5.1. Submitted (thesis) papers

Background Paper 1 (Introduction)

Paddick SM, Gray WK, McGuire J, Richardson J, Dotchin C and Walker RW. **Cognitive screening tools for identification of dementia in illiterate and low-educated older adults, a systematic review and meta-analysis**, International Psychogeriatrics 2017 (Accepted for publication, December 2016)

Background Paper 2 (Introduction)

Paddick SM, Kalaria RN, Mukaetova-Ladinska EB. **The prevalence and clinical manifestations of delirium in sub-Saharan Africa: A systematic review with inferences**. Journal of the Neurological Sciences. 2015 Jan 15; 348(1):6-17

5.2. Key papers

Key Paper 1

Paddick SM, Gray WK, Ogunjimi L, Lwezuala B, Olakehinde O, Kisoli A, Kissima J, Mbowe G, Mkenda S, Dotchin CL, Walker RW, Mushi D, Collingwood C, Ogunniyi A. **Validation of the Identification and Intervention for Dementia in Elderly Africans (IDEA) cognitive screen in Nigeria and Tanzania**. BMC Geriatrics. 2015 Apr 25; 15(1):1.

Key Paper 2

Gray WK, **Paddick SM**, Collingwood C, Kisoli A, Mbowe G, Mkenda S, Lissu C, Rogathi J, Kissima J, Walker RW, Mushi D, Chaote P, Ogunniyi A, Dotchin CL. **Community validation of the IDEA study cognitive screen in rural Tanzania.** International Journal of Geriatric Psychiatry. 2016 Jan 1.

Key Paper 3

Collingwood C, **Paddick SM**, Kisoli A, Dotchin CL, Gray WK, Mbowe G, Mkenda S, Urasa S, Mushi D, Chaote P, Walker RW. **Development and community-based validation of the IDEA study Instrumental Activities of Daily Living (IDEA-IADL) questionnaire.** Global Health Action. 2014 Dec 29; 7.

Key Paper 4

Paddick SM, Lewis EG, Duinmaijer A, Banks J, Urasa S, Tucker L, Kisoli A, Cletus J, Lissu C, Kissima J, Dotchin C, Gray W, Mukaetova-Ladinska E, Cosker G, Walker R. **Identification of delirium and dementia in older medical inpatients in Tanzania. A comparison of screening and diagnostic methods,** Journal of the Neurological Sciences, 2017

5.3. Supplementary papers informing this work

Prevalence and subtypes of dementia in rural Tanzania

Supplementary Paper 1

Longdon AR, **Paddick SM**, Kisoli A, Dotchin C, Gray WK, Dewhurst F, Chaote P, Teodorczuk A, Dewhurst M, Jusabani AM, Walker R. The prevalence of dementia in rural Tanzania: a cross-sectional community-based study. International journal of geriatric psychiatry. 2013 Jul 1; 28(7):728-37.

Supplementary Paper 2

Paddick SM, Longdon A, Kisoli A, Gray WK, Dotchin CL, Jusabani A, Iqbal A, Hughes J, Teodorczuk A, Chaote P, Walker RW. The Prevalence of Dementia Subtypes in Rural Tanzania. The American Journal of Geriatric Psychiatry. 2014 Dec 31; 22(12):1613-22.

Low literacy and difficulties in dementia screening in rural Tanzania

Supplementary Paper 3

Paddick SM, Longdon AR, Kisoli A, Dotchin C, Gray WK, Dewhurst F, Chaote P, Kalaria R, Jusabani AM, Walker R. Dementia prevalence estimates in sub-Saharan Africa: comparison of two diagnostic criteria. Global health action. 2013 Apr 2; 6

Supplementary Paper 4

Paddick SM, Longdon A, Gray WK, Dotchin C, Kisoli A, Chaote P, Walker R. The association between educational level and dementia in rural Tanzania. Dementia & Neuropsychologia. 2014 Jun; 8(2):117-25

Preparatory Work

Supplementary Paper 5

Gray WK, **Paddick SM**, Kisoli A, Dotchin CL, Longdon AR, Chaote P, Samuel M, Jusabani AM, Walker RW. Development and validation of the identification and Intervention for Dementia in Elderly Africans (IDEA) study dementia screening instrument. Journal of geriatric psychiatry and neurology. 2014 Feb 26

Supplementary Paper 6

Paddick SM, Dotchin C, Gray WK, Kisoli A, Kisima J, Chaote P, Walker R. Utility of the mini-Mental State Examination (MMSE) for identification of Dementia in a low-literacy setting in rural Tanzania. Age and Ageing. 2015 Sep 1; 44 (suppl 2):ii25-ii25.

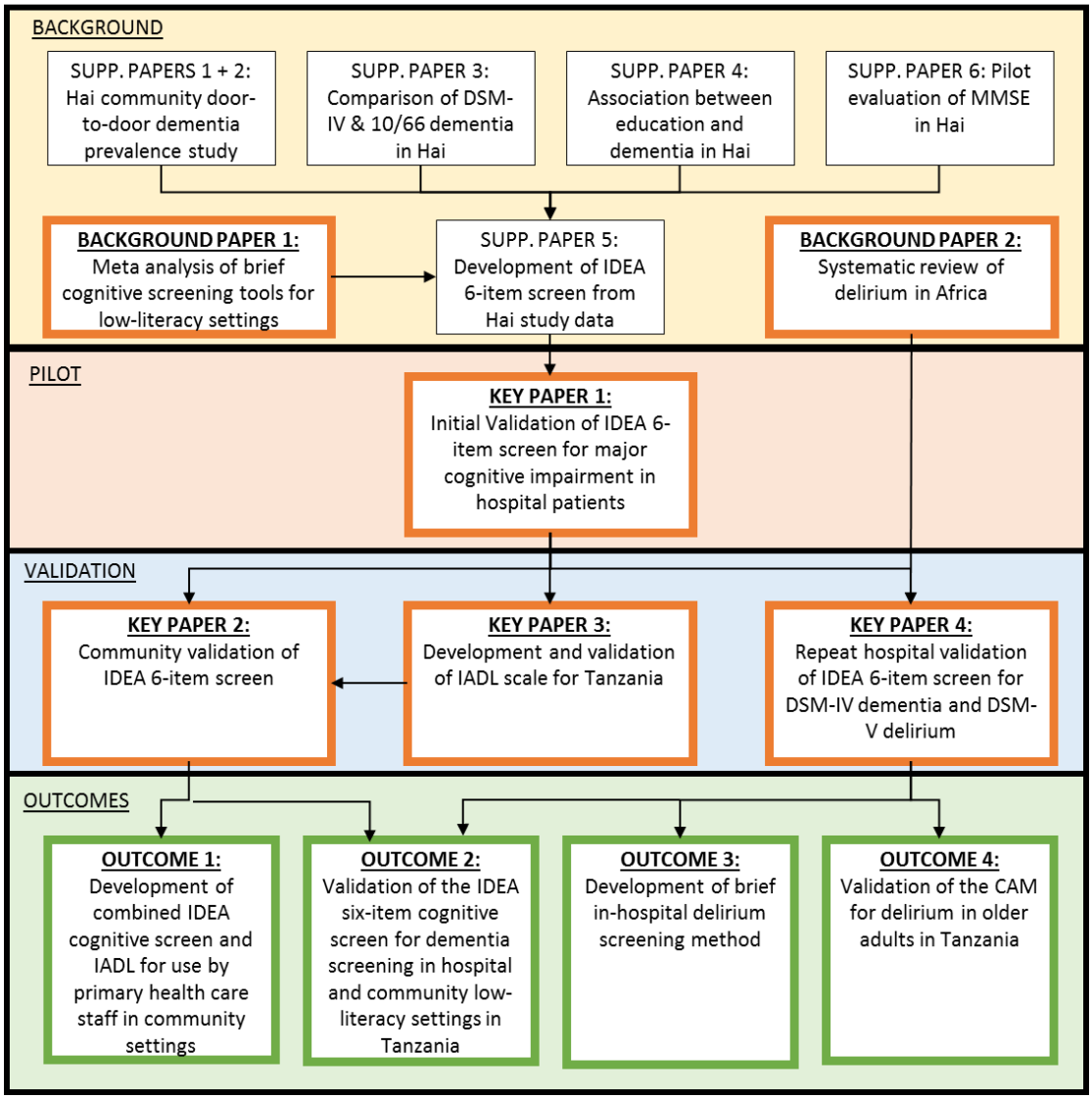

Figure 1. Thesis Outline

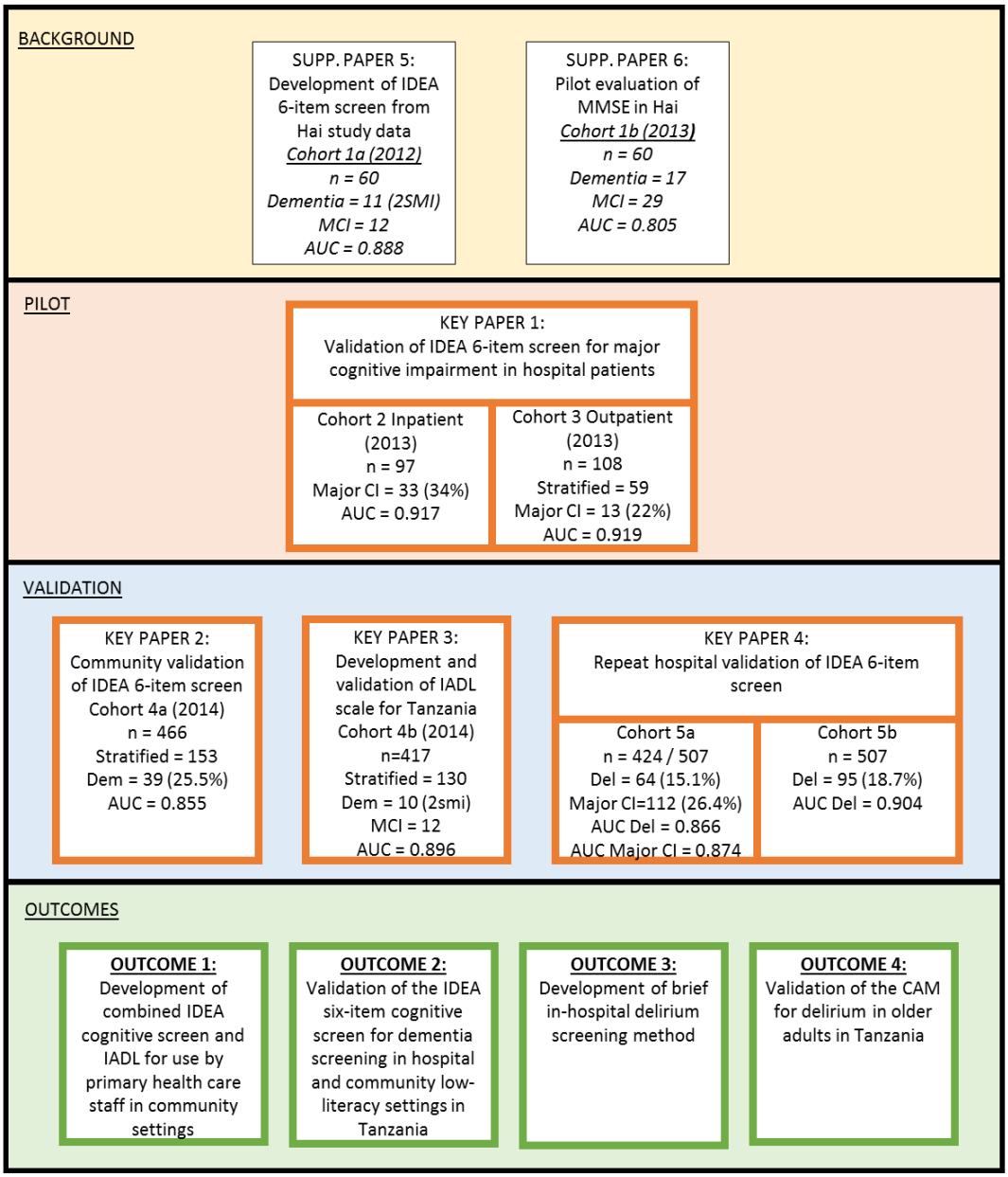

Figure 2. Cohorts and key data in each paper

Key to study cohorts in Figure 2

Cohort 1a 60 rural community dwelling individuals aged 70 and over in 2010. Initially recruited in Hai door-to-door prevalence study in 2010 and meeting consensus MCI criteria at that time. Two year follow-up in 2012 therefore aged 72 and over.

Cohort 1b Individuals from sample 1a followed up one year later, as part of MCI follow-up study.

Cohort 2 Consecutive sample of older adults aged 60 and over admitted to medical wards of a Government secondary care hospital in Moshi Municipality, (Mawenzi Regional Referral Hospital).Validation for cognitive impairment rather than dementia due to incomplete collateral histories.

Cohort 3 Older adults aged 60 and over attending an outpatient free-of-charge medical clinic at a Government secondary care hospital in Moshi Municipality, (Mawenzi Regional Referral Hospital). Systematic sample screened with randomised subset of all those with intermediate or high probability of dementia and 10% of normal controls blindly selected received blinded second stage clinical dementia assessment. Validation for cognitive impairment rather than dementia due to incomplete collateral histories.

Cohort 4a Community sample of rural dwelling individuals aged 60 and over recruited through a widely advertised dementia screening programme. Randomised subset of all those with intermediate or high probability of dementia and 10% of normal controls blindly selected received blinded second stage clinical dementia assessment. Validation for dementia by DSM-IV criteria. Collateral history available for almost all participants, and follow-up when indicated.

Cohort 4b Individuals from cohort 4a with complete cognitive and blinded functional assessment data.

Cohort 5 Consecutive sample of all adults aged 60 and over admitted to medical wards of a tertiary care hospital in Northern Tanzania during January 2015 (pilot) and March-August 2016. Follow-up at 6 months available where necessary. Validation for delirium and dementia.

6. Aims and objectives of this presented work

This series of four published papers aims to establish the validity and utility of a brief, culturally appropriate cognitive screening tool (the IDEA six-item screen) designed for use in low-literacy settings in sub-Saharan Africa (SSA), in a range of clinical settings in Northern Tanzania for identification of both dementia and delirium in older adults. Additional aims are to consider additional screening items to improve diagnostic accuracy by considering the presence of functional impairment, and to differentiate dementia and delirium in hospital settings. Cohorts and key data are outlined in Figure 2.

The objectives of the four key papers presented are outlined below

Objectives of the four key papers

1. To conduct a pilot assessment of diagnostic accuracy and clinical utility of the IDEA six-item cognitive screen for major cognitive impairment (delirium or dementia by DSM-IV criteria) in individuals aged 60 and over admitted to medical wards of a Government hospital in Northern Tanzania (Thesis paper 1)
2. To assess pilot diagnostic accuracy and clinical utility of the IDEA six-item cognitive screen for major cognitive impairment (delirium or dementia by DSM-IV criteria) in individuals aged 60 and over attending a free-of-charge clinic for older people at a Government hospital in Northern Tanzania (Thesis paper 1)
3. To assess diagnostic accuracy and clinical utility of the IDEA six-item cognitive screen for dementia by DSM-IV criteria in rural community-dwelling individuals aged 60 and over presenting to a community dementia screening programme in Northern Tanzania (Thesis papers 2 and 3)
4. To develop and validate a culturally appropriate functional assessment scale (the IDEA-IADL) to assist in identification of dementia in sub-Saharan Africa (Thesis paper 2)
5. To assess whether use of this culturally appropriate functional assessment tool (the IDEA-IADL) improves the diagnostic accuracy of the IDEA six-item cognitive screen for identification of dementia when used by non-specialist health workers in community settings in Northern Tanzania (Thesis paper 2)
6. To re-validate the IDEA six-item screen for identification of dementia by DSM-IV criteria in individuals aged 60 and over admitted to medical wards of a tertiary referral hospital, against gold standard DSM-IV dementia diagnosis by consensus supported by informant history and follow-up home visits at 6 months post discharge (Thesis paper 4)

7. To assess the diagnostic accuracy and clinical utility of the IDEA six item screen for identification of delirium by DSM-5 criteria in individuals aged 60 and over admitted to medical wards of a tertiary referral hospital in Northern Tanzania (Thesis paper 4)
8. To compare the diagnostic accuracy and clinical utility of the IDEA six-item screen with that of the Confusion Assessment Method (CAM) for identification of delirium in a tertiary referral setting against a gold standard diagnosis of delirium by DSM-5 consensus criteria (Thesis paper 4)
9. To conduct a secondary analysis of data in order to determine those screening items most predictive of delirium, and;
10. To propose a screen for identification of delirium suitable for use in a non-specialist setting in sub-Saharan Africa (Thesis paper 4)
11. To assess whether the IDEA six-item cognitive screen is educationally biased in these settings (Thesis papers 1, 3 and 4).

Part One

Introduction

Dementia in sub-Saharan Africa

7. Introduction

7.1. Dementia in low and middle income countries

Dementia is a worldwide public health priority. An estimated 35.6 million people currently have dementia, and the prevalence is predicted to double every 20 years, to 115.4 million in 2050[1].

The dementia syndrome is one of acquired and progressive decline in cognitive function caused by a number of neurodegenerative processes, the most prevalent of which are Alzheimer's disease (ADD), vascular dementia (VAD), Dementia with Lewy Bodies (DLB) and Parkinson's disease dementia (PDD). Multiple higher cognitive functions including memory, executive functioning, visuospatial ability, language and judgement are typically affected and the result is significant disability, dependence and caregiver burden. In addition to the personal and societal cost, is a significant economic cost estimated at over 400 billion USD in 2009[2]. Informal care constituted over a quarter of this cost[2].

Ageing is the greatest risk factor for dementia and projected increases in dementia worldwide are largely due to population ageing. In high income countries (HICs) where demographic transition is complete, awareness of dementia as a public health issue for ageing populations has resulted in substantial research activity supported by government policy.

The majority of people with dementia live in low and middle income countries (LMICs) and population ageing in these regions is the largest contributor to the projected increases in dementia worldwide. Recent epidemiological projections suggest that by 2050 over 80% of people with dementia will live in LMICs as demographic transition progresses in these world regions and their population continues to age[2]. Awareness of dementia as a significant issue in LMICs is relatively recent and therefore very few studies have taken place, with very limited epidemiological data available for many areas and few interventional studies[3].

The current situation therefore is that least is known about aetiology, risk factors or intervention strategies for dementia in the areas of the world where the majority of people with dementia live.

7.2. Dementia in sub-Saharan Africa (SSA)

In sub-Saharan Africa (SSA) an estimated 2.6 million older people currently have dementia and this number is projected to increase by 371% by 2030[1]. These prevalence estimates are based on very few studies, most of which have taken place in the last decade, and have acknowledged methodological issues[1]. Dementia was previously thought to be rare in SSA. Earlier Nigerian studies reported complete absence of dementia in community samples[4, 5] or significantly lower prevalence

when comparing US and Nigerian community samples of older adults using similar methodology[6]. More recent studies have reported dementia prevalence of between 2.29%[7] and 2.79%[8] in Nigeria, 6.4% in Tanzania[9] and 8.1% in an urban centre in the Central African Republic[10] using standard diagnostic criteria. Studies reporting dementia identified by cognitive screening alone, or in combination with an informant interview have reported prevalence of over 10% for cognitive impairment[11, 12] and 8.6-10.1% for dementia[13]. Geographical location of studies is shown in Figure 3. There is a general trend for more recently published studies to report higher prevalence of dementia, although the reasons for this are unclear[3]. The apparent increase in prevalence may mirror changes in disease burden from communicable to non-communicable (NCD) associated with demographic transition worldwide [14, 15] or may be due in part to methodological issues. Community-based prevalence studies of dementia in SSA are summarised in Table 1.

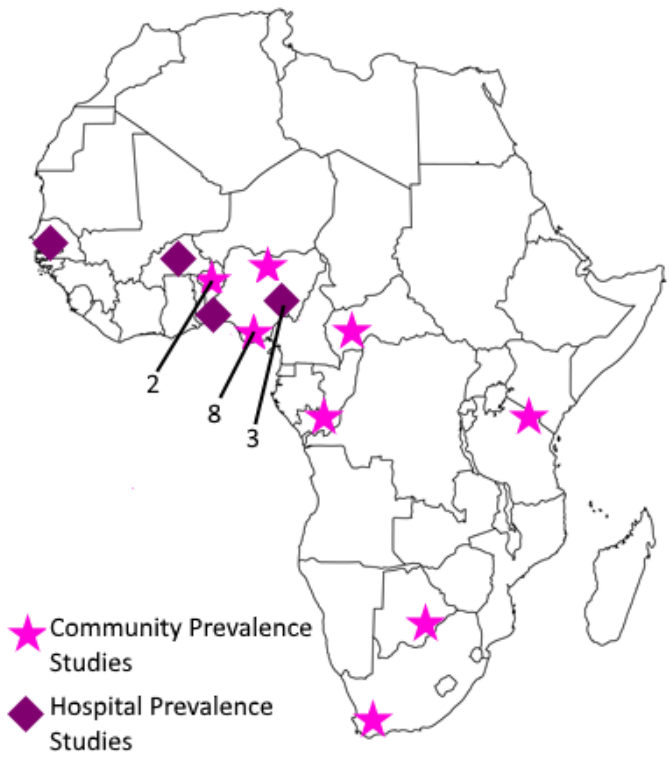

Figure 3. Geographical location of sub-Saharan African dementia and cognitive impairment studies 2016

Hospital or clinic-based studies are even more limited, with many utilising a retrospective case-note review design. Those utilising clinical criteria are summarised in Table 2. Most existing data are

limited to prevalence estimates. Incidence, risk factor and aetiology data are very limited, but suggest that risk factors and aetiology may differ between HICs and SSA.

For example, the APOE4 allele has a well-established association with ADD in HICs but not in the published studies examining this association in SSA[16-18]. Only one interventional study has taken place to date[19]. In summary, very little is currently known about dementia in SSA. It seems likely that dementia is as prevalent as in HICs, but little is known about aetiology, risk factors or potential interventions in this setting.

Table 1. Community based prevalence studies of neurodegenerative dementia in sub-Saharan Africa (older studies listed first)

Study	Location	Age range	Screening tool used	Diagnostic criteria	Dementia prevalence
Ogunniyi, 1992[4]	Nigeria N=932	40+	MMSE	DSM-III-R	Zero
Hendrie, 1995[6] Ogunniyi, 1997[20] Ogunniyi, 2000[7]	Nigeria N=2494	65+	CSI-D (cog +informant)	DSM-III-R ICD-10 NINCDS-ADRDA (AD) ICD-10 VAD	2.29% (age-adjusted) 1.4% AD (limited neuroimaging)
Uwakwe, 2000[21]	Nigeria N=164	60+	GMS SRQ	ICD-10	Zero
Baiyewu, 2002[22]	Nigeria N=2487	65+	CSI-D	Clinical assessment CERAD including MMSE	6.3% CI
Clausen, 2005 [11]	Botswana rural/ urban N=372	60+	MMSE 16/26 minus literacy items	Screen only	9% prevalence (cognitive impairment)
Gureje, 2006[13]	Nigeria N=2152	65+	CERAD 10 word learning list	Screen only	'probable dementia' 10.1%
Ochayi, 2006[23]	Nigeria, Jos n=280	65 +	CSI-D (cog) 28.5/33	DSM-IV	6.4%
Guerchet, 2009[12]	Benin, rural N=502	65+	CSI-D (cog) 25/30, 5WT	DSM-IV NINCDS-ADRDA	2.6% (no neuroimaging)
Uwakwe, 2009[24]	Nigeria N=914	65+	CSI-D	10/66 protocol	11.8% CI (no dementia diagnosis though used 10/66 protocol)
Guerchet, 2010[25]	Central African Republic (CAR) n=496 Congo n=520	65 +	CSI-D (cog) , 5WT	DSM-IV NINCDS-ADRDA	8.1% (CAR) no neuroimaging 6.7% (Congo).
Paraiso, 2011[26]	Benin, urban N=1139	65+	CSI-D (cog) 25/30, 5WT	DSM-IV NINCDS-ADRDA	3.7% no neuroimaging
Yusuf, 2011[8]	Nigeria, Zaria N=320	75.5 ± 9.4	CSI-D (cog)	ICD-10 DSM-IV	2.79%
Longdon, 2013[9]/ Paddick, 2014[27]	Tanzania, rural N=1198	70 +	CSI-D (cog +informant)	DSM-IV NINCDS-ADRDA/NCDDS AIREN	6.4% (age-adjusted) (some neuroimaging)

Table 2. Hospital-based prevalence studies of dementia in SSA (clinical criteria, not records-based). Older studies listed first.

Author and year	Location	Population	Reported literacy or educational level	Screening tools	Diagnostic criteria	Reported prevalence
Baiyewu, 1997[28]	Nigeria, nursing home	N=23 'elderly' no age given	14/23 no formal schooling	One stage assessment MMSE used as part of diagnosis	DSM-III-R GMS AGECAT	11/23 47.83%
Uwakwe, 2000[21]	Nigeria, medical wards, teaching hospital. Prospective cohort study	60+, N=119	68.5% no formal ed	MMSE, self-report, GMS	ICD-10 research criteria	2.8%
Napon, 2009[29]	Burkina Faso, (medical/ neurology/ neuro-surgical wards) Teaching hospital	15+ Mn 62.2 N=2396	51% illiterate	MMSE, 4 item IADL, clock drawing test, verbal fluency	DSM-IV criteria by neurologist.	2.2%
Ramlall, 2013[30]	South Africa, Nursing Home	60+ N=140	<12 years ed	MMSE	DSM-IV-TR	7.9%
Coume, 2012[31]	Senegal, University OPD	N=872 55+	49.3% some ed	Test of Senegal, Fillenbaum IADLs and brief mental test	Clinical diagnosis, Nigerian MMSE and IADL assessment	6.6%.
Toure, 2012[32]	Senegal, geriatric OPD	65 + N=507	47% formal ed	Test of Senegal	DSM-IV	8.87%
Yusuf, 2012[33]	Nigeria, urology OPD	N=121.	Not stated	CERAD 10 word list, stick design test. Blessed dementia Scale	Physical examination ICD-10 DSM-IV by consensus	
Gnonlonfoun 2014[34]	Benin Neurology department	N=251 50+	Not stated	MMSE	DSM-IV Hachinski	8.8% 50% AD

Key: MMSE Mini-Mental State Examination, IADL – Instrumental Activities of Daily Living, GMS – Geriatric Mental State, CERAD – Consortium for Establishing a Registry for Alzheimer's Disease, DSM-IV Diagnostic and Statistical Manual –Fourth Edition, OPD – Outpatient department

7.3. Diagnosis and screening for dementia in LMIC settings

A major challenge in dementia research in LMIC settings is availability of appropriate and validated screening and assessment methods. Most existing tools have been developed and validated in HIC populations which are likely to differ markedly from those in LMICs culturally and educationally. Attempts have been made to address these issues through development of screening and diagnostic methods designed to be used in different cultural settings.

The 10/66 international research collaboration developed a dementia screening and diagnostic method suitable for epidemiological studies in LMIC settings and designed to reduce known cultural biases[35]. The work completed using the 10/66 protocol has been instrumental in raising awareness and informing prevalence estimates of dementia in LMICs, and in informing policy makers worldwide. Although sites in SSA were involved in the initial stages of this collaboration, published validation data include very small numbers of SSA participants[36]. No separate validation studies of the SSA sites have been published. The 10/66 dementia identification protocol uses the Community Screening Instrument for Dementia (CSI-D) for initial dementia screening. The CSI-D was developed for cross-cultural dementia research, initially in the First Nations Cree ethnic group in North America and uses a cognitive assessment and informant questionnaire to stratify individuals into low, intermediate and high dementia probability groups[37]. The algorithm is weighted in favour of the informant interview to compensate for poor cognitive performance due to educational level. Most community-based prevalence studies in SSA have used the CSI-D but it is lengthy and designed for research rather than for use in routine care. A major focus of the 10/66 collaboration is that determination of functional impairment, needed for dementia diagnosis, may be difficult in LMIC settings due to differing cultural expectations and that studies using DSM-IV criteria in LMIC settings may underestimate prevalence[38, 39].

A number of hospital-based studies of dementia in SSA have used the mini-mental state examination (MMSE)[29, 34, 40]. The MMSE remains the most widely used dementia screening instrument worldwide despite well-established shortcomings including educational and cultural bias[41]. Use in these studies is therefore likely to reflect lack of validated alternatives to the MMSE as well as usual clinical practice.

7.4. Dementia screening in low-resource settings

Data from HIC settings suggests that over half of dementia cases remain undiagnosed[42]. Dementia is difficult to identify by doctors and other health professionals in primary care unless a structured screening tool is used[43]. Validated dementia screening tools are lacking in SSA therefore there is

likely to be a similar diagnostic gap. An additional problem in SSA is the large human resource gap. Across SSA there are estimated to be 200 times fewer trained mental health workers per 100,000 population when compared to HIC settings[44]. Specialist clinicians such as geriatricians, neurologists and psychiatrists are also very few, especially outside large urban centres[45, 46]. For example, in Tanzania where this work took place, there are a total of 15 registered psychiatrists for a total population of 50.8 million.

The World Health Organisation (WHO) recommended strategy for addressing this resource gap is one of task-shifting, or training non specialist staff to carry out tasks usually performed by specialist workers[47]. In mental health, the recommendation is to increase coverage of health interventions by integrating screening and monitoring of mental disorders into primary care and routine clinics. This strategy requires clear protocols and decision making support for non-specialist staff if it is to be achievable.

In LMIC settings, the possibility of using a case-finding approach for dementia identification by primary health workers has been explored in two studies from India[48] and from Brazil[49]. These studies did not involve the use of cognitive screening tools, and relied instead on training health workers in the typical clinical presentation of dementia. Both studies were small, and found similar positive predictive value of approximately 60% of dementia diagnosis by standard criteria in individuals identified by primary health care workers. This strategy used alone is unlikely to identify most people with dementia, and relies on the availability of a specialist to confirm diagnoses. Validated brief screening tools are likely to be useful in assisting non-specialist staff in identifying individuals with probable dementia but are currently not available in SSA. At present, only two cognitive screening tools have been validated in SSA. These include the CSI-D (validated in Nigeria[37] and Kenya[16]) and the Test of Senegal, a thirty-nine item cognitive screening test developed and validated in an urban University clinic in Senegal[32]. The CSI-D is primarily a research tool because it is lengthy, requires an informant interview in addition to cognitive screening and utilises an algorithm for risk stratification. The Test of Senegal has to date only been validated in an urban and relatively well-educated cohort which is likely to differ markedly from individuals needing assessment in rural SSA. Neither the Test of Senegal, nor the CSI-D have been validated across different healthcare settings such as hospital inpatients, outpatients and community clinics. Both are relatively lengthy and unlikely to be suitable for use in routine assessment, particularly by non-specialist clinicians in rural areas.

7.5. Illiteracy, low-literacy and cognitive assessment

An estimated seven hundred million people are illiterate worldwide[50]. Although the literacy rate is increasing, around 15% of the world's population are still illiterate[50]. Definitions of illiteracy vary, but the World Health Organisation (WHO) definition is inability to read and write a simple statement about everyday life. The majority of illiterate individuals live in LMIC countries, and prevalence is highest amongst older people in rural areas where access to education may have been limited previously. In SSA the illiteracy rate is currently 40% in adults[50].

Difficulties in cognitive assessment in illiterate and low-literate populations are well recognised[39]. Many cognitive screening tools developed in HIC settings include literacy-dependent items which are difficult or impossible for illiterate people to complete. Cultural differences such as familiarity with testing as a consequence of formal school attendance have also been frequently noted[51].

The differences in cognitive performance between individuals with and without previous formal education are not limited to reading, writing and drawing tasks. Illiterate individuals and those with no previous formal education underperform in most neuropsychological tests when compared to individuals with higher levels of education[52-55].

The greatest differences are observed between those with no formal education and those with elementary education[52]. Several studies have reported significant performance improvements with just one year of education[52, 56]. Language comprehension, phonological verbal fluency (due to increased vocabulary) and abstract thought/concepts such as explaining similarities have been noted to be significantly better in those with primary education in comparison to those with minimal education (one to two years)[52]. Schooling-related differences in cognitive performance in individuals with at least primary education are typically much smaller than those seen between those with no and at least minimal education[52]. This has been attributed in part to significant ceiling effects in neuropsychological tests designed for full marks to be achievable by cognitively normal individuals.

On formal neuropsychological testing, the most consistent cognitive differences between illiterate and literate individuals are in visual perception, logical reasoning, remembering strategies, formal operational thinking and verbal ability alongside reading, writing and calculation tasks which illiterate people would be expected not to be able to complete[52, 53, 55, 57]. There appear to be no real differences in problem-solving ability, orientation (taking into account cultural differences) and verbal memory for familiar categories or real objects[58, 59]. Short term recall, and especially cued recall or recognition memory appear to be indistinguishable in literate and illiterate groups[52]. The largest differences are seen in verbal ability or language tests including phonological verbal

fluency[60], and some tests of visuo-perception including figure copying and recall of a semi-complex figure[53].

Verbal (letter) fluency is typically severely impaired in illiteracy, as might be expected in individuals unable to write[60]. Asking individuals to list words beginning with a particular sound does not improve performance and may be because illiterate people are less able to perceive separate words[60]. Similar difficulty has been noted in repetition tasks[61]. Median phonological verbal fluency score is around 2 words per minute in illiterate individuals compared with up to 20 in unimpaired educated controls. Performance is typically much better in categorical verbal fluency[62], and almost normalises when categories relate to real experiences such as supermarket items[63]. Wider categories such as four legged animals are limited to those directly experienced in those without access to books[62]. Comprehension appears to be significantly affected in illiteracy, illustrated by inability to follow a three stage command[55].

Surprising differences are seen in spatial awareness and in fine finger movements[54, 55]. Luria's fist-palm-side test of frontal lobe function is performed poorly in individuals with low levels of formal education[64]. Performance in tests for apraxia by illiterate individuals such as 'show me how you blow out a candle', or 'show me how you strike a match' has been equated to that seen in individuals with neurological damage to the parietal lobe[55]. It has been suggested that learning to write leads to improvements in fine motor coordination and spatial awareness that might not otherwise be acquired[64, 65].

In visual perception, illiterate people have significant difficulty when asked to name objects presented as two dimensional line drawings[66]. Photographs appear to be easier to interpret, and performance improves to near-normal when naming real objects[55, 66]. Interpretation of pictures involving actions may be especially difficult, and in one study illiterate people were unable to differentiate 'girl running' and 'girl walking' and had difficulty with opposites such as 'girl pulls horse' and 'horse pulls girl'.

Other tests of two and three dimensional construction such as drawing a map or interpreting a 3D figure are difficult for illiterate people to perform in comparison to literate people from the same socioeconomic background and cultural group[53]. Tasks of pencil drawing are typically performed very poorly, but performance improves markedly when matchsticks are used to construct shapes[67]. [68] Similarly, large differences are seen between illiterate and those with elementary education in figure copying, and recall of a semi-complex figure[53].

In summary, it is clear that literate and illiterate people differ in performance on formal cognitive and neuropsychological testing. These differences in performance appear to result from real cognitive differences and not simply from a lack of familiarity with a testing situation.

There are consistent structural and functional neuroimaging differences between literate and illiterate individuals which are thought to represent differences in cognitive neurodevelopment. Illiterate individuals may have less lateralisation of language[69], and are therefore likely to suffer total aphasia following a left anterior circulation stroke[70] although this is a controversial finding[57, 71]. The corpus callosum of illiterate individuals is thinner, with fewer white matter pathways in the splenium[72, 73] and the role of the corpus callosum in literacy is supported by lesion studies showing that alexia results from lesions in this region. Functional neuroimaging studies suggest that illiterate individuals engage both cerebral hemispheres to complete certain tasks where literate individuals only use one, despite overall similar performance[63].

Current theories suggest that literacy changes the functional and structural organisation of the brain through interaction with the visual system[61, 74]. For example, learning to read leads to increased connectivity between the left and right angular gyri[61, 73] . These changes may increase development of the cortex and specifically the association areas, through increases in dendritic arborisation[74].

It has been suggested that the ability for abstract thought may be difficult to acquire without literacy, because literacy leads to symbolic representation through development of the visuospatial sketch pad[60, 65]. Classic neurological studies of illiterate individuals by Vygotsky and Luria noted that symbolic representation was necessary for abstract thought and memory, and that illiterate individuals relied more on direct perception and context when problem-solving[75]. In preliterate societies with oral traditions, illiteracy may not have been as problematic, as concepts could be represented and communicated in other ways, but these traditions are now rare, and those who are illiterate now are likely to be disadvantaged.

Attempts have been made to separate the effects of literacy and formal education in studies of the Vai people of Liberia, where traditionally a local script was taught at home due to lack of access to formal schooling. These studies concluded that simply learning to use written script did not improve cognition to the same degree as formal school attendance[76, 77]. Those with formal schooling demonstrated better overall cognitive performance and verbal ability. For example they were able to give a clear verbal explanation of test answers[65].

These observed differences have been difficult to separate from socioeconomic disadvantage. An association between lower socioeconomic status and dementia has been reported in LMIC settings[78].

Lack of access to education may be associated with other markers of disadvantage such as early childhood adversity or undernutrition[78]. The effect of literacy on cognition and neurodevelopment independent of other markers of childhood disadvantage is supported by studies of literate and illiterate individuals from the same socioeconomic background. Studies of literate and illiterate sister pairs from areas of rural Portugal where it was customary for the oldest daughter to assist with housework[61] whilst younger siblings attended school, and of adult ex-guerrillas in Colombia from similar socioeconomic backgrounds before and after commencing adult education classes, [73] support the role of literacy and education in cognitive neurodevelopment separate from childhood disadvantage.

The differences described between literate and illiterate individuals in cognitive neurodevelopment may not be simple variants, but may also be due to increased risk of cognitive decline and of dementia in illiterate individuals.

7.6. Education and dementia

Education and literacy are thought to reduce risk of dementia through increasing cognitive reserve. Cognitive reserve is a potentially modifiable risk factor for dementia which is currently the subject of much research interest [79-82]. The concept originates from evidence that there is often little relationship between observed degree of neuropathology and cognitive impairment, with some individuals able to tolerate a much greater degree of disease burden without demonstrating clinical evidence of dementia [79, 83, 84]. Educational exposure is thought to increase cognitive reserve through neuroplasticity and creation of more complex neural networks, resulting in the ability to compensate for greater degrees of neuropathology in later life[83]. Conversely, the observed neurocognitive differences observed in illiterate individuals may signify reduced cognitive reserve. Illiterate individuals have been reported to utilise both cerebral hemispheres to perform tasks performed using one hemisphere by literate individuals despite similar performance. Similarly studies of older and younger people demonstrate that despite similar overt cognitive performance, older people utilise both hemispheres to complete memory retrieval tasks, suggesting a degree of compensation for cognitive decline. It follows that if illiterate individuals are employing compensatory strategies throughout life, they may not be able to compensate for cognitive decline later in life.

Education is frequently used as a proxy for cognitive reserve in studies[85] but is not the only element of cognitive reserve. In individuals with similar access to formal education, higher measures of general intelligence at age 11 and linguistic ability in young adulthood have been linked to reduced risk of late onset dementia[86-88].

Similarly, opportunities for informal learning may contribute to cognitive reserve. In illiterate and low-literate settings men have been noted to outperform women, but this difference disappears in individuals with a high school education[65]. It has been suggested that this might be because of increased opportunities for employment and social interaction outside the home for illiterate men that might not be open to women in traditional societies.

In high-income countries, educational attainment is consistently associated with reduced dementia risk [89-92] as well as a delay in onset of the dementia syndrome. Meta-analyses report relative risk (RR) of 1.59 for all dementias for those with lower education and pooled OR of 2.61 (95% CI 2.21-3.07)[85, 93] The association appears greater for Alzheimer's disease (AD) with a RR of 1.88[93]. The majority of these studies include subjects with relatively high levels of education in high-income countries and are difficult to compare to populations in SSA. Studies in LMIC countries, including SSA, have been less likely to report an independent association between educational background and dementia, although an overall doubling of dementia risk with illiteracy was reported in one review of Latin American dementia studies[75]. It has been suggested that educational attainment is less likely to correlate with intellectual ability in these settings due to historical lack of availability or access to schooling. Existing studies of dementia prevalence from SSA report illiteracy rates of between 46 and 90%[94] and therefore educational background and even literacy are less likely to reflect childhood educational ability. Data are very limited in SSA because the vast majority of studies focussing on education and literacy as risk factors for dementia, and examining cognitive reserve have taken place in HIC settings.

Since low educational attainment and illiteracy appear to be risk factors for dementia, and may be associated with the rate of cognitive decline, cognitive screening tools developed in higher literacy settings but employing lower threshold values for illiterate or low-educated individuals may be reducing validity by failing to identify cognitive decline in those who may be at greatest risk[95]. It is clear also that individuals who are illiterate or with very low levels of formal education have major neurocognitive differences compared to educated individuals and that simply removing literacy and numeracy dependent items from screening tools is unlikely to be an effective strategy. Tools minimally modified in this way are likely to contain significant bias towards illiterate individuals are described above.

7.7. Dementia subtypes and cognitive assessment

Worldwide, the most common cause of dementia is thought to be Alzheimer's disease (AD), totalling 60-70% of cases[96]. The next most common cause is vascular dementia (VAD), comprising around 20% of cases worldwide[96]. Data on aetiology of dementia in LMICs are scarce, and limited by lack of access to neuroimaging or other biomarkers. There is some evidence that vascular cognitive impairment and vascular dementia are (were) more common in some East and South East Asian countries, particularly prior to transition to a Western lifestyle[97, 98]. There is also some limited evidence that development and globalisation with adoption of a high-income country lifestyle can result in a change in dementia subtype prevalence from VAD to AD[99, 100]. The underlying causes of this change are not known, and these findings are not universally accepted. Data on aetiology of dementia in SSA are particularly limited. Subtype diagnoses are reported in very few studies, and fewer are supported by neuroimaging or neuropathology[101]. There are some limited data from our team supported by neuroimaging suggesting that VAD is more prevalent in Tanzania than typically reported in HICs, and supported by neuroimaging data[27]. Although current data are lacking, the profile of dementia may differ in SSA to HIC settings. This is important when considering dementia screening.

Different patterns of neuropsychological impairment are typically evident in different subtypes of dementia and can be demonstrated on formal neuropsychological testing. ADD is characterised by early verbal and non-verbal memory impairment, followed by visuospatial impairment, difficulties with abstract reasoning and judgement, verbal fluency and naming. In VAD, memory impairment is typically less severe than that seen in AD, particularly in the early stages. Verbal fluency and other measures of executive function tend to be more severely affected. Dementia with Lewy bodies (DLB) is characterised by attentional and visuospatial impairment, verbal (particularly letter) fluency, processing speed and abstract reasoning. Screening tools developed and used in HIC settings are often biased towards ADD and may be less effective in screening for other dementia subtypes[102].

A comprehensive screening tool for dementia should therefore cover six core domains or abilities. These include attention and working memory, verbal learning and recall, visual construction, expressive language, executive functioning and abstract reasoning[102]. This is the case in dementia globally, but particularly in LMIC settings, including SSA.

Background Paper 1

Cognitive assessment tools validated in low-literacy settings

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Cognitive screening tools for identification of dementia in illiterate and low-educated older adults, a systematic review and meta-analysis

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ABSTRACT

Background: The majority of older adults with dementia live in low- and middle-income countries (LMICs). Illiteracy and low educational background are common in older LMIC populations, particularly in rural areas, and cognitive screening tools developed for this setting must reflect this. This study aimed to review published validation studies of cognitive screening tools for dementia in low-literacy settings in order to determine the most appropriate tools for use.

Method: A systematic search of major databases was conducted according to PRISMA guidelines. Validation studies of brief cognitive screening tests including illiterate participants or those with elementary education were eligible. Studies were quality assessed using the QUADAS-2 tool. Good or fair quality studies were included in a bivariate random-effects meta-analysis and a hierarchical summary receiver operating characteristic (HSROC) curve constructed.

Results: Forty-five eligible studies were quality assessed. A significant proportion utilized a case–control design, resulting in spectrum bias. The area under the ROC (AUROC) curve was 0.937 for community/low prevalence studies, 0.881 for clinic based/higher prevalence studies, and 0.869 for illiterate populations. For the Mini-Mental State Examination (MMSE) (and adaptations), the AUROC curve was 0.853.

Conclusion: Numerous tools for assessment of cognitive impairment in low-literacy settings have been developed, and tools developed for use in high-income countries have also been validated in low-literacy settings. Most tools have been inadequately validated, with only MMSE, cognitive abilities screening instrument (CASI), Eurotest, and Fototest having more than one published good or fair quality study in an illiterate or low-literate setting. At present no screening test can be recommended.

Keywords: cognitive assessment, screening, education, developing country, meta-analysis, low- and middle-income countries

Introduction

Dementia is a global public health priority with an estimated 300 million people currently affected (Prince *et al.*, 2013b). Current epidemiological data and projections suggest that the majority of affected individuals reside in low- and middle-income countries (LMICs) and that this proportion will rise to over 71% of the world total by 2050 (Prince *et al.*, 2013a). Identification of dementia allows early intervention and can improve outcomes (Prince *et al.*, 2013b). In LMICs, scarcity of healthcare and human resources has resulted in a lack of trained clinicians able to correctly identify dementia (Saxena *et al.*, 2007). The World Health Organization's (WHO) mental health strategy addresses this resource gap through training non-specialist clinicians to carry out tasks normally completed by specialists in better resourced areas (Dua *et al.*, 2011). This approach requires well validated and accurate screening tools to assist non-specialists.

Worldwide, over 700 million people are illiterate (UNESCO, 2015). Illiteracy and low rates of formal education are more common in LMICs, particularly in older adults (UNESCO, 2015),

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but can also be found in some HICs due to similar historical difficulties with resources and conflicts affecting the older population as well as recent population shifts due to globalization and migration.

Illiteracy and low educational level are associated with increased risk of dementia and have been hypothesized to account for some of the observed differences in reported prevalence (Caamano-Isorna *et al*., 2006; Meng and D'Arcy, 2012). Conversely, rates of cognitive impairment and dementia may be overestimated in LMIC populations due to poor performance in cognitive screening tests which require some degree of literacy (Paddick *et al*., 2015). Illiterate and low-educated adults can perform poorly on many conventional cognitive tests, without evidence of cognitive or functional decline on clinical history and examination. Most cognitive screening tests for dementia in frequent use, even in LMICs, were developed and validated in HIC settings with higher levels of formal education than those found amongst older adults in many LMICs. These differences in performance are not simply restricted to those aspects of cognitive screening traditionally taught in schools such as reading, writing or calculation, but include visuospatial and language ability (Rosselli *et al*., 1990; Ostrosky-Solis *et al*., 1998). Performance differences have been attributed to simple lack of confidence or familiarity with test situations, but evidence exists of differences in cortical organization and development in non-demented individuals without formal schooling (Castro-Caldas *et al*., 1998; Ardila *et al*., 2010). These differences have been noted between individuals with just one year of formal schooling in comparison with those without formal schooling (Ostrosky-Solis *et al*., 1998).

Difficulties in screening and diagnosis of dementia in low-literacy settings are widely recognized. Epidemiological studies of dementia from sub-Saharan Africa (SSA) report illiteracy rates of 47–97% in older adults (Guerchet *et al*., 2009; Yusuf *et al*., 2011). Similarly, the majority of participants in an international dementia prevalence study from LMICs including China, India, and South America reported either no formal education or incomplete primary education (Sosa *et al*., 2009). In rural Tanzania, our research group has reported that only 7% of females and 18% of males aged 70 years and over had 4 years of education or greater (Paddick *et al*., 2014).

The effect of lower levels of formal education on cognitive screening performance has been demonstrated in HIC settings, but the overall level of education in these studies is generally higher than that found in older populations in LMICs (Crum *et al*., 1993). More recently, a cross-cultural protocol for dementia diagnosis has been developed for use in low-literacy LMIC settings, but this is lengthy and not suitable for routine use by non-specialists (Prince *et al*., 2003). Existing dementia prevalence studies in SSA hospital settings often utilize tools designed and validated in HICs such as the Mini-Mental State Examination (MMSE), suggesting that these tools are common in routine practice in LMICs (Uwakwe, 2000; Touré *et al*., 2008; Napon *et al*., 2009; Ramlall *et al*., 2013).

We aimed to systematically review existing literature on brief, non-specialist cognitive screening tools with criterion validity against a clinical dementia diagnosis in older adults with very low or no formal education or literacy ability. We wished to determine whether existing brief cognitive screening tools can be used in populations of older adults with low or no formal education with similar levels of accuracy to those reported in HIC settings.

Methods

This systematic review followed published guidelines on reporting of systematic reviews of diagnostic accuracy studies, including PRISMA (Moher *et al*., 2009).

Search strategy

We searched four major databases Medline (1946–), Embase (1981–), Psychinfo (1806–), and Cinahl (1981–) for studies published prior to December 01, 2014. Included search terms were dementia (subject headings: dementia, cognitive impairment/defect/disorders, Alzheimer's disease (AD), memory disorders), questionnaires (subject headings: questionnaires, brief cognitive screening; keyword – assess*, screen*), low literacy (subject headings: educational status, educational attainment level, educational background, illiteracy; keyword – illitera* and low literacy), and validity (subject headings: validity, test validity; keyword – valid).

Reference lists of review articles and included studies were hand searched, alongside online databases of LMIC based literature including SCIELO (Central and South America) and African Journals online in order to identify non-indexed peer reviewed articles and ensure a global perspective. Results were not restricted to English language, but only abstracts available in English, Spanish, French, Italian, or Portuguese were reviewed due to resource availability.

Eligibility/inclusion criteria

Abstracts and titles were initially screened by S-MP and WKG separately, with full text articles requested for further assessment where it was not clear whether or not studies met the inclusion criteria. Disagreements were resolved through discussion.

Diagnostic accuracy studies of any cognitive measure, assessment, instrument, or test for face-to-face cognitive screening of dementia were included if they measured criterion validity against a gold standard diagnosis of dementia in individuals aged 45 years and over in a low-literacy setting, and were suitable for non-specialists to use in routine care. Self-assessment, telephone, and informant measures were excluded. We defined gold standard diagnoses as those using standard criteria including ICD or DSM, or clinical diagnoses made by a specialist clinician such as a neurologist, psychiatrist, or geriatrician. Studies simply reporting correlation between a cognitive screening tool and a more established screening test were excluded. The age cut-off of 45 years was selected based on previous epidemiological literature from LMICs. Low-literacy was defined as four years of formal education or less. Illiteracy was defined by self-report or less than one year of formal education. Suitability for use by non-specialists was determined by test duration (20 minutes or less) and ability to be performed without specialist training. In determining whether included screening tools met this criterion, information was sought from the index article or reference lists. Where unavailable, likely duration and eligibility were determined based on clinical experience of the researchers. Detailed neuropsychological batteries and tests for dementia subtype were excluded, as were studies from specialist settings, such as post-head injury or stroke. Illiteracy and educational background based on self-report were acceptable, as existing large epidemiological studies from LMIC settings have also used self-report and standardized literacy assessments are not routinely available (Sosa *et al.*, 2009).

Since research interest in this area is relatively recent, we wished to accurately reflect the current knowledge base and data quality. Both case–control (stage one diagnostic studies) and cross-sectional studies were therefore eligible for review.

Where studies described a low-education population, but data on individuals with 4 years of education or less were not presented, authors were contacted directly and requested to provide this data. In the absence of this additional data, only those studies where a minimum of 25% of participants were illiterate or had no formal schooling were included. Studies including combined cognitive screening and informant questionnaires were included if cognitive screening accuracy could be separately extracted from presented data. Although cultural differences may impact on test performance, consideration of such differences was beyond the scope of this review. Therefore, studies from any geographical location were included if eligibility criteria were met.

Data extraction

Data were extracted by one author (S-MP) and a selection checked by another author (WKG). Demographic data extracted included geographical location and clinical setting, screening test used, age and gender balance of cohort, dementia prevalence, overall median education, and proportion of individuals with less than one year of education or illiteracy. Diagnostic accuracy data including sensitivity, specificity, AUROC, and cut-off used were also extracted for each screening tool. Cross-sectional community (lower prevalence), primary/secondary care (higher prevalence), and case–control studies were considered separately. Cognitive domains assessed in each screening test were determined, and test subsequently categorized into single domain or multiple domain tests.

For meta-analysis, true positive, true negative, false positive, and false negative screening results were extracted or calculated where possible from published data or original data supplied by authors. Where possible, these data were extracted separately for the illiterate/no formal education subgroup.

Quality assessment

Study quality was evaluated using the Quality Assessment of Diagnostic Accuracy Studies version 2 (QUADAS-2) tool (Whiting *et al.*, 2011). QUADAS-2 consists of 4 domains and 14 items assessing the risk of bias, applicability, and quality. Each item is scored as "yes," "no," or "unclear." Two reviewers (SMP and WKG) independently evaluated each of the included studies using agreed criteria based on the QUADAS-2 core questions and applicability to the study question. Core criteria included: (1) method of patient selection (consecutive or random selection, study design and inclusion/exclusion criteria); (2) index test used and blinding to results of the reference standard assessment; (3) use of an appropriate reference standard independent of the screening test result; and (4) flow and timing (appropriate interval between index test and reference standard, all participants assessed with the same reference standard, all participants included in the analysis).

Studies meeting all four core criteria were rated good quality. Fair quality studies failed to meet one core criterion but were otherwise robust. Case–control studies were assessed separately and acknowledged not to meet criterion 1.

Meta-analysis

A bivariate diagnostic random-effects meta-analysis was conducted using the mada open source package for R software (Doebler and Holling, 2012). Bivariate meta-analysis is recommended in studies of diagnostic tests due to threshold effects and underlying between studies variability. A random-effects model was used to adjust for heterogeneity. Only cross-sectional studies with at least three individuals with dementia in a low-literacy population were included in meta-analyses. Studies of insufficient quality on QUADAS-2 assessment were not included in meta-analysis. This included those with a case–control design and where inadequate blinding in screening test administration or gold standard diagnosis resulted in significant bias.

Combined sensitivity, false positive rate, and diagnostic odds ratios (DOR) were used to summarize screening test accuracy. Forest plots were used to summarize the variability in the thresholds used. Between study heterogeneity was assessed using both the I^2 statistic and Cochran's Q with $p < 0.10$ considered statistically significant. A hierarchical summary receiver operating characteristic (HSROC) curve was constructed to present summary estimates of sensitivity and specificity alongside 95% CI and prediction region in each subgroup. Area under curve (AUC) and partial AUC statistics corrected for observed data and false positive rates were also calculated.

Accuracy was assessed using this method for all screening tools in low-literacy groups in both community or low prevalence and clinic-based or higher prevalence settings. There is evidence that both sensitivity and specificity can vary with disease prevalence alongside positive predictive value, possibly due to the differing spectrum of patients assessed in each setting (Leeflang *et al.*, 2013). Studies in these different settings were therefore analyzed separately. All screening tools were initially analyzed together, in order to assess the accuracy of cognitive screening methods. This approach has been used in previous meta-analyses of screening tools with a focus on HIC settings (Mitchell and Malladi, 2010). Where possible, accuracy was evaluated for illiterate/no education groups only. It was intended to analyze performance of specific tests where sufficient data were available.

Results

Included studies

The study selection process is shown in Figure 1. A number of cognitive assessment tools developed for use in low-educated and illiterate populations did not meet our inclusion criteria. These included the Community Screening Instrument for Dementia (CSI-D) used in dementia prevalence studies across LMIC countries. The CSI-D requires an informant, has a duration of over 30 minutes and utilizes a computer algorithm for risk stratification therefore cannot be used by non-specialists (Prince *et al.*, 2003). A brief CSI-D has been modeled and internally validated but not evaluated in clinical practice (Prince *et al.*, 2011). Similarly the Literacy Independent Cognitive Assessment (LICA) and shorter version (S-LICA) were felt to be too complex and/or lengthy for routine use (Choi *et al.*, 2011). The Rowland Universal Dementia Scale (RUDAS) was designed for cross-cultural assessment (Basic *et al.*, 2009), but we were unable to identify a low-literacy validation study of the RUDAS for inclusion in this review. A total of 45 studies meeting our study criteria were identified. A summary of included studies is presented in Tables 1–3.

A total of 27 different screening tests were evaluated, of which four were cultural adaptations of the MMSE. A total of 14 tests (12 multi-domain and 2 single domain) were specifically developed for use in low-literacy settings. A summary of the cognitive domains assessed is presented in Table 4. A majority of studies are related to multi-domain, rather than single domain, cognitive tests. Of those tests evaluated, only the MMSE, cognitive abilities screening instrument (CASI), Eurotest, Fototest, and KICA were validated in more than one good or fair quality study. The low-literacy validations identified for each study are also included in Table 4.

The geographical distribution of good or fair quality studies is shown in Figure 2. Although the majority originated in LMICs, a significant number did not. Twelve studies were conducted in low-literacy populations in Spain, and two in minority Aboriginal populations in Australia. Similarly, three of the most-validated tests, such as the Eurotest, Fototest, and KICA, were developed in low-literacy settings in HICs.

Population and community studies

Fourteen cross-sectional community or population-based studies were identified and are summarized in Table 1. Geographical location of these studies included China (five studies), India (two studies), Spain (two studies), Australia (two studies), Brazil,

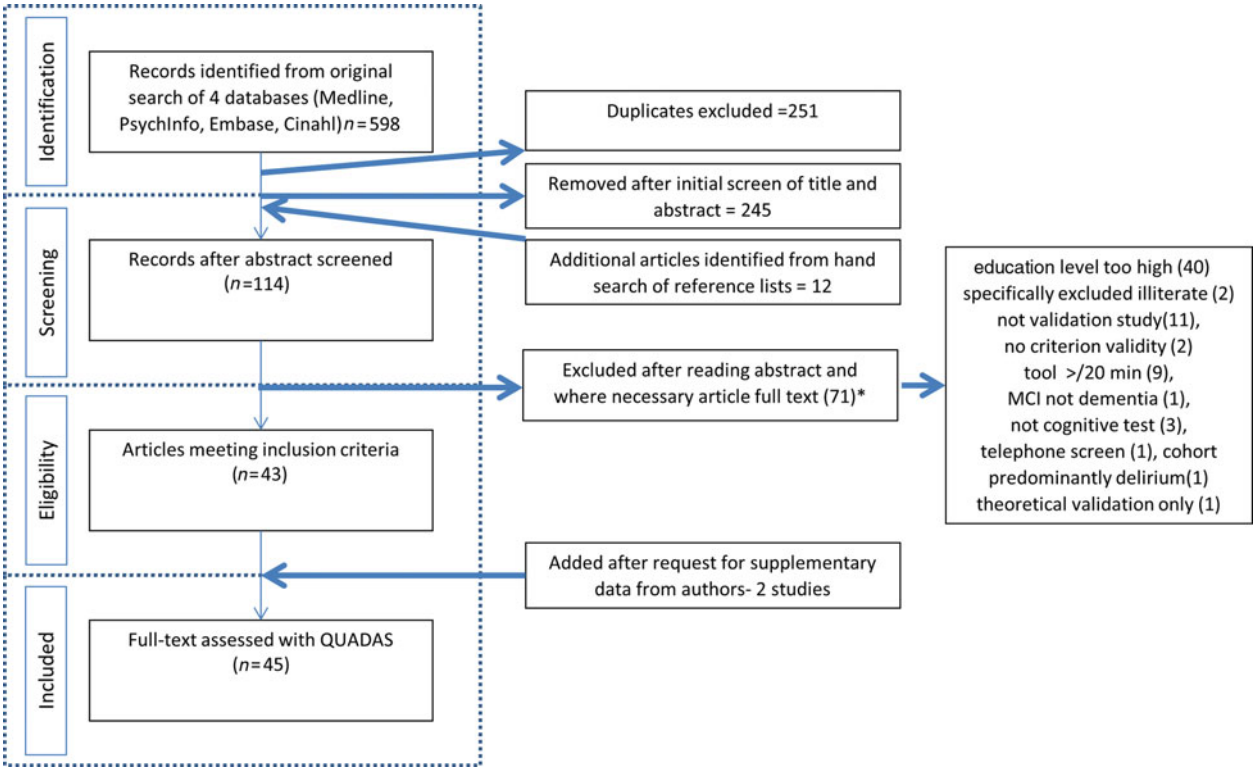

Figure 1. (Colour online) Prisma flowchart of study selection.

Turkey, and Nigeria. A total of 12 screening tools were validated in this setting. Sample size ranged from 455 to 8,411 in population-based studies and 101–490 in smaller community based studies. One small study from India included both community and outpatient clinic cohorts, reported separately, and another in Australia used community health contacts to oversample for cognitive impairment. Reported rates of illiteracy or no formal education ranged from 25% to 91%. Dementia prevalence was generally low, ranging from 3% to 21% with the exception of one study reporting a prevalence of 34% in a population over-sampled for cognitive impairment. All studies utilized DSM-IV, DSM-III, or DSM-III-TR criteria by consensus or specialist clinician, with the exception of one study utilizing an algorithm-based DSM-IV diagnosis. Two studies also applied research criteria for dementia subtypes.

Prevalence/clinic settings

Thirteen screening tests were evaluated over 16 studies conducted in clinic settings. The majority of studies took place in Spain (eight studies) with four taking place in Brazil, two in India, and one each in Thailand and China. These studies are summarized in Table 2. Prevalence of dementia ranged from 10.4% in primary care (Baos Sánchez *et al.*, 2007), 17.8% in nursing home residents (Jitapunkul *et al.*, 1996), and 19–33% in more specialist clinics. Illiteracy rates in these studies varied from 5.3% (Verghese *et al.*, 2012) to 65% (Martínez de la Iglesia *et al.*, 2001) with the majority quoting rates from 25% to 40%. However those studies reporting lower illiteracy levels quoted rates of none or minimal schooling of 41.4% to 49% (Carnero Pardo *et al.*, 2007; Saez-Zea *et al.*, 2008) amongst participants. Included studies where less than a quarter of the sample were illiterate or had no formal studies are those where supplementary information on a low-literacy subgroup was obtained from the study authors. Most studies used DSM-III, DSM-III-TR, or DSM-IV dementia criteria, with two studies utilizing dementia subtype diagnoses.

Case–control studies

Case–control designs are recommended for use only in the first stage of assessment of a diagnostic test, and the majority of these studies related to initial validations of newly developed tests, or initial studies of well-established tests in a low-literacy setting, see Table 3. These studies were nevertheless relevant to our study question with level of illiteracy ranging from 20% to 100%. Identified case–control studies validated 16

Table 1. Summary of screening tools validated in low-education settings – population and community (low prevalence) studies

TOOL	STUDY NUMBER (AUTHOR, DATE)	COUNTRY	SETTING	DEMENTIA	NUMBER OF PARTICIPANTS	MEAN AGE	% FEMALE	EDUCATION, YEARS	DIAGNOSTIC ACCURACY	COMMENTS
Multiple domain tests										
7MS	20 (Del Ser *et al.*, 2006)	Spain, suburban city Leganes	Community, long term epidemiological study	DSM-IV and DSM-III-R clinical consensus	527 (10.8% dementia), 416 after exclusions (11.5% dementia)	79	51.7%	10.6% illiterate; 25% no formal education; 38% incomplete primary	Sensitivity 100, specificity 95.1, AUC 0.996; separate results for illiterate not given	Excluded severe sensory or physical impairment
Blessed-Roth IMC cut off 12/13	22 (Jin *et al.*, 1989)	Shanghai,	Community	DSM-III cognitive and functional tests/history	5,055/5,313, 55+; 77/190 clinical diagnosis; 65/190 DSM-III		57.7%	26.5% no education; 36.65% elementary	Cut-off 12 – sensitivity 84.6, specificity 66.4; cut-off 13 – sensitivity 78.5, specificity 76.8; all – sensitivity 80.4, specificity 70.1 (cut-off 13 in no education); 1–4 years of education – sensitivity 77.8, specificity 88.1	Validation based on 190 stratified
CASI	28 (Liu *et al.*, 1994)	China, southern	Community township, stratified sample 50+	DSM-III-R	455 (16 dementia) 3.5%	68.6	51.4%	71.2% less than 1 year education	Sensitivity 88, specificity 94	
CASI 2.0	27 (Lin *et al.*, 2002)	China,	Rural population from epidemiological study and memory clinic	DSM-IIIR and DSM-IV; AD – NINCDS-ADRA	2,096 (263 dementia) 12.5%	76.1	51.9%	40% illiterate	No education – sensitivity 82.5, specificity 84.9; 1–5 years of education – sensitivity 83.5, specificity 91.0	

Table 1. Continued

TOOL	STUDY NUMBER (AUTHOR, DATE)	COUNTRY	SETTING	DEMENTIA	NUMBER OF PARTICIPANTS	MEAN AGE	% FEMALE	EDUCATION, YEARS	DIAGNOSTIC ACCURACY	COMMENTS
Hasegawa Dementia Scale (HDS)	42 (Tsai and Gao, 1989)	Shanghai, urban and rural	Community	DSM-III-R by psychiatrist	2,573 from 3,063 (21.2% dementia)	Not given (range 60–85)	63%	61% illiterate	Sensitivity 71.4, specificity 95.9	
HMSE used cut point ≤19 as 10th centile	34 (Pandav *et al.*, 2002)	North India, rural	Community	DSM-III-R dementia and CDR by research medical team	5,126 (4810 complete), 632 second stage assessment, 32 dementia (43 including VA)	66.5	46.9%	73.3% illiterate	Sensitivity 81.3, specificity 60.2, AUC 0.804	Calculations based only on 32 non-VA diagnoses. Second stage assessment completed if below 10th centile (not just for MMSE, other tests)
KICA-COG 32/33 cut off	29 (LoGiudice *et al.*, 2006)	Aboriginal population, Australia	Community	DSM-IV and ICD-10 by specialist clinician (subtypes clinical)	27/70 dementia	72	57.1%	61.4% no education; 21 different languages	Sensitivity 90.6, specificity 92.6, AUC 0.95	Age 45 years and over (but mean age similar to other studies)
KICA-Cog	38 (Smith *et al.*, 2009)	Aboriginal population, Australia Kimberley /Northern Territory	Community	DSM-IV and ICD-10 by specialist clinician (subtypes clinical)	47/17 (36% dementia) (NT), 363/45(12.4% dementia)	72	73.1% 55%	46.8% no education 40% no education; 144 no education (36 dementia, 25%)	1 – sensitivity 82.3, specificity 87.5, AUC 0.95; 2 – sensitivity 93.3, specificity 94.8, AUC 0.984; no education – sensitivity 88.9, specificity 87.5, AUC 96.1	

Table 1. Continued

TOOL	STUDY NUMBER (AUTHOR, DATE)	COUNTRY	SETTING	DEMENTIA	NUMBER OF PARTICIPANTS	MEAN AGE	% FEMALE	EDUCATION, YEARS	DIAGNOSTIC ACCURACY	COMMENTS
MMSE-Brazil – 14/15 no education; 17/18 more than 1 year of education	37 (Scazufca *et al.*, 2009)	Brazil, urban	community	DSM-IV by 10/66 algorithm	1,933 (84 dementia)	72.2	60.5%	38.5% no education; 9% had 4 years or more education	No education – sensitivity 78.7, specificity 77.8, AUC 0.87; 1 year of education – sensitivity 91.9, specificity 81.5, AUC 0.94	
MMSE-Turkish -r 18/19 uneducated	24 (Keskinoglu *et al.*, 2009)	Turkey	Community, home visit followed up by hospital	DSM-IV dementia by neurology team	490 (63 dementia)	71.8	59.2%	1.6 years mean education; 34.7% illiterate; 50.4% less than primary	Sensitivity 82.7, specificity 92.3, AUC 0.907	Cluster sampling in community
MOCA Beijing –13/14 illiterate 19/20 with 1–6 years of education; 24/25 with more than 7 years of education	32 (Lu *et al.*, 2011)	China urban and rural	Community	DSM-IV, NINCDS-ADRA, NINDS-AIREN by consensus	8,411	73	53.7%	5.8 (1.1); 2,279/8,411 no education	Dementia and CI – sensitivity 80.9, specificity 83.2 (no education); dementia – sensitivity 96.9, specificity 82.5 at education adjusted cut-offs (all)	Normal cutoff 25/26 in HIC studies

Table 1. Continued

TOOL	STUDY NUMBER (AUTHOR, DATE)	COUNTRY	SETTING	DEMENTIA	NUMBER OF PARTICIPANTS	MEAN AGE	% FEMALE	EDUCATION, YEARS	DIAGNOSTIC ACCURACY	COMMENTS
PCL Cut point 22/32	19 (de Yébenes *et al.*, 2003)	Spain, suburban	Community, population-based	DSM-IV dementia	375 from 527 without sig sensory impairment	78.6	49.1%	9.1% illiterate;, 25.6% no formal studies; 72.5% less than 4 years	Sensitivity 93.94, specificity 94.72, AUC 0.985	Excluded significant sensory impairment
VSID-P	39 (Stanley *et al.*, 2009)	Vellore, South India	OPD and community	DSM-IV	90 (20 dementia) OPD, 101 (3 dementia) community	71.53 OPD 72.5 com	42.2% OPD 59.4% com	37.8 illiterate hospital-based; 53.5% illiterate community	Hospital – sensitivity 94.4, specificity 86.1, AUC 0.92; community – sensitivity 66.7, specificity 77.6, AUC 0.81	Excluded delirium and significant sensory impairment
Single domain tests										
Stick design	4 (Baiyewu *et al.*, 2005)	Nigeria, urban	Community	DSM-III-R consensus or CIND criteria	2,535 – 724 stratified, 88 dementia, 296 CIND, 340 normal (12.2% dementia)	78.8	78.3%	9% had any education, 658 (83 dementia)	All education – AUC 0.779; no education – sensitivity 58.0, specificity 88.0, AUC 0.772	

Note: CIND: cognitive impairment no dementia, MCI: mild cognitive impairment.

Table 2. Summary of screening tools validated in low-education settings – clinic (higher prevalence) studies

TOOL	STUDY NUMBER (AUTHOR, DATE)	COUNTRY	SETTING	DEMENTIA	NUMBER OF PARTICIPANTS	MEAN AGE	% FEMALE	EDUCATION, YEARS	DIAGNOSTIC ACCURACY	COMMENTS
Multi-domain tests										
Chula mental test, CMT (cut off 16)	23 (Jitapunkul *et al.*, 1996)	Thailand, Bangkok	Care home	DSM-III-R by neurologist	212 (17.8% dementia)	77.7	87%	24% illiterate	Sensitivity 100, specificity 90, AUC >90 (from graph); separate illiterate results not given	Expected to be self-caring on admission. Severe dementia cared for at home
Clock (Manos, Shulman, Wolf–Klein, Sunderland)	31 (Lourenço *et al.*, 2008)	Brazil, urban	Medical OPD (convenience sample)	DSM-IV clinical consensus neurologist neuro-psychologist	306 (293 complete data); data only presented for 211 with < 4 years of education; 32.3% dementia	72.8	72.5%	4 years or less	AUC – 0.668 Manos, 0.684 Shulman, 0.684 Wolf–Klein, 0.657 Sunderland	Excluded significant sensory impairment, not all had collateral hx
Eurotest cut-off 20/21	11 (Carnero-Pardo *et al.*, 2006)	Spain, multi-centre	Neurology OPD, consecutive	DSM-IV TR	516; 101 dementia; 35 excluded	73	53.4%	38.7% illiterate; 45.5% no formal education	Sensitivity 91, specificity 82, AUC 0.93	Scores not affected by education
Eurotest 20/21	14 (Carnero-Pardo *et al.*, 2011a)	Spain, southern	Referrals from primary care with suspected CI	DSM-IV TR by consensus neurologists	156 (139 included); 47 MCI, 36 dementia	72	72.7%	14.4% illiterate; 36.0 % less than primary	Sensitivity 73, specificity 96	Did not exclude on basis of sensory impairment
Eurotest	15 (Carnero-Pardo *et al.*, 2012)	Spain, multi-centre	Neurology OPD	DSM-IV TR	548/589 total (101 MCI, 98 dementia)	72.69	56.5%	7% illiterate 49% minimal education	AUC 0.95	Demographic data of primary sample of 589

Table 2. Continued

TOOL	STUDY NUMBER (AUTHOR, DATE)	COUNTRY	SETTING	DEMENTIA	NUMBER OF PARTICIPANTS	MEAN AGE	% FEMALE	EDUCATION, YEARS	DIAGNOSTIC ACCURACY	COMMENTS
Fototest 26/27	14 (Carnero-Pardo *et al.*, 2011a)	Spain, southern	Referrals from primary care with suspected CI	DSM-IV TR by consensus neurologists	156 (139 complete data)	72	72.7%	14.4% illiterate; 36.0 % less than primary	Sensitivity 74, specificity 97	Did not exclude on basis of sensory impairment
Fototest	12 (Carnero-Pardo *et al.*, 2007)	Spain, urban	Neurology OPD patients plus 70 added normal controls	DSM-IV TR Research consensus criteria (Spain) for MCI	225 no CI; 58 MCI; 95 dementia	72.4	61.1%	11.6% illiterates; 41.4% none/ minimal education	Sensitivity 88, specificity 90, AUC 0.95 (dementia/MCI)	
Fototest	15 (Carnero-Pardo *et al.*, 2012)	Spain, multi-centre	Neurology OPD	DSM-IV TR	589 (106 MCI, 122 dementia)	72.69	56.5%	7% illiterate; 49% minimal education	Sensitivity 88, specificity 0.87, AUC 0.94	
Fototest	36 (Baos Sánchez *et al.*, 2007)	Spain, urban	Primary care clinics	DSM-IV TR	241 assessed; 10.4% dementia	76.67	56.7%	45.6% illiterate	Sensitivity 84, specificity 85.6	Random sample separate sensitivity for illiterate not given
Memory Alteration Test (M@T)	14 (Carnero-Pardo *et al.*, 2011a)	Spain, southern	Referrals from primary care with suspected CI	DSM-IV TR by consensus neurologists	156 (139 complete data)	72	72.7%	14.4% illiterate; 36.0 % less than primary	Sensitivity 0.79, specificity 0.90	Did not exclude on basis of sensory impairment
MMSE 19/20 no ed 23/24 all	1 (Almeida, 1998)	Brazil, urban	Outpatient psychiatric clinic	ICD-10 dementia	211 (70 dementia)	69.38	69%	26.5% no education	No education – sensitivity 80, specificity 71; education – sensitivity 84.3, specificity 60.3	Consecutive attendees of clinic less spectrum bias, included severe depression

Table 2. Continued

TOOL	STUDY NUMBER (AUTHOR, DATE)	COUNTRY	SETTING	DEMENTIA	NUMBER OF PARTICIPANTS	MEAN AGE	% FEMALE	EDUCATION, YEARS	DIAGNOSTIC ACCURACY	COMMENTS
MMSE Cut 17/18	16 (Carnero-Pardo *et al.*, 2013)	Spain, urban	Primary care	DSM-IV TR	407 (49% dementia); 180 (52 dementia)	70.8	70.8%	8.3% illiterate; 180 <4 years of education	Sensitivity 89, specificity 86, AUC 0.89	Results for lower educated cohort from author
MMSE 23/24 ed 18/19 no ed(ill)	30 (Lourenço and Veras, 2006)	Brazil,	Geriatric outpatient clinic	DSM-IV dementia	78/dementia; 303 total	73	71.6%	26.4% illiterate; 46% 1–4 years of education	No education – sensitivity 73.5, specificity 73.9; education – sensitivity 75, specificity 69.7	Consecutive, less spectrum bias. Excluded no informant or severe sensory problem
MMSE chinese illiterate 20 literate 22	45 (Xu *et al.*, 2003)	China, Xian province. 'less developed province'	Geriatric outpatient clinic, attached to teaching hospital	Clinical diagnosis by consensus two neurologists, NINCDS-ADRA for AD AIREN for VAD	370 (93 dementia)	70.23	49.9% (d) 40.4% (c)	4.66 years of mean education; 19% whole sample illiterate	Sensitivity 83.87, specificity 84.48	Excluded severe dementia or disability
SPMSQ (cut point 3, 4 for illiterates)	33 (Martínez de la Iglesia *et al.*, 2001)	Spain	General medical clinic	ICD-10 - standardised interview	255 (22% dementia)	74.5	66.7%	65.5% illiterate	Illiterate – sensitivity 85.7, specificity 79.3, AUC 0.89. All – sensitivity 92,0, specificity 84,7, AUC 0.926	No exclusions, likely convenience sample, /oversample for CI
Verbal Fluency	15 (Carnero-Pardo *et al.*, 2012)	Spain, multi-centre	Neurology OPD	DSM-IV TR	578/589 total (103 MCI, 114 dementia)	72.69	56.5%	7% illiterate; 49% minimal education	AUC 0.94	Demographic data of primary sample of 589

Table 2. Continued

TOOL	STUDY NUMBER (AUTHOR, DATE)	COUNTRY	SETTING	DEMENTIA	NUMBER OF PARTICIPANTS	MEAN AGE	% FEMALE	EDUCATION, YEARS	DIAGNOSTIC ACCURACY	COMMENTS
VSID-P	39 (Stanley *et al.*, 2009)	Vellore, South India	OPD	DSM-IV	90 (20 dementia)	71.53	42.2	37.8 illiterate	Sensitivity 94.4, specificity 86.1, AUC 0.92	Excluded delirium and significant sensory impairment
Single Domain Tests										
PMIS cut off 5	44 (Verghese *et al.*, 2012)	Kerala, India	Neurology clinic, consecutive, but additional volunteer controls.	DSM-IV dementia by consensus	304 (65 dementia) 55 <4 years of education	68.3	47.4%	Mean education 8 years, 167 (54.9%) (<10 years), 16 (5.3%) no formal education	Sensitivity 95.4, specificity 99.2,	Excluded sensory, psychiatric or other impairment likely to affect test performance
Mini-cog recall cut point 2/3	21 (Ribeiro Filho and Lourenço, 2009)	Brazil, urban	OPD polyclinic	DSM-IV geriatrician and neuro-psychologist consensus. No subtype	306 (293 complete data); 211 with 4 years or less education – data analyzed; 32.2% dementia	72.8	72.5%	All 4 years of education or less; 78/211 no education	Specificity 60.3, specificity 65.0	Excluded significant sensory impairment
Semantic VF Animal VF	35 (Saez-Zea *et al.*, 2008)	Spain	Consecutive attendees of "cognitive and behavioral disorders" clinic	DSM-IV dementia, MCI by consensus criteria	226 (dementia 83 (31.7%), MCI 53 (20.2%))	72.6	57.2%	9.9% illiterate; 42.7% no formal education	AUC 0.88 (VF animals); AUC 0.90 (VF names)	VF names not associated with education (animals were)

Note: CI: illiterate control, OPD: out patient department.

Table 3. Summary of screening tools validated in low-education settings – case–control studies

TOOL	STUDY NUMBER (AUTHOR, DATE)	COUNTRY	SETTING	DEMENTIA	NUMBER OF PARTICIPANT	MEAN AGE	% FEMALE	EDUCATION, YEARS	DIAGNOSTIC ACCURACY	COMMENTS
Multi-domain tests										
Clock	2 (Aprahamian *et al.*, 2011)	Brazil, urban	Outpatient geriatric clinic, all participants	NINCDS-ADRA for AD mild/ moderate only	66 AD; 40 controls	80.28 (AD), 77.97 (C)	71.7%	All illiterate, no formal education self-defined	Sensitivity 66.7, specificity 82.8, AUC 0.829	Excluded severe dementia CDR3 and sig sensory impairment
Clock	26 (Lam *et al.*, 1998)	China, Hong Kong	Psychogeriatric clinic/ controls social centre	DSM-IV dementia	106 (53 dementia (39 AD); 53 no dementia)	75.7	Not stated	Mean education 4 years	Cut point ¾, sensitivity 0.83, specificity 0.79	
Cognitive state test COST 23/30 (ILL) 24/30 (1-5y) 26/30 (6+y)	3 (Babacan-Yildiz *et al.*, 2013)	Turkey	Outpatient geriat-ric/neurology clinic	AD by NINCDS-ADRA only included CDR 1,2,3 and 0	114 NC; 74 D (AD)	64.9 (NC), 67.2 (AD)	50/114 (NC), 55/74 (D)	21/114 (NC), 37/74 (D) illiterate; mean education – 5.3 years (NC), 3.3 years (D)	Illiterate – sensitivity 81, specificity 99, AUC .094; 1–5 years of education – sensitivity 75, specificity 86, AUC 0.9; more than 6 years of education – sensitivity 77, specificity 84, AUC 0.86	Excluded MCI/CDR 0.5. Appears to have screened all referrals
Eurotest cut 23	10 (Carnero-Pardo and Montoro-Ríos, 2004a)	Spain, southern (Urban)	Specialist clinic (dementia) OPD (no dementia)	DSM-IV dementia	60; 30 mild dementia (CDR 3–4); 30 no dementia; 50%	73.9 (D), 73.8 (NC)	63.3% (D), 56.6% (NC)	8/30 (D), 10/30 (NC) illiterate	Sensitivity 0.93, specificity 0.87, AUC 0.96	Excluded uncorrected sensory impairment. Controls assessed to exclude dementia

Table 3. Continued

TOOL	STUDY NUMBER (AUTHOR, DATE)	COUNTRY	SETTING	DEMENTIA	NUMBER OF PARTICIPANT	MEAN AGE	% FEMALE	EDUCATION, YEARS	DIAGNOSTIC ACCURACY	COMMENTS
Fototest	9 (Carnero-Pardo and Montoro-Ríos, 2004b)	Spain, urban	Research clinic	DSM-IV TR	30 dementia; 30 controls; 50%	73.97 (D), 73.8 (NC)	63.3% (D), 56.6% (NC)	8/30 (D), 10/30 (c) illiterate	Sensitivity 0.93, specificity 0.80, AUC 0.94	Excluded severe sensory impairment
FULD object-memory test, TR 31 DR 7	17 (Chung, 2009)	China	Community centers (NC), dementia day centers (D)	Clinical diagnosis dementia	57 dementia (CDR1); 135 no dementia (CDR 0); 29.7%	79.42 (D), 75.53 (NC)	70.2 (D), 76.3 (NC)	27/57 (D), 45/135 (ND) no education	TR – sensitivity 93, specificity 90, AUC 0.969; DR – sensitivity 91, specificity 82, AUC 0.931	Convenience sample. CDR 1 and 0 only
Hindi MMSE (HMSE) cut-off 23	43 (Tsolaki *et al.*, 2000)	Greece rural	Community, referrals from primary care, assessed in neurology OPD	DSM-IV NINCDS-ADRA for AD	50 AD; 50 no dementia (spouses of patients); 50%	72.98 (D), 72.62 (NC)	*F* ratio not given	All illiterate	Sensitivity 94, specificity 98	
MMSE 17.5 cut- off	2 (Aprahamian *et al.*, 2011)	Brazil, urban	Outpatient geriatric clinic, all participants	NINCDS-ADRA for AD mild/ moderate only	66 AD; 40 controls; 62%	80.28 (AD), 77.97 (C)	71.7%	All illiterate, no formal education and self-defined	Sensitivity 95, specificity 72.7, AUC 0.913	Excluded severe dementia CDR3 and sig sensory impairment

Table 3. Continued

TOOL	STUDY NUMBER (AUTHOR, DATE)	COUNTRY	SETTING	DEMENTIA	NUMBER OF PARTICIPANT	MEAN AGE	% FEMALE	EDUCATION, YEARS	DIAGNOSTIC ACCURACY	COMMENTS
MMSE Cut off 26	5 (Bottino *et al.*, 2009)	Brazil, urban	Outpatient geriatric and research psychiatry clinic	ICD-10 DSM-III-R mild/ moderate only	34 dementia; 59 controls; 36%	73.7 (D), 69.25 (NC)	52.9% (D), 79.7% (NC)	5.44 (D), 4.9 (C)	Sensitivity 94.1, specificity 78.0, AUC 0.941	Convenience sample, assessments were blinded
MMSE cut-off 23/24	6 (Bustamante *et al.*, 2003)	Brazil, urban	Outpatient geriatric and research psychiatry clinic	ICD-10 DSM-III-R mild/ moderate only	30 dementia; 46 controls; 39%	73.9 D, 68.8 (NC)	53.3% (D), 78.3% (NC)	45/76; 0–4 years of education	Sensitivity 80, specificity 91.3, AUC 0.929	No significant difference in median MMSE between high/low education, 17.9 low education dem, 28 low education controls
MMSE Cut-off 24	10 (Carnero-Pardo and Montoro-Ríos, 2004a)	Spain, southern (Urban)	Specialist clinic (dementia) OPD (no dementia)	DSM-IV dementia	60; 30 mild dementia (GDR 3–4); 30 no dementia; 50%	73.9 (D), 73.8 (NC)	63.3% (D), 56.6% (NC)	8/30 (D), 10/30 (NC) illiterate	Sensitivity 67, specificity 0.90, AUC 0.89	Excluded uncorrected sensory impairment. Controls assessed to exclude dementia
MMSE cut-off 21 illiterate	25 (Kochhann *et al.*, 2010)	Brazil, urban	Neurology clinic patients, convenience sample, others OPD, relatives, staff	DSM-IV dementia	968 (162 dementia) 16.7%	70.6	65%	7.2 years of mean education; 72/168 illiterate	Sensitivity 93, specificity 82, AUC 0.955	Markedly higher cut-off for illiterate than in other Brazilian studies, spectrum bias

Table 3. Continued

TOOL	STUDY NUMBER (AUTHOR, DATE)	COUNTRY	SETTING	DEMENTIA	NUMBER OF PARTICIPANT	MEAN AGE	% FEMALE	EDUCATION, YEARS	DIAGNOSTIC ACCURACY	COMMENTS
MMSE-I (Turkish) 22/30 ILL 24 1–5 y ed 24 6+ y ed	3 (Babacan-Yildiz *et al.*, 2013)	Turkey	Outpatient geriatric/neurology clinic	AD by NINCDS-ADRA only included CDR 1,2,3 and 0	114 (NC); 74 (D) (AD); 39.36%	64.9 (NC), 67.2 (AD)	43.86 (NC), 74.33 (D)	21/114 (NC), 37/74 (D) illiterate; mean education – 5.3 years (NC), 3.3 (D)	Illiterate – sensitivity 97, specificity 96, AUC 0.98; 1–5 years of eduaction – sensitivity 96, specificity 99, AUC 0.99; More than 6 years of education – sensitivity 92, specificity 100, AUC 1.0	Also validated COST and MOCA in the same study
SPMSQ Cut-off 7	10 (Carnero-Pardo and Montoro-Ríos, 2004a)	Spain, southern (Urban)	Specialist clinic (dementia) OPD (no dementia)	DSM-IV dementia	60 participants – 30 mild dementia (GDR 3–4), 30 no dementia	73.9 (D), 73.8 (NC)	63.3% (D), 56.6% (NC)	8/30 (D), 10/30 (NC) illiterate	Sensitivity 83, specificity 90, AUC 0.91	Excluded uncorrected sensory impairment. Controls assessed to exclude dementia
T7M (7 minute screen) Cut-off 20	10 (Carnero-Pardo and Montoro-Ríos, 2004a)	Spain, southern (prob urban)	Specialist clinic (dementia) OPD (no dementia)	DSM-IV dementia	60 participants – 30 mild dementia (GDR 3–4), 30 no dementia	73.9 (D), 73.8 (NC)	63.3% (D), 56.6% (NC)	8/30 (D), 10/30 (NC) illiterate	Sensitivity 87, specificity100, AUC 0.98	Excluded uncorrected sensory impairment. Controls assessed to exclude dementia

Table 3. Continued

TOOL	STUDY NUMBER (AUTHOR, DATE)	COUNTRY	SETTING	DEMENTIA	NUMBER OF PARTICIPANT	MEAN AGE	% FEMALE	EDUCATION, YEARS	DIAGNOSTIC ACCURACY	COMMENTS
Test of Senegal Cut-off 28/39	41 (TourÉ *et al.*, 2008)	Senegal, Dakar Urban	Outpatient clinic55+	DSM-IV dementia	58 dementia, 58 no dementia	67.2	37.4%	50.7% no education	Sensitivity 93.1 Specificity 89.6 AUROC 0.967	
The Money Test	8 (Carnero-Pardo *et al.*, 1999)	Spain, urban	Dementia/ memory clinic	DSM-IV	211 no dementia, 114 dementia	67.4 (D), 68.65 (no dementia)	66.35%	26% illiterate, 19/97 dementia, 36/114 no dementia	Sensitivity 89, specificity 92	Included MCI, subjective memory impairment, but then analyzed as case–control
Single domain tests										
Categorical verbal fluency Cut-off 9 illiterate	7 (Caramelli *et al.*, 2007)	Brazil, urban	Outpatient neurological Clinic	DSM-III-R All probable AD NINCDS-ADRA	88 dementia, 117 (NC), 42.9%	78.2 AD, 77 (NC)	73.7%	52 (25%) Illiterate, 46(22%)1–3 years of education	Illiterate – sensitivity 90.5, specificity 80.6, AUC 0.922; 1–3 years of education – sensitivity 95.2, specificity 80.0, AUC 0.914	
Recall DR-BCRB	40 (Takada *et al.*, 2006)	Brazil	Community	DSM-IV AD subtype	95 (34 dementia), 35.8%	74.0 (CI), 79.65 (DI), 73.57 (DL), 81.35 (CL)	46.3%	40/95 illiterate	All – sensitivity 90.3, specificity 98, AUC 0.977; illiterate – sensitivity 93.3, specificity 95.7, AUC 0.975	Excluded CDR 3 severe dementia controls, excluded depression and stroke and >MMSE adjacent scores

Table 3. Continued

TOOL	STUDY NUMBER (AUTHOR, DATE)	COUNTRY	SETTING	DEMENTIA	NUMBER OF PARTICIPANT	MEAN AGE	% FEMALE	EDUCATION, YEARS	DIAGNOSTIC ACCURACY	COMMENTS
Recall DR-CERAD	40 (Takada *et al.*, 2006)	Brazil	Community	DSM-IV AD subtype	95 (34 dementia)	74.0 (CI), 79.65 (DI), 73.57 (DL), 81.35 (CL)	46.3%	40/95 illiterate	All – sensitivity 81.2, specificity 94.1, AUC 0.929; illiterate – sensitivity 80, specificity 87, AUC 0.845	Excluded CDR 3 severe dementia controls, excluded depression and stroke and >MMSE adjacent scores
Stick design STD	18 (de Paula *et al.*, 2013)	Brazil, urban	Community, assessed in OPD	DSM-IV NINDS-AIREN	128	Median – 75 for both groups	Not given	Median education – 4 years for both groups	AUC 0.756	Only included normal and mild dementia, CDR 0.5-1.0. does not give proportion illiteracy
Verbal fluency Cut off 7.5	2 (Aprahamian *et al.*, 2011)	Brazil, urban	Outpatient geriatric clinic, all participants	NINCDS-ADRA for AD mild/ moderate only	66 AD, 40 controls, 63.3%	80.28 (AD), 77.97 (C)	71.7%	All illiterate, no formal education and self-defined	Sensitivity 85, specificity 60.6, AUC 0.790	Excluded severe dementia, CDR3, and significant sensory impairment

Note: AD: Alzheimer's disease, NC: normal control C-patient control, TR: total recall, DR: delayed recall, CI: illiterate control, DI: illiterate dementia, CL: control literate, DL: dementia literate, OPD: out-patient department.

Table 4. Characteristics of cognitive tests included in the review

		ATTENTION			MEMORY		LANGUAGE			EF/ FRONTAL LOBE				PARIETAL/ VISUOSPATIAL				PRACTICALITIES	
TEST	STUDIES	ORIEN-TATION	REGIST-RATION	ATTEN-TION AND CONCEN-TRATION	REMOTE MEMORY	SHORT-TERM RECALL	NAMING	REPET-ITION	COMMAND (NO. STAGE)	LANG-UAGE SPO-KEN WRIT-TEN	ABSTRACT	VF	OTHER EF	COPY	IDEATIONAL PRAXIS	AGNOSIA	CALC	FREE TO USE?	SCHOOLING DEPENDENT ITEMS
Duration <5 minutes																			
CDT	2, 26, 31												*	*				Yes	Draw
Fototest	9,11,14,15,36		*			*F+C	*					*						Yes	N
Mini-Cog	21		*			*								CDT				Yes (licensed)	Draw
PMIS	44		*			*F+C	*											?	N
SPMSQ	13, 33	*		*	*												*	Permission	Y
STD	4,18													*				Yes	N
VF	2, 12, 35											*						Yes	N
VSID-P	39 (2 cohorts)		*		*	*	*		*3	*					*	*		Yes	N
Duration 5–10 minutes																			
7 MS	13, 20	*				* F+C	*					*		CDT				Yes	Draw
CASI-S	28	*	*			*F+C						*						On request	N
COST	3		*	*	*	*	*	*	* 2S		*	*		*	*	*		Yes	Copy
DR-BCSB	40					*	*											On request	N
DR-CERAD	40					*												On request	N
Eurotest	10,12,13				*	*							*				*	Yes	Calc
M@T	12		*			*												Yes	N
MOCA	32	*	*	*		*	*	*			*	*	TMT	CDT				Yes (copy-right)	Draw
Money test	8				*	*							*				*	Yes (now Eurotest)	Calc

Table 4. Continued

		ATTENTION			MEMORY		LANGUAGE			EF/ FRONTAL LOBE				PARIETAL/ VISUOSPATIAL				PRACTICALITIES	
TEST	STUDIES	ORIENTATION	REGISTRATION	ATTENTION AND CONCENTRATION	REMOTE MEMORY	SHORT-TERM RECALL	NAMING	REPETITION	COMMAND (NO. STAGE)	LANGUAGE SPOKEN WRITTEN	ABSTRACT	VF	OTHER EF	COPY	IDEATIONAL PRAXIS	AGNOSIA	CALC	FREE TO USE?	SCHOOLING DEPENDENT ITEMS
PCL	19	*	*		*	*	*											Yes	None
Duration 10–15 (+) minutes																			
B-R-IMC	22	*	*	*	*	*												Yes	N
CASI	27	*		*	*	*				*	*	*		*				Yes	Draw
CMT	23	*	*	*	*		*	*	* 3		*						*	Yes	N
FOME	17		*			* F+C Del	*											No	N
H- MMSE	34, 43	*	*	*		*	*	*	*	*				*			*	? (based on MMSE)	Copy
HDS	42	*	*	*	*	*											*	? (based on MMSE)	Calc
KICA	29, 38	*	*			* F+C	*		*1+2			*		*	*			Yes	N
MMSE	1,2,3,5,6,13,16, 24,25,30,37, 45	*	*	*		*	*	*	* 3S	*				*			*	No	Calc, draw
Test of Senegal	41	*	*	*	*	*				*			*	*			*	Yes	Calc

Note: F + C: free and cued (recall), Del: delayed (recall), TMT: trail making test, CDT: clock drawing test, S: stage (command), HDS: Hasegawa Dementia Scale, CMT: Chula Mental Test, VSID-P: Vellore Screening Instrument for Dementia-Patient, S-LICA: Literacy Independent Cognitive Assessment (short form), KICA: Kimberley Indigenous Cognitive Assessment, CDT: clock drawing test (Sutherland scoring), CDT: clock drawing test (Shulman scoring), 7MS: seven minute screen, PCL: Prueba Cognitiva de Leganes, SPMSQ: short portable mental status questionnaire, MOCA: Montreal Cognitive Assessment, COST: cognitive state test, CASI-S: cognitive abilities screening instrument (short version), SDT: stick design test, Mini-Cog: Mini Cognitive Screen, MMSE: Mini-Mental Status Examination, FOME: Fuld Object Memory Test, B-IMC: Blessed Roth Memory Concentration test, CASI: cognitive abilities screening instrument memory alteration test (M@T)*: domain tested, ?: unclear. NB Filho Mini-Cog article only includes registration and recall items, not the clock test score in scoring.

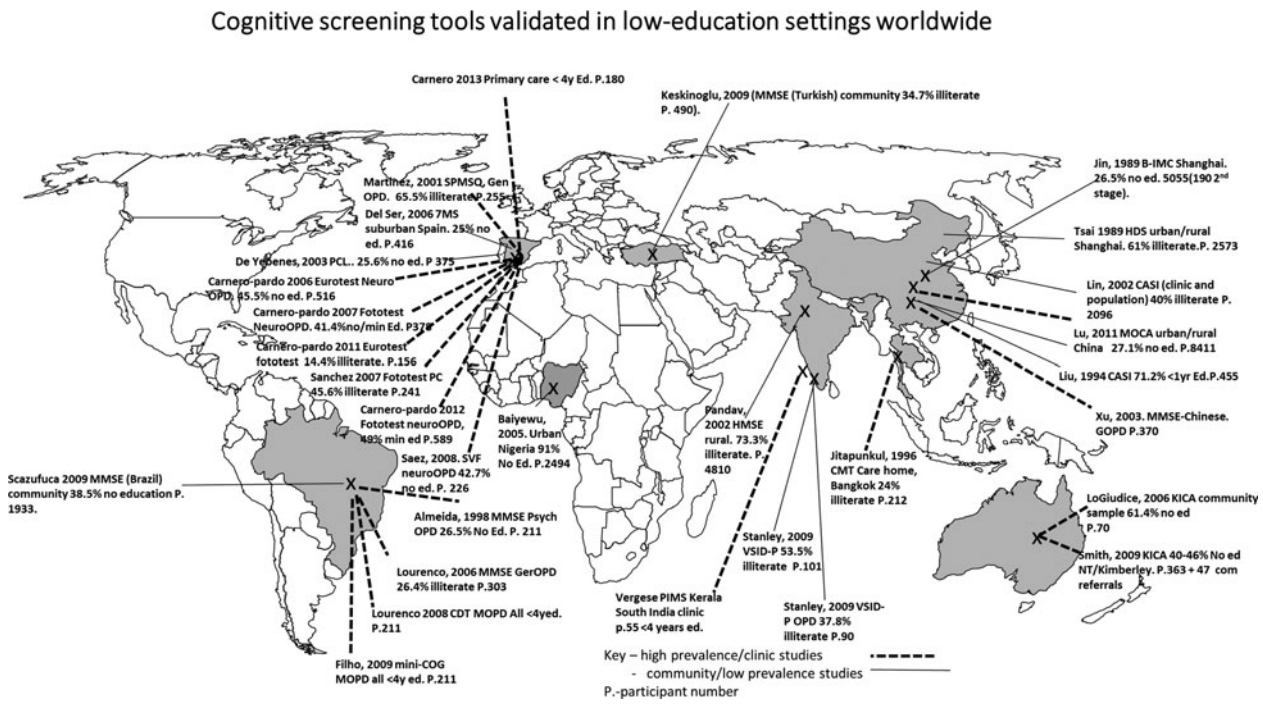

Figure 2. Map of good and fair quality low-literacy screening tool validation studies.

different cognitive tests (including two cultural adaptations of the MMSE) over 15 studies. The majority of studies took place in Brazil. Other studies were located in Spain, Greece, China, Korea, Hong Kong, Senegal, and Turkey.

Sample size in these studies ranged from 60 to 968 with most studies including around 200 participants. Dementia prevalence ranged from 16.75 to 63%, with most studies aiming to include 50% of participants with dementia and 50% control participants. Two studies employed consecutive sampling, but subsequently included only normal controls and individuals with mild/moderate dementia in the analysis. All but two took place in clinic/high prevalence settings, and the majority utilized NINCDS-ADRA criteria for AD alongside DSM-III or DSM-IV dementia criteria with some studies only including patients with AD dementia. Sensitivity and specificity for each included screening test are summarized in Table 3.

Quality assessment

A total of 24 of the 45 included studies were of good or fair quality, see Table 5. Of those rated as being of poorer quality, a significant number (15) utilized a case–control design. Additional spectrum bias was evident amongst case–control studies with most including only individuals with mild dementia alongside healthy controls. Six cross-sectional studies were found to have inadequate blinding procedures in administration of the index screening test, or gold standard reference diagnosis or screening tests applied to persons with established diagnoses. Most community studies used population samples from cross-sectional or longitudinal studies. Others utilized cluster sampling or a stratified sample from two stage community-based studies. Two studies oversampled for cognitive impairment resulting in potential spectrum bias. The majority of clinic-based studies sampled consecutive or randomized referrals (eight studies) (Almeida, 1998; Xu *et al*., 2003; Carnero-Pardo *et al*., 2006; Baos Sánchez *et al*., 2007; Saez-Zea *et al*., 2008; Carnero-Pardo *et al*., 2011b; Carnero-Pardo *et al*., 2012). Others utilized convenience sampling (Lourenço *et al*., 2008; Ribeiro Filho and Lourenço, 2009), oversampled for cognitive impairment (Martínez de la Iglesia *et al*., 2001) or supplemented additional unimpaired controls (Carnero Pardo *et al*., 2007; Verghese *et al*., 2012). Generalizability of both community and clinic-based studies was limited by exclusion of individuals with "severe" (De Yebenes *et al*., 2003; Del Ser *et al*., 2006; Lourenço and Veras, 2006; Stanley *et al*., 2009) or "significant" sensory impairment (Stanley *et al*., 2009) and neurological or psychiatric disorders (Stanley *et al*., 2009; Lu *et al*., 2011; Verghese *et al*., 2012).

Three studies provided insufficient information about study design most commonly in the domain of patient flow and timing; these were rated "fair" if no information in the manuscript led reviewers to suspect serious methodological flaws.

Meta-analyses

Studies were excluded from meta-analyses due to insufficient quality, as assessed by the QUADAS-2 tool; all case–control studies were excluded for this reason. A full description of the reasons for exclusion from meta-analyses is listed in Table 5. Four separate meta-analyses were conducted.

Community or low prevalence studies

Population and community studies included in the meta-analysis included twelve cohorts from eleven primary studies with a total of 15,939 participants of whom 1,376 were diagnosed with dementia (8.6%). Screening tests included variations of the MMSE (four cohorts), and single studies of the HDS, KICA, MOCA, CASI, 7MS, B-IMC, PCL, and VSID-P. All are multi-domain cognitive tests. One community study of a single-domain test (Stick design, Nigeria) was excluded from the meta-analysis after failing to meet the QUADAS-2 quality standard as the screening test formed part of the diagnostic assessment. Two other studies where participants were oversampled for cognitive impairment were considered more appropriately analyzed with high prevalence studies.

There was non-significant heterogeneity between studies when measured by Cochran's *Q*: (17.704 (11 df, p = 0.089)), but moderate heterogeneity when measured with Higgins' I2, a measure of the percentage of total variability due to between studies variability (37.9%).

Combined data in a bivariate random-effects model resulted in a sensitivity estimate of 0.869 (95% CI = 0.791–0.921) and specificity of 0.886 (0.823–0.923). The combined DOR for the model was 50.529 and a HSROC was plotted with an AUC of 0.937and partial AUC (restricted to observed FPRs and normalized) of 0.901, see Figure 3. The most accurate screening tests were 7MS, PCL, and KICA-Cog in Australia. The least accurate were the Hindi MMSE and VSID-P, although the VSID is designed to be used alongside an informant history.

Higher prevalence or clinic-based studies

A total of 13 clinic-based or higher prevalence primary studies including 17 validation cohorts were suitable for inclusion in meta-analysis. Other studies were excluded where low-literacy data could not be extracted or supplied by study authors. Higher prevalence studies included 3,487 individuals of whom 899 were diagnosed with dementia (25.8%). Tests evaluated were the Spanish MMSE (MEC) (two studies) Chinese MMSE, Brazilian MMSE (two studies) the VSID-P, KICA-Cog (two studies), CASI (2 cohorts from one study), Fototest (two studies), Eurotest, PMIS, MAT, CMT, and SPMSQ.

There was little heterogeneity between studies (Cochran's *Q*: 16.235; p = 0.437, I^2 1.449%).

Pooled sensitivity was estimated at sensitivity of 0.845 (0.817–0.869) and specificity of 0.847 (0.805–0.882). The combined DOR was 35.681 and the HSROC resulted in an AUC of 0.881 (partial AUC 0.843). The least accurate test was the Brazilian MMSE, and the most accurate were the CMT and PMIS in Thailand and India albeit with wide confidence intervals. All are multi-domain tests with the exception of the PMIS, which is a picture-based recall test.

Studies of illiterate individuals

Studies including only illiterate individuals or where data for illiterate individuals could be extracted included 2,098 individuals (392 with dementia) across seven primary studies. These included three clinic-based studies, three community studies, and one combining memory clinic and population study participants. Screening tests were all multi-domain and included Brazilian and Chinese variants of the MMSE, the KICA (Aboriginal population in Australia), the SPMSQ (Spain), the CASI (China),and the BR-IMC (China). One large study of the MOCA was excluded as diagnostic accuracy data for illiterate individuals related to cognitive impairment rather than dementia. Similarly, studies of insufficient quality on the QUADAS-2 were also excluded, a large proportion of those identified.

There was little heterogeneity between studies (Cochran's *Q*: 6.734; p = 0.346, I^2 −10.9%). Combined sensitivity estimate was 0.818 (0.769–0.859) and specificity was 0.801 (0.745–0.848). The combined diagnostic odds ratio was 18.753 and the HSROC resulted in an AUC of 0.869 (partial AUC 0.812). The least accurate tests were the Brazilian MMSE and B-IMC in China with similar performance for the MMSE in another Brazilian study and for the Chinese MMSE. The most accurate tests were the KICA-Cog and SPMSQ.

Validation studies of the MMSE

A total of eight primary studies (nine separate cohorts) validated variants of the MMSE in a low-education setting. These included MMSE-Brazil, Hindi MMSE, MMSE-Turkish, Chinese MMSE, and MMSE Spanish version (MEC). These are analyzed together because despite cultural and educational variations, all retain the structure of the original and cover similar cognitive domains. A total of 3,559 individuals were included of which

Table 5. QUADAS-2 assessment of study quality

STUDY	AUTHOR, DATE	TOOL	QUADAS-1-PATIENT SELECTION	QUADAS-2 INDEX TESTS	QUADAS-3 REFERENCE STANDARD	QUADAS-4 FLOW AND TIMING	INCLUDED IN META ANALYSIS?	REASON FOR EXCLUSION
1	Almeida, (1998), Brazil	MMSE	-	?	?	+	Y	
2	Aprahamian *et al.* (2011), Brazil	MMSE, VF, CDT	?	?	-	?	N	CC
3	Babacan-Yildis *et al.* (2013), Turkey	COST, MMSE, MOCA	+	?	-	?	N	CC
4	Baiyewu *et al.* (2005), Nigeria	Stick design	-	-	+	+	N	Part of DX
5	Bottino *et al.* (2009), Brazil	MMSE	+	?	-	-	N	CC
6	Bustamante *et al.* (2003), Brazil	MMSE	+	-	-	-	N	CC
7	Caramelli *et al.* (2007), Brazil	Categorical Verbal Fluency	+	-	-	?	N	CC
8	Carnero-Pardo *et al.* (1999), Spain	The Money Test	+* analyzed as case–control	+	-	+	N	CC
9	Carnero-Pardo and Montoro-Ríos (2004a), Spain	Fototest	+	-	-	?	N	CC
10	Carnero-Pardo *et al.* (2006), Spain	Eurotest	-	+	-	+	N	Post DX
11	Carnero-Pardo *et al.* (2011a), Spain	Fototest	-	-	-	?	Y	
12	Carnero-Pardo *et al.* (2011b), Spain	Eurotest, Fototest, M@T	-	-	-	?	Y	
13	Carnero-Pardo and Montoro-Ríos (2004b), Spain	Eurotest, MMSE, SPMSQ, 7MS	+	-	?	?	N	CC

Table 5. Continued

STUDY	AUTHOR, DATE	TOOL	QUADAS-1-PATIENT SELECTION	QUADAS-2 INDEX TESTS	QUADAS-3 REFERENCE STANDARD	QUADAS-4 FLOW AND TIMING	INCLUDED IN META ANALYSIS?	REASON FOR EXCLUSION
14	Carnero-Pardo *et al.* (2007), Spain	Fototest	-	+	-	?	N	Post DX
15	Carnero-Pardo *et al.* (2012), Spain	Fototest, Eurotest, VF	-	+	-	?	N	Post DX
16	Carnero-Pardo *et al.* (2013), Spain	MMSE	-	-	-	-	Y	
17	Chung (2009), China	FULD object-memory test	+	-	-	?	N	CC
18	De Paula *et al.* (2013), Brazil	Stick design	+	-	-	?	N	CC
19	De Yebenes *et al.* (2003), Spain	PCL	-* severe sensory	-	-	-	Y	
20	Del Ser *et al.* (2006), Spain	7MS	-	-	-	-	Y	
21	Ribeiro Filho and Lourenço (2009), Brazil	Mini-Cog	- (convenience)					
			*sev sensory/ hand	+	+	+	N	Part of DX
22	Jin *et al.* (1989), China	Blessed-Roth IMC	-	?	?	?	Y	
23	Jitapunkul *et al.* (1996), Thailand	Chula Mental Test	-	-	-	?	Y	

Table 5. Continued

STUDY	AUTHOR, DATE	TOOL	QUADAS-1-PATIENT SELECTION	QUADAS-2 INDEX TESTS	QUADAS-3 REFERENCE STANDARD	QUADAS-4 FLOW AND TIMING	INCLUDED IN META ANALYSIS?	REASON FOR EXCLUSION
24	Keskinoglu *et al.* (2009), Turkey	MMSE-Turkish-r	-	-	-	-	Y	
25	Kochhann *et al.* (2010), Brazil	MMSE-Brazil	+	?	-	?	N	CC
26	Lam *et al.* (1998), China	Clock drawing test	+	-	?	+	N	CC
27	Lin *et al.* (2002), China	CASI	? pop study and memory clinic	-	-	-	Y	
28	Liu *et al.* (1994), China	CASI 2	-	-	-	-	Y	
29	LoGiudice *et al.* (2006), Australia	KICA-COG	-	-	-	-	Y	
30	Lourenço and Veras (2006), Brazil	MMSE-Brazil	-* convenience	-	-	-	Y	
31	Lourenco *et al.* (2008), Brazil	Clock drawing test	- (convenience) * severe sensory/ hands	-	+	+	N	Part of DX
32	Lu *et al.* (2011), China	MOCA Beijing version	-* psych/neur	-	-	?	N	(missing essential data)

Table 5. Continued

STUDY	AUTHOR, DATE	TOOL	QUADAS-1-PATIENT SELECTION	QUADAS-2 INDEX TESTS	QUADAS-3 REFERENCE STANDARD	QUADAS-4 FLOW AND TIMING	INCLUDED IN META ANALYSIS?	REASON FOR EXCLUSION
33	Martinez de la Iglesia *et al.* (2001), Spain	SPMSQ	- (convenience)	-	-	-	Y	
34	Pandav *et al.* (2002), India	HMSE	-	-	-	+	Y	
35	Saez *et al.* (2008), Spain	Semantic verbal fluency/animal fluency	-	+	+	+	N	Not independent of reference test
36	Baos Sánchez (2007), Spain	Fototest	-* excluded severe sensory impairment	-	-	-	Y	
37	Scazufuca *et al.* (2009), Brazil	MMSE-Brazil	-	-	-* algorithm	-	Y	
38	Smith *et al.* (2009), Australia	KICA-Cog	-	-	-	-	Y	
39	Stanley *et al.* (2009), India	VSID-P	-* neur/sensory/ hands	-	-	-	Y	
40	Takada *et al.* (2006), Brazil	DR-BCRB. DR CERAD	+* excluded CDR3	?	?	?	N	CC
41	Toure *et al.* (2008), Senegal	Test of Senegal	+	?	?	?	N	CC
42	Tsai and Gao (1989), China	Hasegawa Dementia Scale	-	-	?	?	Y	
43	Tsolaki *et al.* (2000), Greece	HMSE	+	?	?	?	N	CC
44	Verghese *et al.* (2012), India	PIMS	-* nb extra rel. controls/ excluding severe sensory/neurol	?	-	-	Y	
45	Xu *et al.* (2003), China	MMSE-Chinese	+* exc dep/dem, dependence, severe sensory	-	-	-	Y	

Note: CC: case control design, +: substantial risk of bias present, −: no substantial risk of bias, ?: unclear from text, DX: diagnosis.

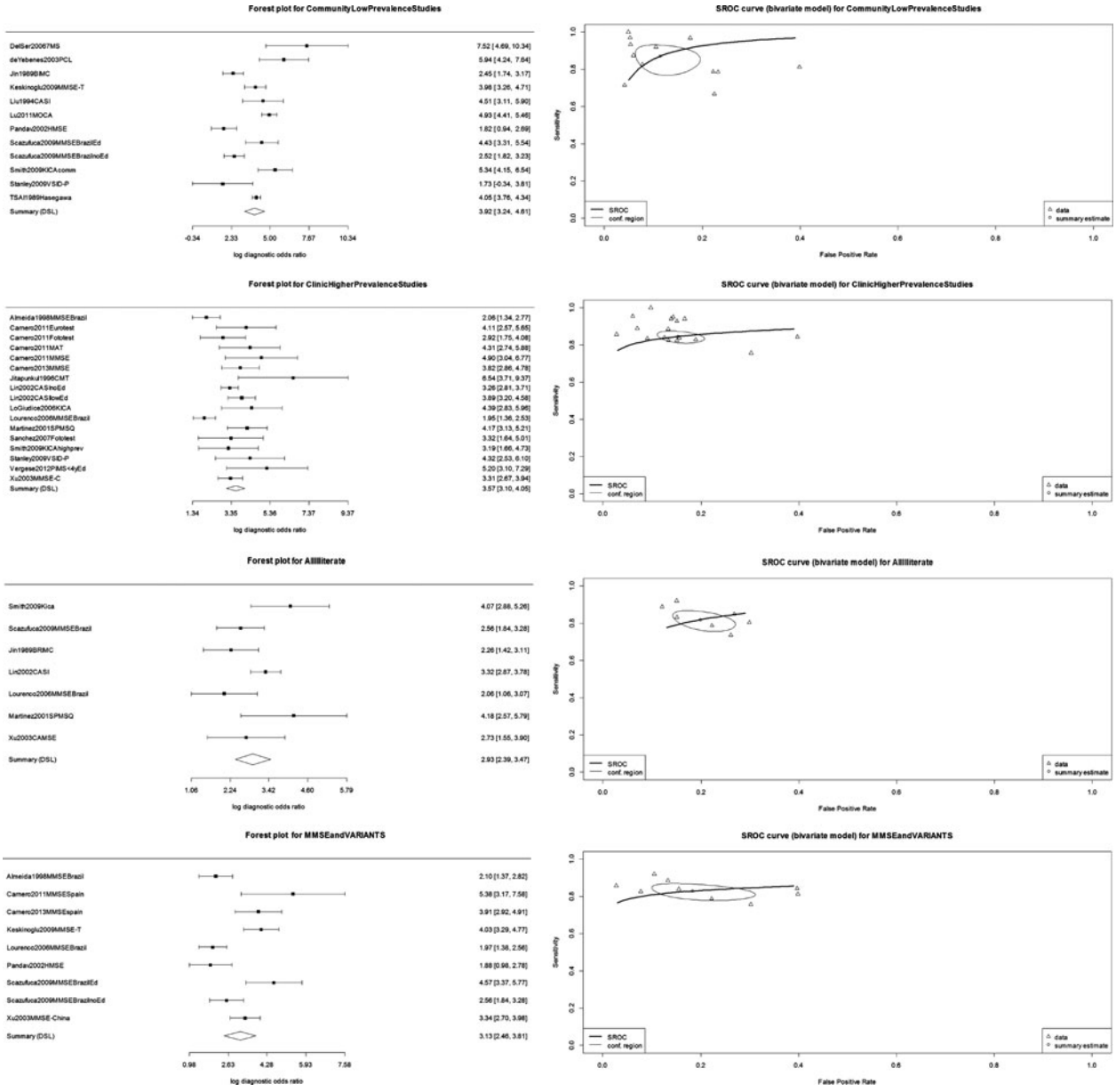

Figure 3. Results of meta-analysis. Forest plots of diagnostic odds ratio (DOR) and hierarchical summary ROC (HRSROC) curves.

397 had dementia (11.2%). Cut off points for dementia screening varied widely and ranged from 14 to 20 for those who were illiterate or without formal education and 17 to 23 in those with at least one year of education. Most studies utilized different cut off points for those with and without formal education.

There was no significant heterogeneity between studies (Cochran's Q: 9.894; p = 0.273, I^2 19.147%). Combined sensitivity estimate was 0.828 (0.789–0.862), and specificity was 0.817 (0.717–0.887). The combined DOR was 22.981 and AUC was 0.853 (partial AUC 0.819). The MMSE demonstrated the most accuracy when used in low-literacy cohorts in Spain and Brazil, but performed poorly in some of the lowest literacy settings in LMICs.

Discussion

The overall diagnostic accuracy of cognitive screening tests for dementia in low-literacy settings is similar to that reported in reviews of diagnostic accuracy in HICs. A meta-analysis of brief cognitive screening tools for identification of dementia in HICs reported a pooled sensitivity and specificity of 72% and 88.2%, respectively, in community settings (dementia prevalence 16%), 88.9% and 88.4%, respectively, in secondary/specialist care

(dementia prevalence 28%; Mitchell and Malladi, 2010). In comparison, we calculated a sensitivity of 86.9% and 84.5% and specificity of 88.6% and 84.7% in community and clinical studies, respectively. Although this degree of accuracy might be acceptable in a HIC setting, with higher levels of access to specialist clinicians, in LMIC settings higher sensitivity and specificity are necessary to improve dementia case-finding and screening, especially in primary care or community settings.

In lower prevalence or community studies, the most accurate tests were the 7MS, PCL, and KICA-Cog conducted in Spain and Australia, and in higher prevalence or clinical studies, the most accurate were the CMT and PMIS. In illiterate individuals, the best-performing tests were the KICA-Cog and SPMSQ. In all three settings, the worst-performing tests were adaptations of the MMSE, alongside the VSID-P in the community and the B-IMC in illiterate individuals. However, the VSID was designed to be utilized alongside an informant interview, and we have analyzed only the performance of the cognitive screening tool. No studies of hospital inpatients were identified that met our study criteria.

Overall, we found the diagnostic accuracy of cognitive screening tools to be best in community or population settings compared to clinic settings. This may be related to the spectrum of participants seen. Some community studies excluded individuals with significant sensory impairment, which may have artificially increased the diagnostic accuracy of the screening test. Clinic-based studies taking place in geriatric medicine clinics might also be expected to have a higher proportion of individuals with general frailty or medical conditions adversely affecting performance on a cognitive test. Performance of screening tools included within these studies is therefore representative of routine clinical practice conditions.

Diagnostic accuracy was reasonable (DOR 18, AUC 0.869) in studies only including illiterate individuals, although, in general, screening test performance was lowest in this group. A few good or fair quality studies were identified in this group, with a significant proportion utilizing a case–control design.

Heterogeneity between studies was generally low to moderate, and highest in community settings. This may be partially due to the fact that we selected studies relevant to a specific low-literacy population only, but is interesting in that these studies took place in many different geographical locations and where cultural background would be likely to differ.

Many briefer screening tools focused on recall only. Recall is affected early in AD dementia but less so in other dementia subtypes. There is evidence that vascular dementia is more common in LMIC settings, although overall knowledge of dementia subtypes in these regions is limited. Tools focusing on AD-type pathology only may therefore be of limited utility. Similarly, most good or fair quality studies did not report or assess for dementia subtypes, and many case–control studies focused only on individuals with AD.

Screening tool length was variable, with tests ranging from 1 to 20 minutes in length. As expected, longer tests generally assessed a wider range of cognitive domains. Evidence from HICs suggests that screening tools should be of 5 minutes duration or less in order to be practical for use in primary care (Brodaty *et al.*, 2006). Of the screening tools included in this study, only the COST, Eurotest, Fototest, and VSID included most cognitive domains within 4–7 minutes and might therefore have potential for use in primary care. Of these, only Eurotest and Fototest have been independently validated, but not in a substantial low-literacy cohort, independent validation studies of these tests in low-literacy LMIC settings have yet to take place. These tests were also not among the most accurate identified.

In resource-poor settings, cost is also a consideration. The MMSE is subject to license restrictions and its use now requires payment. Most but not all of the tests reviewed are in the public domain or free to use with permission, see Table 4.

A significant proportion of the identified studies utilized a case–control design, the majority of which took place in urban clinical settings, frequently teaching hospitals, and university clinics. These therefore had limited generalizability. Similarly, a large number of validation studies initially identified did not meet our study criteria as the overall level of education among participants was relatively high. The majority of these studies appeared to have been carried out in teaching hospital clinics and may not be representative of the older population in these settings.

The majority of screening tools identified in this study, whether developed for a low-literacy setting or validation of an established screening tool in a low-literacy setting, had been validated only once. Few had an identifiable independent validation with the exception of the MMSE variations, Eurotest, Fototest, KICA-Cog, and CASI. Only for the MMSE, were sufficient studies identified to separately analyze diagnostic performance.

Performance of the MMSE overall in this review resulted in a combined sensitivity estimate of 82.8% and specificity of 81.7%. In comparison, a recent meta-analysis including 149 studies of the MMSE reported similar findings with combined sensitivity

of 81% and specificity of 89% (Tsoi *et al.*, 2015). When compared to other screening tests included in this review, the MMSE performed poorly as a screening test for dementia despite inclusion of culturally relevant adaptations. Better performance was seen in HIC settings or settings with relatively higher formal education and worst in those with the lowest literacy, reflecting the well-evidenced educational bias of the instrument.

Variations of the MMSE are therefore least likely to be accurate and should be avoided for dementia screening in low-literacy settings. Despite this, the MMSE remains the most widely used dementia screening test worldwide (Shulman *et al.*, 2006), including in low-literacy LMIC settings.

The cut-off values utilized for the MMSE varied widely. Some studies utilized different cut-off values for participants with and without formal education, frequently based on normative data. Although a bivariate method of meta-analysis takes threshold effects into account (Reitsma *et al.*, 2005), the approach of varying screening cut-off values in different populations has been criticized for reducing validity and this is also likely to reduce generalizability to other populations. This approach is also likely to lead to considerable ceiling effects in those with better cognitive performance (Kraemer *et al.*, 1998).

Many screening tests included in this review were developed both for a low-literacy population and specific to the cultural and geographical setting in which the study was carried out. Examples include the KICA-Cog test developed for the Aboriginal minority group in Australia, VSID in India, and Chula Mental Test (CMT) in Thailand. Therefore, although the CMT and KICA-Cog were among the best-performing screening tests, performance cannot be generalized to, or recommended in other settings. Other tests are more easily transferable such as the picture recall tests of the PMIS and Fototest, but these currently lack independent validation in a low-literacy cohort in a LMIC.

Limitations

This review assessed cognitive screening in low-literacy populations regardless of geographical location. Cultural differences are likely to affect performance on cognitive testing, and this issue has not been the focus of this review.

It is possible that other articles meeting our search criteria exist, but were not identified using our search criteria if they included a low-literacy population and did not refer to this in the article abstract or search terms. Since we also reviewed reference lists of included studies, articles not identified are likely to be a few. We only reviewed articles in English, Spanish, French, Italian, or Portuguese, and therefore we may have missed studies published in other languages. Nevertheless, all articles identified through database search had an English abstract and were excluded through not meeting the study criteria. Although we attempted to contact study authors for additional data, for many older studies this was not possible and therefore studies had to be excluded from meta-analysis. This may have led to bias in the study.

Conclusion

This systematic review and meta-analysis of brief cognitive screening tools validated in illiterate and low-literacy settings demonstrated that cognitive screening tools have a diagnostic accuracy in low-literacy or illiterate populations similar to that reported in meta-analyses of screening tool performance in identification of dementia in higher literacy settings. This accuracy is likely to be inadequate to allow accurate case identification by non-specialists in LMIC settings. Published high quality studies are few, and few screening tools have been independently validated in a low-literacy setting. Differing cut-off values further reduce generalizability. At present, although existing screening tools demonstrate reasonably good accuracy in low-literacy settings, the available evidence is inadequate to allow recommendation of any one particular test. We recommend that further high-quality independent validations of tests designed for low-literate populations should take place in LMIC settings in order to establish diagnostic utility in these settings.

Conflict of interest

None.

Description of authors' roles

S. Paddick and W. Gray designed the study and completed data extraction and assessment of study quality. S. Paddick wrote the first draft and conducted statistical analysis supervised by W. Gray. J. Richardson and J. McGuire conducted and advised on the literature searches. Professor Walker and C. Dotchin designed the study and supervised S. Paddick. All co-authors reviewed the final version of the study prior to publication.

References

Almeida, O. P. (1998). Mini exame do estado mental e o diagnóstico de demência no Brasil. *Arq Neuropsiquiatria*, 56, 605–612.

Aprahamian, I., Martinelli, J. E., Cecato, J. and Yassuda, M. S. (2011). Screening for Alzheimer's disease among illiterate elderly: accuracy analysis for multiple instruments. *Journal of Alzheimer's Disease*, 26, 221–229.

Ardila, A. *et al.* (2010). Illiteracy: the neuropsychology of cognition without reading. *Archives of Clinical Neuropsychology*, 25, 689–712.

Babacan-Yildiz, G. *et al.* (2013). COST: cognitive state test, a brief screening battery for Alzheimer disease in illiterate and literate patients. *International Psychogeriatrics*, 25, 403–412.

Baiyewu, O. *et al.* (2005). The stick design test: a new measure of visuoconstructional ability. *Journal of the International Neuropsychological Society*, 11, 598–605.

Baos Sánchez, L., Ruiz Muñoz, M. A., Bernal López, M. D., Ballester Rodríguez, B. and Ángora Mazuecos, F. (2007). Estudio de la validez del Test de las Fotos en el cribado de Deterioro Cognitivo en Atención Primaria. *Revista Clínica de Medicina de Familia*, 2, 57–62.

Basic, D. *et al.* (2009). The validity of the rowland universal dementia assessment scale (RUDAS) in a multicultural cohort of community-dwelling older persons with early dementia. *Alzheimer Disease & Associated Disorders*, 23, 124–129.

Bottino, C. M. C. *et al.* (2009). Combined instruments for the screening of dementia in older people with low education. *Arquivos de Neuro-Psiquiatria*, 67, 185–190.

Brodaty, H., Low, L. F., Gibson, L. and Burns, K. (2006). What is the best dementia screening instrument for general practitioners to use? *American Journal of Geriatric Psychiatry*, 14, 391–400.

Bustamante, S. E. Z. *et al.* (2003). Instrumentos combinados na avaliação de demência em idosos: resultados preliminares. *Arquivos de Neuro-Psiquiatria*, 61, 601–606.

Caamano-Isorna, F., Corral, M., Montes-Martinez, A. and Takkouche, B. (2006). Education and dementia: a meta-analytic study. *Neuroepidemiology*, 26, 226–232.

Caramelli, P., Carthery-Goulart, M. T., Porto, C. S., Charchat-Fichman, H. and Nitrini, R. (2007). Category fluency as a screening test for Alzheimer disease in illiterate and literate patients. *Alzheimer Disease & Associated Disorders*, 21, 65–67. 10.1097/WAD.1090b1013e31802f31244f.

Carnero-Pardo, C., Lendinez-Gonzalez, A. and Navarro-Gonzalez, E. (1999). The coin test. *Revue Neurologique*, 29, 801–804.

Carnero-Pardo, C. and Montoro-Ríos, M. (2004a). Evaluación preliminar de un nuevo test de cribado de demencia (Eurotest). *Revue Neurologique*, 38, 201–209.

Carnero-Pardo, C. and Montoro-Ríos, M. (2004b). Test de las fotos. *Revue Neurologique*, 39, 801–806.

Carnero-Pardo, C., Orduna, I. C., Martínez, B. E., Viedma, S. C., García, P. T. and Rodríguez, J. O. (2013). Efectividad del mini-mental en la detección del deterioro cognitivo en atención primaria. *Atención Primaria*, 45, 426–433.

Carnero-Pardo, C., Sáez-Zea, C., De la Vega Cotarelo, R. and Gurpegui, M. (2012). Estudio FOTOTRANS: estudio multicéntrico sobre la validez del Fototest en condiciones de práctica clínica. *Neurologia*, 27, 68–75.

Carnero-Pardo, C. *et al.* (2006). Diagnostic accuracy of the Eurotest for dementia: a naturalistic, multicenter phase II study. *BMC Neurology*, 6, 1.

Carnero Pardo, C. *et al.* (2007). Diagnostic accuracy of the phototest for cognitive impairment and dementia]. *Neurologia*, 22, 860–869.

Carnero-Pardo, C. *et al.* (2011a). Diagnostic accuracy, effectiveness and cost for cognitive impairment and dementia screening of three short cognitive tests applicable to illiterates. *PLoS One*, 6, e27069.

Carnero-Pardo, C. *et al.* (2011b). Effectiveness and costs of phototest in dementia and cognitive impairment screening. *BMC Neurology*, 11, 92.

Castro-Caldas, A., Petersson, K. M., Reis, A., Stone-Elander, S. and Ingvar, M. (1998). The illiterate brain. Learning to read and write during childhood influences the functional organization of the adult brain. *Brain*, 121, 1053–1063.

Choi, S. H. *et al.* (2011). Validation of the literacy independent cognitive assessment. *International Psychogeriatrics*, 23, 593–601.

Chung, J. C. (2009). Clinical validity of Fuld Object Memory Evaluation to screen for dementia in a Chinese society. *International Journal of Geriatric Psychiatry*, 24, 156–162.

Crum, R. M., Anthony, J. C., Bassett, S. S. and Folstein, M. F. (1993). POpulation-based norms for the mini-mental state examination by age and educational level. *JAMA*, 269, 2386–2391.

de Paula, J. J., Costa, M. V., Bocardi, M. B., Cortezzi, M., De Moraes, E. N. and Malloy-Diniz, L. F. (2013). The stick design test on the assessment of older adults with low formal education: evidences of construct, criterion-related and ecological validity. *International Psychogeriatrics*, 25, 2057–2065.

De Yebenes, M. J., Otero, A., Zunzunegui, M. V., Rodriguez-Laso, A., Sanchez-Sanchez, F. and Del Ser, T. (2003). Validation of a short cognitive tool for the screening of dementia in elderly people with low educational level. *International Journal of Geriatric Psychiatry*, 18, 925–936.

Del Ser, T., Sanchez-Sanchez, F., Garcia de Yebenes, M. J., Otero, A. and Munoz, D. G. (2006). Validation of the seven-minute screen neurocognitive battery for the diagnosis of dementia in a spanish population-based sample. *Dementia and Geriatric Cognitive Disorders*, 22, 454–464.

Doebler, P. and Holling, H. (2012). Meta-analysis of diagnostic accuracy with mada. cran.mtu.edu; last accessed 8 February, 2017.

Dua, T. *et al.* (2011). Evidence-based guidelines for mental, neurological, and substance use disorders in low-and middle-income countries: summary of WHO recommendations. *PLoS Medicine*, 8, e1001122.

Guerchet, M. *et al.* (2009). Cognitive impairment and dementia in elderly people living in rural Benin, West Africa. *Dementia and Geriatric Cognitive Disorders*, 27, 34–41.

Jin, H. *et al.* (1989). Cross-cultural studies of dementia: use of a Chinese version of the blessed-Roth information-memory-concentration test in a Shanghai dementia survey. *Psychology and aging*, 4, 471.

Jitapunkul, S., Lailert, C., Worakul, P., Srikiatkhachorn, A. and Ebrahim, S. (1996). Chula mental test: a screening test for elderly people in less developed countries. *International Journal of Geriatric Psychiatry*, 11, 715–720.

Keskinoglu, P., Ucku, R., Yener, G., Yaka, E., Kurt, P. and Tunca, Z. (2009). Reliability and validity of revised Turkish version of mini mental state examination (rMMSE-T) in community-dwelling educated and uneducated elderly. *International Journal of Geriatric Psychiatry*, 24, 1242–1250.

Kochhann, R., Varela, J. S., de Macedo Lisboa, C. S. and Chaves, M. L. F. (2010). The Mini Mental State Examination. *Population*, 11, 15.

Kraemer, H. C., Moritz, D. J. and Yesavage, J. (1998). Adjusting mini-mental state examination scores for age and educational level to screen for dementia: correcting bias or reducing validity? *International Psychogeriatrics*, 10, 43–51.

Lam, L. C. W. *et al.* (1998). Clock-face drawing, reading and setting tests in the screening of dementia in Chinese elderly adults. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences*, 53, P353–P357.

Leeflang, M. M. G., Rutjes, A. W. S., Reitsma, J. B., Hooft, L. and Bossuyt, P. M. M. (2013). Variation of a test's sensitivity and specificity with disease prevalence. *Canadian Medical Association Journal*, 185, E537–E544.

Lin, K. N., Wang, P. N., Liu, C. Y., Chen, W. T., Lee, Y. C. and Liu, H. C. (2002). Cutoff scores of the cognitive abilities screening instrument, Chinese version in screening of dementia. *Dementia and Geriatric Cognitive Disorders*, 14, 176–182.

Liu, H.-C. *et al.* (1994). Assessing cognitive abilities and dementia in a predominantly illiterate population of older individuals in Kinmen. *Psychological Medicine*, 24, 763–770.

LoGiudice, D. *et al.* (2006). Kimberley indigenous cognitive assessment tool (KICA): development of a cognitive assessment tool for older indigenous Australians. *International Psychogeriatrics*, 18, 269–280.

Lourenço, R. A., Ribeiro-Filho, S. T., Moreira, I. d. F. H., Paradela, E. M. P. and Miranda, A. S. d. (2008). The clock drawing test: performance among elderly with low educational level. *Revista Brasileira de Psiquiatria*, 30, 309–315.

Lourenço, R. A. and Veras, R. P. (2006). Mini-exame do estado mental: características psicométricas em idosos ambulatoriais. *Revista de Saúde Pública*, 40, 712–719.

Lu, J. *et al.* (2011). Montreal cognitive assessment in detecting cognitive impairment in Chinese elderly individuals: a population-based study. *Journal of Geriatric Psychiatry and Neurology*, 24, 184–190.

Martínez de la Iglesia, J., DueñasHerrerob, R., Carmen Onís Vilchesa, M., Aguado Tabernéa, C., Albert Colomerc, C. and Luque Luquec, R. (2001). Adaptación y validación al castellano del cuestionario de Pfeiffer (SPMSQ) para detectar la existencia de deterioro cognitivo en personas mayores e 65 años. *Medicina Clínica*, 117, 129–134.

Meng, X. and D'Arcy, C. (2012). Education and dementia in the context of the cognitive reserve hypothesis: a systematic review with meta-analyses and qualitative analyses. *PLoS one*, 7, e38268.

Mitchell, A. J. and Malladi, S. (2010). Screening and case finding tools for the detection of dementia. Part I: evidence-based meta-analysis of multidomain tests. *American Journal of Geriatric Psychiatry*, 18, 759–782.

Moher, D., Liberati, A., Tetzlaff, J. and Altman, D. G. (2009). Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ* 339, b2535.

Napon, C., Traore, S., Niakara, A., Ouango, G., Ouango, A. and Kabore, J. (2009). Les démences en Afrique subsaharienne: aspects cliniques et étiologiques en milieu hospitalier à Ouagadougou (Burkina Faso). *African Journal of Neurological Sciences*, 28, 37–43.

Ostrosky-Solis, F., Ardila, A., Rosselli, M., Lopez-Arango, G. and Uriel-Mendoza, V. (1998). Neuropsychological test performance in illiterate subjects. *Archives of Clinical Neuropsychology*, 13, 645–660.

Paddick, S.-M. *et al.* (2014). The association between educational level and dementia in rural Tanzania. *Dementia & Neuropsychologia*, 8, 117–125.

Paddick, S. M. *et al.* (2015). Utility of the mini-mental state examination (MMSE) for identification of dementia in a low-literacy setting in rural Tanzania. *Age and Ageing*, 44, ii25–ii25.

Pandav, R., Fillenbaum, G., Ratcliff, G., Dodge, H. and Ganguli, M. (2002). Sensitivity and specificity of cognitive and functional screening instruments for dementia: the Indo-US dementia epidemiology study. *Journal of the American Geriatrics Society*, 50, 554–561.

Prince, M., Acosta, D., Chiu, H., Scazufca, M. and Varghese, M. (2003). Dementia diagnosis in developing countries: a cross-cultural validation study. *The Lancet*, 361, 909–917.

Prince, M., Bryce, R. and Ferri, C. (2013a). *World Alzheimer Report 201: The Benefits of Early Diagnosis and Intervention*. Alzheimer's Disease International.

Prince, M., Guerchet, M. and Prina, M. (2013b). *Policy Brief for Heads of Governments*. N/A Ed. London: Alzheimer's Disease International.

Prince, M. *et al.* (2011). A brief dementia screener suitable for use by non-specialists in resource poor settings-the cross-cultural derivation and validation of the brief community screening instrument for dementia. *International Journal of Geriatric Psychiatry*, 26, 899–907.

Ramlall, S., Chipps, J., Pillay, B. J. and Bhigjee, A. I. (2013). Mild cognitive impairment and dementia in a heterogeneous elderly population: prevalence and risk profile. *African Journal of Psychiatry*, 16, 119–135.

Reitsma, J. B., Glas, A. S., Rutjes, A. W., Scholten, R. J., Bossuyt, P. M. and Zwinderman, A. H. (2005). Bivariate analysis of sensitivity and specificity produces informative summary measures in diagnostic reviews. *Journal of Clinical Epidemiology*, 58, 982–990.

Ribeiro Filho, S. T. and Lourenço, R. A. (2009). The performance of the mini-cog in a sample of low educational level elderly. *Dementia & Neuropsychologia*, 3, 81–87.

Rosselli, M., Ardila, A. and Rosas, P. (1990). Neuropsychological assessment in illiterates: II. Language and praxic abilities. *Brain and Cognition*, 12, 281–296.

Saez-Zea, C., Carnero-Pardo, C. and Gurpegui, M. (2008). Names of persons: a verbal fluency test without socioeducational influences. *Neurologia*, 23, 356–360.

Saxena, S., Thornicroft, G., Knapp, M. and Whiteford, H. (2007). Resources for mental health: scarcity, inequity, and inefficiency. *The Lancet*, 370, 878–889.

Scazufca, M., Almeida, O., Vallada, H., Tasse, W. and Menezes, P. (2009). Limitations of the Mini-Mental State Examination for screening dementia in a community with low socioeconomic status. *European Archives of Psychiatry and Clinical Neuroscience*, 259, 8–15.

Shulman, K. I. *et al.* (2006). IPA survey of brief cognitive screening instruments. *International Psychogeriatrics*, 18, 281–294.

Smith, K. *et al.* (2009). Assessing cognitive impairment in Indigenous Australians: re-evaluation of the Kimberley indigenous cognitive assessment in Western Australia and the northern territory. *Australian Psychologist*, 44, 54–61.

Sosa, A. L. *et al.* (2009). Population normative data for the 10/66 dementia research group cognitive test battery from Latin America, India and China: a cross-sectional survey. *BMC Neurology*, 9, 1.

Stanley, R. *et al.* (2009). The Vellore screening instruments and strategies for the diagnosis of dementia in the community. *International Psychogeriatrics*, 21, 539–547.

Takada, L. T. *et al.* (2006). Comparison between two tests of delayed recall for the diagnosis of dementia. *Arquivos de Neuro-Psiquiatria*, 64, 35–40.

Touré, K. *et al.* (2008). The test of Senegal: a valid and reliable screening tool to assess for dementia in a Senegalese elderly population. *African Journal of Neurological Sciences*, 27, 4.

Tsai, N. and Gao, Z. X. (1989). Validity of Hasegawa's Dementia Scale for screening dementia among aged Chinese. *International Psychogeriatrics*, 1, 145–152.

Tsoi, K. F., Chan, J. C., Hirai, H. W., Wong, S. S. and Kwok, T. Y. (2015). Cognitive tests to detect dementia: a systematic review and meta-analysis. *JAMA Internal Medicine*, 175, 1450–1458.

Tsolaki, M., Iakovidou, V., Navrozidou, H., Aminta, M., Pantazi, T. and Kazis, A. (2000). Hindi Mental State Examination (HMSE) as a screening test for illiterate demented patients. *International Journal of Geriatric Psychiatry*, 15, 662–664.

UNESCO (2015). *Education Data 2015*. Quebec, Canada: UNESCO.

Uwakwe, R. (2000). Psychiatric morbidity in elderly patients admitted to non-psychiatric wards in a general/teaching hospital in Nigeria. *International Journal of Geriatric Psychiatry*, 15, 346–354.

Verghese, J. *et al.* (2012). Picture-based memory impairment screen for dementia. *Journal of the American Geriatrics Society*, 60, 2116–2120.

Whiting, P. F. *et al.* (2011). QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. *Annals of Internal Medicine*, 155, 529–536.

Xu, G., Meyer, J. S., Huang, Y., Du, F., Chowdhury, M. and Quach, M. (2003). Adapting Mini-Mental State Examination for dementia screening among illiterate or minimally educated elderly Chinese. *International Journal of Geriatric Psychiatry*, 18, 609–616.

Yusuf, A. J., Baiyewu, O., Sheikh, T. L. and Shehu, A. U. (2011). Prevalence of dementia and dementia subtypes among community-dwelling elderly people in northern Nigeria. *International Psychogeriatrics*, 23, 379–386.

8. Commentary on Background Paper 1

8.1. Overview and summary

Although the need for culturally appropriate cognitive screening tools designed for low-literacy settings is well-recognised, few screening tools have been adequately validated. We conducted a systematic review and meta-analysis of cognitive screening tools for dementia suitable for non-specialists to use in routine clinical care and of 15-20 minutes duration or less (Background Paper 1). We were specifically interested in performance in illiterate and low-literate populations which we defined as having 4 years of education or fewer, as previous evidence suggested this to be the level at which educational differences had the greatest effect on cognitive performance. The review followed PRISMA guidelines and studies were quality assessed using the QUADAS-2 tool. We focussed specifically on cognitive rather than informant or function-based assessments for this review.

A total of 45 eligible studies were quality assessed. A significant proportion of studies utilised a case control design, resulting in spectrum bias. Many of these studies were small and took place in university teaching hospitals in urban centres and therefore have limited generalisability. We elected to include these studies in the review as this reflected the preliminary nature of the existing evidence.

A number of cognitive assessment tools developed for use in low-educated and illiterate populations did not meet our inclusion criteria. These included the Community Screening Instrument for Dementia (CSI-D) used in the 10/66 protocol. The CSI-D requires an informant, has a duration of over 30 minutes and utilises a computer algorithm for risk stratification therefore cannot be used by non-specialists. Similarly the Literacy Independent Cognitive Assessment (LICA) and shorter version the S-LICA were felt to be too complex and/or lengthy for routine use. The Rowland Universal Dementia Scale (RUDAS) was designed for cross-cultural assessment, but we were unable to identify a low-literacy validation study.

Studies included in the review are described in Figure 4. Surprisingly, many studies of illiterate and low-literate populations identified were conducted in rural or minority groups in HIC settings where older people had previously had difficulties accessing formal education and these may not therefore be generalizable to LMIC settings due to cultural differences. A number of screening tests were developed for specific cultural and geographical settings. Examples included the KICA-Cog developed for the Aboriginal minority group in Australia, VSID in India and Chula Mental Test (CMT) in Thailand. These tests may also not be generalizable to other settings.

Few tools were adequately validated with only four identified tests having at least one independent validation. Despite well evidenced shortcomings, the most validated test was the MMSE, including cultural variations and translations.

Good or fair quality studies were included in a bivariate random effects diagnostic meta-analysis and a hierarchical summary receiver operating characteristic (HSROC) curve constructed. The AUROC was 0.937 for community/low prevalence studies, 0.881 for clinic based/higher prevalence studies and 0.869 for illiterate populations. For the MMSE and adaptations AUROC was 0.853.

The overall diagnostic accuracy of cognitive screening tests for dementia in low-literacy settings was similar to that reported in reviews of diagnostic accuracy in HICs. Overall, we found the diagnostic accuracy of cognitive screening tools to be best in community or population settings compared to clinic settings, but there was evidence that this might be due to spectrum bias. No studies of hospital inpatients were identified that met our study criteria. Studies including only illiterate individuals were of lower quality, and generally had the lowest diagnostic accuracy, but diagnostic accuracy was reasonable (DOR 18, AUC 0.869). The worst-performing tests included adaptations of the MMSE.

The MMSE remains the most widely used dementia screening test worldwide[41], and has been used for dementia screening in many hospital-based dementia prevalence studies in SSA. The cut-off values utilised for the MMSE varied widely. Some studies utilised different cut-off values for participants with and without formal education, frequently based on normative data. Varying cut-off values in different populations has been criticised for reducing validity and this is also likely to reduce generalisability to other populations[95]. This approach is also likely to lead to considerable ceiling effects in those with better cognitive performance.

As might be expected, diagnostic accuracy of the MMSE was lowest in those with the lowest literacy. Performance was similar to that reported in a meta-analysis of 149 studies of the MMSE (combined sensitivity of 0.81 and specificity of 0.89)[103] but an additional consideration in LMIC settings is shortage of specialist clinicians and therefore screening tools with a higher level of accuracy overall are needed.

Few screening tools evaluated in low-literacy settings and included in the systematic review covered the majority of core domains. Those that did cover the majority of domains were not the most accurate, and many briefer tools focussed on recall only. These might therefore be less useful in non-AD dementia

Overall we concluded that although a large number of screening tools have been evaluated, studies of those tools developed for low-literacy settings are generally of poor quality and can generally be

considered preliminary. Few have independent validation in a low-literacy setting, and others used a case-control design or internal validation only. Few studies were generalizable to other settings and many tools that we might have expected to be validated in a low-literacy group in fact had not.

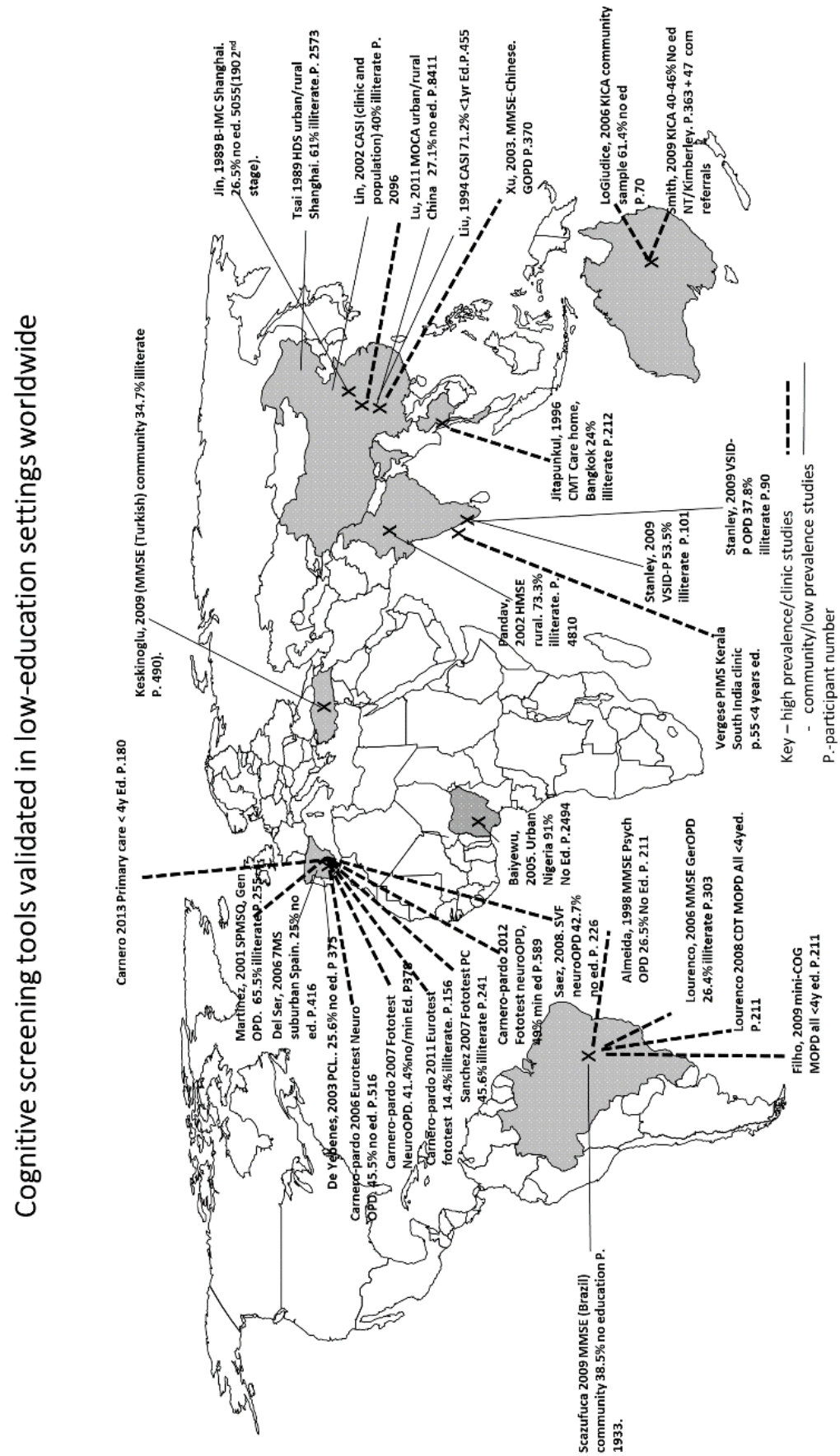

Figure 4. Geographical location of cognitive screening tools validated in LMIC setting

8.2. Functional assessment for dementia diagnosis in LMIC settings

In order to make a diagnosis of dementia it is necessary to demonstrate functional impairment occurring as a consequence of functional impairment. Functional assessment is generally agreed to include two main elements; activities of daily living (ADLs) and instrumental (or extended) activities of daily living (IADLs). ADLs are basic self-care activities such as bathing, feeding and dressing independently and assessment of these is often useful in identifying care needs and dependence. IADLs are more complex activities generally agreed to be affected earlier in cognitive impairment as they require more intact neurocognitive abilities to complete.

Assessment of function can be difficult in LMICs where cultural norms and social roles differ. Existing IADL scales developed in HICs are often inappropriate, particularly where multigenerational living is common, and older people may not be directly responsible for household tasks measured on existing scales. Performance on other tasks may be restricted by lack of availability or access to amenities such as transport, or adherence to traditional gender roles. These issues in functional assessment are well recognised and have been previously thought to be responsible for falsely low dementia prevalence rates reported in LMICs, particularly those in SSA. A number of IADL scales designed for use in LMIC settings have been devised. These are often highly specific to the location in which they were developed, reflecting cultural differences. No scales suitable for use by non-specialist clinicians in SSA have been published. The only scale developed in SSA is a clinician-rated scale based on expert observation and designed to be used in a home-visit context (the Clinician Home-based Interview to Assess Function, CHIF). This approach is reasonable in areas where specialist clinicians are available, but this is unlikely to be the case across much of sub-Saharan Africa, particularly in rural areas.

Table 3 Functional assessment scales designed for use in low and middle income countries (LMIC)

Author, Year	Location, setting	Development method	Validation sample	Validation method	Key findings
Fillenbaum, 1999 (EASI)[104]	Kerala, India low-literacy community	Community discussion with elders and health workers related to usual social roles and activities of the elderly	Pilot testing 100 people, initial validation 387 people aged 55 years and over; mean age 69.5 years	Hindi MMSE score < 22	Cronbach's alpha =0.82. Lower scores in females, older people, illiterate people and those with lower cognitive function
Hendrie, 2006 (CHIF)[105]	Nigeria	Expert opinion of clinicians. Also took into account 'items usually included in assessments of ADL	Community sample of 295	DSM dementia Blessed dementia scale, MMSE.	AUROC 0.925 for dementia Cronbach's alpha 0.83 Correlated with Blessed DS 0.56 and MMSE 0.44
Jitapunkl, 1994 (Chula ADL)[106]	Thailand, community sample	Factor analysis of items from the Barthel index and Office of Populations Censuses and Surveys (OPCS) disability score	703 people aged 60 years and over; mean age 68 years	Agreement with OPCS and Barthel Index.	Aim of scale was to measure disability appropriately in local population
Mathuranath, 2005 (E-ADL)[107]	India memory clinic	Development and validation of scale based on Lawton IADL. Input from senior citizens group and clinicians on suitable IADL	Validation on 240 memory clinic attendees and 135 controls from background population	DSM dementia	AUROC 0.97. Sensitivity 0.91, specificity 0.99
Senanarong, 2003 (THAI-ADL)[108]	Thailand, community and specialist clinic	Specialist panel discussion	181 memory clinic attendees; mean age 69 years	Agreement with Thai MMSE FAQ, Barthel, CDR	Correlation with Thai MMSE (r = 0.69), CDR (r = 0.81), Barthel Index (r = 0.80) and FAQ (r = 0.88)

Umayal et al 2010[109]	Sri Lanka, nursing home population	Validation of a modified Blessed dementia scale and Bristol ADL. Scores were modified by expert/clinician opinion	Nursing home residents aged 65 years and over; mean age 73 years	Dementia ICD-10 criteria by consultant psychiatrist	Modified Bristol scale: AUROC 0.933. Sensitivity 100%, specificity 74.2%. Modified Blessed scale: AUROC 0.892. Sensitivity 100%, specificity 71%.

Delirium in sub-Saharan Africa

Background Paper 2

Delirium in sub-Saharan Africa; a systematic review with inferences.

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Review article

The prevalence and clinical manifestations of delirium in sub-Saharan Africa: A systematic review with inferences

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ABSTRACT

Background: In high-income countries with ageing populations, delirium is most prevalent in older adults and in palliative and intensive care settings. The prevalence and aetiology of delirium are likely to differ in low income countries, including sub-Saharan Africa (SSA), due to different population demographics, disease burden and exposure to pathogens. We reviewed published literature relating to the prevalence, clinical features and underlying causes of delirium in SSA and compare this with that published in high-income countries in order to identify knowledge and clinical service gaps, and priorities for further research.
Methods: We performed a narrative review by comprehensively searching the following databases: Medline, PsychInfo, Embase and PubMed. Studies published between January 1 1975 and December 31 2013 in all languages, including the terms 'delirium', 'acute brain syndrome', 'organic brain syndrome', or 'acute confusion' originating from SSA were included. In addition, reference lists of included articles and online databases of African medical literature were hand-searched. We also included case series and case reports due to paucity of published studies.
Results: We identified a total of 46 relevant studies. Delirium was the main focus of only one cross-sectional study, whereas most included delirium in studies on neuropsychiatric conditions. Only two studies reported prevalence in older adults. Most studies reported very low (<2%) delirium prevalence, whereas delirium in psychiatric inpatient and outpatient settings was higher than expected (18.2%–29.9%). Descriptive studies of 'bouffee delirante' from psychiatry settings were often describing delirium. Infection and HIV seropositivity were common associations of delirium throughout these studies. There were no studies of intensive, critical or surgical care settings or of management strategies.
Conclusions: We currently know very little about the prevalence, presentation and aetiology of delirium in developing countries. This knowledge gap should be tackled with some urgency, in order to address questions of screening, diagnosis, prevention and management in this setting.

Contents

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1. Introduction

Delirium is a neuropsychiatric syndrome which is rapidly becoming a public health priority in high-income countries with ageing populations [1–3]. An episode of delirium is associated with adverse short and long term outcomes, including elevated risk of mortality [4–6], longer term cognitive impairment [7,8], institutionalisation [6] and increased healthcare costs [9]. These outcomes occur in all age groups [10], although older people are more affected [6,11]. Timely identification is crucial, with mortality increasing by 11% for every 48 h of ongoing delirium in an older person [12]. Up to two thirds of delirium cases remain undiagnosed [5], largely due to symptom variation causing difficulties for non-specialists [13].

In hospital inpatient studies, delirium is reported in up to 31% of all medical admissions [5], in two thirds of hospitalised older adults [2] and in more than half of emergency orthopaedic surgical patients [14], and those with an acute stroke [15]. In intensive and palliative care settings, the prevalence is substantially higher (80% [4] and 88% [16], respectively). In contrast, the community prevalence of delirium has been estimated at 0.4% in adults aged 55 and younger [17] and 1–2% in older people [18], whereas the prevalence in children is unclear with data limited to case reports and small case series [19].

Although described for over 2000 years, delirium still remains poorly understood [13,20–22]. The delirium 'brain failure' is thought to result from disrupted neurotransmission in a vulnerable individual following an insult to brain function [3,20,23]. Amongst numerous insults causing delirium, inflammation and infection are most consistent aetiological factors in all settings [3,21]. The most vulnerable are those with decreased cognitive reserve, including older people, and especially those with dementia [2,11].

Dramatic changes in life expectancy have occurred over the past century largely due to reductions in mortality from an infectious disease [24]. In high-income countries, those aged 65 and over now make up 13–17.5% of the population in the USA and Europe, respectively. Mortality from an infectious disease has been superseded by an increasing burden of a chronic disease [25] so that in high-income countries, cardiovascular disease, cancer and stroke are now the major causes of mortality and morbidity [26]. As the population ages, the number of people with dementia has also increased, with 5.4–6.4% of those aged 65 and over in Europe and the USA having dementia [27]. These demographic changes all contribute to a high number of older people vulnerable to delirium.

In tandem with this, incidence of infectious disease is again increasing by 4.8% per annum [24]. Much of this increase is due to food borne and antibiotic-resistant organisms [24]. Older people are more susceptible to these infections and have an estimated three fold increased risk of community acquired pneumonia and twenty fold higher risk of urinary tract infection [28]. Susceptibility to tuberculosis (TB) and hospital and institutionally acquired infections is similarly increased [28]. These higher rates of infection are likely to lead to corresponding increases in delirium.

In sub-Saharan Africa (SSA), population demographics differ markedly from those in high-income countries. In 1900, life expectancy in the USA was 47 years, and pneumonia, TB and diarrhoea were the three most common causes of mortality [24]. This situation is not dissimilar to that in SSA today, where the current life expectancy projections are 63 for women and 58 for men [26]. However, by 2030 more than three quarters of the elderly population worldwide will live in developing countries [29]. Already there are an estimated 2.1 million people with dementia in SSA and this will increase by 70–90% by 2030 [30]. Prevalence of non-communicable diseases is also increasing with a third of deaths now attributed to them [26].

Nevertheless, diarrhoea, lower respiratory tract infection, TB, malaria and HIV/AIDS remain the most common causes of death in SSA [26]. The vast majority of those with HIV/AIDS live in SSA and although life expectancy has increased in all countries of SSA, HIV/AIDS has resulted in a reversal of demographic transition in some of the worst affected countries [31]. Tropical diseases, especially that group of 17 infectious diseases known as the 'neglected tropical diseases' remain prevalent [32]. In addition, increasing urbanisation is leading to increases in infectious diseases due to poor sanitation, increased transmission of pathogens and inability of health systems to keep pace with development [33]. The older population in developing countries is at increased risk of infection, but is a group about which surprisingly little is known [34]. It is likely that delirium is also prevalent in SSA, but presentation and clinical features may differ due to differing disease burden(s).

We therefore reviewed the published literature relating to the prevalence, clinical features and underlying causes of delirium in SSA. We compare the literature findings with that published in high-income countries and highlight potential knowledge gaps and priorities for further research and clinical service developments.

2. Methods

This narrative review was based on a comprehensive search that included Medline, PsychInfo, Embase and PubMed databases for studies published between January 1 1975 and December 31 2013. To ensure a global perspective, articles in English, French, Spanish, German and Russian were reviewed for potential inclusion. Articles not in English were translated by S-MP (Spanish and French) and EML (German and Russian). The key words used in the current search were: 'delirium', 'acute brain syndrome', 'organic brain syndrome', or 'acute confusion' (Box 1). All countries and regions of SSA were included as keyword and title search terms using the United Nations list of countries.

In addition, reference lists of selected articles were hand searched for potentially relevant articles. Content lists of African medical journals including the East African Medical Journal, Tropical Doctor and the African Journal of Psychiatry were also hand-searched. Due to the small number of articles retrieved, case reports and case series were included where delirium was a major focus of the report. All age groups and healthcare settings were included.

All abstracts were critically reviewed and the full text of relevant articles was obtained. Where there was doubt regarding relevance, particularly in cases of differing nomenclature, the full text was also sought. All abstracts and articles were initially reviewed by S-MP and in cases of doubt these were reviewed by EBM-L and a consensus decision reached. Criteria for inclusion were that the article related directly to prevalence, phenomenology, aetiology, outcome and/or management of delirium. Articles were excluded if they related primarily to description of a specific disease where delirium was simply listed as a symptom, without further elaboration. This category consisted predominantly of case reports of uncommon infectious diseases where delirium might occur. There was no requirement for delirium to be diagnosed using standard criteria, provided there was

Box 1
Search strategy terms.

Search strategy
1. exp Delirium/or delirium.mp.
2. Confusion/or acute confusion.mp.
3. organic brain syndrome.mp.
4. acute brain syndrome.mp.
5. acute brain syndrome.mp. [mp = ti, ab, ot, nm, hw, kf, px, rx, ui, an, sh, tn, dm, mf, dv, kw, tc, id, tm]
6. 1 or 2 or 3 or 4 or 5
7. delirium.m_titl.
8. 1 or 6 or 7
9-94 all countries in SSA searched separately by .ti and .mp
95 9-94 or
96. Africa, Western/or South Africa/or Africa, Eastern/or africa.mp. or "Africa South of the Sahara"/or Africa, Central/or Africa/or Africa, Southern/
97. 95 or 96
98. 8 and 97

sufficient evidence from the text of the article that delirium was being described. The selection process is detailed below.

3. Results

A total of 46 relevant studies were identified. The risk factors and data are summarised and listed in accompanying Tables 1–10 (see Fig. 1).

3.1. Geographical location of studies

All the studies came from primarily 3 areas in SSA, two historically domineered by French and German influence and South Africa, being the most developed country in the region. It is, therefore not surprising that the quality of the studies similarly varies between these 3 regions (Fig. 2).

Table 1
Most frequent causes of delirium in SSA.[a]

Disorder	Findings	Delirium prevalence
HIV		
	HIV positive admissions with psychiatric disorder [50]	30.1%
	HIV positive mineworkers [87]	13%
	40% HIV positive amongst psychiatric admissions with delirium (overall prevalence of delirium 3.7%)	3.7%
Typhoid fever		
	Typhoid fever 136 cases [42]	14%
	Typhoid fever 50 cases [88]	≤8.4%
	'Typhoid psychosis': 17 cases from a total of 414 children assessed by neuropsychiatric service over a four year period in Nigeria [55]	4.1%
Malaria		
	Cerebral malaria in 129 consecutive cases in Senegal [65]	10.7%
Other causes		
	Liver cirrhosis [43]	12.9%
	Infectious endocarditis (IE) [52] (toxic encephalopathy)	12.5%
	Chronic obstructive pulmonary disease (COPD) [89]	3.3%
	Polypharmacy in the elderly, based on a small audit [90] (7 of 9 with delirium from 100 admissions)	7%
	Ingestion of an anticholinergic drug [91] (4 cases)	NA

[a] Data from inpatient studies included.

3.2. Diagnostic criteria utilised in studies

Most studies did not use formalised criteria and assessment tools for delirium. The DSM-IV criteria for delirium were used in only four studies [35–38] although one other retrospectively applied DSM-III criteria for 'organic brain syndrome' to case notes [39]. ICD-9 and -10 criteria were somewhat more widely used [40–45], but only one study applied a formal screening tool such as the Confusion Assessment Method (CAM) [46]. Of those studies using formal criteria, only four are based on clinical interviews [37,41,43,45], with most retrospectively applying criteria to case notes.

Of the remainder, delirium diagnoses are based on clinical expertise and include a variety of different terms for delirium. Some record delirium as a clinical diagnosis [47–49]. Other terms include 'syndrome confusionnel' [50], 'organic brain syndrome' [39], 'acute confusional state' [51], 'toxic encephalopathy' [52], 'organic psychotic disorder' [53], 'acute delirious episode' [54] and 'typhoid psychosis' [55]. Despite the wide variety of terms, where symptomatology is recorded it is consistent with delirium. This is similar to the situation in high-income countries, where a wide range of terms for delirium (e.g. acute mental status change, confusional status, encephalopathy, postoperative psychosis, acute organic syndrome, and septic encephalopathy) continues to be in use resulting in difficulties [22]. More recent studies from high income countries indicate increasing agreement on use of the term delirium and the use of standardised criteria and assessment methods.

In SSA, an important issue remains around the use of the terms 'acute delusion psychosis' and 'acute delirious episode' in some studies [54,56]. These are referred to from the point of view of psychiatry and relate to episodes of short lived psychosis from the French school of psychiatry termed as the 'bouffee delirante' [57]. The bouffee delirante is most closely related to the ICD-10 classification of F23 acute and transient psychotic episode [57]. The description is typically of an acute onset of psychosis in a young person associated with polymorphic presentation, which has a good outcome. Both studies on bouffee delirante type of psychotic episode describe a selection of patients presenting with predominantly visual hallucinations alongside disturbance of consciousness, poor sleep, periods of lucidity throughout the day and mood disturbance [56,58]. A number presented following surgical procedures or following diagnoses of HIV infection. Since the majority of patients in these series were not tested for the presence of infectious disease, we would argue that it is probable that at least a proportion of these patients were in fact experiencing delirium from which they recovered.

3.3. Healthcare settings

In contrast to high-income countries, the majority of the reviewed studies originate from psychiatric services: a total of twelve inpatient and two outpatient psychiatric studies. In addition, most case reports and series relate to individuals wrongly referred or treated for a psychiatric disorder when they in fact had delirium, usually due to an infective cause [38,59–61].

Perhaps surprisingly, a high proportion of studies involve children [37,44,55,62–64]. Of those studies undertaken in medical inpatient settings, only one specifically studied patients over the age of 60 [41]. This reflects the demographic composition of SSA where currently only 4.6% of the population are aged 65 and over [29]. Two studies originate in infectious diseases departments [50,65] and one in a palliative care setting [49], but there are no studies of surgical or critical care patients. Miscellaneous studies include two on forensic patients; one describing those referred for psychiatric opinion by police in South Africa [47] and another a retrospective description of court report assessments [66], highlighting an unusual finding of three of twelve accused of murder or attempted murder having delirium [66].

Table 2
Aetiology of delirium in HIC and SSA.

Categories	High income countries (HIC)	SSA	p-Value
Community prevalence of delirium			
Community prevalence of delirium	0.5%–2 [17]	NA	
Hospital prevalence of delirium			
Older people (>65 years)	14–56% [92,93]	9.4% [40]	<0.0001
Adults (17–64 years)	9.9% [94]	29.9% [44]	<0.0001
Children and adolescence	8.18% [95]	15% [43]–26% [36]	<0.0001
Most common causes of delirium			
Critical illness/intensive care	86% [4]	NA	
Palliative care	88% [16]	15% [48]	<0.0001
Orthopaedic surgery	>50% [14]	NA	
Acute stroke	>48% [15,96]	NA	
Dementia	41% [97]	NA	
Urinary tract infection	35% [98]	NA	
HIV	46% [99]	3.7–30.1% [49]	0.0289
Infection in older people	43% [100]	NA	
Pulmonary diseases	21.2% [101]	3.35% [65]	<0.0001
Malaria	83.3% [102] 5/6 cases	10.7 [64]	<0.0001
Typhoid fever	NA	14% [42]–15.5% [41]	
Liver diseases	2.1%	12.9% [42]	0.0073
Heart diseases	8.4% [103]	12.5% [51]	0.0035
Polypharmacy	50%	7% [66]	<0.0001

Abbreviations: NA, not available; SSA, sub-Saharan Africa.

3.4. Cross sectional studies

Cross sectional studies report prevalence of delirium amongst referrals to psychiatric services, including inpatient wards [35], outpatient psychiatric clinics [46] and consultation liaison psychiatry [37,44,45]. Of the few medical inpatient studies, prevalence appears remarkably low (<2%) [51], and this is evident even in better designed studies, including the only one conducted on older inpatients (>60 year) [41]. In the latter study, delirium prevalence, based on the ICD-10 criteria, was 9.4%. An overwhelming lack of expertise in diagnosing delirium was evident in this study with only one of out of the 10 people with delirium being appropriately diagnosed by a physician [41]. The only

Table 3
Studies in inpatient and outpatients.

Author and year	Location	Type of study	Study population	Definition or description of delirium	Aetiology	Outcome/results
Ukwaja, 2010 [38]	Nigeria, rural health centre.	Case report	12 year old girl presenting with delirium and depression symptoms	DSM-IV	Typhoid fever	Initially treated for depression, full recovery when typhoid diagnosed.
Perret, 2000 [104]	Senegal, urban	Case series	Four destitute French expatriates, two with delirium.	Clinical symptom	Meningoencephalitis, cerebral malaria, delirium tremens	Two of the four presented with delirium. Malnutrition and destitution appeared contributory.
Thiam, 2000 [60]	Dakar, Senegal	Case report	20 year old man with mental confusion, no previous psychiatric history.	Mental confusion	Pulmonary TB	Cause of confusion was tuberculosis (TB)
Djibo, 2000 [91]	Niger	Case report	Four adolescent cases in Niger.	Clinical symptom	Intoxication with DATURA plant	Adolescents presenting with agitated delirium alongside symptoms similar to atropine intoxication
Cisse, 2008 [105]	Guinea	Case series	13 consecutive Wernicke's encephalopathy in refugee camp.	Confusion	Wernicke's encephalopathy	11 of 13 had 'confusion' as part of the syndrome.
Thiam,2002 [59]	Dakar, Senegal	Case series	Four patients presenting to psychiatric department 1998 to 1999. Age 13 to 22	Delirium syndrome	Cerebral malaria	All four were found to have falciparum malaria with high parasite load and improved on treatment. No psychiatric relapse at one year.
Avode, 1994 [106].	Benin	Case report	Adult patient with confusional syndrome, epilepsy and myositis.	Confusional syndrome	Diffuse cysticercosis.	Treated successfully with praziquantel and corticosteroids
Kyebambe, 2010 [107]	Uganda	Case report	40 year old woman with weakness, delirium, aphasia and epilepsy	Clinical symptom	Neurosyphilis	Improved on treatment
Acosta-Rabassa, 1985 [108]	Guinea-Bissau	Case series	6 patients with acute 'psychotic delirious reaction' in the context of physical illness	Clinical 'psychotic delirious reaction'	Not stated	Conclude that despite physical illness the cause was in fact psychological
De Wet, 1980 [61]	South Africa	Case series	2 cases of rabies presenting with delirium.	Clinical symptom	Rabies	Both were initial thought to have a psychiatric problem.

Table 4
Studies in specific patient groups.

Author and year	Location	Type of study	Study population	Definition or description of delirium	Aetiology	Outcome/results
Soumare, 2008 [65]	Senegal, urban Dakar hospital, infectious disease department	Retrospective case note review	129 cases of cerebral malaria admitted to 2001 to 2005	Mental confusion	Cerebral malaria	Case fatality rate of 20.2%. 10.7% presented with mental confusion, 90.4% with coma
Aghanwa, 2002 [43]	Nigeria, gastroenterology clinic	Cross sectional, prospective	31 consecutive patients with liver cirrhosis admitted between July 1996 and August 1998.	ICD-10 using clinician interview and GHQ	Liver cirrhosis	55% of liver cirrhosis patients had diagnosable psychiatric conditions, 12.9% delirium.
Aghanwa and Erhabor 2001 [89]	Nigeria.	Cross sectional	Thirty COPD (chronic obstructive pulmonary disease) patients compared to 30 uncomplicated hypertensive patients and 30 healthy controls.	Clinical diagnoses using the present state examination and PHQ-9	Not stated, COPD comorbid	3.3% of the COPD patients had delirium.
Bademosi, 1976 [52]	Nigeria, general hospital	Retrospective case note review	95 individuals (adults and children)—majority 20–29 with diagnosed infective endocarditis	Clinical diagnosis 'toxic encephalopathy'	Infectious endocarditis	12.5% presented with 'toxic encephalopathy'
Sall, 2009 [87]	South Africa	Retrospective case note review	38 consecutive presenting HIV positive mineworkers	Clinical diagnosis	Linked to HIV status	Five of 38 presented with delirium.
Aghanwa, 2001 [42]	Nigeria, general hospital	Retrospective case note review	All cases of typhoid fever admitted over a six year period 136 cases total.	ICD-9 using case note data	Typhoid fever	19.1% had psychiatric morbidity of these, 73% delirium. 15.5% had symptoms of delirium insufficient for ICD-9 diagnosis
Hafiez, 1987 [88]	Sudan, psychiatric department of general hospital.	Prospective	All cases of typhoid fever presenting with psychiatric symptoms over a two year period. 50 cases total.	Clinical symptom description including clouding of consciousness. Delirium not defined.	Typhoid fever	8.4% of cases had 'psychiatric symptoms' of which 74% had clouding of consciousness, 56% visual hallucinations, and 46% delusions.
Karambe, M, 2010 [50]	Mali, Bamako hospital infectious diseases department	Cross sectional, prospective.	166 HIV positive admissions found to have psychiatric disorder (from total of 286 admissions). Age 18 to 65 mean 36. A 15 month study period.	'Syndrome confusionnel' diagnosed by a psychiatrist. Criteria not stated. HIV status, CD4	All HIV positive. 48.8% on antiretroviral medication, 94% of those with delirium had CD4 less than 60.	Delirium in 30.1% of those 166 with psychiatric disorder. 56% mortality of cohort.
Ovunga, 1985 [109]	Kenya, psychiatric hospital	Case series	11 patients with sickle cell trait admitted to psychiatric ward	Clinical diagnosis delirium	Sickle cell crisis	6 of the 11 presented with delirium which resolved within 1–2 weeks.
Fainsinger, 2000 [49]	South Africa, palliative care	Multi-centre cross sectional study	94 consecutive patients requiring palliative care in multi-centre study including South Africa	Delirium as symptom	Not stated	Delirium present in 15% of South Africa cohort compared with 60% Madrid, 29% in Israel, differences are significant at p. 0.001

Table 5
Cross sectional studies in children and adolescents.

Author and year	Location	Type of study	Study population	Definition or description of delirium	Aetiology	Outcome/results
Hatherill, Flischer and Nassen, 2010 [37]	South Africa, national specialist children's hospital.	Retrospective, cross sectional, and descriptive case series	23 consecutive child and adolescent referrals to liaison psychiatry service with delirium. Age 2 to 16.	DSM-IV criteria and delirium subtype i.e. hyper, hypo active and mixed.	Variety of causes, including severe burn injury, sepsis, post-transplant, organ and multiorgan failure.	Mortality 26%. Delirium represented 18% of all liaison psychiatry referrals. Predominance of hyperactive cases.
Oyewumi, 1989 [62]	Nigeria, child and adolescent mental health service	Cross sectional descriptive	80 adolescents aged 12–20 admitted to inpatient facilities	Organic brain syndrome	Infection and drug abuse more common causes	23% had organic brain syndrome as main diagnosis
Lustig, 1999 [63]	Nigeria, outpatient child and adolescent psychiatry clinic	Retrospective case note review	53 adolescents admitted over 24 weeks who had definite diagnoses recorded in the case notes	'Organic brain syndrome'	Causes not given	Organic brain syndrome listed as diagnosis in 7.4% of those assessed
Tunde-Ayinmode 2010 [44]	Nigeria, psychiatric clinic of teaching hospital.	Retrospective case note review	94 children aged 7–19. Mean age 16.3. Outpatients and inpatients referred to the psychiatric clinic over a 4 year period.	ICD 10 criteria, applied retrospectively.	Infections and cerebral malaria most common cause of delirium. Numerical prevalence not stated.	Delirium in 15% of referrals.
Seck, 1998 [64]	Senegal, child and adolescent mental health service	Retrospective case note review	275 admissions and 750 consultations over first year of operation of service			
Stanley, 2008 [55]	Nigeria, liaison psychiatry service	Retrospective case note review	All children under 19 years seen for neuropsychiatric review in outpatient clinic and emergency department	'Typhoid psychosis' clinically	S. typhi	17 cases of typhoid psychosis from 414 neuropsychiatric consults for children. Outcome not recorded. Symptom pattern consistent with delirium.

Table 6
Studies in liaison psychiatry.

Author and year	Location	Type of study	Study population	Definition or description of delirium	Aetiology	Outcome/results
Ajiboye, 2004 [67]	Nigeria, general hospital—liaison psychiatry service	Cross sectional, prospective	47 consecutive referrals to liaison psychiatry service over a 6 month period. Used present state examination and BPRS.	'Acute organic brain syndrome' as clinical diagnosis	Not stated	32% of 47 referrals had acute organic brain syndrome.
Aghanwa, 1996 [68]	Nigeria, teaching hospital, liaison psychiatry referrals	Retrospective case note review	Inpatients referred to liaison psychiatry over a 5 year period. Age range unclear—under 15 to over 56.	Diagnosis recorded by attending psychiatrist	Not stated	25.3% of 87 cases were recorded as acute brain syndrome. Low overall referral rate of 0.48%.

Table 7
Inpatient and outpatient psychiatric clinic studies.

Author and year	Location	Type of study	Study population	Definition or description of delirium	Aetiology	Outcome/results
Ola, 2010 [46]	Nigeria, urban teaching hospital.	Prospective	264 consecutive referrals to outpatient teaching hospital psychiatric clinic	Confusion assessment method (CAM)	52.1% had infections of which 33.3% had GI infection and 10.4% malaria. 16.7% non-infectious physical illness. 31.3% undiagnosed illness.	18.2% of new outpatient referrals presented delirium. 21.4% referrals medical OPD, 31.6% ER and 17.7% private hospital referrals had delirium.
Maling, 2011 [35]	Uganda, national psychiatric referral hospital, general hospital	Cross sectional	272 first time psychiatric admissions—age 18 and over.	DSM IV psychiatric diagnosis HIV status, CD4 count	HIV prevalence 18.4% in study population. Delirium more likely to have HIV, but CD4 counts over 500 c/o other mental disorders.	3.7% of all psychiatric admissions had delirium of which 40% were HIV positive.
Charbonnier, 2008 [40]	Mayotte, Comoros	Retrospective case note review	1212 psychiatric reports analysed against ICD criteria for psychiatric disorder	ICD-10		
Van Rensberg, 2007 [36]	South Africa, psychiatric inpatient hospital	Retrospective audit	438 admissions aged 10–79	DSM-IV	None stated	4 cases of delirium identified from 438. 35 of psychosis secondary to a medical condition. Age of those with delirium not stated.
Adeyemi, 1996 [45]	Nigeria, teaching hospital, psychiatric referrals		77 consecutive inpatient referrals to the psychiatric service of a teaching hospital over a one year period compared to a control sample of 75 unreferred patients	ICD-10 following clinical interview	The most common causes were infection predominantly *Salmonella* typhi. 41.3%	68% had mental disorders, psychoses 50.7%, delirium 29.9%.
Abiodun, 2000 [69]	Nigeria, psychiatric hospital	Cross sectional	Study of 191 inpatients, focus was the presence of physical disorder	ICD-10 delirium and evidence of physical illness from case notes and laboratory tests	Of 191 patients 27.2% had significant physical illness, 57.4 of these were infections	7.8% met ICD-10 criteria for delirium. In 70% of those referred, physical illness was not recognised by referring team.
Abiodun, 1988 [39]	Nigeria, psychiatric hospital.	Retrospective case note review of mortality	138 deaths of psychiatric inpatients over a 10 year period 1976 to 1985	DSM-III for acute brain syndrome		34.8% of deaths had acute brain syndrome of which 20.8% were referred by medical doctors failing to recognise delirium.
Gureje, 1986 [110]	Nigeria, outpatient neuropsychiatric unit.	Prospective validation of screening tool	350 consecutive referrals to neuropsychiatry service over a three month period	Seven item screening checklist for organic brain syndrome, validated by clinician and medical history and examination.	12/20 a direct medical cause of presentation identified 4/20 medical cause aggravating presentations.	5.7% referrals met criteria for organic brain syndrome
Nubukpo, 2005 [54]	Togo, psychiatric hospital	Cross sectional	Descriptive study of symptomatology of those presenting with 'acute delirious episode' ADE	'Acute delirious episode'		A significant number appear to be delirium. 79% visual hallucinations 3 new diagnoses HIV remainder not tested.
Berk, 1992 [48]	South Africa, inpatient psychiatric service	Retrospective case–control	Comparison of 42 patients examined with CT scan from 381 total admissions vs 42 randomly selected control inpatients	Clinical diagnosis delirium	Not recorded	19% of those receiving CT vs 2.3% of those not receiving CT had delirium
Andriambano, 1976 [56]	Madagascar	Retrospective descriptive study	Descriptive study of 92 cases of acute delirious episode	Clinical diagnosis	Some associated with infection or post surgical state. Figures not stated	A significant number appear to be delirium and associated with infectious or surgical cause.
Acuda, 1985 [53]	Kenya, psychiatric hospital	Retrospective case note review		Organic psychotic disorder	Causes not stated	Organic psychotic disorder in 28%

Table 8
Neurology studies.

Author and year	Location	Type of study	Study population	Definition or description of delirium	Aetiology	Outcome/results
Winkler, 2011 [51]	Northern Tanzania, rural hospital	Prospective study cross sectional	All patients presenting with a neurological or psychiatric disorder. Age 1 to 97 mean 38.	Clinical assessment by neurologist. Acute confusion diagnosed clinically. GCS for conscious level.	HIV testing not possible. Of acute confusional state (ACS) 25% undiagnosed, 13.8% non-infectious encephalopathy, 6.9% cerebral malaria.	Of 8676 admissions 18.3 per 1000 acute confusional state (ACS) and 51.5 per 1000 impairment of consciousness (IOC). In both groups, non-infectious causes predominated.
Melka, 1997 [70]	North west Ethiopia, teaching hospital.	Prospective study	202 patients with altered states of consciousness admitted to medical wards between January 1994 and December 1995.	Altered state of consciousness was defined as confusion, stupor and coma. Aetiology defined by history, clinical examination, and laboratory tests.	Infection 55%, metabolic disorders 22.3%, structural lesions 14.9% and poisoning 3.5%, cause unknown in 4.5%. Of infectious causes cerebral malaria most common then meningitis and encephalitis.	Mortality rate in hospital 60.4%. Overall prevalence amongst admissions not stated.

study of palliative care patients reported a prevalence of delirium of only 15%, in contrast to other arms of the same study from high-income countries that reported higher delirium rates of 30–60% [49].

Psychiatry inpatient and outpatient studies are more numerous. In adults, delirium prevalence appears strikingly high but variable, ranging from <1% [36] up to 29.9% [45]. However, when clinical interviews and listings of some form of formalised diagnostic criteria or screening method is used, the, prevalence is somewhat higher, e.g. ranging between 18.2% and 29.9% [45,46], with the exception of one study [35]. In all the analysed studies, differing assessment methods were used, making comparisons difficult. Furthermore, some studies were performed retrospectively (e.g. case note reviews) and not surprisingly report lower prevalence. Nevertheless, these rates are much higher than expected for the adult population and suggest a high rate of inappropriate referrals to psychiatry.

Prevalence in children and adolescents in psychiatric outpatient and inpatient facilities is similarly high (7.4% to 23%) [44,62,63]. Delirium is reported in 15%–18% of children [37,44] and 25–32% of adults [67,68] referred to liaison psychiatry, with a low overall referral rate being noted [68].

3.5. Aetiology

Whilst a number of studies were carried out in selected patient groups, the majority of these did not attempt to causally link the presence of delirium to the presenting physical illness. For the most part, possible aetiologies were simply listed, and no attempt was made to control for other potential causes such as ingestion of psychoactive substances or alcohol. In the majority of studies, patients were not tested for HIV (Table 1).

Of those cross sectional studies which address aetiology, one outpatient psychiatry study reported that 52.1% of those with delirium had infections; the majority had gastrointestinal infections with a smaller proportion (6.9%) having cerebral malaria [46]. Over a third of patients had an undiagnosed physical illness that might have contributed to the delirium. A large prospective neurological study from Tanzania, that did not include HIV testing, found non-infectious causes to be predominant in those with 'acute confusion', whereas only 13.8% had cerebral malaria [51]. Interestingly, a small prospective series of child and adolescent referrals to liaison psychiatry in a tertiary centre in South Africa reported a very different aetiological contribution to delirium. In this study, a variety of causes including severe burns, sepsis and multi-organ failure were associated with delirium [37], and not only infectious diseases as in previous studies.

3.6. Mortality and outcome

The majority of studies do not report information on mortality rates post delirium. A retrospective case note review of deaths in a Nigerian psychiatric hospital over a ten year period found that 34.8% met DSM-III delirium criteria for acute brain syndrome before death. In this study, over 20% of cases were not recognised as having delirium by referring general physicians [39]. Although this report is now 25 years old and we would expect practices to have changed considerably, a more recent study argues that medical practice has not changed overtly, with one third of psychiatric admissions having physical illness of which 7.8% had delirium. Over two thirds of physical illness, most of which were infections were not notified by the admitting physicians [69].

Of those prevalence studies reporting in-hospital mortality, rates are variable but remain high. A mortality rate of 26% was recorded in a small case series of children referred to liaison psychiatry [37]. A larger case series of cerebral malaria noted a case fatality rate of 20.2% of whom 10.7% had presented with confusion [65]. Mortality was 60.4% in 202 patients with 'altered states of consciousness' in Ethiopia, but the proportion of these meeting criteria for delirium was not clear [70]. Finally, in a HIV positive cohort with psychiatric symptoms, 30.1% of the cohort of 166 met criteria for delirium [50]. Mortality for the entire cohort was 56%, but the mortality of those with delirium was not recorded. Since these studies only record in-hospital mortality, overall mortality may be even higher. Infectious diseases are still the major causes of mortality

Table 9
Studies of older adults (60 and over).

Author and year	Location	Type of study	Study population	Definition or description of delirium	Aetiology	Outcome/results
Uwakwe, 2000 [41]	Nigeria, teaching hospital.	Prospective observational study	All patients aged over 60 years admitted to non-psychiatric wards. 119 total.	ICD-10.	Not stated	Prevalence of delirium was 9.4%. Attending physicians identified only one of ten delirium cases.
Verrier-Jones, 1978 [90]	South Africa, psychogeriatric unit	Cross sectional, prospective	First 100 consecutive admissions to a specialised p unit. Mean age 70.3 years. All but 3 over 60	Clinical diagnosis 'confusional state'	Polypharmacy was the cause in 7/9	9 from 100 had delirium—those with dementia not included.

Table 10
Miscellaneous studies.

Author and year	Location	Type of study	Study population	Definition or description of delirium	Aetiology	Outcome/results
Jonsson, 2013 [47]	South Africa, police referrals to hospital	Retrospective case note review	718 individuals referred for psychiatric assessment by police under the mental health act over a 6 month period	Clinical diagnosis	Not states	Delirium listed as admission diagnosis in 2.1%. More likely to be transferred to medical hospital.
Mbassa, 2009 [66]	Cameroon, court reports	Retrospective review of forensic court reports.	12 offenders assessed for the purpose of court reports following murder or attempted murder. 8 men and 4 women, age 17 to 43 mean 18.	ICD-10 criteria	Not given	Of 12 offenders, 3 or 25% were diagnosed with chronic delirium, 41.7% or 5 cases with schizophrenia and 1 patient 8.3% with personality disorder.

in SSA, and 70% of deaths from HIV/AIDS occur in Africa. The evidence presented here suggests that a substantial proportion of these may present with delirium.

4. Discussion

Our systematic review highlights the currently limited knowledge of prevalence, aetiology, clinical presentation and outcome of delirium in SSA. The analysis included an extensive literature search and many articles not referenced in standard medical indexes. Despite this, delirium was not the focus in many of these publications. The majority of cross sectional studies were of all psychiatric, neuropsychiatric and/or neurological presentations in which delirium was listed as a diagnosis. Furthermore, terminology differed markedly and a number of delirium synonyms were used making comparisons difficult. Only a few studies used standard criteria for delirium and only one reported delirium subtypes. In addition, most studies were small. A substantial proportion of them were retrospective case note reviews or clinical audits, which provide less robust evidence. A further limitation is that descriptions of symptoms and presentations are generally limited to case reports and small case series.

The limited data on aetiology suggests that infectious aetiology is common, in particular HIV/AIDS, malaria and typhoid fever (Table 2). The prevalence in children is relatively high and rates of referral to psychiatric services appear similar to those in adults. Nevertheless, in high-income countries, published evidence on delirium on children is limited and largely based on case series and case reports. A greater knowledge base of delirium in childhood may in fact exist in SSA [37].

Where we have the most information is on prevalence. This suggests that delirium is lower than expected in hospital inpatients, but considerably higher in psychiatric populations with high rates of inappropriate psychiatric referral. This is supported by those studies on acute non-

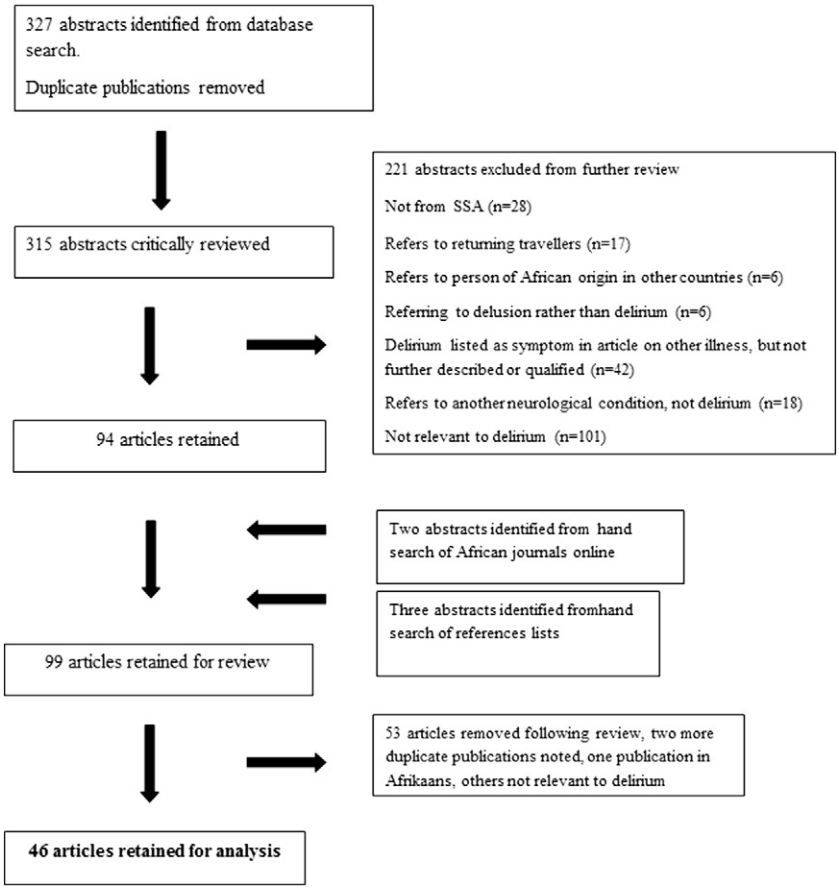

Fig. 1. Selection strategy for articles for the review.

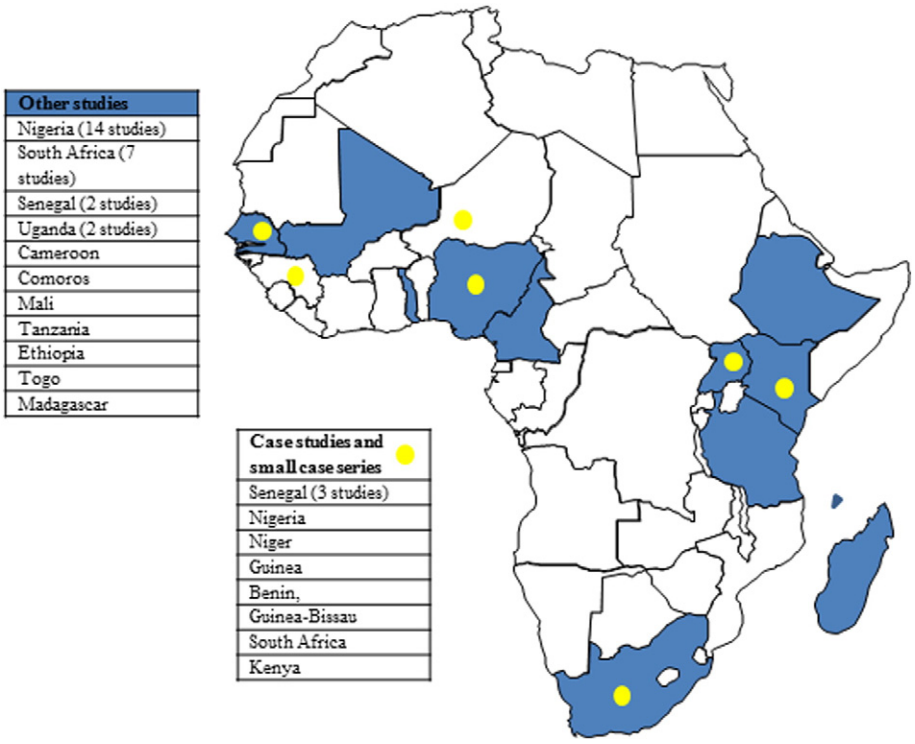

Fig. 2. Map of Africa to show location of studies in delirium. Shaded (blue) countries show where at least one prevalence study or audit was conducted. Dots (yellow) show countries where there was at least one case report or small case series.

affective psychosis written from a psychiatry perspective but which nevertheless appear to be describing delirium in at least some of the cases.

It is recognised that there are currently severe scarcity of neurologists, psychiatrists and geriatricians across SSA [71,72]. For psychiatrists, there are currently two hundred times fewer per head of population in SSA compared to those working in high-income countries [73]. The majority of studies in this review where delirium was diagnosed using formal criteria took place in teaching hospitals in Nigeria where psychiatrically trained doctors were available. It is likely that the distinction between psychosis and delirium will be difficult in most settings across SSA if trained medical personnel are not available. In high-income countries, reports suggest that more than two thirds of delirium cases are missed by physicians [74], and our review suggests that a high number of cases are similarly missed in SSA. The high prevalence of delirium seen inappropriately in psychiatric settings, alongside the high mortality from our limited data, suggests that education and training of non-specialist staff on recognition of delirium are priorities which could significantly reduce mortality. This task shifting approach to scaling up services through non specialist staff is recommended by the World Health Organisation [75].

It is also unclear whether the low prevalence observed in medical patients reflects a real difference, failure of diagnosis or failure to present to medical services. A number of reviewed case studies noted that patients had sought traditional medical care prior to attending conventional medical services [63]. Those with psychiatric disorders are particularly likely to attend traditional healers in SSA [76,77] and therefore we do not know what proportion of individuals presented too late or not at all. This raises the issue whether delirium may not be more prevalent in the community, if not recognised, or not registered by medical professionals.

In the current review, no studies of patients with dementia and delirium were identified, despite those with dementia being at high risk of delirium in high income countries [74]. Dementia was previously considered uncommon in SSA, but recent studies report a similar rate (6.4–8.1%) to those in the US and Europe [78,79]. With demographic transition the number of people with dementia is predicted to rise rapidly alongside the growing elderly population. Studies of delirium in this group are therefore needed. Furthermore, of the 20 million HIV positive individuals estimated to live in SSA, around 40% have neurocognitive impairment [80], resulting in a younger cohort of individuals who may be vulnerable to delirium. Furthermore, HIV positive men tend to be treated more readily than women [81,82] and they can expect to live longer, thus being at risk to develop HIV-related encephalopathy with ageing. This is the realm with few reports, and the information from these cohorts would be of an enormous boost for planning future health resources.

In general, little is known about cognitive impairment post delirium. However, deterioration in cognitive performance in adults [83] and school performance and behaviour in children [84,85] following malaria is well documented. Since delirium appears to be more common in childhood, young adulthood and in adults in SSA compared to high-income countries (Table 2) this is a priority for further research that will also help understand the mechanisms of cognitive dysfunction post-delirium. In fact, the mechanisms of delirium manifest in various disorders need to be explored at large even in HIC [86].

5. Conclusions

We currently know little about the prevalence, presentation and aetiology of delirium associated with various conditions in sub-Saharan Africa. This paucity in knowledge needs to be addressed with some urgency, to provide guidelines regarding screening, diagnosis, prevention and management in this setting. This is also likely to benefit clinicians in high-income countries where a significant population of HIV positive individuals exists. Psychiatrists and physicians currently working in high-income countries are less likely to be familiar with neuropsychiatric presentations of HIV, leading to the possibility of misdiagnosis or failure to consider HIV as a possibility. Transfer of knowledge and experience from colleagues working in SSA is therefore likely to be of much benefit. Furthermore, due to globalisation, increasing travel and ethnic diversity, rates of presentation with more unusual psychiatric presentations as a result of infectious disease are likely to

rise. These patients may be misdiagnosed with psychosis and deprived of timely treatment and management. Tackling delirium in different cultures as well as in less common infectious diseases is likely to directly benefit our practice.

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Contributors

Stella-Maria Paddick: literature search, drafting, interpretation of the reports and revising the manuscript at various stages of preparation.

Raj N Kalaria: editing, revising the manuscript at various stages and interpretation.

Elizabeta Mukaetova-Ladinska: literature search, editing and revising the manuscript, and interpretation.

Conflicts of interest

None declared that relate to this article.

Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.jns.2014.10.034.

References

[1] O'Mahony R, Murthy L, Akunne A, Young J. Synopsis of the National Institute for Health and Clinical Excellence Guideline for prevention of delirium. Ann Intern Med 2011;154:746–51.
[2] Inouye SK. Delirium in older persons. N Engl J Med 2006;354:1157–65.
[3] Maclullich AMJ, Anand A, Davis DHJ, Jackson T, Barugh AJ, Hall RJ, et al. New horizons in the pathogenesis, assessment and management of delirium. Age Ageing 2013;42:667–74.
[4] Ely EW, Shintani A, Truman B, Speroff T, Gordon SM, Harrell Jr FE, et al. Delirium as a predictor of mortality in mechanically ventilated patients in the intensive care unit. JAMA 2004;291:1753–62.
[5] Siddiqi N, House AO, Holmes JD. Occurrence and outcome of delirium in medical in-patients: a systematic literature review. Age Ageing 2006;35:350–64.
[6] Witlox J, Eurelings LM, de Jonghe JM, Kalisvaart KJ, Eikelenboom P, van Gool WA. Delirium in elderly patients and the risk of postdischarge mortality, institutionalization, and dementia: a meta-analysis. JAMA 2010;304:443–51.
[7] Adamis D, Treloar A, Martin FC, Macdonald AJ. Recovery and outcome of delirium in elderly medical inpatients. Arch Gerontol Geriatr 2006;43:289–98.
[8] Davis DHJ, Muniz Terrera G, Keage H, Rahkonen T, Oinas M, Matthews FE, et al. Delirium is a strong risk factor for dementia in the oldest-old: a population-based cohort study. Brain 2012;135:2809–16.
[9] Leslie DL, Marcantonio ER, Zhang Y, Leo-Summers L, Inouye SK. One-year health care costs associated with delirium in the elderly population. Arch Intern Med 2008;168:27–32.
[10] Pandharipande PP, Girard TD, Jackson JC, Morandi A, Thompson JL, Pun BT, et al. Long-term cognitive impairment after critical illness. N Engl J Med 2013;369:1306–16.
[11] Levkoff SE, Evans DA, Liptzin B, Cleary PD, Lipsitz LA, Wetle TT, et al. Delirium. The occurrence and persistence of symptoms among elderly hospitalized patients. Arch Intern Med 1992;152:334–40.
[12] Gonzalez M, Martinez G, Calderon J, Villarroel L, Yuri F, Rojas C, et al. Impact of delirium on short-term mortality in elderly inpatients: a prospective cohort study. Psychosomatics 2009;50:234–8.
[13] MEAGHER DJ, MORAN M, RAJU B, GIBBONS D, DONNELLY S, SAUNDERS J, et al. Phenomenology of delirium: assessment of 100 adult cases using standardised measures. Br J Psychiatry 2007;190:135–41.
[14] Bruce AJ, Ritchie CW, Blizard R, Lai R, Raven P. The incidence of delirium associated with orthopedic surgery: a meta-analytic review. Int Psychogeriatr 2007;19:197–214.
[15] McManus J, Pathansali R, Stewart R, Macdonald A, Jackson S. Delirium post-stroke. Age Ageing 2007;36:613–8.
[16] Hosie A, Davidson PM, Agar M, Sanderson CR, Phillips J. Delirium prevalence, incidence, and implications for screening in specialist palliative care inpatient settings: a systematic review. Palliat Med 2013;27:486–98.
[17] Folstein MF, Bassett SS, Romanoski AJ, Nestadt G. The epidemiology of delirium in the community: the Eastern Baltimore Mental Health Survey. Int Psychogeriatr 1991;3:169–76.
[18] Andrew M, Freter S, Rockwood K. Prevalence and outcomes of delirium in community and non-acute care settings in people without dementia: a report from the Canadian Study of Health and Aging. BMC Med 2006;4:15.
[19] Hatherill S, Flisher AJ. Delirium in children and adolescents: a systematic review of the literature. J Psychosom Res 2010;68:337–44.
[20] Lipowski ZJ. Delirium (acute confusional states). JAMA 1987;258:1789–92.
[21] Cerejeira J, Firmino H, Vaz-Serra A, Mukaetova-Ladinska EB. The neuroinflammatory hypothesis of delirium. Acta Neuropathol 2010;119:737–54.
[22] Morandi A, Pandharipande P, Trabucchi M, Rozzini R, Mistraletti G, Trompeo AC, et al. Understanding international differences in terminology for delirium and other types of acute brain dysfunction in critically ill patients. Intensive Care Med 2008;34:1907–15.
[23] Cerejeira J, Lagarto L, Mukaetova-Ladinska EB. Behavioral and psychological symptoms of dementia. Front Neurol 2012;3:73.
[24] Cohen ML. Changing patterns of infectious disease. Nature 2000;406:762–7.
[25] De Flora S, Quaglia A, Bennicelli C, Vercelli M. The epidemiological revolution of the 20th century. FASEB J 2005;19:892–7.
[26] Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012;380:2095–128.
[27] Ferri C, Prince M, Brayne C, Brodaty H, Fratiglioni L, Ganguli M, et al. Global prevalence of dementia: a Delphi consensus study. Lancet 2005;366:2112–7.
[28] Gavazzi G, Krause K-H. Ageing and infection. Lancet Infect Dis 2002;2:659–66.
[29] United Nations Population Division DoEaSA, Report World Population Ageing. World population ageing reports. New York, USA: United Nations Population Division; 2013. 2013.
[30] George-Carey R, Adeloye D, Chan KY, Paul A, Kolcic I, Campbell H, et al. An estimate of the prevalence of dementia in Africa: a systematic analysis. J Glob Health 2012;2:20401.
[31] Kalemli-Ozcan S. AIDS, "reversal" of the demographic transition and economic development: evidence from Africa. J Popul Econ 2012;25:871–97.
[32] Mathers CD, Ezzati M, Lopez AD. Measuring the burden of neglected tropical diseases: the global burden of disease framework. PLoS Negl Trop Dis 2007;1:e114.
[33] Alirol E, Getaz L, Stoll B, Chappuis F, Loutan L. Urbanisation and infectious diseases in a globalised world. Lancet Infect Dis 2011;11:131–41.
[34] Gavazzi G, Herrmann F, Krause K-H. Aging and infectious diseases in the developing world. Clin Infect Dis 2004;39:83–91.
[35] Maling S, Todd J, Van der Paal L, Grosskurth H, Kinyanda E. HIV-1 seroprevalence and risk factors for HIV infection among first-time psychiatric admissions in Uganda. AIDS Care 2011;23:171–8.
[36] van Rensburg AB Janse. Clinical profile of acutely ill psychiatric patients admitted to a general hospital psychiatric unit. Afr J Psychiatry (Johannesbg) 2007;10:159–63.
[37] Hatherill S, Flisher AJ, Nassen R. Delirium among children and adolescents in an urban sub-Saharan African setting. Journal of Psychosomatic Research. 69:187–92.
[38] Ukwaja KN. Typhoid fever presenting as a depressive disorder—a case report. Rural & Remote Health. 10:1276.
[39] Abiodun OA. Mortality from acute organic brain syndrome: a Nigerian psychiatric hospital experience. East Afr Med J 1988;65:366–71.
[40] Charbonnier C, Massoubre C, Szekely D, Airault R, Lang F. Psychopathologies encountered on the island of Mayotte between 1998 and 2004. Encéphale 2008;34:123–31.
[41] Uwakwe R. Psychiatric morbidity in elderly patients admitted to non-psychiatric wards in a general/teaching hospital in Nigeria. Int J Geriatr Psychiatry 2000;15:346–54.
[42] Aghanwa HS, Morakinyo O. Correlates of psychiatric morbidity in typhoid fever in a Nigerian general hospital setting. Gen Hosp Psychiatry 2001;23:158–62.
[43] Aghanwa HS, Ndububa D. Specific psychiatric morbidity in liver cirrhosis in a Nigerian general hospital setting. Gen Hosp Psychiatry 2002;24:436–41.
[44] Tunde-Ayinmode MF. Audit of child and adolescent psychiatry in a teaching hospital in Nigeria: prevalence, pattern and implication for improved services; 2010.
[45] Adeyemi JD. In-patient psychiatric referrals in a teaching hospital: a case controlled report. J Psychosom Res 1996;41:427–33.
[46] Ola BA, Crabb J, Krishnadas R, Erinfolami AR, Olagunju A. Incidence and correlates of delirium in a West African mental health clinic. General Hospital Psychiatry. 32:176–81.
[47] Jonsson G, Moosa MY, Jeenah FY, Musenge E. The outcome of mental health care users admitted under Section 40 of the South African Mental Health Care Act (No 17 of 2002). Afr J Psychiatry (Johannesbg) 2013;16:94–103.
[48] Berk M. Indications for computed tomographic brain scanning in psychiatric inpatients. South African medical journal. S Afr Med J 1992;82:338–40.
[49] Fainsinger RL, Waller A, Bercovici M, Bengtson K, Landman W, Hosking M, et al. A multicentre international study of sedation for uncontrolled symptoms in terminally ill patients. Palliat Med 2000;14:257–65.
[50] Karambe M, Zoungrana J, Dembele JP, Fofana AS, Oumar AA, Sissoko M, et al. [The psychiatric manifestations of people living with HIV in Mali]. Mali Medical. 25:32–5.
[51] Winkler AS, Tluway A, Schmutzhard E. Aetiologies of altered states of consciousness: a prospective hospital-based study in a series of 464 patients of northern Tanzania. J Neurol Sci 2011;300:47–51.
[52] Bademosi O, Falase AO, Jaiyesimi F, Bademosi A. Neuropsychiatric manifestations of infective endocarditis: a study of 95 patients at Ibadan, Nigeria. J Neurol Neurosurg Psychiatry 1976;39:325–9.
[53] Acuda SW, Ovuga EB. Psychiatric disorders in a general provincial hospital in Kenya. East Afr Med J 1985;62:229–35.

[54] Nubukpo P, Clement JP, Grunitzky EK, Leger JM, Dumas M. Epidemiologic, clinical, and etiologic features of acute delirious episodes (ADE) in Togo: findings of a hospital survey. Med Trop 2005;65:137–42.
[55] Stanley PC, Nwaneri DU, Stanley CN. The pattern of typhoid psychosis in childhood at the University Hospital of Port Harcourt, Port Harcourt January 2000 to December 2003. Res J Med Sci 2008;2:1–4.
[56] Andriambao D, Rakotobe ARR, Tristan M, Ranaivoarison J, Rasidy N, Raharisoa MA. Characteristic aspects of acute delusion psychosis in Madagascar. Encéphale 1976; 2:367–83.
[57] Weibel H, Metzger JY. Psychoses dÃ©lirantes aiguÃ«s. EMC Psychiatr 2005;2:40.
[58] Nubukpo P, Clement JP, Grunitzky EK, Leger JM, Dumas M. Epidemiologic, clinical, and etiologic features of acute delirious episodes (ADE) in Togo: findings of a hospital survey. Med Trop 2005;65:137–42.
[59] Thiam MH, Diop BM, Dieng Y, Gueye M. Mental disorders in cerebral malaria. Dakar Med 2002;47:122–7.
[60] Thiam MH, Karfo K, Sylla O, Gueye M. Mental confusion and multifocal lymphatic and pulmonary tuberculosis. A case report. Med Trop 2000;60:372–4.
[61] de Wet JS. Rabies presenting as an acute psychiatric emergency. S Afr Med J 1980; 58:297–8.
[62] Oyewumi LK. Inpatient adolescent psychiatry in a teaching hospital in Nigeria. Acta Psychiatr Scand 1989;80:639–43.
[63] Lustig SL, Maldonado JR. Diagnoses of children and adolescents on initial presentation to a Nigerian outpatient psychiatry clinic. Int J Soc Psychiatry 1999;45:190–7.
[64] Seck B, Dassa SK. R S. Le premierservice de pédopsychiatrie de l'Afrique de l'Ouest. Bilan et perspectives d'une première année de fonctionnement après rénovation. Neuropsychiatr Enfance Adolesc 1998;3:179–86.
[65] Soumare M, Seydi M, Diop SA, Diop BM, Sow PS. Cerebral malaria in adults at the Infectious Diseases Clinic in the Fann Hospital in Dakar, Senegal. Bull Soc Pathol Exot 2008;101:20–1.
[66] Mbassa Menick D. Characteristics of murder and attempted murder in Cameroon. Study based on expert psychiatric court reports. Med Trop 2009;69:255–62.
[67] Ajiboye PO, Adelekan ML. A prospective analysis of in-patient consultation–liaison psychiatry in a Nigerian teaching hospital. East Afr Med J 2004;81:620–5.
[68] Aghanwa HS, Morakinyo O, Aina OF. Consultation–liaison psychiatry in a general hospital setting in west Africa. East Afr Med J 1996;73:133–6.
[69] Abiodun OA. Physical morbidity in a psychiatric population in Nigeria. Gen Hosp Psychiatry 2000;22:195–9.
[70] Melka A, Tekie-Haimanot R, Assefa M. Aetiology and outcome of non-traumatic altered states of consciousness in north western Ethiopia. East Afr Med J 1997;74:49–53.
[71] Bower JH, Zenebe G. Neurologic services in the nations of Africa. Neurology 2005; 64:412–5.
[72] Dotchin CL, Akinyemi RO, Gray WK, Walker RW. Geriatric medicine: services and training in Africa. Age Ageing 2013;42:124–8.
[73] Saxena S, Thornicroft G, Knapp M, Whiteford H. Resources for mental health: scarcity, inequity, and inefficiency. The Lancet. 370:878–89.
[74] Fick DM, Agostini JV, Inouye SK. Delirium superimposed on dementia: a systematic review. J Am Geriatr Soc 2002;50:1723–32.
[75] Lancet Global Mental Health Group. Scale up services for mental disorders: a call for action. Lancet 2007;370:1241–52.
[76] Ngoma MC, Prince M, Mann A. Common mental disorders among those attending primary health clinics and traditional healers in urban Tanzania. Br J Psychiatry 2003;183:349–55.
[77] Ae-Ngibise K, Cooper S, Adiibokah E, Akpalu B, Lund C, Doku V, et al. 'Whether you like it or not people with mental problems are going to go to them': a qualitative exploration into the widespread use of traditional and faith healers in the provision of mental health care in Ghana. Int Rev Psychiatry 2010;22:558–67.
[78] Ochayi B, Thacher TD. Risk factors for dementia in central Nigeria. Aging Ment Health 2006;10:616–20.
[79] Guerchet M, M'Belesso P, Mouanga AM, Bandzouzi B, Tabo A, Houinato DS, et al. Prevalence of dementia in elderly living in two cities of Central Africa: the EDAC survey. Dement Geriatr Cogn Disord 2010;30:261–8.
[80] Habib AG, Yakasai AM, Owolabi LF, Ibrahim A, Habib ZG, Gudaji M, et al. Neurocognitive impairment in HIV-1-infected adults in Sub-Saharan Africa: a systematic review and meta-analysis. Int J Infect Dis 2013;17:e820–31.
[81] Siu GE, Wight D, Seeley JA. Masculinity, social context and HIV testing: an ethnographic study of men in Busia district, rural eastern Uganda. BMC Public Health 2014;14:33.
[82] Differences between HIV-infected men and women in antiretroviral therapy outcomes—six African countries, 2004–2012. MMWR Morb Mortal Wkly Rep 2013;62:945–52.
[83] Peixoto B, Kalei I. Neurocognitive sequelae of cerebral malaria in adults: a pilot study in Benguela Central Hospital, Angola. Asian Pac J Trop Biomed 2013;3:532–5.
[84] Nankabirwa J, Wandera B, Kiwanuka N, Staedke SG, Kamya MR, Brooker SJ. Asymptomatic plasmodium infection and cognition among primary schoolchildren in a high malaria transmission setting in Uganda. Am J Trop Med Hyg 2013;88: 1102–8.
[85] Bangirana P, Menk J, John CC, Boivin MJ, Hodges JS. The association between cognition and academic performance in Ugandan children surviving malaria with neurological involvement. PLoS One 2013;8:e55653.
[86] Kalaria RN, Mukaetova-Ladinska EB. Delirium, dementia and senility. Brain 2012; 135:2582–4.
[87] Sall L, Salamon E, Allgulander C, Owe-Larsson B. Psychiatric symptoms and disorders in HIV infected mine workers in South Africa. A retrospective descriptive study of acute first admissions. Afr J Psychiatry 2009;12:206–12.
[88] Hafeiz HB. Psychiatric manifestations of enteric fever. Acta Psychiatr Scand 1987; 75:69–73.
[89] Aghanwa HS, Erhabor GE. Specific psychiatric morbidity among patients with chronic obstructive pulmonary disease in a Nigerian general hospital. J Psychosom Res 2001;50:179–83.
[90] Verrier-Jones P, Pascoe FD, Gillis LS, King JB. The first 100 patients in the Valkenberg Psychogeriatric Assessment Unit. S Afr Med J 1978;54:113–5.
[91] Djibo A, Bouzou SB. Acute intoxication with "sobi-lobi" (Datura). Four cases in Niger. Bull Soc Pathol Exot 2000;93:294–7.
[92] Inouye SK. Delirium in hospitalized older patients. Clin Geriatr Med 1998;14: 745–64.
[93] Fong TG, Tulebaev SR, Inouye SK. Delirium in elderly adults: diagnosis, prevention and treatment. Nat Rev Neurol 2009;5:210–20.
[94] Ryan DJ, O'Regan NA, Caoimh RO, Clare J, O'Connor M, Leonard M, et al. Delirium in an adult acute hospital population: predictors, prevalence and detection. BMJ Open 2013;3.
[95] Turkel SB, Tavare CJ. Delirium in children and adolescents. J Neuropsychiatry Clin Neurosci 2003;15:431–5.
[96] Ferro JM, Caeiro L, Verdelho A. Delirium in acute stroke. Curr Opin Neurol 2002;15: 51–5.
[97] Margiotta A, Bianchetti A, Ranieri P, Trabucchi M. Clinical characteristics and risk factors of delirium in demented and not demented elderly medical inpatients. J Nutr Health Aging 2006;10:535–9.
[98] Kamel HK. The frequency and factors linked to a urinary tract infection coding in patients undergoing hip fracture surgery. J Am Med Dir Assoc 2005;6:316–20.
[99] Uldall KK, Berghuis JP. Delirium in AIDS patients: recognition and medication factors. AIDS Patient Care STDS 1997;11:435–41.
[100] Rahkonen T, Makela H, Paanila S, Halonen P, Sivenius J, Sulkava R. Delirium in elderly people without severe predisposing disorders: etiology and 1-year prognosis after discharge. Int Psychogeriatr 2000;12:473–81.
[101] Suzuki H, Hirashima T, Kobayashi M, Okamoto N, Matsuura Y, Tamiya M, et al. Impact of pneumonia on hyperactive delirium in end-stage lung cancer patients. Support Care Cancer 2013;21:281–5.
[102] Botella de Maglia J, Espacio Casanovas A. Severe and complicated malaria. Report of six cases. Rev Clin Esp 1998;198:509–13.
[103] Bucerius J, Gummert JF, Borger MA, Walther T, Doll N, Falk V, et al. Predictors of delirium after cardiac surgery delirium: effect of beating-heart (off-pump) surgery. J Thorac Cardiovasc Surg 2004;127:57–64.
[104] Perret JL, Sane M, Mbaye PS, Fall F, Diop M, Jousseaume JF. The new poor expatriates in the third world. Med Trop 2000;60:375–7.
[105] Cisse AF, Camara N, Diallo LL, Morel Y, Kone S, Camara MI, et al. Gayet–Wernicke's encephalopathy. A study of 13 cases observed in a refugee population hospitalized at the Conakry Teaching Hospital. Bull Soc Pathol Exot 2008;101:402–3.
[106] Avode DG, Bouteille B, Avimadje M, Adjien C. Epilepsy, intracranial hypertension, confusional syndrome and cutaneous cysticercosis. Apropos of 1 case observed in a hospital in Benin. Bull Soc Pathol Exot 1994;87:186–8.
[107] Kyebambe PS. Neurosyphilis masquerading as hemiparesis and Jacksonian epilepsy in an HIV positive patient: a case report. African Health Sciences. 10:211–4.
[108] Acosta Rabassa C, Castro González A. Reacción psicótica delirante aguda y enfermedad somática. Una experiencia en Guinea Bissau (Acute delirious psychotic reaction and somatic disease: an experience in Guinea Bissau). Rev Hosp Psiquiátrico La Habana 1985;26:97–113.
[109] Ovunga EB, Acuda SW. Neuro-psychiatric disorders in sickle cell trait. East Afr Med J 1985;62:730–4.
[110] Gureje O. Screening for organic brain syndromes in Nigerians. East Afr Med J 1986; 63:447–51.

Supplementary material: Further details on search strategy

Medline, Embase, PsychInfo

1. exp Delirium/ or delirium.mp.
2. Confusion/ or acute confusion.mp.
3. organic brain syndrome.mp.
4. acute brain syndrome.mp.
5. acute brain syndrome.mp. [mp=ti, ab, ot, nm, hw, kf, px, rx, ui, an, sh, tn, dm, mf, dv, kw, tc, id, tm]
6. 1 or 2 or 3 or 4 or 5
7. delirium.m_titl.
8. 1 or 6 or 7
9. angola.mp. or Angola/
10. angola.m_titl.
11. benin.mp. or Benin/
12. benin.m_titl.
13. botswana.mp. or Botswana/
14. botswana.m_titl.
15. burkina faso.mp. or Burkina Faso/
16. burkina faso.m_titl.
17. chad.mp. or Chad/
18. chad.m_titl.
19. burundi.mp. or Burundi/
20. burundi.m_titl.
21. cameroon.mp. or Cameroon/
22. cameroon.m_titl.
23. cape verde.mp. or Atlantic Islands/ or Cape Verde/
24. cape verde.m_titl.
25. central african republic.mp. or Central African Republic/
26. central african republic.m_titl.
27. comoros.mp. or Comoros/
28. comoros.m_titl.
29. congo.mp. or Congo/ or "Democratic Republic of the Congo"/
30. congo.m_titl.
31. cote d'ivoire.mp. or Cote d'Ivoire/
32. cote d'ivoire.m_titl.
33. eritrea.mp. or Eritrea/
34. eritrea.m_titl.
35. ethiopia.mp. or Ethiopia/
36. ethiopia.m_titl.
37. gabon.mp. or Gabon/
38. gabon.m_titl.
39. gambia.mp. or Gambia/
40. gambia.m_titl.
41. ghana.mp. or Ghana/
42. ghana.m_titl.
43. guinea.mp. or Guinea/ or Equatorial Guinea/ or Guinea-Bissau/
44. guinea.m_titl.

45. kenya.mp. or Kenya/
46. kenya.m_titl.
47. lesotho.mp. or Lesotho/
48. lesotho.m_titl.
49. liberia.mp. or Liberia/
50. liberia.m_titl.
51. madagascar.mp. or Madagascar/
52. madagascar.m_titl.
53. malawi.mp. or Malawi/
54. malawi.m_titl.
55. mali.mp. or Mali/
56. mali.m_titl.
57. mauritania.mp. or Mauritania/
58. mauritania.m_titl.
59. mauritius.mp. or Mauritius/
60. mauritius.m_titl.
61. mozambique.mp. or Mozambique/
62. mozambique.m_titl.
63. namibia.mp. or Namibia/
64. namibia.m_titl.
65. Niger/ or niger.mp.
66. niger.m_titl.
67. nigeria.mp. or Nigeria/
68. nigeria.m_titl.
69. rwanda.mp. or Rwanda/
70. rwanda.m_titl.
71. senegal.mp. or Senegal/
72. senegal.m_titl.
73. seychelles.mp. or Seychelles/
74. seychelles.m_titl.
75. sierra leone.mp. or Sierra Leone/
76. sierra leone.m_titl.
77. somalia.mp. or Somalia/
78. somalia.m_titl.
79. Sudan/ or south sudan.mp.
80. sudan.m_titl.
81. swaziland.mp. or Swaziland/
82. swaziland.m_titl.
83. tanzania.mp. or Tanzania/
84. tanzania.m_titl.
85. togo.mp. or Togo/
86. togo.m_titl.
87. uganda.mp. or Uganda/
88. uganda.m_titl.
89. zambia.mp. or Zambia/
90. zambia.m_titl.
91. zimbabwe.mp. or Zimbabwe/
92. zimbabwe.m_titl.

93. sao tome.mp.
94. sao tome.m_titl.
95. 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94
96. Africa, Western/ or South Africa/ or Africa, Eastern/ or africa.mp. or "Africa South of the Sahara"/ or Africa, Central/ or Africa/ or Africa, Southern/
97. 95 or 96
98. 8 and 97

9. Commentary on Background Paper 2

Delirium is an acute onset syndrome of cognitive dysfunction presenting with deficits in attention, arousal and global cognition[110]. In high-income countries (HICs), the syndrome is highly prevalent in older hospitalised adults[111]. Well-evidenced adverse outcomes include cognitive decline[111-114], disability[115, 116]and increased mortality rates[112, 115]. Prompt interventions can improve outcome[117], but delirium is under-diagnosed, and may be missed in up to half of cases[27, 118]. Identification of delirium is most difficult amongst those at the greatest risk: older adults and those with pre-existing cognitive impairment. Use of validated screening and diagnostic measures improve detection rates of delirium[118, 119]. Routine cognitive screening is therefore recommended for older hospitalised adults in HIC countries[120]. Delirium and dementia can be difficult to differentiate particularly in acute hospital settings.

We conducted a comprehensive narrative review of delirium prevalence and risk factors in SSA in all languages (background paper 1)[121]. Existing data were very limited, and a significant proportion of studies consisted of case reports and small case series. Very few studies used standard diagnostic or assessment criteria such as the DSM or the CAM, and in the remainder, a wide range of terminology or synonyms for delirium were employed. A substantial number relied on retrospective case note review rather than clinical assessment. A large proportion of studies took place in inpatient, outpatient and liaison psychiatry settings and demonstrated significant rates of misdiagnosis of delirium as psychiatric disorder and inappropriate referral to psychiatric services. The most substantial evidence appeared to come from paediatric populations, and only two studies of older adults were discovered, one of which took place in a psychogeriatric unit using retrospective case note review, and one in a hospital setting using clinical criteria. Prevalence in these studies was 9 and 9.6% respectively[40], and a large diagnostic gap was noted with only one case of hospital delirium identified by the treating medical team.

It was notable that our review did not uncover any validation studies of assessment tools for delirium in SSA, and it was hypothesised that absence of appropriate screening tools may contribute to the potentially large diagnostic gap in delirium, especially in older adults.

The overall outcome of our review was that almost no data on delirium in older adults in SSA exist and no screening or diagnostic tools had been validated. The large number of apparent inappropriate referrals to psychiatric services and overall poor outcomes suggested that validated screening tools were urgently needed. This was the reason for investigation of screening and diagnostic methods for delirium as part of this presented work. If non-specialist health workers are to identify dementia through cognitive screening, the ability to identify delirium is crucial in order to

ensure the safety of individuals with delirium through appropriate referral and urgent investigation. Therefore any screening method developed must consider delirium identification.

10.Summary and statement of problem

In summary, the available evidence suggests that brief screening tools for dementia are currently lacking in SSA. Human resource shortages and the need for a task-shifting approach for dementia assessment indicate that a brief and accurate screening tool is needed which is suitable for non-specialists to use in routine care.

The available data on cognitive neurodevelopment and psychometric assessment in illiterate individuals suggests that real cognitive differences exist between literate and illiterate individuals. Although performance differences are present in most cognitive domains, certain tests appear to be less affected by literacy or previous school attendance and these tests could be considered to be the most 'culture fair' in low-literacy settings. These include categorical verbal fluency, orientation and delayed recall.

Importantly, since problem solving and other practical assessments appear unaffected by literacy, it is likely that functional assessment will be useful in differentiating those with poor or borderline cognitive performance due to illiteracy and those with dementia in this setting

The need to screen for all dementia subtypes would suggest that a test focussed on orientation and recall will be inadequate at screening for dementia in this setting.

Delirium is important to identify alongside dementia as it needs prompt intervention and diagnosis can improve overall outcome. No delirium screening or assessment tools have been validated in Africa to date and these are urgently needed.

Existing screening tools designed for low-literacy settings have been inadequately validated, and most validation studies have utilised the MMSE in low-literacy settings despite well evidenced shortcomings of this approach.

11. Context – The IDEA study

The work submitted for this doctoral thesis was completed as part of the identification and Interventions for Dementia in Elderly Africans (IDEA) study. The IDEA study was a three year collaboration between Newcastle University and Northumbria Healthcare NHS Foundation Trust (NHCFT) in the UK, the University of Ibadan in Nigeria, and Kilimanjaro Christian Medical College (KCMCo), in Tanzania. I was the research doctor for the Tanzanian site from June 2013 to June 2016. The overall aims of the project were as follows: 1) to develop and validate a brief cognitive assessment for dementia suitable for use by non-specialist health workers in SSA, and 2) to develop and trial an adaptation of cognitive stimulation therapy (CST), a group based non-pharmacological intervention for dementia, for use in this setting. The focus of this thesis is on the first of these two project outcomes.

12.Setting

12.1. Hai demographic surveillance site (DSS) Tanzania

This work took place in the Kilimanjaro region of Northern Tanzania. Tanzania is a low-income country with an average per capita income of $930. The literacy rate in 2010 was 73%. Life expectancy is 61 years at birth and 5% of the population are aged 65 or over.

The community-based work described here took place in the Hai district, a rural area on the slopes of Mount Kilimanjaro. The majority of the population are subsistence farmers, although some families cultivate cash crops such as coffee and tomatoes. The official language is Swahili, but most also speak a tribal language at home. A significant minority of older women may only speak a tribal language. Most health professionals speak some English because degree-level courses are now taught in English.

Hai has been a demographic surveillance site (DSS) since 1992, and regular population censuses have been carried out over the past 20 years. The population of the DSS was 161,119 in 2009, with a further census planned for 2017.Hai is a well demarcated area with natural boundaries and little migration in and out of the area occurs. Villages in Hai, and elsewhere in rural Tanzania, are highly organised. Households are grouped into ten-household cells with an elected representative called a balozi. The balozi is expected to answer to the village committee on matters related to their 10-household cell, holds office for 5 year terms and is generally a well-known individual in the village. This organisational system ensures that censuses and epidemiological work can be carried out, as the name of the balozi is used to locate households and subsequently individuals in the same way as a postcode might be used in Europe. Each village has one or two enumerators, elected by the village committee with a role in health surveillance and public health measures. The village enumerators are experienced in carrying out epidemiological work, and this system has resulted in successful epidemiological studies of stroke, epilepsy, Parkinson's disease, neurological disorders, atrial fibrillation and dementia.

Figure 5 and Figure 6 show the location and setting of Hai in Tanzania.

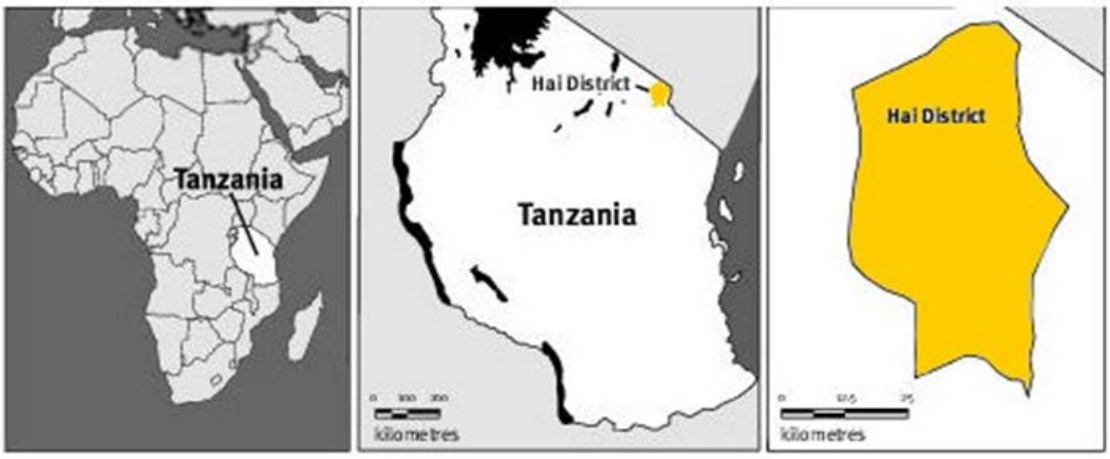


Figure 5 Location of the Hai district

Figure 6 The Hai district

12.2. Hospital settings

12.2.1. Mawenzi Regional Referral Hospital

Mawenzi Regional Referral Hospital (MRRH) (see Figure 7) is a government hospital in Moshi, Kilimanjaro with 200 beds and two inpatient medical wards. Over 300 outpatient appointments take place per day. The hospital serves an urban and rural population of over 100000 people. Patients requiring more specialist services are referred to the local tertiary referral hospital. In line with current Government policy, MRRH has a geriatric medicine clinic which is intended to be free of charge for all individuals able to demonstrate their age to be 60 and over. The usual method of age verification is a letter from the village chairperson.

Figure 7. Screening at Mawenzi Regional Referral Hospital

12.2.2. Kilimanjaro Christian Medical Centre

Kilimanjaro Christian Medical Centre (KCMC) (see Figure 8) is an 800 bedded tertiary referral hospital in Moshi, Kilimanjaro which serves a predominantly rural population of over eight million people over an area of more than 170,000km2. The hospital is funded through a partnership between central government and a charitable foundation, with treatments funded through both national health insurance and user-payments. This study took place in the 107-bedded internal medicine department including two inpatient medical wards, a high dependency unit and small private ward. In 2014 16.1% of 4590 total admissions to the department were aged 60 and over. In-hospital mortality in this age group is estimated at 25.1% and hospital stay is typically short (median 5 days) in survivors.

Figure 8. Kilimanjaro Christian Medical Centre (KCMC)

12.3. Ethical approval

Ethical approval for the studies described was obtained from both the Kilimanjaro Christian Medical Centre (KCMC) local ethical committee and the National Institute of Medical Research (NIMR) in Dar-es-Salaam, Tanzania. Consent was also obtained from the managerial boards of the hospitals included in the study and oral presentations describing the project were delivered to clinical staff of the participating hospitals prior to commencing the project to ensure that all were properly informed of the nature and purpose of the study. Likewise consent was obtained from the district medical officer (DMO) for the Hai district and permission granted for local primary health care workers to assist with the project.

All studies followed a similar informed consent procedure. All participants were given oral and written information about the project by a trained research nurse or medical officer. Since these studies included significant numbers of people with cognitive impairment, those deemed not to have capacity to consent by the assessing health worker were allowed to take part if written assent was obtained from a close relative. For those unable to write, consent was recorded using a thumbprint.

13. Preliminary work informing this study (supplementary papers 1, 2, 3 and 4)

13.1. Hai dementia prevalence study, 2010

Difficulties of cognitive screening for dementia in rural Tanzania, consideration of different diagnostic criteria in this setting, and effect of education.

The Hai dementia prevalence study was a two stage door-to-door community-based prevalence study of individuals aged 70 and over from 6 villages randomly selected within the Hai district. The age-adjusted dementia prevalence by DSM-IV clinical criteria was 6.4. The assessment method followed the 10/66 international collaboration protocol, developed to be culture-fair and previously used to estimate dementia prevalence across a number of LMIC settings as described in section 2.2 'Diagnosis and screening for dementia in LMIC settings' above. A total of 1198 participants aged 70 and over from a total of 1277 identified using census data, were screened using the CSI-D. As described above, the CSI-D was developed as a research tool for epidemiological studies and consists of a cognitive screen developed for use in cross-cultural settings (COGSCORE), and an informant interview (RELSCORE).The CSI-D was administered by trained primary health care research workers, in participants own homes. Scores are entered into an algorithm and result in stratification into 'probable dementia', 'possible dementia' and 'no dementia' categories. All those with high probability, 50% of those with intermediate probability 'possible dementia' and 5% of those with low probability 'no dementia' underwent second stage clinical assessment based on the 10/66 protocol. A total of 296 individuals were assessed in the second stage. This structured assessment included the geriatric Mental State (GMS), a neurological examination, the Neuropsychiatric Inventory (NPI), a detailed informant history for dementia subtype, caregiver burden questionnaire (Zarit caregiver burden questionnaire) and detailed risk factor questionnaire. Second stage assessment was completed by a research doctor assisted by a trained study nurse. In addition to the 10/66 protocol, designed for use by non-medically qualified graduates, additional history and examination took place where required in order to clarify diagnosis by DSM-IV clinical criteria.

The overall educational level in this cohort was strikingly low, with over two thirds of older women having never attended school. Of 668 females, only 44 (6.8%) had more than 4 years of education, 205 (30.7%) had 4 years or less, with 419 (62.7%) having had no education at all. Educational level was generally higher in males with 96 (18.5%) reporting more than 4 years of education, 256 (49.4%) had 4 years of education or less and 166 (32.0%) having had no education at all. Females were 3.56 times (95% CI 2.80-4.55) more likely to have had no education than males.

Although designed for use in cross-cultural LMIC settings, results in Hai indicated educational bias in the 10/66 algorithm-based diagnosis, compared with clinically diagnosed DSM-IV dementia (see Table 4).

Any previously formal education was found to have a significant association with cognitive performance on the CSI-D and with 10/66 algorithm-based dementia diagnosis but not with DSM-IV dementia diagnosis based on clinical history and examination. Education and literacy were also independently associated with CSI-D COGSCORE and 'probable dementia' by CSI-D in males, but not in females fully assessed in phase two of the study. The lack of association in women was attributed to a lack of statistical power due to the lower level of schooling amongst female participants (see Table 6).

We concluded that since comprehensive clinical interviews and informant histories had been used to make diagnoses of dementia by DSM-IV criteria with doctors and locally experienced clinical staff, these diagnoses were likely to be correct. The reported prevalence by 10/66 criteria of over 20% of individuals having dementia simply did not reflect the functional ability of older people in the Hai district seen clinically by the research team and by health workers familiar with the local area. The 10/66 protocol were designed for LMIC settings, but most published study sites included individuals with markedly higher levels of education than those seen in our rural SSA study. Although the 10/66 collaboration included at least one study site in SSA, data have been published for cognitive impairment rather than dementia so cannot be compared to our findings in Tanzania.

Considering known literature on cognitive performance in illiterate and low-literate people, outlined in section 2.4 above, the CSI-D includes a number of items which are likely to be educationally biased. The 10/66 protocol attempts to compensate this by weighting the informant interview, but a number of SSA prevalence studies have used the cognitive scale of the CSI-D alone for dementia screening, dementia diagnosis and prevalence estimates of cognitive impairment. In these studies, CSI-D COGSCORE totals of 28/33 and 25.5/33 have been used as indicative of cognitive impairment or dementia respectively. This approach is less likely to be valid, especially in low-literacy settings and in these studies illiteracy rates are broadly similar to those in Hai ranging from 40-96%.

In Hai, overall cognitive performance on the CSI-D COGSCORE was poor, with median COGSCORE totals of only 25.7 for women and 27.7 for men. These scores are similar to the cut-off scores for cognitive impairment used in prevalence studies in SSA and other LMIC settings.

In the original cross-cultural validation of the CSI-D across high and low literacy settings, mean COGSCORES for those who did not have dementia ranged from 28-30 with the exception of a cohort

in Nigeria who had similar educational levels to our cohort in Hai. In this cohort, mean COGSCORES were 25.42, similar to median scores in older women in Hai (25.7%).

In conclusion, in rural SSA, the best-validated existing dementia screening tools are significantly educationally biased and cognitive assessment tools designed for use in this low literacy setting are needed to inform research studies and clinical practice. In addition to the educational bias noted, the CSI-D is lengthy, and was designed primarily as a research tool for epidemiological studies. The algorithm-based risk stratification yielded by the combination with the informant interview is unlikely to be useful to non-specialist clinicians working with older people in rural SSA and a different approach is needed.

Table 4. Comparison of dementia diagnosis by 10/66 dementia collaboration criteria (designed to be culture-fair in LMIC settings) and DSM-IV clinical criteria based on detailed structured clinical interview and informant history by research doctor (supplementary paper 3)

Prevalence of 10/66 and clinically diagnosed DSM-IV dementia				
	Cases within 168 people with 'probable dementia'	Cases within 56 people with 'possible dementia'	Cases within 72 people with 'no dementia'	Extrapolated dementia prevalence (%)
10/66 dementia'				
Females	103	37	2	28.5
Males	45	7	1	16.3
70–74 years	22	5	1	13.1
75–79 years	33	8	1	19.4
80–84 years	27	13	1	29.7
≥85 years	66	18	0	43.7
Total all cases	148	44	3	23.5
Age-standardised all cases	–	–	–	21.6
DSM-IV clinically diagnosed dementia				
Females	51	5	0	9.3
Males	22	0	0	4.8
70–74 years	9	1	0	3.5
75–79 years	10	1	0	3.8
80–84 years	15	1	0	8.6
≥85 years	39	2	0	19.3
Total all cases	73	5	0	7.5
Age-standardised all cases	–	–	–	6.4

Table 5. Association between any education and dementia diagnosis by 10/66 collaboration criteria (designed to be culture-fair in LMIC settings) and DSM-IV clinical dementia criteria based on clinical interview and informant history. Formal education was not independently associated with DSM-IV criteria dementia. The 10/66 algorithm protocol appeared educationally biased in this setting (supplementary paper 3)

Logistic regression models of the role of education after adjusting for the effect of age and gender					
				95% CI for OR	
	B	Sig.	OR	Lower	Upper
10/66 dementia					
70–74 years	–	–	1	–	–
75–79 years	0.894	0.016	2.444	1.180	5.061
80–84 years	1.406	0.001	4.079	1.832	9.082
85 years or over	1.817	<0.001	6.156	2.938	12.898
Female gender	0.633	0.030	1.884	1.065	3.333
Education*	0.800	0.004	2.225	1.284	3.855
Constant	−0.837	0.005	0.433		
Clinical DSM-IV dementia					
70–74 years	–	–	1	–	–
75–79 years	0.147	0.759	1.158	0.454	2.952
80–84 years	0.807	0.077	2.242	0.918	5.478
85 years or over	1.279	0.002	3.592	1.619	7.971
Female gender	0.230	0.456	1.259	0.688	2.304
Education*	0.103	0.730	1.108	0.619	1.985
Constant	−1.940	<0.001	0.144		

OR=odds ratio, CI=confidence interval.

*Education was coded as 1=none, 0=some primary education or higher level. There were 13 missing values and the model is based on 283 cases.

Table 6. Relationship between literacy, schooling and life experience and median CSI-D cognitive score (COGSCORE) in Hai 2010 dementia prevalence study. Although the CSI-D has was designed to be culture-fair, total scores were much lower in those without formal education and/or illiterate (supplementary paper 3)

Literacy, schooling and life experience data in relation to CSI-D cognitive score						
Yes				No		
		Number	CSI-D score (median, IQR)	Number	CSI-D score (median, IQR	Significance
Females	Ever attended school (n=668)	249 (37.3%)	26.9 (24.7 to 28.9)	419 (62.7%)	24.8 (21.6 to 27.4)	U=34866.5, z= –6.688, **p<0.001**
	Can read and write (n=668)	232 (34.7%)	26.9 (24.7 to 28.7)	436 (65.3%)	24.9 (21.8 to 27.5)	U=34449.5, z= –6.791, **p<0.001**
	Born outside Hai (n=673)	70 (10.4%)	25.2 (23.6 to 27.3)	603 (89.6%)	25.8 (22.6 to 28.1)	U=19397.0, z= –1.109, p=0.267
	Ever lived outside Hai (n=673)	96 (14.3%)	26.1 (24.1 to 28.0)	577 (85.7%)	25.6 (22.6 to 28.0)	U=26581.0, z= –0.632, p=0.527
Males	Ever attended school (n=518)	352 (68.0%)	28.3 (26.3 to 29.9)	166 (32.0%)	26.5 (24.0 to 28.0)	U=20757.0, z= –6.278, **p<0.001**
	Can read and write (n=518)	337 (65.1%)	28.2 (26.3 to 29.8)	181 (34.9%)	26.8 (24.0 to 28.6)	U=21481.5, z= –6.039, **p<0.001**
	Born outside Hai (n=525)	66 (12.6%)	27.1 (26.1 to 28.3)	459 (87.4%)	27.9 (25.5 to 29.5)	U=13771.5, z= –1.194, p=0.233
	Ever lived outside Hai (n=525)	157 (29.9%)	28.0 (26.2 to 29.6)	368 (70.1%)	27.5 (25.3 to 29.4)	U=26422.5, z= –1.549, p=0.121

IQR: inter quartile range.

Table 7. Association between markers for cognitive function and schooling in phase II cohort (Supplementary paper 4)

Association between markers for cognitive function and schooling in phase II cohort. N=296			
		Univariate odds ratio (95% CI, significance)	Age adjusted odds ratio (95% CI, significance)
Females	CSI-D patient cognitive score	1.01 (0.96 to 1.05, p=0.786)	1.00 (0.95 to 1.04, p=0.858)
	CERAD 10 word list score	1.13 (0.97 to 1.31, p=0.115)	1.08 (0.92 to 1.26, p=0.339)
	Probable dementia by CSI-D	0.83 (0.61 to 1.11, p=0.211)	0.85 (0.63 to 1.16, p=0.316)
	DSM-IV dementia diagnosis	0.91 (0.47 to 1.77, p=0.776)	1.11 (0.55 to 2.22, p=0.774)
Males	CSI-D patient cognitive score	1.11 (1.03 to 1.20, p=0.010)	1.09 (1.01 to 1.18, p=0.028)
	CERAD 10 word list score	1.12 (0.91 to 1.37, p=0.273)	1.09 (0.87 to 1.37, p=0.452)
	'Probable dementia' by CSI-D	0.48 (0.31 to 0.75, p=0.001)	0.54 (0.34 to 0.86, p=0.010)
	DSM-IV dementia diagnosis	0.44 (0.16 to 1.18, p=0.103)	0.59 (0.20 to 1.76, p=0.345)

14. Evaluation of the Mini-Mental State Examination (MMSE) in Hai (Supplementary Paper 3, cohort 1b)

The mini-mental state examination (MMSE) is the most widely used cognitive screening test worldwide despite well described shortcomings relevant to potential use in sub-Saharan Africa. These shortcomings include well-evidenced educational bias, inclusion of literacy and numeracy-dependent items, and lack of items assessing frontal lobe or executive function. Nevertheless, the MMSE is the most extensively validated cognitive test in low-literacy settings as evidenced by the data presented in the systematic review of brief cognitive screening tools. We felt that due to this very widespread use of the MMSE for cognitive screening, including in hospital settings in SSA as detailed in Table 2, it was appropriate to evaluate the performance of the MMSE in Tanzania.

The version of the MMSE used for the pilot was minimally adapted in order to be understood in Tanzania. The sentence for repetition was changed to a similar phrase well known in Swahili. Likewise the attention task was simplified to serial subtractions of three. The item on street name was changed to 'who lives next door' because street names were not relevant in Hai. Translations to instructions were made with discussion with the district medical supervisors, a group of assistant medical officers with extensive public health experience and forwards and backwards translated to ensure that instructions would be clearly understood as intended.

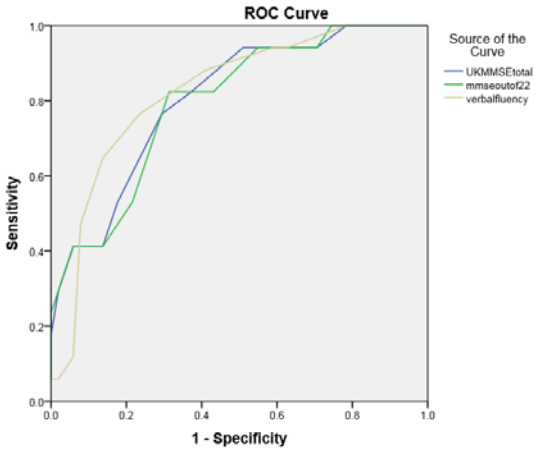
The MMSE was evaluated in sixty participants under follow-up as part of a study of mild cognitive impairment (MCI). Demographic data are summarised in Table 8. Median MMSE score for individuals with no cognitive impairment following detailed home-based clinical assessment was 19, within the range normally classified as moderate dementia in high income countries. This was similar to findings from other LMIC studies with high levels of illiterate participants identified during the systematic review of cognitive screening tools. Surprisingly, the majority of participants could not name the country and replied by giving the name of the region, or nearest large town, despite prompting. As expected, most illiterate participants were reluctant to attempt the drawing task and most refused.

The performance of the MMSE is summarised below in in Table 8. The optimum cut-off for the MMSE in our sample was 13.5/30 or 13.5/22 with sensitivity of .77 and specificity of .71. A cut off of 14 resulted in sensitivity of .824 but specificity of 0.63. Removing the literacy-dependent items did not change the optimum cut-off score with 13.5/22 resulting in sensitivity of .824 and specificity of .69. Auroc was fair (0.80-0.796). Categorical verbal fluency was superior to the MMSE in dementia screening. Of the domains assessed in the MMSE, the best-performing were orientation and delayed

recall. Results supported evidence from other low-literacy settings that performance on categorical verbal fluency and orientation are less affected by illiteracy. Generally those with normal cognition performed poorly in all individual tasks in the MMSE with the exception of repetition and simple naming, a similar finding to that reported in another low literacy setting in Brazil. The optimal cut-off of 13/30 was at the lower end of normative scores reported in other low-literacy settings (13-18). The previously described validity issues when using artificially low scores for illiterate people on the MMSE and other cognitive screening tests, and the result of this pilot study, indicate that the MMSE cannot be recommended for dementia screening in SSA.

Table 8. MMSE for dementia screening in Hai pilot study

*=missing	Dementia n=17	MCI N=29	Normal cognition N=14
Age (med, IQR)	81.0 (16.50) *=1	85.0 (10.0)	80.00 (14.0)
Female (n, %)	11 (64.71)	19 65.52	11 (78.57)
Ever attended formal school (n, %)	4 (23.53)	10 34.48	7 (50.0)
Years of education (med, IQR)	0.00 (1.00)	0.00 (3.00)	0.50 (4.0)
Self-reported basic literacy (n, %)	4 (23.53)	7 (24.14)	7 (50.0)
Verbal fluency (category, animals) (med, IQR)	4.00 (2.50)	6.00 (3.50)	8.50 (3.75)
CERAD delayed recall (med, IQR)	1.00 (2.250) *=5	1.00 (2.0) *=5	1.50 (4.0) *=4
Minimally adapted MMSE total score (med, IQR)	12.00 (4.50)	15.0 (5.0)	19.50 (3.75)
MMSE total disregarding literacy and numeracy based items /22	12.00 (4.50)	14.0 (4.0)	19.00 (2.5)
Subset scores			
MMSE orientation/10	4.00 (3.00)	6.00 (2.0)	8.00 (2.5)
MMSE registration/3	3.00 (1.00)	3.00 (0.0)	3.00 (0.0)
MMSE recall/3	0.00 (1.00)	1.00 (2.0)	2.00 (0.0)
MMSE commands/3	2.00 (2.50)	2.00 (2.0)	2.00 (1.25)
MMSE naming/2	2.00 (0.00)	2.00 (0.0)	2.00 (0.0)
MMSE writing/1	0.00 (0.00)	0.00 (0.0) *=4	0.00 (0.0) *=1
MMSE written command/1	0.00 (0.00) *=1	0.00 (1.0)	0.00 (1.0)
MMSE copying/1	0.00 (0.00) *=4	0.00 (0.0) *=4	0.00 (0.0) *=1
MMSE attention and concentration (calculation)/5	0.00 (0.00)	0.00 (0.0)	0.00 (1.0)
MMSE repetition/1	1.00 (0.00)	1.00 (0.0)	1.00 (0.0)



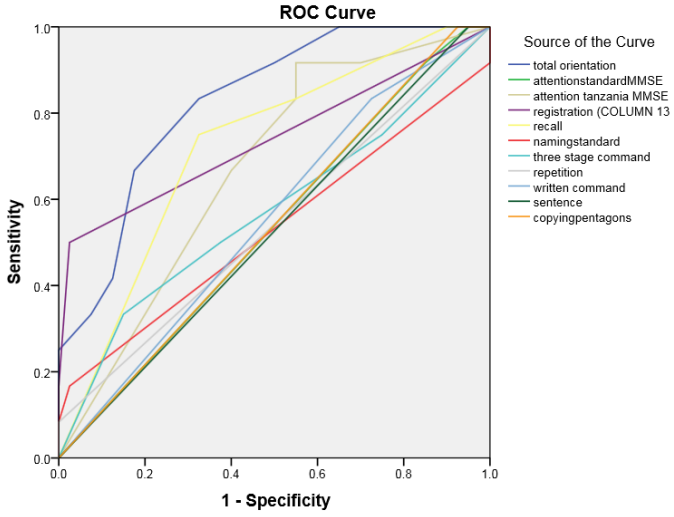
Area Under the Curve

Test Result Variable(s)	Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
UKMMSEtotal	.805	.059	.000	.690	.920
mmseoutof22	.796	.060	.000	.678	.913
verbalfluency	.824	.056	.000	.713	.934

The test result variable(s): UKMMSEtotal, mmseoutof22, verbalfluency has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5



Area Under the Curve

Test Result Variable(s)	Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
total orientation	.827	.062	.001	.705	.949
attentionstandardMMSE	.535	.092	.712	.354	.717
attention tanzania MMSE	.671	.083	.075	.509	.833
registration (COLUMN 13	.740	.097	.013	.550	.929
recall	.721	.081	.021	.562	.880
namingstandard	.531	.107	.745	.322	.741
three stage command	.572	.102	.454	.371	.773
repetition	.542	.099	.664	.347	.736
written command	.554	.092	.572	.373	.735
sentence	.525	.093	.794	.342	.708
copyingpentagons	.538	.092	.696	.357	.718

Figure 9. Performance of cognitive domains from MMSE for prediction of dementia

The IDEA six-item cognitive screen

15.The IDEA six-item cognitive screen for Africa (SIDSA)

The SIDSA is a brief cognitive screening tool designed for use by non-specialist workers in primary care in a rural SSA setting, and to be used in a low-literacy setting. Items scored assess orientation, short-term recall, long term memory, abstract thought, category (animal) fluency and visuo-construction.

Four items are taken from the Community Screening Instrument for Dementia (CSI-D). These are as follows, to describe the function of a bridge, naming the day of the week, naming the village chairperson, town mayor or equivalent, and categorical verbal fluency (animals in one minute). An additional item, the 10 word list is an adaption of the Consortium to Establish a Registry for Alzheimer's disease (CERAD) 10 word recall task. This was adapted in India to allow auditory rather than written presentation of the words, and adaptation of the words to a LMIC setting. Three learning trials are given, and then recall of the 10 previously learned words is scored after a five minute delay with one point given for each correct answer up to a maximum of 5 points. This task forms part of the 10/66 international dementia collaboration protocol. The final item is a measure of praxis and visuoconstruction using a matchstick construction task taken from the stick design test, originally validated in a community cohort in Nigeria with a very low level of literacy. This is scored from zero to three points. Weighting of individual questions for item scoring was derived from the parameter estimates of the regression models. The maximum possible score on the IDEA screen is therefore 15 points and the minimum is zero, with higher scores indicating better cognitive performance.

The IDEA six-item screen appears to address some of the issues of educational bias noted in other screening tools. There are no included items requiring reading writing drawing or calculation in order to avoid overt educational bias. In addition, the items included are amongst those evidenced to be less affected by exposure to formal education. Orientation (if culturally appropriate items are asked) has been shown to be less affected by exposure to formal education than other cognitive tests. Likewise although verbal fluency performance is related to educational attainment, categorical fluency and in particular categories related to everyday life are less educationally biased. The 10 word learning list, and particularly the adaptation used here was originally used in a low-literacy setting in India. It has been shown to have minimal educational bias, with scores on total word learning and delayed recall appearing fairly consistent across a range of LMIC urban and rural settings with higher or lower levels of education[36]. In the Hai dementia prevalence study, delayed recall performance using this 10-word list was similar in men and women with a median of two words recalled in both groups (U=9142.0, z= –0.603, p=0.547), despite the lower education levels

and greater age of the female group, suggesting a lack of educational bias in this assessment. The IDEA six-item screen, although brief, includes items screening frontal and parietal lobe function. This avoids the focus on registration and recall seen in other brief screening tools and may therefore have utility in screening for dementias of subtypes other than Alzheimer's disease dementia (ADD). This is important since there is evidence of an increased prevalence of non-ADD dementias in Tanzania.

Six Items Dementia Screening for Africa- SIDSA

Vitusitavyakuchunguzaugonjwawa dementiakwaAfrika – SIDSA

Date of Interview:	INTERVIEWER
Subjects' Name:	Subject ID
A.1.1 Gender:	Location of Interview:
Home Address/village	Ballozi:
Telephone number (essential)	
A.1.2 Date of Birth (if known):	A.1.3 Current Age
(If not known/unsure, estimate using historical events):	
A.1.4 Occupation:	A.1.5 Still working?
CAN THE PATIENT READ AND WRITE? (Please circle)	YES NO
EDUCATIONAL LEVEL REACHED	
None Grades 1-4 Grades 5-7 Grade 8 or above	Completed secondary school Further education

Preparation for ten-word list (Question 5) *Maandalizi kwa ajili ya orodha maneno-kumi (Swali la 5)*

I am going to read out a list of words. Please listen carefully and I will ask you to repeat them back to me once I have finished (read out the words slowly).
Mimi nitakusomea orodha ya maneno. Tafadhali sikiliza kwa makini na nitakuomba wewe kuyarudia mara baada ya mimi kumaliza (soma maneno polepole).

First attempt: Now tell me all the words you can remember (tick on the grid the words remembered)

Jaribu la kwanza: *Sasa uniambie maneno yote unayoweza kukumbuka (weka alama ya vema mbele ya neno lililokumbukwa)*

Second attempt: Now I will read out the words again, listen carefully and I will ask you to repeat as many as you can. Now tell me all the words you can remember (tick on the grid the words remembered)

Jaribu la pili: *Sasa mimi nitasoma orodha ya maneno tena, sikiliza kwa makini na mimi nitakuuliza wewe kuyarudia kwa wingi kadri unavyoweza. Sasa niambie maneno yote unayoweza kukumbuka (weka alama ya vema mbele ya neno lililokumbukwa)*

Third attempt: Now I will read out the words one last time, listen carefully and I will ask you to repeat as many as you can. Now tell me all the words you can remember (tick on the grid the words remembered)

Jaribu la tatu*: Sasa mimi nitasoma tena orodha ya maneno mara moja ya mwisho, sikiliza kwa makini na mimi nitakuuliza wewe kuyarudia kwa wingi kadri utakavyoweza. Sasa niambie maneno yote unayoweza kukumbuka (weka alama ya vema mbele ya neno lililokumbukwa*

Word/ *neno*	First attempt *jaribu la kwanza*	Second Attempt *Jaribu la pili*	Third Attempt *Jaribu la tatu*
Butter /*Siagi*			
Arm /*Mkono*			
Letter /*Barua*			
Queen/ *Malkia*			
Ticket /*Tikiti*			
Grass / *Nyasi*			
Corner /*Kona*			
Stone /*Jiwe*			
Book /*Kitabu*			
Stick /*Fimbo*			

1. I will tell you the name of something and I want you to describe what it is. What is a bridge? (correct answer: something that goes across a river, canyon or road) Mimi nitakuambia jina la kitu na Mimi nataka wewe kuelezea ni nini.Je, daraja nini? (Jibu sahihi: kitu ambacho huenda juu ya mto, korongo au barabara)	0 if incorrect / kama si sahihi 2 if correct / kama sahihi	Score / Alama:___/2
2. I want you to name as many different animals as you can in one minute. Nitapendautajemajinayawanyamawengikadriuwezavyondan iyadakikamoja.	/ 0 - 0-3 animals named / kama ametaja wanyama 0-3 1 - 4-7 animals named / kama ametaja wanyama 4-7 2 - 8 or more animals named / kama ametaja wanyama 8 au zaidi	Score / Alama:___/2
3. Who is the chief/head/leader of this village? Ni nanimtawala/mkuu/kiongoziwakijijihiki?	0 if incorrect / kama si sahihi 1 if correct / kama sahihi	Score / Alama:___/1
4. What day of the week is it? Ni sikuganiya wiki leo?	0 if incorrect / kama si sahihi 2 if correct / kama sahihi	Score / Alama:___/2
5. Can you tell me the ten words we learned earlier? Try to remember as many as you can. Je, unaweza kuniambia maneno kumi tuliojifunza mapema? Jaribu kukumbuka majina mengi kadri utakavyoweza	0 for no words remembered /kama hakuna neon lililokumbukwa 1 for 1 word / 1 kwa neno 1	Score / Alama:___/5

	2 for 2 words / 2 kwa maneno 2 3 for 3 words / 3 kwa manneno 3 4 for 4 words / 4 kwa maneno 4 5 for 5 or more / 5 kwa maneno 5	
6. Can you make the design shown below using these four matchsticks? I will show you once and then you have to copy exactly. (The examiner should make the design first using the matchsticks and specifically point out to the person that the heads of the matchsticks all need to point the same way. Once the examiner has made the shape, collect up the matchsticks in a bunch and place them in front of the person being interviewed.) Je, unaweza kufanya maumbokama inavyoonekana hapa chini kwa kutumia njiti nne za kiberiti. Mimi nitakuonyesha mara moja na kisha wewe utarudia kama mimi nilifanywa) (Mtahini anapaswa kufanya maumbo ya kwanza kwa kutumia njiti za kiberiti na hasa kuelezea kwa ufasaha kuwa vichwa vyote vinne vielekee upande mmoja. Mara mtahini anapomaliza kufanya umbo, kusanya njiti za kiberiti katika rundo na kuziweka. mbele ya mtu kuwa anayehojiwa, ni sawa mtu kuona umbo hili hapa chini wakati wakitengeneza umbo). 	Score 1 for each part of the design that is performed correctly Toa maksi 1 kwa kila sehemu ya umbo inayofanywa sawa. 1 - Middle two matchstick heads pointing same way Vichwa vya njiti mbili vinaelekea upande mmoja 1 - Outside two matchsticks pointing at an angle Kwa upandewa nje njiti mbili zinaelekea kwenye kona 1 - Matchstick heads are orientated correctly vichwa vya njiti vimeelekezwa sawa Total number of points */ Jumla ya alama* ___/3	Total number of points */ Jumla ya alama* ___/3 *ONLY ENTER BEST SCORE ON MATCHSTICK TEST HERE*
Repeat matchstick task allowing the patient to see the design above as they make the shape Rudia njiti ukimpa mgonjwa aone muundo huu hapa juu wakati akitengeneza umbo Total number of points */Jumla ya alama* ___/3		
Total points:		/15

Does the person have visual impairment which has prevented him/her from scoring? YES / NO
Je mtu uliyemwona ana shida ya kuona iliyomfanya asiweze kukamilisha zoezi

Does the person have hearing impairment which has prevented him/her from scoring YES / NO
Je mtu uliyemwona ana shida ya kusikia iliyomfanya asiweze kukamilisha zoezi

Start time.....Finishing time.....

16. Development and internal validation of the IDEA six-item cognitive screen for Africa (supplementary paper 5)

The IDEA six-item cognitive screen was developed from data collected during the 2010 prevalence study of dementia in Hai (supplementary papers 1, 2 and 3). All cognitive assessment data collected during the screening phase of the study, were analysed with the aim of selecting those items most predictive of dementia in this setting. Data were therefore available for 296 individuals aged 70 and over seen and fully clinically assessed for dementia during the second phase of the study. Available data included all items from the CSI-D and also the 10/66 adaptation of the CERAD 10 word learning list. The drawing items included in the CSI-D (drawing interlocking circles and interlocking pentagons) were not included in analysis as the vast majority of individuals had either refused to attempt this task or failed in completion of it. Subjective feedback from health workers conducting the screening had been that many individuals stated it was the first time they had been asked to use a pencil.

Two methods of scale development were used, Mokken scale analysis (MSA) based on Item Response Theory (IRT), and a combination of factor analysis and logistic regression. The model was developed using 80% of the available data, with cases selected at random, and internally validated on the remaining 20% of cases in order to avoid overfitting. The preferred model used the second method. This model demonstrated the best performance on internal validation (AUROC 0.871 vs 0.786 for the MSA-based model). Although MSA is a frequently-used method for scale development, in cognitive assessment for dementia it presents some difficulty. MSA assumes an underlying latent trait, and is a hierarchical method, assuming hierarchical levels of difficulty amongst items. This may work well in assessment of items assumed to have a hierarchical difficulty scale, such as questions in an exam grading level of knowledge, but may not work so well in a condition such as dementia. Dementia is a syndrome, and especially in this environment, screening tools are required to identify individuals who may have disparate cognitive deficits. Attempting to identify one underlying latent trait of ‘cognitive impairment’ may not be an effective strategy, particularly when attempting to identify individuals with differing dementia subtypes.

In order to increase generalisability, and to ensure that a more comprehensive cognitive assessment took place, one further test of praxis and visuoconstruction was added. The data available for modelling and internal validation was lacking in this regard, since the CSI-D assesses this cognitive domain through drawing, and this task had had to be removed from analysis due to non-completion by a large proportion of participants. The item added was a matchstick construction task selected from the Stick Design Test, a test of praxis validated in a low-literacy setting in Nigeria. The shape

selected (rake) was the most discriminating between dementia and 'no dementia' in published validation data related to this task. Performance of the modelled 6 item screen on internal validation is illustrated below in Figure 10 Internal and pilot validation of IDEA six-item screen*Figure 10*. Interestingly, the brief CSI-D, developed and internally validated using a similar process of modelling screening data from the 10/66 international collaboration did not work well in our cohort. The reasons for this are not clear, although the educational level in our cohort was lower than that of most sites included in the 10/66 collaboration as mentioned previously.

17. Pilot external validation of IDEA six-item screen and feasibility study (supplementary paper 5, cohort 1a)

17.1. Pilot external validation (cohort 1a)

The IDEA screen was piloted in a cohort of 60 individuals aged 70 and over. Half of these (30 individuals) were identified during the 2010 dementia prevalence study as meeting mild cognitive impairment (MCI) international consensus criteria after case discussion with a UK based old age psychiatrist. This cohort were followed up at home annually for four years, and this pilot evaluation took place two years after baseline assessment. Additional control participants (30) were recruited through random selection of individuals rated cognitively normal on initial screening with the CSI-D in 2010. Absence of major cognitive impairment was verified by repeat CSI-D screening and only those in the CSI-D 'low probability' group were included as controls. The IDEA screen was administered by a nurse or clinical officer, in participants' own homes and blind to the outcome of clinical assessment and psychiatric diagnosis. Participants were subsequently clinically assessed for the presence of dementia using a protocol similar to that used in the baseline dementia study and including history, mental state examination, bedside cognitive testing, neurological examination and detailed informant history for cognitive or functional impairment.

Prevalence of dementia in the sample was 11/60 (18.3%). Differential diagnosis was challenging, with 12 individuals meeting MCI criteria and two having other mental illness (late onset schizophrenia and depression with psychosis). Diagnostic accuracy of the initial 5-item scale developed through factor analysis and logistic regression was good (sensitivity 81.8%, specificity 71.4%, AUROC 0.867 (0.752-0.982)) at a cut off of 7/12. Addition of the matchstick construction item improved AUROC to 0.888 (0.766-1.00). At a cut off of 7/15, sensitivity was 81.8 and specificity 84.4, and at the higher cut-off of 10/15 sensitivity improved to 90.9 but there was a substantial reduction in specificity to 62.2%.

	AUROC (95% CI)	Maximum Score	Dementia Cutoff	Sensitivity, %	Specificity, %
Validation data set (n = 60)					
5-Item instrument	0.871 (0.768-0.975)	12	≤7	91.7	61.7
7-Item instrument	0.786 (0.648-0.925)	9	≤6	91.7	38.3
CSI-D cognitive section	0.847 (0.714-0.980)	33	≤21	88.9	64.9
Brief CSI-D	0.792 (0.637-0.947)	9	≤6	91.7	42.6
Fieldwork testing data set (n = 60)					
5-Item instrument	0.867 (0.752-0.982)	12	≤7	81.8	71.4
Matchstick design item	0.842 (0.708-0.977)	3	≤1	90.9	77.8
6-Item IDEA study instrument	0.888 (0.766-1.000)	15	≤7	81.8	84.4
			≤10	90.9	62.2

Abbreviations: AUROC, area under the receiver–operating characteristic; CSI-D, community screening instrument for dementia; IDEA, Identification and Intervention for Dementia in Elderly Africans.

Figure 10 Internal and pilot validation of IDEA six-item screen

18.Summary and research questions

In summary, the IDEA six-item cognitive screen developed through modelling appeared to have substantial advantages in terms of face validity for dementia screening in this setting. Use of the screen by non-specialist workers in community settings appeared feasible, and the screen appeared accurate in identification of dementia based on pilot data and a small sample. Further refinement and testing appeared useful considering the current lack of alternative cognitive screening tools validated in this setting, and the shortcomings of existing tools validated in low-literacy settings.

18.1. Research questions

1. What is the clinical effectiveness of the IDEA six item cognitive screen as a screening tool for dementia in hospital inpatient, outpatient and community settings in sub-Saharan Africa?
2. Is the IDEA six-item cognitive screen educationally biased in these settings?
3. How might we identify functional impairment as a result of cognitive impairment to assist with dementia diagnosis in sub-Saharan Africa?
4. Can we improve upon the accuracy of cognitive screening using the IDEA six-item screen by adding a culturally appropriate measure of functional ability?
5. What is the clinical effectiveness of the IDEA six-item cognitive screen for identification of delirium in hospital inpatient settings in Tanzania?
6. What might be the most effective method of screening for delirium in older hospitalised adults in sub-Saharan Africa taking into account the lack of access to specialist clinicians in this setting?

Part Two

Validation of the IDEA six-item cognitive screen

Key paper 1

(Initial validation for major cognitive impairment in older hospital inpatients and outpatients)

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RESEARCH ARTICLE Open Access

Validation of the Identification and Intervention for Dementia in Elderly Africans (IDEA) cognitive screen in Nigeria and Tanzania

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Abstract

Background: We have previously described the development of the Identification and Intervention for Dementia in Elderly Africans (IDEA) cognitive screen for use in populations with low levels of formal education. The IDEA cognitive screen was developed and field-tested in an elderly, community-based population in rural Tanzania with a relatively high prevalence of cognitive impairment. The aim of this study was to validate the IDEA cognitive screen as an assessment of major cognitive impairment in hospital settings in Nigeria and Tanzania.

Methods: In Nigeria, 121 consecutive elderly medical clinic outpatients reviewed at the University College Hospital, Ibadan were screened using the IDEA cognitive screen. In Tanzania, 97 consecutive inpatients admitted to Mawenzi Regional Hospital (MRH), Moshi, and 108 consecutive medical clinic outpatients attending the geriatric medicine clinic at MRH were screened. Inter-rater reliability was assessed in Tanzanian outpatients attending St Joseph's Hospital in Moshi using three raters. A diagnosis of dementia or delirium (DSM-IV criteria) was classified as major cognitive impairment and was provided independently by a physician blinded to the results of the screening assessment.

Results: The area under the receiver operating characteristic (AUROC) curve in Nigerian outpatients, Tanzanian outpatients and Tanzanian inpatients was 0.990, 0.919 and 0.917 respectively. Inter-rater reliability was good (intra-class correlation coefficient 0.742 to 0.791). In regression models, the cognitive screen did not appear to be educationally biased.

Conclusions: The IDEA cognitive screen performed well in these populations and should prove useful in screening for dementia and delirium in other areas of sub-Saharan Africa.

Keywords: Dementia, Delirium, Screening, Nigeria, Tanzania, Africa, Validation

Background

The prevalence of dementia, alongside other non-communicable diseases (NCDs), is increasing rapidly as populations age globally, with 135.5 million people expected to have dementia by 2050 [1]. The greatest increases are predicted in low- and middle-income countries (LMICs) with 71% of the global total of people with dementia residing in LMICs by 2050 [1]. In sub-Saharan Africa (SSA) the number of cases of dementia is expected to increase from 1.31 million in 2013 to 5.05 million by 2050 [1]. Identification of dementia and other major cognitive impairments in LMICs can be problematic, due to the lack of culturally appropriate validated screening tools. The vast majority of cognitive screening tools in common use worldwide have been developed and validated in high income countries (HIC) and usefulness in LMIC settings is greatly limited by cultural and educational differences. Illiteracy is highly prevalent in older adults in many LMICs, particularly in rural areas. Minimising educational bias in cognitive screening tools would improve their clinical utility. In SSA, perhaps more than in other LMIC settings, this problem is compounded

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by a serious shortage of specialist clinicians including neurologists, geriatricians and psychiatrists [2,3]. There are 200 times fewer qualified mental health workers per 100,000 population in SSA compared to HICs [4]. One way to overcome this problem is to develop and validate cognitive screening tools suitable for use by non-specialist healthcare workers and clinicians. These tools must be brief, simple to use and have excellent predictive properties. This task-shifting approach is recommended by the World Health Organization (WHO) for other mental and neurological conditions in low-resource settings [5]. We have recently described the development, internal validation and fieldwork testing of the Identification and Interventions for Dementia in Elderly Africans (IDEA) study cognitive screening tool [6]. This screening tool was developed using data collected from 1198 older adults screened for dementia in rural Tanzania, a low-literacy setting. It was subsequently piloted in a follow up cohort with relatively high levels of cognitive impairment. The aim of the current study was to externally validate the IDEA cognitive screen for use in a cohort of older adults in hospital settings in Nigeria and Tanzania.

Methods

This current study took place as part of the larger IDEA study of dementia in SSA. In Nigeria, the study was approved by the University of Ibadan and Oyo state Ministry of Health research ethics committees. In Tanzania, the study was approved nationally by the National Institute for Medical Research, and locally by Kilimanjaro Christian Medical University College. Written informed consent was obtained from each participant. We obtained a thumbprint for those that could not read or write after the purpose and implications of the study were verbally explained. In cases where patients were unable to give informed consent due to cognitive deficit, written assent was obtained from a close relative.

Participants and setting

Nigerian cohort

Outpatient sample Participants were geriatric patients, aged 65 years and over, seen at the medical outpatient clinic of University College Hospital Ibadan (UCH) during May 2013. UCH is an 850-bed teaching hospital in the city of Ibadan, Oyo state, western Nigeria. The city has a population of approximately 3 million people. Patients were included if they consented to participate and were 65 years or older.

Tanzanian cohort

Mawenzi Regional Hospital (MRH) in Moshi is a government hospital with approximately 200 beds and provides care for around 300 outpatients per day. The hospital serves an urban and rural population of around 100,000 people. Those requiring more specialist services are referred to Kilimanjaro Christian Medical Centre, a tertiary referral hospital in Moshi.

Outpatient sample

Outpatients were recruited from the geriatric medicine outpatient clinic at MRH. The geriatric clinic offers a free-of-charge service for those able to demonstrate that they are aged 60 years or over, usually with a letter from their village committee. All attendees at the clinic aged 65 years or over were invited to take part. Screening was conducted daily for a four-week period during October and November 2013. Screening did not take place on public holidays and weekends, as the clinic was closed. Due to resource limitations, a stratified sample of outpatients were clinically assessed. A full clinical assessment of all those scoring ≤ 8 on the IDEA screen was completed. A score of ≤ 7 was considered the optimal cut-off for detection of major cognitive impairment, but the higher cut-off was chosen to try to ensure high sensitivity. We aimed to clinically assess a random selection of at least 40% of those who scored > 8 on the screen. Randomisation involved drawing lots.

Inpatient sample

All admissions to the medical wards of MRH aged 65 years and over, from 8th October to 20th December 2013 were invited to take part in the study. The ward admission records were consulted daily and a physical check was made of all wards for new admissions. Patients were excluded if they refused to participate, or if the assessing clinician felt they were too unwell to participate.

Inter-rater reliability

This was carried out in the outpatient clinic of St Joseph's Catholic Mission hospital in Moshi, Tanzania. St Joseph's was chosen for the assessment of inter-rater reliability to ensure that all patients were previously unknown to the raters, thus avoiding the possibility that their scores could be influenced by prior information. All outpatients aged 65 years and over were invited to take part. Screening was carried out by three trained raters (AK, SM or JK), randomly coded A, B and C. To minimise the confounding influence of a training effect, rater A and rater B were each randomly assigned to see half of the patients on the first assessment and the other half on the second assessment. The third assessment was completed by rater C. For the third assessment, not all patients could be followed up due to having been discharged from the clinic. A minimum gap of two days was left between consecutive assessments to minimise carryover effects. Assessments were timed, where possible, to coincide with existing outpatient appointments

in order to avoid additional unnecessary travel for participants, some of whom were frail.

Assessments

At both sites, basic demographic data (age, gender and highest education level) were collected from each participant. In both countries, birth registration is not universal, and many older people do not know their date of birth. Where age was not accurately known, a validated method of estimation based on significant past events was used [7]. The method has been shown to have excellent concordance during validation work in other SSA populations (intra-class correlation coefficient (ICC) 0.87).

Cognitive screening

The IDEA cognitive screen has six items derived from existing cognitive assessments used in LMIC [6]. The screen is shown in Figure 1. Items 1–4 are taken from the Community Screening instrument for Dementia (CSI-D) [8]. These involve being able to name a bridge from a description of its use, knowing the day of the week, knowing the name of the village chief/ town mayor/ city governor and naming as many animals as possible in one minute (score 2 for ≥ 8 animals, score 1 for 4–7 animals, score 0 for 0–3 animals). Item 5 is taken from Consortium to Establish a Registry for Alzheimer's Disease (CERAD) 10-word recall test [9], with recall of 10 common words after 5 minutes delay (score 1 point for each word up to a maximum of 5 points). The sixth item is designed to measure praxis and involves a matchstick design test originally developed by Baiyewu et al. [10], with scores ranging from 0 (no matchsticks placed correctly), to 3 (all four matchsticks placed correctly in the shape of a rake). The maximum possible score is 15 and the minimum 0, with a higher score indicating better cognitive function. The IDEA screen therefore includes delayed recall, orientation, two measures of frontal lobe function, verbal fluency and abstract reasoning, praxis and long-term memory. An assessment of ability for new learning is also possible from performance on the 10-word learning list. No items are included requiring reading, writing, drawing or calculation in order to reduce possible educational bias. The screen was administered in the local language (Yoruba in Nigeria, Swahili or Chagga in Tanzania) with the words from the 10-word list translated into the local equivalent.

In Nigeria, the cognitive screen was administered by a study nurse, prior to formal assessment for cognitive impairment by a doctor. The nurse was therefore blind to the clinical diagnosis at the time of assessment. In Tanzanian inpatients and outpatients, the cognitive screen was completed by one of three assessors: an MSc qualified nurse (AK), occupational therapist (GM) or assistant medical officer (JK). As in Nigeria, to ensure blinding, cognitive screening was conducted prior to clinical assessment by a doctor. After administration, all screening tools were filed and not seen by the doctor completing cognitive and neurological assessment.

Clinical assessment

At both sites, participants were assessed clinically for major cognitive impairment. A focused neurological examination, further physical examination (where appropriate) and informant history including usual level of functioning were completed wherever possible. Clinical assessment included bedside cognitive screening designed to cover all major cognitive domains, including orientation, registration and delayed recall, attention and concentration, receptive and expressive language, praxis and frontal lobe function using Luria's three-step hand position test. A formal mental state examination with completion of the geriatric depression scale (in order to exclude psychiatric disorder as a cause of poor cognitive performance), neurological examination and careful questioning of informants on history and instrumental activities of daily living (IADLs) appropriate to the setting in order to assess functional impairment were also completed. Due to the lack of validated appropriate cognitive screening tools in our setting, greater weight was placed on the informant history and psychiatric and neurological examination than the outcome of bedside cognitive assessment when reaching a clinical diagnosis.

In inpatients, the Confusion Assessment Method (CAM) was completed where there was evidence of cognitive impairment. Care was taken to ensure that the assessing doctor remained blinded to the outcome of screening when completing the clinical assessment.

Diagnosis of major cognitive impairment

After interview and assessment, a diagnosis of major cognitive impairment was provided as appropriate by the study doctor at each site (AO and LO in Nigeria and S-MP in Tanzania). Diagnoses of dementia, delirium and other significant mental illness, where present, were based on DSM-IV criteria [11]. Informant histories were extremely useful in attempting to differentiate between dementia and delirium and these were sought wherever possible, by telephone if necessary. In cases of diagnostic difficulty, cases were discussed with a specialist in old age psychiatry and a consensus on the most likely clinical diagnosis reached. Anyone with a diagnosis of dementia or delirium was identified as having major cognitive impairment.

Sample size

For multivariable analysis, a sample size was chosen that would avoid over-fitting the model. Although estimates vary, a minimum of seven cases per predictor was deemed

Preparation for ten-word list item (Question 5)

I am going to read out a list of words. Please listen carefully and I will ask you to repeat them back to me once I have finished (read out the words slowly).

First attempt: Now tell me all the words you can remember (tick on the grid the words remembered)

Second attempt: Now I will read out the words again, listen carefully and I will ask you to repeat as many as you can. Now tell me all the words you can remember (tick on the grid the words remembered)

Third attempt: Now I will read out the words one last time, listen carefully and I will ask you to repeat as many as you can. Now tell me all the words you can remember (tick on the grid the words remembered).

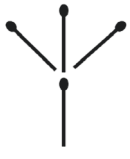
	First attempt	Second attempt	Third attempt
Butter			
Arm			
Letter			
Queen			
Ticket			
Grass			
Corner			
Stone			
Book			
Stick			
1	I will tell you the name of something and I want you to describe what it is. What is a bridge? (*correct answer: something that goes across a river, canyon or road*)	**0** if incorrect **2** if correct	Score:____/2
2	I want you to name as many **different** animals as you can in one minute.	Number of animals named:____ **0** for 0–3 animals named **1** for 4–7 animals named **2** for 8 or more animals named	Score: ____/2
3	Who is the chief/head/leader of this village?	**0** if incorrect **1** if correct	Score:____/1
4	What day of the week is it?	**0** if incorrect **2** if correct	Score:____/2
5	Can you tell me the ten words we learned earlier? Try to remember as many as you can.	**0** for no words remembered **1** for 1 word **2** for 2 words **3** for 3 words **4** for 4 words **5** for 5 or more words	Score:____/5
6	Can you make the design shown below using these four matchsticks. I will show you once and then you have to copy exactly *The examiner should make the design first using the matchsticks and specifically point out to the person that the heads of the matchsticks all need to point the same way. Once the examiner has made the shape, collect up the matchsticks and place them in front of the person being interviewed.* 	Score **1** for each part of the design that is performed correctly **1** Middle two matchstick heads pointing same way **1** Outside two matchsticks pointing at an angle **1** Matchstick heads are orientated correctly	Total number of points:____/3
			Total Score:___/15

Figure 1 The IDEA cognitive screen in English.

acceptable. Any model was thought unlikely to contain more than eight predictor variables, and so a minimum sample size for each cohort of 56 was calculated.

Statistical methods

Statistical analysis was conducted using IBM SPSS statistics version 21 (IBM corporation, Armonk, NY, USA). All data (including age) were not normally distributed and so non-parametric tests (Mann–Whitney U test and chi-squared test) were used. For data analysis, education was dichotomised into some education (attended school) and no education (never attended school). Sensitivity, specificity and likelihood ratio (LR) were calculated. Positive predictive value (PPV) was calculated for Nigerian outpatients and Tanzanian inpatients, but not for Tanzanian outpatients. Since not all screened Tanzanian outpatients were clinically assessed, prevalence, and therefore an accurate PPV, could not be estimated. The area under the receiver operating characteristic (AUROC) curve was used as an overall measure of the performance of the IDEA cognitive screen. Cronbach's α was calculated to assess the consistency of the screen.

We used regression modeling to investigate whether the IDEA cognitive screen was educationally biased. Major cognitive impairment becomes more common with increasing age and is thought to be more common in women than men and more common in those with no formal education [12,13]. However, these three variables are also confounded with each other, with women tending to be overrepresented in older age groups and, in many areas of SSA, less likely to have attended school than men. To assess the independent influence of age, gender and education on screening performance, univariate and multivariable logistic regression models were developed with screening tool score (dichotomised into ≤ 7 and > 7) as the dependent (outcome) variable. Age, gender, education and the presence of major cognitive impairment were forced into a multivariable model as independent (predictor) variables. Univariate models were initially investigated within each of the three cohorts separately. Given the similarity in the results of the univariate analysis, and to increase statistical power, multivariable models were constructed using the combined data from all three cohorts. Education was dichotomised as no formal education or some formal education and age was split into five-year age bands. Inter-rater reliability was assessed using the ICC and by comparing the level of agreement in terms of clinical decision-making. The significance level was set at 5% and two-tailed tests were used throughout.

Results

In Tanzania, 97 inpatients were seen, of whom 33 (34.0%) had major cognitive impairment (20 dementia, 13 delirium). Of 108 outpatients seen in Tanzania, 16 (14.8%) scored ≤ 8 and all were clinically assessed. Of the remaining 92 who scored > 8, 43 (46.7%) were randomly selected for clinical assessment, giving a Tanzanian outpatient cohort of 59, of whom 13 (22.0%) had major cognitive impairment. All 13 had dementia, though one person with dementia was also thought to have delirium at the time of assessment and was referred for further investigations. In Nigeria, data were available for 121 outpatients, of whom 12 (9.9%) had major cognitive impairment (all dementia).

Thus, 277 were included in this validation study across all three settings. The median time taken to complete the screen was 10 minutes (inter quartile range: 8 to 12 minutes).

Demographic data

Age, gender and education level data for those with and without major cognitive impairment are presented in Table 1. In Nigeria, those with major cognitive impairment had significantly higher levels of education than those without major cognitive impairment and in Tanzanian outpatients, those with major cognitive impairment were significantly older than those without major cognitive impairment.

Performance of the IDEA cognitive screen

Cronbach's α for the IDEA cognitive screen was 0.807 in Tanzanian inpatients, 0.738 in Tanzanian outpatients and 0.741 in Nigerian outpatients, suggesting it to have an acceptable degree of internal consistency in all three settings.

AUROC curves for each cohort are presented in Figure 2. Across all three settings no one with major cognitive impairment scored more than 10, and only eight scored greater than the suggested cut off of ≤ 7 (three Tanzanian outpatients and one Tanzanian inpatient scored 8, one Tanzanian outpatient scored 9 and one Tanzanian outpatient and two Tanzanian inpatients scored 10). Of 15 people without major cognitive impairment who scored ≤ 7, three had mild cognitive impairment (MCI) and five were aphasic or unable to perform well due to physical or mental illness. Sensitivity, specificity, PPV, LR and AUROC curve data, are shown in Table 2. The AUROC curve was above 0.9 in all settings.

The influence of age, gender and education on IDEA cognitive screen performance

Univariate logistic regression models investigating the influence of age, gender, education and the presence of major cognitive impairment on screening performance (outcome variable) are summarised in Table 3. Major cognitive impairment was associated with a cognitive screening score ≤ 7 in all three cohorts, with age as an additional correlate in Tanzanian inpatients. In multivariable

Table 1 Validation of the Identification and Intervention for Dementia in Elderly Africans (IDEA) cognitive screen in 2013: Demographic data

	Major cognitive impairment	No major cognitive impairment	Significance of difference
Outpatients Nigeria			
Number of patients	12	109	
Median age (IQR)	71 (65.3 to 77.5)	70 (67 to 75.5)	U = 619.0, z = −0.305, p = 0.761
Number of females	8 (66.7%)	49 (45.0%)	$\chi^2 = 2.045$, p = 0.153
Level of education*	None: 0	None: 36 (33.0%)	$\chi^2 = 5.619$, p = 0.018
	Some: 11 (91.6%)	Some: 67 (61.5%)	
	Not known: 1 (8.3%)	Not known: 6 (5.5%)	
Outpatients Tanzania			
Number of patients	13	46	
Median age (IQR)	79.5 (73.3 to 89.8)	72 (67.3 to 78.8)	U = 162.5, z = −2.030, p = 0.042
Number of females	7 (53.8%)	21 (45.7%)	$\chi^2 = 2.045$, p = 0.153
Level of education	None: 5 (38.5%)	None: 11 (23.9%)	$\chi^2 = 0.273$, p = 0.601
	Some: 8 (61.5%)	Some: 35 (76.1%)	
Inpatients Tanzania			
Number of patients	33	64	
Median age (IQR)	78 (72.5 to 90)	75.5 (70.3 to 81)	U = 846.0, z = −1.601, p = 0.109
Number of females	14 (42.4%)	37 (57.8%)	$\chi^2 = 2.068$, p = 0.150
Level of education	None: 15 (45.5%)	None: 22 (34.4%)	$\chi^2 = 1.407$, p = 0.236
	Some: 17 (51.5%)	Some: 42 (65.6%)	
	Not known 1 (3.0%)		

IQR = interquartile range.
U = the test value of the Mann–Whitney U test.
* For data analysis education was dichotomised into some education (attended school for at least a year) and no education (never attended school).

analysis, with data for all three cohorts combined (n = 277), female gender, greater age and the presence of major cognitive impairment were independent predictors of low screening score, but education was not, see Table 4. Even after removing gender and age from the model, education level remained a non-significant predictor.

Inter-rater reliability

For inter-rater reliability assessment, 30 patients were seen by raters A and B and 19 by rater C. The median time from the first to the second assessment was 3 days (IQR 2 to 4 days) and the median time from the second to the third assessment was 5 days (IQR 4 to 8 days).

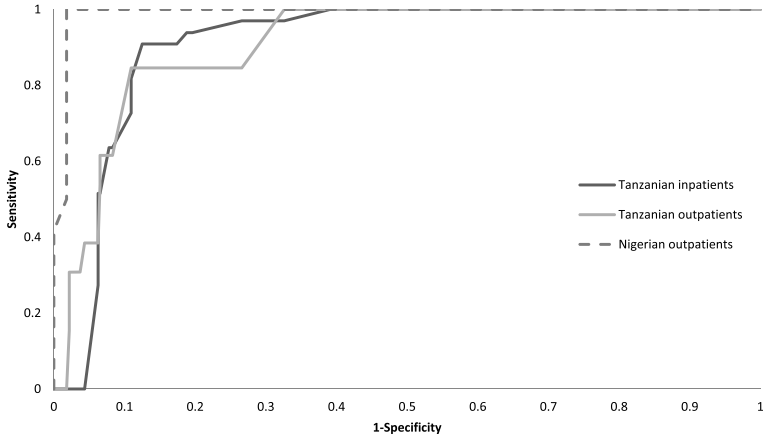


Figure 2 Validation of the Identification and Intervention for Dementia in Elderly Africans (IDEA) cognitive screen in 2013: ROC curves for each cohort.

Table 2 Validation of the Identification and Intervention for Dementia in Elderly Africans (IDEA) cognitive screen in 2013: Sensitivity, specificity, LR and PPV

	Nigerian outpatients	Tanzanian outpatients	Tanzanian inpatients
AUROC curve	0.990	0.919	0.917
Cut-off of ≤ 7	100% sensitivity	61.5% sensitivity	90.9% sensitivity
	96.3% specificity	93.5% specificity	87.5% specificity
	27.0 LR	9.5 LR	7.3 LR
	75.0% PPV	-	78.9% PPV
Cut-off of ≤ 8	100% sensitivity	84.6% sensitivity	93.9% sensitivity
	91.7% specificity	89.1% specificity	81.3% specificity
	12.0 LR	7.8 LR	5.0 LR
	57.1% PPV	-	72.1% PPV

AUROC = area under the receiver operating characteristic.
PPV = positive predictive value.
LR = likelihood ratio.

The level of agreement between the raters was good. Comparing raters A and B, the ICC was 0.791. For the 19 patients seen by rater C, the ICC was 0.787 compared to rater A and 0.742 compared to rater B. The differences in scores between raters were generally small. Comparing the first two raters, 20 assessments (66.7%) were within one point of each other and 27 (90.0%) within two points of each other. Using ≤ 7 as a cut-off, raters A and B agreed, and would have made the same clinical decision for 28 (93.3%) cases. Likewise, raters A and B agreed on 18 (94.7%) cases, with 13 (68.4%) scores within one point of each other and 18 (94.7%) within two points. Finally, raters A and C agreed on 17 (89.5%) cases, with 15 (78.9%) within one point of each other and 17 (89.5%) within two points.

Discussion

The IDEA cognitive screen performed well in all three settings, with good internal consistency and inter-rater reliability. The AUROC curve was generally higher than seen during internal validation and fieldwork testing in Tanzania [6]. The screen appeared to be acceptable and culturally appropriate and no one refused assessment.

The sensitivity in Tanzanian outpatients was relatively low, although lower sensitivity in outpatients was expected in this setting. In rural Tanzania, people who have dementia, and who are able to attend outpatient clinics, are likely to be in the early stages of disease. They may therefore be expected to perform relatively well on brief cognitive screening, with the presence of dementia only becoming apparent on more detailed assessment. It is not clear why the screen performed better in Nigerian outpatients than in Tanzanian outpatients. The fact that UCH in Ibadan is a tertiary referral hospital may have played a part, with a broader spread of patients including those with more severe problems, who may be easier to assess cognitively. Further validation work in other settings in Nigeria is merited.

The IDEA cognitive screen performed well in comparison with other major cognitive impairment screening instruments developed for use in populations with low levels of formal education [14,15]. Touré et al. [14] developed the 'Test of Senegal' and obtained an AUROC curve of 0.967 on comparison with the DSM-IV-R criteria when blind assessment of 58 cases and 58 controls was carried out. However, the test has 39 questions in total and is therefore too lengthy for use in busy non-specialist hospital settings.

The performance of the IDEA cognitive screen also compares well to tests of cognitive performance validated in HICs [16,17]. The six-item screener comprises three orientation questions and a three-word delayed recall test. It was developed for use in emergency departments and has a sensitivity of 63%, a specificity of 81% and an AUROC curve of 0.77 [18]. The mini-cog comprises a clock-drawing test and a three-word delayed recall test; it has a sensitivity of 75% and specificity of 85% [19]. The general practitioner assessment of cognition (GPCOG) combines the clock-drawing test with items assessing recall and orientation; its sensitivity was 85% and specificity 86% [20]. A review of other brief screening instruments was carried out in 2007 [21].

UK and US good practice guidelines recommend cognitive assessment of older adults in higher-prevalence settings including primary care, and routinely in hospital inpatient and outpatient populations [22]. The existing evidence base strongly suggests that identification of cognitive impairment can improve outcomes and reduce morbidity and mortality through prevention of delirium [23]. Cognitive screening should form a core part of assessment for older hospitalised adults. Surprisingly, even in HICs few of the recommended cognitive screening tools have been validated in general hospital settings

Table 3 Validation of the Identification and Intervention for Dementia in Elderly Africans (IDEA) cognitive screen in 2013: Univariate logistic regression models with dichotomised cognitive screen as the dependent (outcome) variable

	Odds ratio (95% CI)
Nigerian outpatients	
Major cognitive impairment present*	-
Female	2.82 (0.92 to 8.69)
No formal education	3.11 (0.67 to 14.58)
Age	
65-69 years	1
70-74 years	1.03 (0.27 to 3.98)
75-79 years	1.88 (0.47 to 7.51)
80-84 years	0.68 (0.07 to 6.26)
85 years and over	1.88 (0.18 to 19.68)
Tanzanian outpatients	
Major cognitive impairment present	22.93 (4.55 to 115.67)
Female	2.25 (0.58 to 8.72)
No formal education	2.80 (0.72 to 10.97)
Age	
65-69 years	1
70-74 years	6.75 (0.61 to 75.27)
75-79 years	4.00 (0.32 to 50.23)
80-84 years	6.00 (0.46 to 78.56)
85 years and over	7.71 (0.68 to 87.25)
Tanzanian inpatients	
Major cognitive impairment present	70.00 (17.28 to 283.59)
Female	1.00 (0.44 to 2.27)
No formal education	1.99 (0.86 to 4.64)
Age	
65-69 years	1
70-74 years	4.57 (0.83 to 25.21)
75-79 years	4.31 (0.76 to 24.38)
80-84 years	7.00 (1.17 to 41.76)
85 years and over	14.00 (2.54 to 77.21)

* An odds ratio cannot be calculated due to zero values. Only four subjects, from the 121 in the cohort, were misclassified, all identified as positive on screen, but negative on clinical assessment.

[24]. Validation of appropriate cognitive screening methods for hospitalised older adults is therefore needed globally, not only in SSA.

Limitations

The main limitation of our study is the relatively small number of people in each cohort who had major cognitive impairment. However, the overall number of people with major cognitive impairment (n = 58) was relatively large and results were similar across all settings, allowing data to be combined for multivariable analysis. Any attempt to increase the number of major cognitive impairment cases by assessing only people previously known to have dementia and a group of controls would have reduced the generalisability of our results and may have resulted in substantial bias.

Table 4 Validation of the Identification and Intervention for Dementia in Elderly Africans (IDEA) cognitive screen in 2013: Multivariable logistic regression model with dichotomised cognitive screen as the dependent (outcome) variable

	Odds ratio (95% CI)	Significance (p)
Major cognitive impairment present	108.82 (36.31 to 326.14)	<0.001
Female	3.32 (1.20 to 9.19)	0.021
No formal education	1.07 (0.40 to 2.88)	0.895
Age		
65-69 years	1	
70-74 years	3.26 (0.83 to 12.74)	0.090
75-79 years	3.52 (0.87 to 14.31)	0.079
80-84 years	5.39 (1.05 to 27.68)	0.044
85 years and over	6.80 (1.58 to 29.21)	0.010

Hosmer and Lemeshow goodness of fit test, χ^2 (7) = 5.60, p = 0.587. Nagelkerke R^2 = 0.66.

In this hospital-based study, we did not attempt to distinguish patients with delirium from those with dementia. It is not expected that a short screen will be able to distinguish such conditions. The value of carrying out screening is to alert the clinician to cognitive impairment meaning that delirium can be promptly recognised and treated, and possible dementia considered in hospital discharge planning. Without an informant history and follow-up it is difficult to be certain that dementia is present in hospital patients. Despite multiple attempts, it was not always possible to obtain a history from a close relative. Those patients who had a carer tended to be younger and more independent, and were probably less likely to have cognitive impairment. Occasionally carers were distant relatives who were less able to give a detailed history. In the Tanzanian sample, patients who were seriously unwell, and were felt to need admission to the tertiary referral hospital, were transferred, and this is again likely to have led to an underestimate of cases of delirium. In the outpatient settings, resource limitations meant that it was not possible to see all screened patients. However, almost half of those who screened negatively were randomly selected for clinical assessment and any bias is likely to be small. Finally, few people had a birth certificate or had had their birth registered and so a validated method of age estimation was used. The method has been shown to have excellent concordance

during validation work in other populations in SSA and we feel that, at a cohort level, any bias will be small.

Conclusions

The IDEA cognitive screen was administered by non-specialist healthcare workers and performed well in hospital settings in Nigeria and Tanzania. Further testing in other regions of SSA, and in primary care, is an important next step.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

S-MP conducted the literature search, collected data in Tanzania, analysed the data, interpreted the results and wrote the first draft. WKG designed the study, conducted the literature search, analysed the data, interpreted the results and wrote the first draft. LO collected data in Nigeria. BI collected data in Nigeria. OO collected data in Nigeria. AK collected data in Tanzania. GM collected data in Tanzania. JK collected data in Tanzania. SM collected data in Tanzania. CLD designed the study, analysed the data and interpreted the results. RWW designed the study and interpreted the results. DM designed the study. CC collected data in Tanzania. AO designed the study, collected data in Nigeria and interpreted the results. All authors read, critically reviewed and approved the final manuscript.

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References

1. Prince M, Guerchet M, Prina M. Policy brief for heads of government: the global impact of dementia 2013–2050. London: Alzheimer Disease International; 2013.
2. Dotchin CL, Akinyemi RO, Gray WK, Walker RW. Geriatric medicine: services and training in Africa. Age Ageing. 2013;42:124–8.
3. Bower JH, Zenebe G. Neurologic services in the nations of Africa. Neurology. 2005;64:412–5.
4. Saxena S, Thornicroft G, Knapp M, Whiteford H. Resources for mental health: scarcity, inequity, and inefficiency. Lancet. 2007;370:878–89.
5. Eaton J, McCay L, Semrau M, Chatterjee S, Baingana F, Araya R, et al. Scale up of services for mental health in low-income and middle-income countries. Lancet. 2011;378:1592–603.
6. Gray WK, Paddick SM, Kisoli A, Dotchin CL, Longdon AR, Chaote P, et al. Development and Validation of the Identification and Intervention for Dementia in Elderly Africans (IDEA) Study Dementia Screening Instrument. J Geriatr Psychiatry Neurol. 2014;27:110–8.
7. Paraiso MN, Houinato D, Guerchet M, Agueh V, Nubukpo P, Preux PM, et al. Validation of the use of historical events to estimate the age of subjects aged 65 years and over in Cotonou (Benin). Neuroepidemiology. 2010;35:12–6.
8. Hall KS, Hendrie HC, Brittain HM, Norton JA, Rodgers DD, Prince CS, et al. The development of a dementia screening interview in 2 distinct languages. Int J Methods Psychiatr Res. 1993;3:1–28.
9. Welsh KA, Butters N, Mohs RC, Beekly D, Edland S, Fillenbaum G, et al. The Consortium to Establish a Registry for Alzheimer's Disease (CERAD). Part V. A normative study of the neuropsychological battery. Neurology. 1994;44:609–14.
10. Baiyewu O, Unverzagt FW, Lane KA, Gureje O, Ogunniyi A, Musick B, et al. The stick design test: a new measure of visuoconstructional ability. J Int Neuropsychol Soc. 2005;11:598–605.
11. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed. Washington DC: American Medical Association; 1994.
12. Paddick S-M, Longdon A, Gray WK, Dotchin C, Kisoli A, Chaote P, et al. The association between educational level and dementia in rural Tanzania. Dementia & Neuropsychologia. 2014;8:117–25.
13. Paddick SM, Longdon AR, Kisoli A, Dotchin C, Gray WK, Dewhurst F, et al. Dementia prevalence estimates in sub-Saharan Africa: comparison of two diagnostic criteria. Glob Health Action. 2013;6:19646.
14. Touré K, Coumé M, Ndiaye NND, Thiam MH, Zunzunegui MV, Bacher Y, et al. The test of senegal: a valid and reliable screening tool to assess for dementia in a senegalese elderly population. Afr J Neurol Sci. 2008;27:4–13.
15. Prince M, Acosta D, Ferri CP, Guerra M, Huang Y, Jacob KS, et al. A brief dementia screener suitable for use by non-specialists in resource poor settings–the cross-cultural derivation and validation of the brief Community Screening Instrument for Dementia. Int J Geriatr Psychiatry. 2011;26:899–907.
16. Mitchell AJ. A meta-analysis of the accuracy of the mini-mental state examination in the detection of dementia and mild cognitive impairment. J Psychiatr Res. 2009;43:411–31.
17. Larner AJ, Mitchell AJ. A meta-analysis of the accuracy of the Addenbrooke's Cognitive Examination (ACE) and the Addenbrooke's Cognitive Examination-Revised (ACE-R) in the detection of dementia. Int Psychogeriatr. 2014;26:555–63.
18. Wilber ST, Carpenter CR, Hustey FM. The Six-Item Screener to detect cognitive impairment in older emergency department patients. Acad Emerg Med. 2008;15:613–6.
19. Wilber ST, Lofgren SD, Mager TG, Blanda M, Gerson LW. An evaluation of two screening tools for cognitive impairment in older emergency department patients. Acad Emerg Med. 2005;12:612–6.
20. Brodaty H, Pond D, Kemp NM, Luscombe G, Harding L, Berman K, et al. The GPCOG: a new screening test for dementia designed for general practice. J Am Geriatr Soc. 2002;50:530–4.
21. Woodford HJ, George J. Cognitive assessment in the elderly: a review of clinical methods. QJM. 2007;100:469–84.
22. National Institute for Health and Care Excellence (NICE). Delirium: Diagnosis, prevention and management. London: NICE; 2010.
23. Fong TG, Tulebaev SR, Inouye SK. Delirium in elderly adults: diagnosis, prevention and treatment. Nat Rev Neurol. 2009;5:210–20.
24. Jackson TA, Naqvi SH, Sheehan B. Screening for dementia in general hospital inpatients: a systematic review and meta-analysis of available instruments. Age Ageing. 2013;42:689–95.

19. Commentary on Key Paper 1

Initial validation of the IDEA six-item cognitive screen for identification of major cognitive impairment (delirium or dementia) in hospital settings (Cohorts 2 and 3)

19.1. Overview

This study describes the initial validation of the IDEA six-item screen in two cohorts of individuals treated at a Government hospital in Tanzania. These include a cohort of 97 older individuals assessed on admission to medical wards of the hospital, and a randomised sample of 59 individuals (from 108 screened) presenting for treatment at a dedicated free-of-charge older persons medical clinic at the same hospital. Data are also reported on validation of the six-item screen in a Nigerian outpatient setting in the accompanying paper, but this is not the main focus of this presented work.

19.2. Materials and methods, Tanzanian site

Inpatient validation

Inpatient validation of the IDEA six item screen took place in a consecutive sample of individuals aged 65 and over admitted to the medical wards of Mawenzi Regional Referral Hospital (MRRH) in 2013. It was aimed to assess 100 consecutive admissions over a three month period. All those admitted from 4th October 2013 to the 20th December 2013 were eligible for inclusion in the study. The admission books of both wards were consulted each morning for new admissions from the previous evening, and a check physically made of both wards for new admissions who might not yet have been registered. All new admissions were approached for consent to be included in the study. Signed informed consent was obtained from all participants, with a thumbprint collected from those who were unable to write. Where informed consent was not possible due to mental status at the time of interview, signed informed consent was sought from an accompanying close relative with assent from the participant. All those consenting to take part were then screened for dementia by one of three trained screeners. These included an MSc qualified nurse, occupational therapist and an Assistant Medical Officer. The screening assessment consisted of the IDEA six item screen and demographic data including educational level, literacy and occupation.

On completion of the screening assessment, the completed screening tools were filed in a separate location unseen by the research doctor. All patients were then fully assessed by the research doctor blinded to the outcome of the screening assessment. Clinical assessment took place blinded to the outcome of cognitive screening and included bedside cognitive assessment (registration, delayed recall, orientation, coordination and praxis, comprehension of commands, attention and

concentration and expressive language through use of open questions about changes in the local area (social, environmental, political) from the past to the present day). A focussed mental state examination with further assessment of any issues noted such as suspiciousness or possible psychosis was conducted, alongside a neurological examination focused on signs of Parkinsonism or stroke. All participants were assessed using the Confusion Assessment Method (CAM) to assist in identification of delirium.

A detailed history for cognitive and functional impairment, and dementia risk factors was obtained for all participants from an appropriate informant where possible. The informant questionnaire was an adaptation of a questionnaire used in previous studies in Nigeria, and based on the DSM-IV criteria. This had been revised and agreed by research clinicians in the Tanzanian, Nigerian and UK study sites as part of the development work for the study, and was used to inform a semi-structured informant history but was not used alone to inform diagnosis. An informant interview was always sought, either in person or by telephone if family were unable to visit. Where an informant interview was not possible, but felt to be important in securing a diagnosis, a home visit was attempted. In cases of diagnostic doubt, further discussion with a UK based old age psychiatrist took place. Criterion validity was measured against major cognitive impairment. Dementia, delirium and other mental disorders were diagnosed according to DSM-IV and ICD-10 criteria. The DSM-5 was published four months prior to commencement of the study, but the DSM-IV criteria were used as these were the criteria quoted in the original research proposal and ethical committee application. Mild cognitive impairment (MCI) was diagnosed according to the modified Petersen criteria.

Outpatient validation

Outpatient validation took place in the geriatric outpatient clinic. All individuals aged 65 or over attending the clinic, and present before the cut-off time were eligible for screening. Due to resource limitations a randomised cohort of all those scoring 8 and below, and at least 10% of those scoring 9 or higher randomly selected by drawing lots, underwent blinded clinical assessment following the same format as that detailed for hospital medical inpatients. For those patients attending the clinic without a relative, detailed informant histories were obtained by telephone by a research nurse with training in dementia assessment and history taking from informants.

In both inpatient and outpatient settings, individuals found to have dementia were offered information about dementia and appropriate advice. Those found to meet criteria for another mental disorder, particularly DSM-IV depression or psychotic illness, were referred to the Regional Psychiatric Service (RPS) at MRRH.

19.3. Results

During the study period, 120 patients aged 65 or over were admitted to the inpatient male and female medical wards of MRRH. Of these, 99 were included in our study. 21 were not included (17.5%). Two further participants were excluded from analysis due to having been found subsequently not to have completed the screening tool fully, resulting in a study sample of 97 individuals.

Reasons for exclusion were as follows; 7 (33.3%) were transferred to the regional tertiary hospital KCMC shortly after admission due to illness severity; 3 (14.3%) died before being seen; 7 (33.3%) were discharged before the interview was completed. (This was often unexpected and due to financial and time commitment pressures on family members who were forced to request early discharge). One (4.7%) patient left the ward overnight and did not return, two (9.5%) were recent readmissions and refused to be screened and one (4.7%) was not present on the ward and discharged prior to morning ward round. It was unclear if this occurred with or without medical advice. There were no significant differences in age or gender between those assessed and not assessed. Of those 97 individuals assessed, 33 (34%) were diagnosed with major cognitive impairment (20 DSM-IV dementia and 13 DSM-IV delirium).

Of those 108 outpatients screened, 16 scored 8 or below on the IDEA six-item screen and all were clinically assessed for major cognitive impairment. Of the 92 who scored 9 or above, 43 (46.7%) were randomly selected for second stage assessment. The total randomised sample for the validation study was therefore 59 individuals. Of these, 13 were diagnosed with major cognitive impairment (22%). All of these met dementia criteria, but one participant was felt to have superimposed delirium and was referred for medical admission.

Table 9. Summary of demographic data of those fully assessed as part of validation study

Inpatient	Major CI	No major CI	Significance of difference
Number of patients	33	64	
Median age (IQR)	78 (72.5 to 90)	75.5 (70.25 to 81)	U = 846.0, z = -1.601, p = 0.109
Number of females	14 (42.4%)	37 (57.8%)	$\chi 2 = 2.068$, p = 0.150
Level of education	None: 15 (45.5%) Some: 17 (51.5%) Not known 1 (3.0%)	None: 22 (34.4%) Some: 42 (65.6%)	$\chi 2 = 1.407$, p = 0.236

Outpatient (pilot)			
Number of patients	13	46	
Median age (IQR)	79.5 (73.25 to 89.75)	72 (67.25 to 78.75)	U = 162.5, z = -2.030, p = 0.042
Number of females	7 (53.8%)	21 (45.7%)	$\chi 2 = 2.045$, p = 0.153
Level of education	None: 5 (38.5%) Some: 8 (61.5%)	None: 11 (23.9%) Some: 35 (76.1%)	$\chi 2 = 0.273$, p = 0.601

The initial development work had suggested a screening cut-off of 7 for dementia. No individual with major cognitive impairment scored more than 10 in this study. One outpatient and two inpatient participants scored 10, one outpatient scored 9 and three outpatients and one inpatient scored 8. False positives scoring 7 or below but without major cognitive impairment included three diagnosed with MCI, and five who were aphasic or severely dysphasic or otherwise severely unwell.

Cronbach's Alpha was 0.807 in the inpatient sample and 0.739 in the outpatient sample. This shows an acceptable but not high degree of internal consistency. Since dementia is a syndromal diagnosis, higher values of for internal consistency may not be achievable or even desirable as the screening tool has been designed to pick up a variety of different impairments rather than focussing on memory or one other single construct.

19.4. Strengths and limitations of Key Paper 1

Study design

Previous validation studies of cognitive screening tools in sub-Saharan Africa are very few. Those studies identified in our systematic review (Background Paper 2) validated the Test of Senegal and the Stick Design Test. Both validation studies have methodological difficulties. The Test of Senegal was validated in 58 individuals with dementia and 58 controls in a study using a cross-sectional design. Whilst cross sectional validation study designs are acceptable as stage 1 diagnostic studies, this method results in significant spectrum bias, particularly in a disorder such a dementia where an intermediate category of minor neurocognitive disorder or mild cognitive impairment (MCI) is well recognised. Further validation is required before utility in clinical practice can be evaluated.

The Stick Design Test was validated in a study where the outcome of the screening test formed part of the information used for consensus diagnosis, again resulting in significant bias.

One of the major strengths of this study was that the screening tool was performed blind to the outcome of clinical assessment for dementia, and dementia assessment was performed blind to the outcome of screening tool performance. This therefore avoids the methodological difficulties present in those very few previous studies, and also in a substantial number of other screening tool validation studies conducted in low-literacy settings. Since borderline cases were assessed, this avoids the problem of spectrum bias in stage 1 diagnostic studies. Efforts were made to comprehensively assess study participants, and assessments were informed by previous work and experience by the study team of clinical assessments for dementia in Tanzania.

Clinical Diagnosis

Although a comprehensive assessment was attempted, it was not possible to be certain of underlying dementia in all participants. Follow-up assessments post-discharge were not possible in this cohort due to resource limitations and therefore it was not always possible to exclude underlying dementia in individuals presenting with CAM positive delirium. It is not considered ideal in clinical practice to make a diagnosis of dementia in hospital inpatients, particularly if unwell. Diagnoses were also made by one research doctor (the doctoral candidate) with substantial previous experience of dementia assessment in a similar environment. Difficult or borderline cases were discussed with a specialist in old age psychiatry, but a formal blinded consensus panel diagnosis of dementia was not possible due to lack of follow-up data and other resource issues. For these reasons, this study can only be considered preliminary. Furthermore this study reports validation of the IDEA screen for cognitive impairment, rather than for clearly defined dementia or delirium by standard criteria.

Sampling

There may have been a degree of bias within the inpatient sample, as due to resource issues within the hospital, patients who were more severely unwell, or required specialised diagnostic investigations were transferred elsewhere, usually to the local tertiary referral hospital (KCMC). The sample assessed, although representative of medical inpatients in this government hospital, might not be typical of older hospital inpatients in other settings where tertiary referral services might not be locally available. MRRH is a Government hospital, and charges are made to register at the hospital by opening a file, and for subsequent treatment. Charges are substantially lower than those at private or NGO assisted hospitals, but families are generally responsible for costs of investigations and for purchase of medications although health insurance schemes are growing in popularity. Due to the financial implications of hospital admission, admissions were typically much shorter than expected from clinical practice in the UK. As a result, the time for completion of informant histories

was short, and it was not always possible to obtain a history from the primary carer or nearest relative prior to discharge or transfer. This last point is based upon subjective experience only, since detailed hospital admission and discharge records allowing calculation of median length of stay were not available to the research team, again due to the speed of turnover and nursing resource issues.

Similarly in the outpatient sample, resource issues may have resulted in bias. Although medical treatment was offered free of charge, a number of routine investigations were not available within the hospital, including radiography, electrocardiographs (ECG) and measurement of full blood count (FBC) and blood biochemistry including kidney and liver function. As a result, individuals requiring these investigations were referred to other providers outside the hospital for completion of these. As a result, some participants withdrew consent to take part in the study, or were deemed by the research team to be ineligible to continue since this might delay or otherwise impact clinical care. Those requiring investigations may have been more unwell than those assessed, resulting in a degree of bias in the sample.

19.5. Outcomes and conclusion

This study presented an initial validation of the IDEA six-item screen for major cognitive impairment (dementia or delirium) in hospital settings in Tanzania. The IDEA screen was administered by experienced health professionals of differing clinical backgrounds and a high degree of criterion validity when compared with diagnosis of major cognitive impairment by a research doctor was demonstrated. Although a number of methodological issues are acknowledged and discussed above this study indicated that the IDEA six-item screen had potential as a brief cognitive screening tool for dementia and delirium in hospital settings in Tanzania. There did not appear to be significant educational bias when data were combined with those of the Tanzanian sample. Further validation in a variety of settings was indicated to further examine its clinical utility and also to avoid the issues outlined in the systematic review (Background paper 2) of development and subsequent inadequate validation of screening tools suitable for low-literacy settings. This study also indicated that further work was required with regard to the optimal cut-off score. Initial development work had suggested a cut-off of 7/15 (Supplementary Paper 5) but a cut-off of 8 was used for the randomised sample in hospital outpatients in order to oversample for cognitive impairment.

Table 10. Demographic data for inpatient/outpatient and community samples

Location	n	% female (n. missing)	Age (*= missing) Median, IQR range	Days in hospital Mean, SD	Marital status (n, %) 1.Married 2.Widow/widower 3.Divorced 4.Separated 5.Never married	Household 1.Living alone 2.Living with spouse 3.Living with spouse and others 4.Living with family 5.Other	Literacy n. (%)	Education n. (%)(*=missing) 1= none 2= grade 1-4 3=grade 5-7 4=completed primary 5=completed secondary	Occupation N, %) 1. Agriculture 2. Semi-skilled/ small business 3. Craft/clerical 4. Prof/managerial	Working (n. %)
Inpatient ward	97	51/96 5(3.13) (*=0)	Med 77.0 IQR 12 (65 -111) (*=0)	2.135 (3.227) R. 1-29	1 33 (34.38) 2 58 (60.42) 3 4 (4.17) 5 1 (1.04) (*= 1)	1. 7 (7.37) 2. 3 (3.16) 3. 25(26.32) 4. 59(62.11) 5. 1 (1.05) (*= 2)	59/97 (61.46) (*= 1)	1. 37 (38.54) 2. 42 (43.75) 3. 10 (10.42) 4. 6 (6.25) 5. 1 (1.04) (*= 1)	1 65 (70.65) 2 14 (15.22) 3 9 (9.78) 4 4 (4.35) (*= 5)	17 (18.28%) (*=4)
Outpatient geriatric clinic	107	52/108 (48.6) (*=0)	Med 75.0 IQR 12 (65- 105) (*=3)	n/a	1. 52 (49.5) 2. 45 (42.9) 3. 5 (4.8) 4. 1 (0.95) 5. 2 (1.9) (*= 3)	1. 10 (9.52) 2. 5 (4.76) 3. 37 (35.2) 4. 49 (46.7) 5. 4 (3.8) (*= 2)	78/104 (75.0) (*= 4)	1. 22 (21.15) 2. 49 (47.12) 3. 11 (10.58) 4. 17 (16.35) 5. 3 (2.88) 6. 2 (1.92) (*= 3)	1. 70 (72.92) 2. 10 (10.42) 3. 7 (7.29) 4. 9 (9.38) (*= 12)	48(50%) (*=12)

Community screening programme	472	264/472 55.9% (*=0)	Med 73.0 IQR 12.0 (54 -115)	n/a	n/a	n/a	339/453 74.8% (*=19)	1 87 (19.00) 2 180 (39.30) 3 136 (29.69) 4 46 (10.04) 5 9 (1.97) (*= 14)	n/a (data available only for stage 2 assessment)	n/a (data available only for stage 2 assessment)
Outpatient inter-rater reliability sample	37		Med 71.00 IQR 7.75 (65 – 93)	n/a			32/37 86.5% (*=0)	1 7 (18.92) 2 14 (37.84) 3 5 (13.51) 4 4 (10.81) 5 7 (18.92) (*=0)		

Key Paper 2

Community validation of the IDEA study cognitive screen in rural Tanzania

RESEARCH ARTICLE

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Community validation of the IDEA study cognitive screen in rural Tanzania

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Objectives: The dementia diagnosis gap in sub-Saharan Africa (SSA) is large, partly because of difficulties in screening for cognitive impairment in the community. As part of the Identification and Intervention for Dementia in Elderly Africans (IDEA) study, we aimed to validate the IDEA cognitive screen in a community-based sample in rural Tanzania

Methods: Study participants were recruited from people who attended screening days held in villages within the rural Hai district of Tanzania. Criterion validity was assessed against the gold standard clinical dementia diagnosis using DSM-IV criteria. Construct validity was assessed against, age, education, sex and grip strength and instrumental activities of daily living (IADLs). Internal consistency and floor and ceiling effects were also examined.

Results: During community screening, the IDEA cognitive screen had high criterion validity, with an area under the receiver operating characteristic curve of 0.855 (95% CI 0.794 to 0.915). Higher scores on the screen were significantly correlated with lower age, male sex, having attended school, better grip strength and improved performance in activities of daily living. Factor analysis revealed a single factor with an eigenvalue greater than one, although internal consistency was only moderate (Cronbach's alpha = 0.534).

Conclusions: The IDEA cognitive screen had high criterion and construct validity and is suitable for use as a cognitive screening instrument in a community setting in SSA. Only moderate internal consistency may partly reflect the multi-domain nature of dementia as diagnosed clinically.

Key words: validation; screening; dementia; cognitive impairment; Africa; Tanzania; low- and middle-income countries; developing countries; screening tools
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Introduction

Dementia is being increasingly recognised as a public health concern in many areas of sub-Saharan Africa (SSA) (Mavrodaris *et al.*, 2013; Prince *et al.*, 2013). As populations age, dementia is becoming increasingly common and is associated with high levels of disability (Prince *et al.*, 2011a; Dotchin *et al.*, 2015; Kisoli *et al.*, 2015). Despite the growing body of epidemiological data, diagnosis of dementia in many

parts of SSA can be difficult because of a shortage of specialist physicians (Bower and Zenebe, 2005; Dotchin *et al.*, 2013) and a lack of appropriate screening tools. The World Health Organization (WHO) Mental Health Gap Action Programme (mhGAP) was developed to help address some of the resource issues around identification and management of people with mental health problems, including dementia, in low-resource settings (World Health Organization, 2010).

The Identification and Intervention for Dementia in Elderly Africans (IDEA) cognitive screen was developed as a brief screening instrument for cognitive impairment in SSA (Gray *et al.*, 2014). It can be administered in around 10 min by non-specialist healthcare workers and is designed for use in people with low levels of formal education (Paddick *et al.*, 2015a). It was developed and piloted in rural Tanzania and has been shown to have excellent internal consistency, criterion validity and reliability in hospital-based cohorts in Tanzania and Nigeria (Gray *et al.*, 2014; Paddick *et al.*, 2015a).

Aims

Our aim was to assess the criterion and construct validity and internal consistency of the IDEA cognitive screen in a community-based cohort of people in rural Tanzania. To assess construct validity we hypothesised that lower cognitive function scores would be associated with greater age, female sex, lower education and lower grip strength.

Method

Ethics

Ethical approval for this study was given by the National Institute of Medical Research, Dar-es-Salaam, Tanzania. Additional ethical approval for the validation work was given by Kilimanjaro Christian Medical University College, Moshi, Tanzania.

Setting

The study was conducted in villages in the Hai district of northern Tanzania. Tanzania is a low-income country, with a gross national income of $930 per capita; the average life expectancy is 61 years, with 4.8% of the population aged 60 or over (The World Bank, 2015; United Nations, 2015). Hai district is largely rural, situated at the base of Mount Kilimanjaro. There are two large hospitals in Hai and numerous dispensaries and smaller health centres.

Timing

All screening and initial psychiatric assessment data were collected between March and May 2014. Some follow-up assessments to confirm initial diagnosis were conducted from June to August 2014.

Recruitment

Details of the recruitment process have already been published, and a brief summary is given below (Collingwood *et al.*, 2014). Participation in the study was on a voluntary self-referral basis. Screening days took place at local village offices. Given the voluntary nature of participation, after dissemination of information about the study, consent was assumed for those who volunteered for screening. However, consent was obtained from all those who were selected for assessment by the study doctor. A thumbprint was taken from those who could not read or write and the nature of the study explained verbally.

A few days before each of the screening days, information about the study was announced in local religious meetings (Christian and Muslim) and by local census enumerators, with support from the village committee. Any residents aged 65 years or over wishing to take part, or any family members wishing to refer a relative, were invited to attend one of three screening days in each village. All participants were asked to attend with a relative or carer able to give an informant history. Eleven people were identified by village enumerators as too frail to attend screening and were visited at home. To avoid selection bias, any older people who wished to take part in the study, but were physically unable to attend screening days, were visited at home. Information was collected on the participants' sex, age, literacy and educational level. Contact information for each participant was recorded to allow follow-up of those selected for clinical assessment.

Cognitive screening

Cognitive screening was conducted using the IDEA cognitive screen, which has been validated for use in a hospital setting (Gray *et al.*, 2014; Paddick *et al.*,

2015b). The screen was developed by members of our team using data collected as part of a dementia prevalence study (Longdon *et al.*, 2013). To increase content validity it was piloted and refined based on feedback from health professionals and clinical performance in the pilot study cohort (Gray *et al.*, 2014). The screen has six items: being able to name a bridge from a description of its use, knowing the day of the week, knowing the name of the village chief/town mayor/city governor, naming as many different animals as possible in one minute, delayed recall from a 10 word-list and a matchstick design item (Paddick *et al.*, 2015b). Subjects can score 0–15 points, with zero reflecting the lowest cognitive performance and 15 the highest cognitive performance. A score of 8–9 was taken to indicate possible dementia and a score of ≤7 probable dementia (Gray *et al.*, 2014). Assessments were conducted by nine local healthcare workers who were blinded to all clinical cognitive assessments conducted by the study doctor (S-MP). The healthcare workers administering the screen were blind to the DSM-V diagnosis provided by the doctor. All healthcare workers had attended a 4-day training course regarding dementia and use of the screening instruments.

The assessors were asked to indicate on the study proforma whether, in their opinion, the informant was felt to be reliable based on cognitive and functional assessments. The informant was considered unreliable if they were a non-relative (e.g. neighbour) who on questioning rarely came into contact with the participant and/or the information given by the informant largely contradicted the impression the interviewer had of the participant based on cognitive screening.

Other assessments

Data on age, sex and highest education level attained were collected. Instrumental activities of daily living (IADLs) were assessed using the 11-item IDEA-IADL scale, which was developed by members of our team and has been shown to be valid in this setting (Collingwood *et al.*, 2014). Grip strength was assessed using a Jamar hydraulic hand dynamometer (Model J000105, Lafayette Instruments, Lafayette, IN, USA) with participants seated, their elbow by their side and flexed to right angles, and a neutral wrist position. Three recordings of grip strength in the dominant hand were taken and the best effort used for the purposes of data analysis. All assessors were trained in the use of the dynamometer and practiced the testing procedure prior to assessments.

Diagnosis of dementia

Dementia diagnosis was based on DSM-IV dementia criteria (American Psychiatric Association, 1994). As during pilot fieldwork testing, DSM-IV diagnosis was provided by a UK-based research psychiatrist (S-MP) who was blind to the results of the cognitive and functional assessment conducted by the healthcare workers. All participants had a cognitive examination which included orientation, delayed recall, an assessment of attention and concentration (days of the week backwards), an assessment of language ability based on a structured conversation and ability to follow complex commands. A brief neurological and physical examination was also conducted and patients assessed regarding known dementia risk factors. Screening for depression using the Geriatric Depression Scale (GDS) and for fatigue was also done. Anyone suspected of having depression, based on the GDS, was assessed further using a semi-structured interview. Depression was assessed only in regard to its confounding influence in the diagnosis of dementia. A detailed assessment that would allow a formal diagnosis of depression was not conducted.

An informant interview was completed in line with DSM-IV guidelines (American Psychiatric Association, 1994). In all but one case of suspected dementia an informant history was taken from a close relative. In the one case where an informant could not be identified, a friend was used as the informant. One case was discussed with another psychiatrist to confirm diagnosis and three cases were re-visited at four months follow-up to confirm or refute diagnoses.

Where diagnoses were in doubt, cases were discussed with a UK-based consultant in old age psychiatry.

Based on their IDEA cognitive screen scores, a stratified sample was followed-up and underwent full clinical diagnostic assessment. The aim was to assess all those scoring ≤9 (probable or possible dementia) as well as a randomly selected 15% of those scoring >9 and thought unlikely to have dementia. Random selection involved blindly picking participant's numbers out of a container. Informants who failed to attend for full diagnostic assessment interview were asked to attend on a subsequent day and, where this was not possible, were followed-up on home visits by the clinician.

Statistical methods

Data analysis. Statistical analysis was conducted using Microsoft Excel 2010 and IBM SPSS statistics version

21. Grip strength data were normally distributed. All other data were found to be non-normally distributed and therefore summarised in terms of median, interquartile range (IQR), range and frequency as appropriate. The significance level was set at 5% and two-tailed significance tests used throughout.

Cronbach's alpha was used as a measure of internal consistency and factor analysis used to investigate underlying latent traits within the scale. For factor analysis, the method of principal components was used and a varimax rotation applied to aid data analysis.

The minimally important change (MIC) was estimated using distribution-based methods (Jaeschke *et al.*, 1989; Crosby *et al.*, 2003; de Vet *et al.*, 2006). The MIC was taken as equivalent to the standard error of measurement (SEM), where:

$$\text{SEM} = \text{standard deviation } x\sqrt{(1 - \text{Cronbach's alpha})}.$$

By using Cronbach's alpha as a measure of reliability, the MIC relates to the scale and is not an assessment of the MIC within individuals.

Correlation tests were used to assess construct validity, with Spearman's test used for data measured at the ordinal, interval or ratio level and the point biserial method used for data measured at the nominal level. Grip strength data was split into males and females for analysis. To assess the independent influence of age, sex and education on screening performance, multivariable logistic regression models were developed with screening tool score (dichotomized into ≤ 7 and >7) as the dependent (outcome) variable. Age, sex, education, GDS score and the presence of dementia were forced into a multivariable model as independent (predictor) variables. For multivariable modelling multiple imputation was used to impute 19 missing values for GDS score and 4 missing values for education level. Area under the receiver operating characteristic (AUROC) curve was calculated to give an overall assessment of the predictive ability of each of the scales, with presence of clinical dementia (yes or no) as the state variable.

Results

Four hundred and seventy-three people presented for screening. Exclusions, with reasons are shown in Figure 1. Therefore, data were available for 466 people.

Scores for the IDEA cognitive screen are summarised in Table 1, together with demographic and assessment data. Ninety-three (93.0%) of the 100 people who scored ≤ 9 (possible or probable dementia) were assessed for the presence of dementia by the study doctor (see Figure 1). Of these, three could not be traced for a follow-up and four were not followed up because of administrative errors. A further 60 (16.4%) people were randomly selected for follow-up and assessment from the 366 who scored >9. This gave a stratified validation cohort of 153 (see Figure 1), 39 (25.5%) of whom were diagnosed with DSM-IV dementia.

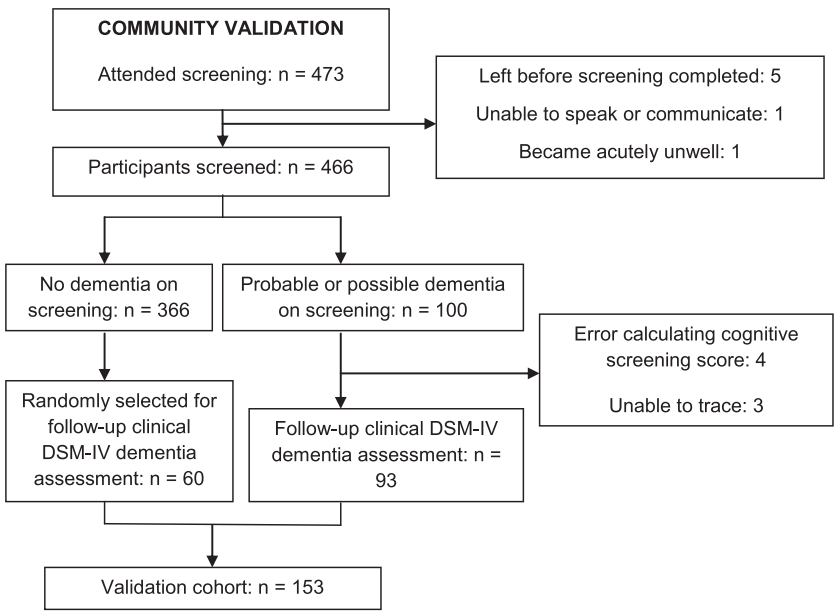

Figure 1 Flow diagram of the recruitment process.

Table 1 Scores for construct validation variables in each IDEA cognitive screen category and overall correlation

	Score ≤7	Score 8 or 9	Score ≥10	Correlation
Number	41	59	366	—
Median age (IQR)	80.0 (73.0 to 85.0)	77.0 (70.3 to 81.0)	72.0 (67.0 to 79.0)	$r = -0.314$, $p < 0.001$[a]
Number of females (%)	35 (85.4%)	42 (71.2%)	184 (50.3%)	$r = -0.271$, $p < 0.001$[b]
Number with some formal education (%)	18 (46.2%), 2 missing values	36 (62.1%), 1 missing value	317 (87.8%), 5 missing values	$r = 0.410$, $p < 0.001$[b]
Male mean grip strength in kg (SD)	23.8 (3.764)	23.8 (5.947), 1 missing value	30.3 (9.310), 11 missing values	$r = 0.334$, $p < 0.001$[a]
Female mean grip strength in kg (SD)	14.2 (5.839), 5 missing values	18.3 (4.096), 3 missing values	21.1 (5.495), 13 missing values	$r = 0.435$, $p < 0.001$[a]
Median IDEA-IADL questionnaire score	13 (4 to 30), 3 missing values	27 (15.5 to 32), 2 missing values	33 (27 to 33), 27 missing values	$r = 0.397$, $p < 0.001$[a]

IQR, inter-quartile range; SD, standard deviation.
[a]Spearman's test.
[b]Point-biserial correlation.

Internal consistency

Factor analysis revealed a single component with an eigenvalue of greater than one (2.222) explaining 37.0% of the variance. The loadings of each question on the factor were: (1) (abstract reasoning item): 0.542, (2) (temporal orientation item): 0.725, (3) (spatial orientation item): 0.581, (4) (verbal fluency item): 0.588, (5) (delayed recall item): 0.696 and (6) (praxis item): 0.484. Cronbach's alpha was 0.534.

Interpretability

The MIC was estimated to be 1.993, based on a standard deviation for IDEA cognitive screen scores of 2.919. Median IDEA cognitive screen scores by age band, sex, education level and clinical diagnosis are presented in Table 2. The difference in the median score for the no education and some education groups was greater than the MIC. There was a general trend towards lower median cognitive screen score with age, with those in the 65–69 age group having a median score of 14.0 and those in the 85 years and over group having a median score of 10.5.

Table 2 Median IDEA cognitive screen scores by age band, sex, educational level and clinical diagnosis

		Median IDEA cognitive screen score (IQR)
Age band	65–69 years ($n = 145$)	14.0 (12.0 to 15.0)
	70–74 years ($n = 108$)	12.0 (9.0 to 14.0)
	75–79 years ($n = 90$)	13.0 (11.0 to 14.0)
	80–84 years ($n = 77$)	11.0 (9.0 to 13.0)
	85 years and over ($n = 46$)	10.5 (8.0 to 12.3)
Sex	Male ($n = 205$)	13.0 (11.0 to 15.0)
	Female ($n = 261$)	12.0 (9.0 to 14.0)
Education level	Attended school ($n = 371$)	13.0 (11.0 to 14.0)
	Never attended school ($n = 87$)	10.0 (8.0 to 12.0)
Clinical diagnosis	No dementia ($n = 114$)	10.0 (8.0 to 13.3)
	Dementia ($n = 39$)	7.0 (6.0 to 8.0)

IQR, inter-quartile range.

Construct validity

The correlation between the IDEA cognitive screen scores and age, sex, education, IDEA-IADL scores and grip strength is shown in Table 1. There was a significant correlation between higher cognitive screen score (better cognition) and lower age, male sex, having attended school, higher grip strength and higher levels of ability in IADLs. Although those who had not attended school performed less well than those who had attended school, the interpretation of this finding is complicated by the fact education is thought to be protective against dementia (Prince *et al.*, 2012; Mortamais *et al.*, 2014). Furthermore females, who are generally at greater risk of dementia than males, were less likely to have attended school than males (189 of 254 (74.4%) females had attended school compared to 182 of 204 (89.2%) males). However, after adjusting for the effects of age, sex, education, GDS score and the presence of dementia in a logistic regression model, the relationship between screening score and

education became non-significant, see Table 3. GDS score was significantly correlated with IDEA cognitive screen score in univariate analysis ($r = 0.322$, $p < 0.001$), but not in multivariable analysis.

Criterion validity

The AUROC curve was 0.855 (95% CI 0.794 to 0.915) for the 153 people who had a clinical examination for the presence or absence of dementia, see Table 4. At a cut-off of ≤7, sensitivity was 59.0% and specificity 86.0% and at a cut-off of ≤8, sensitivity was 87.2% and specificity 67.5%. Although sensitivity was higher at a cut-off of ≤8 than ≤7, the likelihood ratio was higher at ≤7 than at ≤8 (4.21 and 2.68 respectively). The AUROC is similar to that seen in a hospital setting, although a slightly higher cut-off may be optimal if sensitivity is a priority (Paddick *et al.*, 2015b).

Table 3 Multivariable logistic regression model to assess the independent association between IDEA cognitive screening score, education, age, sex and geriatric depression scale score

	Odds ratio (95% CI)	Significance
Age band		
65–69 years	1	—
70–74 years	2.614 (0.476 to 14.353)	0.269
75–79 years	4.202 (0.742 to 23.806)	0.105
80–84 years	2.396 (0.408 to 14.080)	0.334
85 years and over	2.884 (0.450 to 18.502)	0.264
Female	3.096 (1.024 to 9.359)	0.045
Never attended school	1.911 (0.756 to 4.826)	0.171
Clinical dementia present	4.782 (1.789 to 12.783)	0.002
Geriatric depression scale score	1.051 (0.903 to 1.223)	0.519

CI, confidence interval.
The cut-off for the cognitive screening tool was ≤7.

Table 4 Criterion validity of the IDEA cognitive screen against DSM-IV criteria

	Score ≤7	Score 8 or 9	Score ≥10
Number	41	59	366
Seen for DSM-IV diagnostic assessment	39 (95.1%)	54 (91.5%)	60 (16.4%)
Diagnosis of dementia	23/39 (59.0%)	15/54(27.8%)	1/60 (1.7%)

Floor and ceiling effects

Only four people (0.9%) scored zero and only nine people (1.9%) scored four or less. However, higher scores were more common, with 90 people (19.3%) scoring the maximum of 15 points and 281 people (60.3%) scoring 12 or higher.

Discussion

This is the first prospective community-based validation of a brief cognitive screening instrument in SSA. The screening tool displayed good criterion validity and had an AUROC only slightly lower than that seen on hospital-based validation (Paddick *et al.*, 2015a). The lower sensitivity seen in this community cohort is unsurprising. People who are well enough to attended screening are likely to be in an earlier disease stage than those who attend hospital. As such, they may well perform adequately on screening, despite being cognitively impaired. The fact that many participants were in early stage disease may have also contributed to the fact that internal consistency in this community-based sample was only moderate and lower than reported in a hospital setting (Paddick *et al.*, 2015a). Each of the six questions was designed to test a different domain of cognitive function (Gray *et al.*, 2014). Those in early stage disease may have had fewer cognitive domains affected than those in later stage disease, and so scores on each question may have been less consistent.

Previous reports of the community validation of brief cognitive screening tools in SSA are very limited, and most previous validation have followed a case–control approach. The 'Test of Senegal', developed by Touré *et al.* (2008) gave an AUROC curve of 0.967 on comparison with the DSM-IV-R criteria. However, with 39 questions, the test is too long for community screening purposes. Baiyewu *et al.* (2005) used a series of four stick design tests to differentiate people with no cognitive impairment from those with cognitive impairment but no dementia and those with dementia. Across 724 subjects, the AUROC was 0.779 when comparing the dementia group with other participants. The 10/66 research group have also developed a brief CSI-D for use in low- and middle-income countries (Prince *et al.*, 2011b). Although some of the data used for internal validation was from a community-dwelling sample in Nigeria, external validation has not yet been conducted.

Using regression modelling we have investigated the role of education on screening performance. We wished to consider whether use of a higher cut-off in those who have attended school (or a lower cut-off in those who have not attended school) may increase the specificity (or sensitivity) of the instrument. The results of our analysis would suggest that this is not justified.

Construct validity was assessed against a range of measures, and all showed significant correlation in a manner that was consistent with our original hypothesis. The association of cognitive impairment with age, sex, education and IADL score has been noted previously in Hai district (Longdon *et al.*, 2013; Collingwood *et al.*, 2014). The correlation with grip strength has been noted by authors in other world regions (Alfaro-Acha *et al.*, 2006; Wang *et al.*, 2006; Shin *et al.*, 2012). Grip strength is thought to be an important indicator of frailty, with a notable recent publication from a rural Ghanaian population (Koopman *et al.*, 2015). Although grip strength data are likely to be confounded by other variables, particularly age, it is notable that the correlation between grip strength and screening performance in females was the highest of all variables considered. Although most participants completed the grip strength test, those with cognitive impairment often struggled to understand the instructions given and this may have increased the degree of the association. Why this should be particularly the case in females merits further study.

GDS score was used as a measure of depressive symptoms. The lack of association between GDS score and IDEA cognitive screen score after adjusting for the effects of confounding variables suggests that the screen should not falsely identify large numbers of people with depressive symptoms, in the absence of cognitive impairment, as requiring further cognitive assessment. Our study was not designed as a study of depression and as such our data are limited in this regard. There is very little previous data on depression across SSA (Gureje *et al.*, 2010). A well-funded study of depression aetiology and prevalence in SSA is needed to complement the growing body of knowledge on dementia in the region.

The screen also appears to have good interpretability, with clear differences in score between sub-groups, in a manner that would be expected. However, the MIC should be interpreted with caution. It should be noted that the MIC relates to differences in scores for different sub-groups at a single assessment and should not be considered an estimate of the MIC within an individual upon re-test. The IDEA cognitive screen was designed as a brief screen for cognitive impairment in people with low literacy levels that could be used by non-specialist healthcare workers. Therefore, it may be too brief to act as a useful instrument to detect changes in cognitive function over time. The relative simplicity of the screen may also explain the observed ceiling effect, with over half of all subjects scoring 12–15 points. The screen was not designed to distinguish those with good cognitive function from each other and during the design phase emphasis was placed on discrimination between those with and without dementia whilst keeping the instrument as concise as possible. Increasing the complexity of the screen, and so the time taken to complete an assessment, by inclusion of items to discriminate between higher levels of cognitive function could not be justified.

Limitations

Those who were physically unwell or disabled were much less likely to attend for screening at the village health centre. This is likely to have resulted in some selection bias. We offered home visits to patients identified as frail by village enumerators to try to minimise the impact of this and 11 participants were recruited in this way. Nevertheless, if people with dementia living in rural communities in SSA are to be identified, such screening events are likely to be one of the most effective, and sustainable, methods of identifying people with cognitive impairment. Those included in this study are likely to be representative of those who would be screened if the instrument were used routinely.

The MIC was calculated using distribution-based, rather than anchor-based, methods. We recognise the limitations of this approach and accept that use of both distribution-based and anchor based methods is generally seen as a gold standard (Crosby *et al.*, 2003; de Vet *et al.*, 2006). Further work, specifically aimed at estimating the MIC, using an appropriate anchor is needed to refine the estimate provided here. Nevertheless, the estimate given does not seem unreasonable based on our subjective experience.

Conclusions

The IDEA cognitive screen appears acceptable as a cognitive screen in this setting. Good content validity and inter-rater reliability have been demonstrated in previous studies (Gray *et al.*, 2014; Paddick *et al.*, 2015a).

High criterion validity, construct validity and interpretability were observed when used to screen for dementia in this rural community-based Tanzanian population. Only moderate internal consistency may partly reflect the multi-domain nature of dementia as diagnosed clinically and the likely early disease stage of many of those screened.

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Conflicts of interest

There were no conflicts of interest.

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Role of the funding source

The sponsors of this study had no role in designing the study; in the collection, analysis and interpretation of data; in the writing of the report or in the decision to submit the paper for publication.

Contributions

Design/conception—William K. Gray, Stella-Maria Paddick, Richard Walker, Catherine Dotchin, Adesola Ogunniyi, Paul Chaote, Declare Mushi. Literature search—Stella-Maria Paddick, William K. Gray. Data collection—Celia Collingwood, Stella-Maria Paddick, Aloyce Kisoli, Godfrey Mbowe, Sarah Mkenda, John Kissima, Jane Rogathi, Carolyn Lissu. Data analysis—William K. Gray. Interpretation of results—Stella-Maria Paddick, Richard Walker, Catherine Dotchin, William Gray. Writing of paper—William K. Gray, Stella-Maria Paddick, Aloyce Kisoli, Catherine Dotchin, Richard Walker.

Key points

- We aimed to validate the IDEA cognitive screen in a community-based sample in rural Tanzania.
- Criterion validity was assessed against clinical diagnosis of dementia, giving an area under the receiver operating characteristic curve of 0.855.
- Higher scores on the screen were significantly correlated with lower age, male sex, having attended school, better grip strength and improved performance in activities of daily living.
- The IDEA cognitive screen had high criterion and construct validity and is suitable for use as a cognitive screening instrument in a community setting in SSA.

References

Alfaro-Acha A, Al Snih S, Raji MA, *et al.* 2006. Handgrip strength and cognitive decline in older Mexican Americans. *J Gerontol A Biol Sci Med Sci* **61**: 859–865.

American Psychiatric Association. 1994. Diagnostic and Statistical Manual of Mental Disorders. 4th edn. American Medical Association: Washington DC.

Baiyewu O, Unverzagt FW, Lane KA, *et al.* 2005. The Stick Design test: a new measure of visuoconstructional ability. *J Int Neuropsychol Soc* **11**: 598–605.

Bower JH, Zenebe G. 2005. Neurologic services in the nations of Africa. *Neurology* **64**: 412–415.

Collingwood C, Paddick SM, Kisoli A, *et al.* 2014. Development and community-based validation of the IDEA study Instrumental Activities of Daily Living (IDEA-IADL) questionnaire. *Glob Health Action* **7**: 25988.

Crosby RD, Kolotkin RL, Williams GR. 2003. Defining clinically meaningful change in health-related quality of life. *J Clin Epidemiol* **56**: 395–407.

de Vet HC, Terwee CB, Ostelo RW, *et al.* 2006. Minimal changes in health status questionnaires: distinction between minimally detectable change and minimally important change. *Health Qual Life Outcomes* **4**: 54.

Dotchin CL, Akinyemi RO, Gray WK, Walker RW. 2013. Geriatric medicine: services and training in Africa. *Age Ageing* **42**: 124–128.

Dotchin CL, Paddick SM, Gray WK, *et al.* 2015. The association between disability and cognitive impairment in an elderly Tanzanian population. *J Epidemiol Glob Health* **5**: 57–64.

Gray WK, Paddick SM, Kisoli A, *et al.* 2014. Development and Validation of the Identification and Intervention for Dementia in Elderly Africans (IDEA) Study Dementia Screening Instrument. *J Geriatr Psychiatry Neurol* **27**: 110–118.

Gureje O, Uwakwe R, Oladeji B, Makanjuola VO, Esan O. 2010. Depression in adult Nigerians: results from the Nigerian Survey of Mental Health and Well-being. *J Affect Disord* **120**: 158–164.

Jaeschke R, Singer J, Guyatt GH. 1989. Measurement of health status. Ascertaining the minimal clinically important difference. *Control Clin Trials* **10**: 407–415.

Kisoli A, Gray WK, Dotchin CL, *et al.* 2015. Levels of functional disability in elderly people in Tanzania with dementia, stroke and Parkinson's disease. *Acta Neuropsychiatr* **27**: 206–212.

Koopman JJ, van Bodegom D, van Heemst D, Westendorp RG. 2015. Handgrip strength, ageing and mortality in rural Africa. *Age Ageing* **44**: 465–470.

Longdon AR, Paddick SM, Kisoli A, *et al.* 2013. The prevalence of dementia in rural Tanzania: a cross-sectional community-based study. *Int J Geriatr Psychiatry* **28**: 728–737.

Mavrodaris A, Powell J, Thorogood M. 2013. Prevalences of dementia and cognitive impairment among older people in sub-Saharan Africa: a systematic review. *Bull World Health Organ* **91**: 773–783.

Mortamais M, Portet F, Brickman AM, *et al.* 2014. Education modulates the impact of white matter lesions on the risk of mild cognitive impairment and dementia. *Am J Geriatr Psychiatry* **22**: 1336–1345.

Paddick SM, Gray WK, Ogunjimi L, *et al.* 2015a. Validation of the Identification and Intervention for Dementia in Elderly Africans (IDEA) cognitive screen in Nigeria and Tanzania. *BMC Geriatr* **15**: 53.

Paddick SM, Gray WK, Ogunjimi L, *et al.* 2015b. Validation of the Identification and Intervention for Dementia in Elderly Africans (IDEA) cognitive screen in Nigeria and Tanzania. *BMC Geriatr* **15**: 53.
Prince M, Acosta D, Ferri CP, *et al.* 2011a. The association between common physical impairments and dementia in low and middle income countries, and, among people with dementia, their association with cognitive function and disability. A 10/66 Dementia Research Group population-based study. *Int J Geriatr Psychiatry* **26**: 511–519.
Prince M, Acosta D, Ferri CP, *et al.* 2011b. A brief dementia screener suitable for use by non-specialists in resource poor settings—the cross-cultural derivation and validation of the brief Community Screening Instrument for Dementia. *Int J Geriatr Psychiatry* **26**: 899–907.
Prince M, Acosta D, Ferri CP, *et al.* 2012. Dementia incidence and mortality in middle-income countries, and associations with indicators of cognitive reserve: a 10/66 Dementia Research Group population-based cohort study. *Lancet* **380**: 50–58.
Prince M, Bryce R, Albanese E, *et al.* 2013. The global prevalence of dementia: a systematic review and metaanalysis. *Alzheimers Dement* **9**: 63–75 e62.
Shin HY, Kim SW, Kim JM, Shin IS, Yoon JS. 2012. Association of grip strength with dementia in a Korean older population. *Int J Geriatr Psychiatry* **27**: 500–505.
The World Bank. 2015. Data: Countries and economies.
Touré K, Coumé M, Ndiaye NND, *et al.* 2008. The test of senegal: a valid and reliable screening tool to assess for dementia in a senegalese elderly population. *Afr J Neurol Sci* **27**: 4–13.
United Nations. 2015. World Population Prospects: Key Findings and Advance Tables. United Nations: New York, NY.
Wang L, Larson EB, Bowen JD, van Belle G. 2006. Performance-based physical function and future dementia in older people. *Arch Intern Med* **166**: 1115–1120.
World Health Organization. 2010. mhGAP Intervention Guide for Mental, Neurological and Substance Use Disorders in Non-Specialized Health Settings. edn 2013/06/07 edn. World Health Organization: Geneva, Switzerland.

20. Commentary on Key Paper 2

Community validation of the IDEA six item cognitive screen in rural Tanzania (Cohort 4a)

20.1. Overview

This paper presents a community validation of the IDEA 6-item screen in a sample of 466 rural dwelling older adults assessed as part of a widely advertised dementia screening programme in May 2014. In addition to assessment for diagnostic accuracy or criterion validity, this paper considers construct validity, interpretability in terms of minimally important change, internal consistency and floor and ceiling effects of the IDEA six-item screen. A similar methodology is used to that described in Key Paper 1, but with the advantage of collaborative histories for almost all participants, and follow-up home visits for diagnostic clarification. This study also reports feasibility of use of the six-item screen in primary care, administered by health workers from different backgrounds in a rural setting. Dara collection for this study took place between March and August 2014.

Materials and methods

This study took place in six villages in rural Hai, selected from those not involved in previous epidemiological studies of dementia by our team. A dementia screening programme was widely advertised as part of an awareness raising programme taking place as part of the IDEA study. Community stakeholders including Christian and Muslim religious leaders, the District Medical Officer and village committees were involved in the study and agreed to announce the screening programme at community meetings and in the local mosques and churches in the week before the screening took place. Screening took place in rural health centres or village offices in villages without a separate health centre to avoid participants having to travel.

Participants self-referred or were referred by a family member or village health care worker. To avoid bias towards the fittest older people, home assessments were offered to any older person who in the opinion of the village health worker would have difficulty attending the health centre. Village health workers were asked to produce lists of frailer older people who might benefit from screening, and to approach these individuals and ask if the IDEA team could visit and explain the study.

Screening

The IDEA screen was administered by one of 9 trained screeners who were primary health care workers or health professionals working within the local area. Of those 466 screened, a randomised sample of 153 individuals underwent a detailed clinical assessment for dementia by DSM-IV criteria

blind to the outcome of the IDEA six item screen (93% of 100 with possible or probable dementia (IDEA screen 9 or below), alongside16.4% of 366 with no dementia on screening randomly selected through drawing lots).

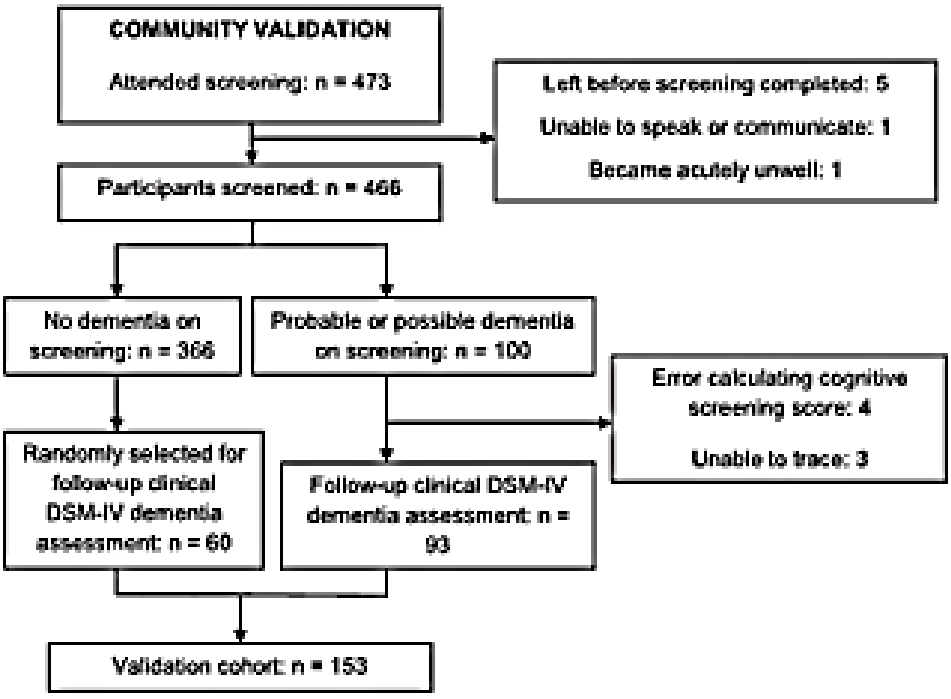


Figure 11. Study flowchart

Clinical assessment for dementia

Clinical assessment was similar to that detailed in cohorts 2 and 3 and included detailed bedside cognitive assessment, focussed mental state examination, neurological examination (and further physical examination where appropriate) as well as history of dementia risk factors. A detailed informant history for cognitive and functional impairment was obtained for all participants, and in all but one case this was from a family member who lived with, or close by the participant. Depression was screened for using the Geriatric Depression Scale (GDS). The GDS has previously been used in epidemiological research in sub-Saharan Africa but has not previously been validated in this setting. In cases of diagnostic doubt, further discussion with a UK based old age psychiatrist took place, and in a small number of cases follow-up assessment took place at the participant's home 2-3 months later in order to clarify diagnosis. These were cases where the history from the informant was not initially clear enough to prove a six month history for dementia diagnosis, or where severe depression by DSM-IV criteria was present, and it was not clear whether there was also an underlying dementia.

Other assessments for validity and reliability of the IDEA six-item screen in this setting

In addition to assessment for dementia by DSM-IV criteria for assessment of criterion validity, a number of other scale properties were examined. These included construct validity, interpretability, internal consistency and determination of minimally important change for interpretability.

Construct validity was examined through correlation with predictor variables. These included age, gender, previous formal education, frailty (using grip strength as a surrogate marker), functional ability measured by the IDEA-IADL (discussed in Key Paper 3) and number of symptoms on the Geriatric Depression Scale (GDS) 15 item.

Internal consistency was re-examined in this cohort using Cronbach's Alpha and factor analysis also used to identify the number of latent traits within the scale (as determined by an Eigenvalue over 1). The minimally important change was estimated using Cronbach's alpha as a measure of reliability. The independent relationship between education and IDEA six-item screen score was further examined in this study. Age, sex, education and GDS score were assessed using multivariable regression using positive IDEA screen score as the dependent variable.

20.2. Results

A total of 39 individuals (25.5%) of the randomised sample met criteria for DSM-IV dementia. The proportion who had never attended school was 19%. Criterion validity was high (AUROC 0.855 (0.794-0.915)) for DSM-IV dementia. Sensitivity at the previously validated cut-off of 7/15 was low (59%) improving to 87.2% at 8/15, with specificities of 86.0% and 67.5% respectively. Internal consistency was moderate (Cronbach's alpha 0.534). I felt this was because the IDEA screen was deliberately designed to screen all lobes of the brain and that this reflected the wide variety of impairments seen clinically. Nevertheless on factor analysis there was only one factor with an Eigenvalue over one, indicating that the scale measures one underlying construct.

As might be expected, higher scores on the IDEA screen were correlated with male gender, less frailty (measured through surrogate marker grip strength), younger age, and previous formal education. The minimally important change (MIC) was estimated at 1.93 (2 points) for the scale as a whole. The IDEA six-item screen appears to have construct validity in terms of correlation with factors commonly expected to be associated with cognitive performance in dementia studies.

Education

Education did appear to affect scores, with those without education scoring lower on the IDEA six-item screen. The difference in median score between those with and without formal education was larger than the minimally important change (MIC) value. Nevertheless, education was no longer a significant predictor of positive IDEA screen score when entered into a logistic regression model

controlling for age, gender, presence of dementia and GDS score. Likewise number of symptoms on the GDS correlated with idea screen score, but on multivariable regression controlling for other variables, depression was no longer a significant predictor.

Illiteracy and lack of formal education are well recognised as risk factors for dementia, and this aspect has been discussed in the Introduction to this study. In our original prevalence study education was associated with dementia on univariable but not multivariable analysis, but the reasons for this are unclear. Other tools used by our team in rural Hai for cognitive assessment had clear educational bias because illiteracy was independently related to a positive cognitive screen for dementia but not for dementia by DSM-IV criteria. This does not appear to be the case for the six-item screen in the hospital and community studies completed.

Very few people scored at floor level, with very few scoring 4 or below. In contrast more than half of individuals scored 12 or more indicating significant ceiling effects. This is not a failing of the screen, since we would expect most cognitively intact older people to score at ceiling on a brief screening tool.

20.3. Strengths and limitations of Key Paper 2

Criterion validity

Clinical diagnoses were made by the study doctor, with access to advice from a specialist in old age psychiatry in the UK where necessary. A major strength of the clinical diagnoses in this study were the access to an informant history for cognitive and functional decline obtained from an individual living with or in regular contact with the participant. Only one participant was not able to identify a suitable informant. Follow-up visits were also available for diagnostic clarification, usually where it was difficult to differentiate dementia and depression. Dementia subtypes were diagnosed on clinical criteria only, with the limitation that no neuroimaging was possible since the CT scanner used in the original study was no longer functioning. Nevertheless a more robust method would have been a formal consensus panel validation of diagnoses by DSM-IV criteria.

Depression

With regard to depression, the GDS has previously been used in epidemiological research in Nigeria, and was translated by health workers with a mental health background and previous experience of dementia research. It is important to note that no formal validation of the 15 item GDS (or in fact longer versions) has taken place in Tanzania or in older adults in sub-Saharan Africa. However because resources for validation of the GDS were not available to us, we felt that use of the GDS was justifiable. Although a focussed mental state examination was completed at each assessment, a full

history for depression was not obtained. Individuals with low scores on the GDS were not questioned extensively on presence of depression symptoms and therefore it is possible that cases of milder depression may have been missed.

The MIC was calculated using Cronbach's alpha as a measure of validity, and therefore relates to the scale as a whole. The MIC between individuals cannot be reliably calculated through this method so should not be used a measure of within-individual change.

The association of education and IDEA six-item screen score is difficult to disentangle. In this study, those with and without formal education differed in median six-item screen score, and this difference was larger than the 2 point calculated MIC score. However, in this study, as in Key Paper 1 previous formal education was associated with IDEA six item screen on univariable but not multivariable analysis, in this case controlling for age, gender and number of depression symptoms. This showed that a positive IDEA screen score was not independently associated with previous formal education, taking these other variables into account. For this reason, varying the screening cut off in this setting for level of education may not be justified. As identified in the Introduction, adjustment of screening score for level of education can have the effect of reducing validity of the screening instrument used

Another possible limitation is that the primary health care workers carrying out this study had received training in dementia including communication skills and carrying out cognitive assessment. Whilst this would of course be the ideal situation, we should be mindful that this screening test may be used by people without this training and consider the effect of this on diagnostic accuracy.

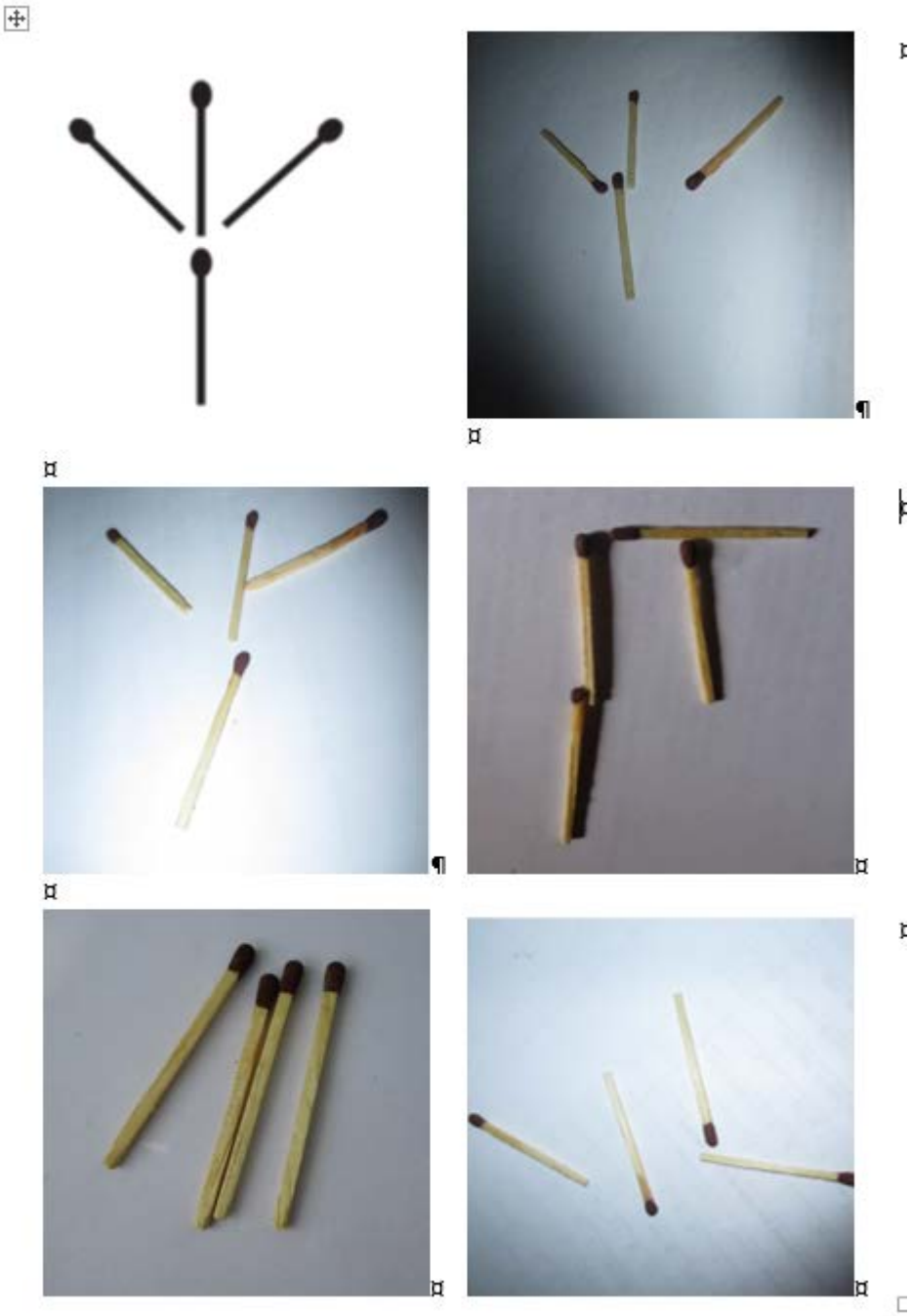
We were unable to carry out inter-rater reliability between raters in this study, although work presented in Key Paper 1 indicates that inter-rater reliability for the six-item screen is high.

20.4. Outcome of Key Paper 2

This paper presents a repeat criterion validation of the IDEA-six item cognitive screen in the context of a community dementia screening programme and in a high-prevalence randomised sample of individuals aged 65 and over. In terms of feasibility, cognitive screening was completed by a range of primary health care workers typical of those likely to use the IDEA six-item screen in this setting. Clinical diagnoses were more robust than those in the initial validation due to almost complete availability of informant histories and follow-up interviews. Absence of delirium, as expected in this community sample, meant that consideration of performance of the IDEA six-item screen in differentiating dementia and delirium was not necessary. Due to the lower sensitivity of the previously determined cut-off score of 7 in this setting (59%), a cut-off score of 8 or below should be

used for dementia in community/primary care. This may be in part due to the absence of delirium in this setting, as these individuals might be expected to achieve very low scores.

Figure 12. Matchstick construction task attempts



Key Paper 3

Development and community-based validation of the IDEA study Instrumental Activities of Daily Living (IDEA-IADL) questionnaire

Global Health Action

ORIGINAL ARTICLE

Development and community-based validation of the IDEA study Instrumental Activities of Daily Living (IDEA-IADL) questionnaire

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Background: The dementia diagnosis gap in sub-Saharan Africa (SSA) is large, partly due to difficulties in assessing function, an essential step in diagnosis.
Objectives: As part of the Identification and Intervention for Dementia in Elderly Africans (IDEA) study, to develop, pilot, and validate an Instrumental Activities of Daily Living (IADL) questionnaire for use in a rural Tanzanian population to assist in the identification of people with dementia alongside cognitive screening.
Design: The questionnaire was developed at a workshop for rural primary healthcare workers, based on culturally appropriate roles and usual activities of elderly people in this community. It was piloted in 52 individuals under follow-up from a dementia prevalence study. Validation subsequently took place during a community dementia-screening programme. Construct validation against gold standard clinical dementia diagnosis using DSM-IV criteria was carried out on a stratified sample of the cohort and validity assessed using area under the receiver operating characteristic (AUROC) curve analysis.
Results: An 11-item questionnaire (IDEA-IADL) was developed after pilot testing. During formal validation on 130 community-dwelling elderly people who presented for screening, the AUROC curve was 0.896 for DSM-IV dementia when used in isolation and 0.937 when used in conjunction with the IDEA cognitive screen, previously validated in Tanzania. The internal consistency was 0.959. Performance on the IDEA-IADL was not biased with regard to age, gender or education level.
Conclusions: The IDEA-IADL questionnaire appears to be a useful aid to dementia screening in this setting. Further validation in other healthcare settings in SSA is required.

Keywords: *instrumental activities of daily living*; *validation*; *screening*; *dementia*; *Africa*; *Tanzania*

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The population of sub-Saharan Africa (SSA) is ageing rapidly with an associated increase in non-communicable diseases, such as dementia, presenting a challenge to already scarce healthcare and human resources. In 2013, there were estimated to be 1.31 million people with dementia in SSA, which will rise to a projected 5.05 million people by 2050 (1). Despite this, the diagnosis of dementia in many parts of SSA can be problematic due to a severe shortage of specialist physicians, such as neurologists, psychiatrists, and geriatricians (2, 3), and an estimated 200 times fewer trained mental health workers in SSA in comparison to European countries (2–4). The World Health Organization (WHO) have developed the Mental Health Gap Action Programme (mhGAP) (5) to help address some of the issues around identification and management of people with mental health problems in low- and middle-income countries (LMICs). In line with the mhGAP, the WHO

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recommended strategy for diagnosis and management of chronic disease and mental disorders in low-resource settings is one of task shifting. Task shifting aims to support and enable non-specialist and primary care workers to provide services delivered by specialists and physicians in higher resourced settings (6, 7). This approach requires use of clearly defined protocols alongside brief assessment tools designed and validated for use in these low-resource environments with high sensitivity and specificity to assist clinical decision making. Unfortunately, assessment tools for dementia designed for use in SSA are currently few, especially those designed for use by non-specialists in primary care.

Cognitive screening tools designed for use in SSA are currently few, despite the difficulties of assessing cognition in this predominantly low-literacy setting. The Community Screening Instrument for Dementia (CSI-D) has been previously validated in Nigeria (8) and Kenya (9) and used in research studies, but is too lengthy for routine screening. A brief CSI-D has been developed by the 10/66 research group from data collected as part of a series of prevalence studies (10). However, it has not yet been externally validated, and the data used for its development were from India, China, and Latin America where background education levels are likely to be much higher than in many areas of SSA. A brief screening instrument [the IDEA (Intervention for Dementia in Elderly Africans) cognitive screen] has been developed and validated by members of our team, specifically for use in SSA. It is intended to minimise educational bias (11).

Used alone, cognitive screening is not adequate as a clinical decision aid, even if using tools specifically designed for SSA. Poor performance may be due to physical illness, sensory impairment or lack of confidence rather than cognitive impairment or dementia. A collateral history from an informant is also required, and functional assessment tools are necessary to assist staff in identifying those with likely dementia, as well as forming a core part of the formal diagnostic criteria for dementia. Functional assessment is generally agreed to include two main elements: activities of daily living (ADLs) and instrumental (or extended) activities of daily living (IADLs). ADLs are basic self-care activities such as bathing, feeding, and dressing independently. Assessment of these is often useful in identifying care needs and dependence. IADLs are more complex activities generally agreed to be affected earlier in cognitive impairment as they require more intact neurocognitive abilities to complete (12).

A number of IADL assessment tools exist, with the most widely used being the Lawton IADL scale (12). Used alone, the Lawton IADL scale is reported to have a sensitivity of 0.85–0.90 and specificity of 0.66–0.98 in identifying dementia (13). Most IADL scales have been developed in high-income countries, and assume independent living. In LMICs, cultural norms and social roles differ, and existing IADL scales are often inappropriate, particularly where multigenerational living is common, and older people may not be directly responsible for household tasks measured on existing scales. Performance on other tasks may be restricted by lack of availability or access to amenities such as transport, or adherence to traditional gender roles. These issues in functional assessment are well recognised and have been previously thought to be responsible for falsely low dementia prevalence rates reported in LMICs, particularly those in SSA. Culturally appropriate IADL scales have been developed for use in LMICs (see Table 1). A culturally specific, semi-structured assessment of IADL to assist in dementia diagnosis has been developed in Nigeria, but must be conducted by a trained clinical assessor and requires a home visit (14).

Aims

Our aim was to develop and validate a brief, and culturally appropriate, assessment of IADL, suitable for use by primary healthcare workers in identifying dementia in SSA when combined with a cognitive screening tool (15). It is hoped that, after completing cognitive and functional assessment, a village health worker would feel confident in choosing an appropriate referral pathway and be able to offer advice to patients and their families.

Method

Ethics

Ethical approval for the pilot fieldwork testing and subsequent validation was given by the National Institute of Medical Research, Dar-es-Salaam, Tanzania. Additional ethical approval for the validation work was given by Kilimanjaro Christian Medical University College, Moshi, Tanzania.

Setting

The study was conducted in six villages in the Hai district of Tanzania. Tanzania is a low-income, developing country; the average life expectancy is 61 years, with around 5% of the population aged 65 or over (16). Hai district is largely rural, and situated at the base of Mount Kilimanjaro, in the north of the country. There are two government hospitals in Hai and numerous dispensaries and smaller health centres.

Since 1992, Hai has contained a demographic surveillance site (DSS) (17). The DSS had a population of 161,119 in 2009, most of whom are subsistence farmers (15). Each village within the Hai DSS has one or two healthcare workers or enumerators with responsibilities for carrying out regular population censuses and completing public health activities under supervision from the

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Table 1. Instrumental activities of daily living scales devised for use in low- and middle-income countries

Author, year	Location, setting	Development method	Validation sample	Validation method	Key findings
Senanarong et al., 2003 (THAI-ADL) (28)	Thailand, community and specialist clinic	Specialist panel discussion	181 memory clinic attendees; mean age 69 years	Agreement with Thai MMSE FAQ, Barthel, CDR	Correlation with Thai MMSE ($r = 0.69$), CDR ($r = 0.81$), Barthel Index ($r = 0.80$) and FAQ ($r = 0.88$)
Jitapunkul et al., 1994 (Chula ADL) (29)	Thailand, community sample	Factor analysis of items from the Barthel index and Office of Populations Censuses and Surveys (OPCS) disability score	703 people aged 60 years and over; mean age 68 years	Agreement with OPCS and Barthel Index	Aim of scale was to measure disability appropriately in local population
Umayal et al., 2010 (30)	Sri Lanka, nursing home population	Validation of a modified Blessed dementia scale and Bristol ADL. Scores were modified by expert/ clinician opinion	Nursing home residents aged 65 years and over; mean age 73 years	Dementia ICD-10 criteria by consultant psychiatrist	Modified Bristol scale: AUROC 0.933. Sensitivity 100%, specificity 74.2% Modified Blessed scale: AUROC 0.892. Sensitivity 100%, specificity 71%
Fillenbaum et al., 1999 (EASI) (31)	Kerala, India low-literacy community	Community discussion with elders and health workers related to usual social roles and activities of the elderly	Pilot testing 100 people, initial validation 387 people aged 55 years and over; mean age 69.5 years	Hindi MMSE score < 22	Cronbach's alpha $= 0.82$. Lower scores in females, older people, illiterate people and those with lower cognitive function
Mathuranath et al., 2005 (E-ADL) (32)	India memory clinic	Development and validation of scale based on Lawton IADL. Input from senior citizens group and clinicians on suitable IADL	Validation on 240 memory clinic attendees and 135 controls from background population	DSM dementia	AUROC 0.97. Sensitivity 0.91, specificity 0.99
Hendrie et al., 2006 (CHIF) (14)	Nigeria	Expert opinion of clinicians. Also took into account 'items usually included in assessments of ADL'	Community sample of 295	DSM dementia Blessed dementia scale, MMSE	AUROC 0.925 for dementia Cronbach's alpha 0.83 Correlated with Blessed DS 0.56 and MMSE 0.44

District Medical Officer. Enumerators reside within the villages for which they are responsible and are well-respected members of their community. They have considerable experience of research projects focussing on chronic diseases and older adults.

Development of the IDEA-IADLs questionnaire

To facilitate the development of an IADL questionnaire for use in the IDEA study (the IDEA-IADL questionnaire), a workshop was held with all district enumerators and local healthcare workers. In total, 55 people attended the workshop. Prior to attending this workshop, the enumerators had received extensive training on dementia as part of a prevalence study conducted in 2010 (15). Additionally, enumerators had obtained practical experience of screening for dementia using the CSI-D. The workshop was facilitated by A.K. and S.-M.P.

It was explained to the group that assessment of functional impairment was reported to be difficult in traditional societies because assessment tools were generally designed for use in high-income countries with different cultural expectations of older individuals. The group was therefore asked to list, based on their experience in their local communities, those activities that would be expected of an elderly person, regardless of gender. It was stressed that this should be regardless of physical

disability or sensory impairment (e.g. poor eyesight or hearing). To avoid biasing the responses obtained, no existing IADLs scales were discussed at the workshops.

Activities were suggested and then discussed with the wider group until a consensus was reached. The discussion was facilitated by a registered nurse with experience of working in the Hai district with people with dementia. It was felt that, in most circumstances, the family or community would attempt to assist the elderly person in carrying out roles or tasks that they found difficult, and therefore a graded response to each question, rather than a dichotomous (yes/no), answer would be more appropriate. No attempt was made to model answers upon an existing assessment scale or to modify an existing scale.

Pilot fieldwork testing of the IDEA-IADL questionnaire

The IDEA-IADL questionnaire developed was piloted on 52 people identified and followed up as part of a dementia prevalence study (15). The scale was administered by a healthcare worker (nurse, clinical officer or assistant medical officer) who recorded responses from an informant (a close relative or friend of the participant). All healthcare workers who administered the questionnaire had been involved in the original development of the scale and subsequent discussion.

Diagnosis of dementia and mild cognitive impairment during pilot fieldwork testing

Once the IADL questionnaire had been administered, formal assessment for cognitive impairment was carried out by a research doctor (S-M.P.) who was blinded to the results of the IDEA-IADL questionnaire. All participants had a cognitive examination which included orientation, delayed recall, an assessment of attention and concentration (days of the week backwards), an assessment of language ability based on a structured conversation and ability to follow complex commands. A brief neurological and physical examination was also conducted and patients assessed regarding known dementia risk factors. Screening for depression was carried out using the geriatric depression scale (GDS) with further clinical assessment if indicated. An informant interview was completed in line with DSM-IV guidelines (18). Dementia diagnosis was based on DSM-IV dementia criteria (18). Mild cognitive impairment diagnosis was based on international consensus criteria (19).

Community validation of the IDEA-IADL questionnaire

Participation in the study was on a voluntary, self-referral basis. A few days before the research team came to each village, information about the study, including what participation involved, was announced in local religious meetings and by local enumerators, with support from the village committee. Any residents aged 65 years or over wishing to take part, or any family members wishing to refer a relative, were invited to attend one of three screening days in each village. All participants were asked to attend with a relative or carer able to give an informant history. Eleven people were identified by village enumerators as too frail to attend screen and were visited at home.

Screening days took place at local village offices. Given the voluntary nature of participation, after dissemination of information about the study, consent was assumed for those who volunteered for screening. To avoid selection bias, any older people who wished to take part in the study, but were physically unable to attend screening days, were visited at home. Information was collected, on the participants' gender, age, literacy, and educational level. Contact information for each participant was recorded to allow follow-up.

Functional assessments and cognitive screening

Function was assessed using the IDEA-IADL questionnaire and the Lawton IADL scale (12). Assessments were conducted by local healthcare workers who were blinded to all cognitive assessments. Both assessments were translated into Swahili and back translated prior to use.

Cognitive screening was conducted using the validated IDEA cognitive screen (11). The screen was administered by a local healthcare worker who was blind to the DSM-IV diagnosis and all functional assessments and who had attended a 4-day training course regarding dementia and use of the screening instruments. Subjects can score 0–15 points, with zero reflecting the lowest cognitive performance and 15 the highest cognitive performance. A score of 8–9 was taken to indicate possible dementia and a score of ≤ 7 probable dementia (11).

The assessors were asked to indicate on the study pro forma whether, in their opinion, the informant was felt to be reliable. The informant was considered unreliable if they were a non-relative (e.g. neighbour) who on questioning rarely came into contact with the participant and/or the information given by the informant largely contradicted the impression the interviewer had of the participant based on cognitive screening.

Diagnosis of dementia during validation

As during pilot fieldwork testing, DSM-IV diagnosis was provided by a UK-based research psychiatrist (S-M.P.) who was blind to the results of the cognitive and functional assessment conducted by the healthcare workers. Where diagnoses were in doubt, cases were discussed with a UK-based consultant in old age psychiatry.

Based on their IDEA cognitive screen scores, a stratified sample was followed up and underwent full clinical diagnostic assessment. The aim was to assess all those with probable and possible dementia as well as a randomly selected 10% of those with no dementia (scoring > 9).

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Random selection involved blindly picking participant's numbers out of a container.

Informants who failed to attend for a full diagnostic assessment interview were asked to attend on a subsequent day and, where this was not possible, were followed up on home visits by the clinician.

Statistical methods

Data analysis

Statistical analysis was conducted using Microsoft Excel 2010 and IBM SPSS statistics version 2.1. All data were found to be non-normally distributed and therefore summarised in terms of median, inter-quartile range (IQR), and range. The significance level was set at 5% and two-tailed significance tests used throughout. Cronbach's alpha was used as a measure of internal consistency and factor analysis used to investigate underlying latent traits within the scale. For factor analysis, the method of principal components was used and a varimax rotation applied to aid data analysis. Area under the receiver operating characteristic (AUROC) curve was calculated to give an overall assessment of the predictive ability of each of the scales, with presence of clinical dementia (yes or no) as the state variable.

To identify the most appropriate weighting to give to the IDEA cognitive screen and IDEA-IADL questionnaire when combined into a single measure, binary logistical regression analysis was performed using the screening instrument scores as covariates and presence of clinical dementia (yes or no) as the outcome variable. Regression coefficients were converted to weights using the method of Sullivan et al. as part of their work on the Framingham Study (20). Linear regression was used to investigate the influence of age, gender, and education level on IDEA-IADL scores after adjusting for the influence of dementia diagnosis. The model validity was assessed by examination of eigenvalues, studentised residuals, and tolerance.

There were very few missing values and these appeared to be missing completely at random and non-informative. No attempt was made to impute these data, and these data were omitted from the analysis.

Results

A flow diagram summarising the steps in the development, and validation of the IDEA-IADL questionnaire is shown in Fig. 1.

Development of the IDEA-IADL questionnaire

Health workers and enumerators from 52 villages within the DSS took part in the workshop. In addition, a number of other health workers involved in research projects attended the workshop including the community psychiatric nurse for the Hai district, and assistant medical officers and clinical officers with public health responsibilities.

A questionnaire consisting of 12 questions each scored from zero ('cannot do this') to three ('can do it with no problems, do not need help') was constructed based on the responses from participants. The questions included are shown in Table 2. The questionnaire was developed in Swahili and later translated into English for those team members not familiar with Swahili.

Pilot fieldwork testing

Of the 52 participants in pilot fieldwork testing of the IDEA-IADL questionnaire, 28 had normal cognition, 14 had mild cognitive impairment, and 10 had dementia. It rapidly became evident that one item initially included on the scale ('they make their will and testament and make decisions on their property after they have gone') was not suitable for inclusion in the scale as some health workers were uncomfortable asking this question, although they felt it was an important part of an elderly person's role. The question was only answered by 22 participants (42.3%) and was not included in subsequent analyses. No attempt was made to replace the item with another question as it was felt all items of interest had been considered.

Cronbach's alpha for the remaining 11 questions was 0.904, indicating high internal consistency. When the presence of dementia was used as the outcome variable, the AUROC curve was 0.814 [95% confidence interval (CI) 0.689–0.939] for the questionnaire. At a cut-off of ≤ 23 as indicative of dementia, sensitivity was 80.0% and specificity 78.6%.

Validation

Of a total 455 who presented for screening, six were excluded (one unable to speak or communicate, one due to acute medical illness requiring immediate hospital admission, and four left the screening event before screening was completed). For the latter four participants, it was assumed that consent had been withdrawn and they were excluded from all analyses. Of the 449 participants for who data were collected, 32 (7.1%) were excluded from the study after screening data was collected. Fourteen (3.1%) were excluded because the informant was deemed unreliable in the opinion of the interviewers, 12 (2.7%) were excluded because a reliable informant could not be identified, and six (1.3%) were excluded due to incomplete IADL data. Thus, complete IDEA-IADL questionnaire and Lawton IADL scale scores were available for 417 subjects (see Fig. 1).

For the IDEA-IADL questionnaire, Cronbach's alpha was 0.959 indicating high internal consistency. Factor analysis revealed only one factor with an eigenvalue greater than one, explaining 71.6% of the variance in the model. Table 3 shows the component matrix for the first three factors, their eigenvalues, and the percentage of

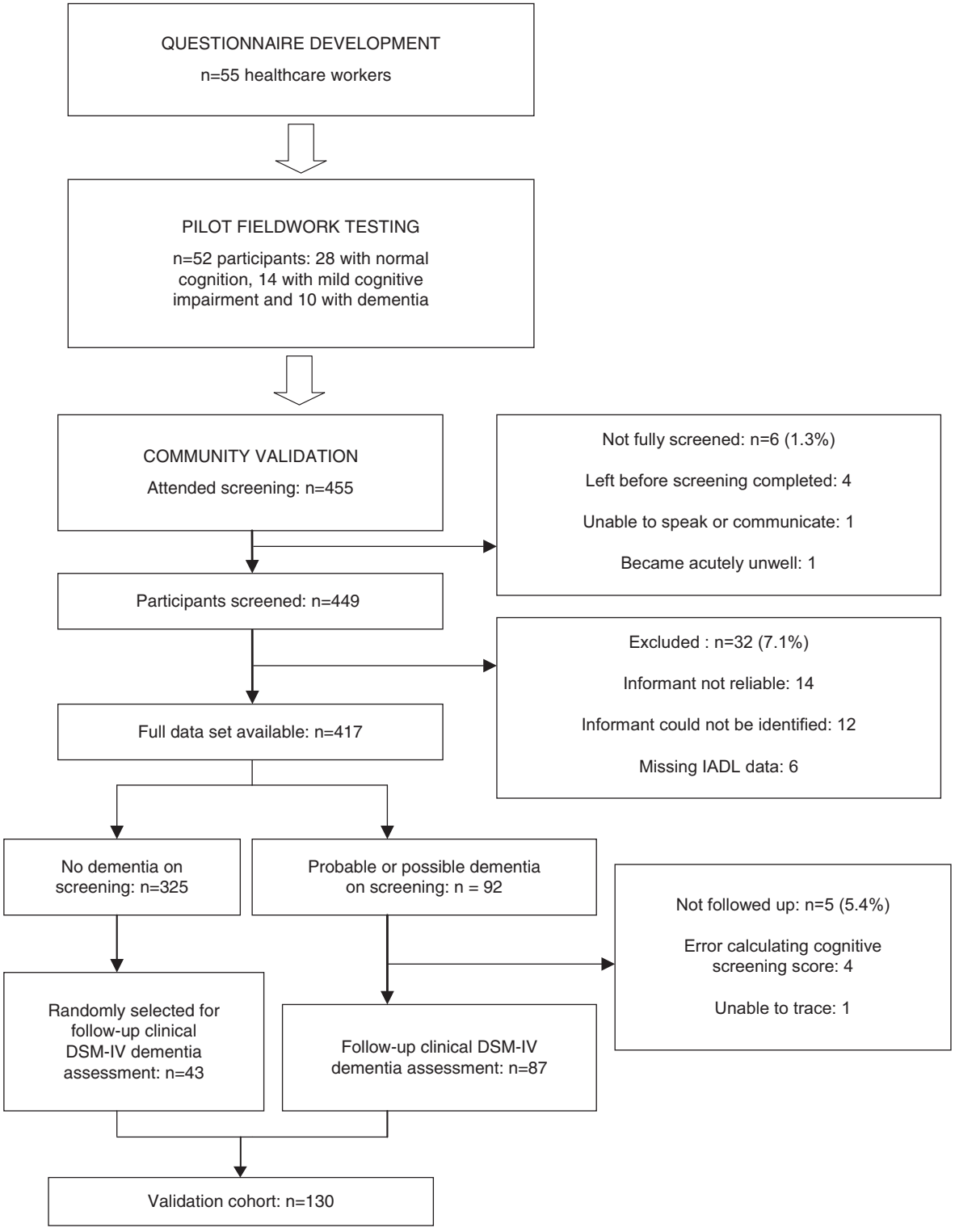

Fig. 1. Flow diagram of the IDEA-IADL development and validation process.

variance explained by each component. The questionnaire took a median of 5 min (IQR 3–7, data available for 320 people) to administer.

Scores for the IDEA cognitive screen are summarised in Table 4, together with demographic data. Ninety-two of the 97 people who scored ≤ 9 (possible or probable dementia) had IADL data available (see Table 4 and Fig. 1). Of these, one could not be traced for a follow-up and four were not followed up due to addition errors in their scores, such that they were initially thought to have

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Table 2. Twelve questions initially included in the scale

	Swahili	English translation
1	Wanatoa historia	They give histories of the family, their life, past events
2	Wana suluhisha	They settle conflicts
3	Wanasaidia shughuli ndogo ndogo	They assist in small works in the home
4	Wanatoa ushauri	They give advice
5	Wanadumisha na kufundisha mila/unyago	They teach the traditions of society
6	Ni walinzi wa nyumbani	They watch over the house when others are out
7	Wanatunza wajukuu	They look after the grandchildren
8	Wanatoa ushawishi	Persuasion or changing people's ideas for the better
9	Wanasaidia katika maswala mazito kama sherehe	They preside over feasts and ceremonies
10	Wanapangia watu majukumu	Delegation of responsibilities to others
11	Wanasimamia haki	They fight for justice within the family and the community. They ensure fairness
12[a]	Wanafanya mirathi	They make their testament and decide on division of possessions after they have gone

[a]After pilot fieldwork, this question was removed for the scale because many people were unwilling to answer questions on this sensitive topic.

scored >9. Thus, 87 people with possible or probable dementia were followed up and clinically assessed for dementia by the study doctor. A further 43 randomly selected people who scored >9 were also followed up and clinically assessed. This gave a validation cohort of 130 (see Fig. 1), 35 (26.9%) of whom were diagnosed with DSM-IV dementia. With the presence of dementia used as the outcome measure, AUROC curves for the IDEA cognitive screen, the IDEA-IADL questionnaire, and the Lawton IADL scale are summarised in Table 5.

Logistic regression analysis indicated that, if combined as a singe measure, the IDEA cognitive screen and the IDEA-IADL questionnaire items should be weighted in a ratio of 5:1, respectively, as shown in Table 6. After doing this, the AUROC curve for the combined score was calculated and is shown in Table 5. Although both screening tools performed well independently, combined use of the IDEA cognitive screen and IDEA-IADL questionnaire resulted in an AUROC curve of 0.937 (0.896–0.979), compared with cognitive screening only (0.846; 95% CI 0.776–0.915) or IDEA-IADL alone (0.896; 95% CI, 0.842–0.951).

Finally, linear regression was used to investigate whether the IDEA-IADL questionnaire was biased to age, gender, or education. Dementia diagnosis (yes or no) was included in the model since it is known to be strongly associated with each of these variables. As shown in Table 6, only dementia diagnosis emerged as an independent predictor of IDEA-IADL score, suggesting the questionnaire to be unbiased to each of the other variables.

Table 3. Factor analysis of IDEA-IADL scores

	Component		
	1	2	3
Eigenvalue	7.881	0.718	0.411
Variance explained (%)	71.6	6.5	3.7
Factor loadings			
Question 1 (give histories)	0.854	−0.245	0.027
Question 2 (settle conflicts)	0.864	−0.165	−0.016
Question 3 (assist in house)	0.784	0.411	0.300
Question 4 (give advice)	0.895	−0.135	−0.119
Question 5 (teach traditions)	0.865	−0.227	0.127
Question 6 (watch over house)	0.782	0.399	−0.322
Question 7 (childcare)	0.781	0.441	0.026
Question 8 (persuade others)	0.876	−0.123	−0.0182
Question 9 (preside over ceremonies)	0.832	−0.080	0.365
Question 10 (delegate)	0.892	−0.026	−0.057
Question 11 (ensure fairness)	0.876	−0.127	−0.126

Discussion

Efficient and effective identification of people with dementia is an important first step in reducing the diagnosis and treatment gap that exists in many countries in SSA. A case-finding approach, in conjunction with a basic training programme on recognition of dementia, has been employed in similar low-resource settings, including Brazil (21) and India (22). This approach has had only moderate success, in part, due to the low overall prevalence of dementia in the community. Our suggested approach, based on validated screening tools, is likely to be more effective and would be in keeping with the protocol driven WHO mhGAP strategy (5).

The aim of this study was to develop an IADL questionnaire that could act as a clinical decision aid in a low-resource setting. Impairment in IADLs has been

Table 4. IDEA cognitive screen scores

	Score ≤7	Score 8 or 9	Score ≥10
Number	40	57	352
Median age (IQR)	80 (73.75–85.5)	76 (70–81.25)	72 (67–79)
Number of females (%)	34 (85.0%)	41 (71.9%)	178 (50.6%)
Number with some formal education (%)	18 (47.4%), 2 missing values	34 (60.7%), 1 missing value	305 (87.6%), 4 missing values
Median Lawton scale score	3 (1–7), 3 missing values	6 (4–7), 2 missing values	7 (5.5–8), 27 missing values
Median IDEA-IADL questionnaire score	13 (4–30), 3 missing values	27 (15–32), 2 missing values	33 (27.5–33), 27 missing values
Seen for DSM-IV diagnostic assessment	36 (90.0%)	51 (89.5%)	43 (12.2%)
Diagnosis of dementia	21 (52.5%)	13/51 (25.5%)	1/43 (2.3%)

found to be predictive of later dementia in large population studies in the USA and France over periods of up to 10 years, irrespective of cognitive assessment scores within the normal range at baseline. In fact, IADL assessment scales have been used alone in population screening for dementia (13, 23). It has been suggested that these are less educationally biased than cognitive assessments in low-literacy settings (24, 25).

Previous IADL assessment instruments tend to be of three types: self-report by patient, informant interview, and direct observation (26, 27). All have their flaws, with the usefulness of self-report and informant interview limited by the cognitive ability of the patient and the reliability of the informant, respectively. Direct observation is often seen as a gold standard, although it can be resource-intensive and require a great deal of staff training, making it generally unsuitable for use in our setting. We have pragmatically chosen to develop a questionnaire that relies on informant interview. In a community setting, finding a reliable informant is usually possible and in the current study, only 3.1% (14 of 449) of informant interviews were considered unreliable by the interviewer.

Although a small number of functional assessment scales have been developed and validated for use in other LMICs (see Table 1), of these, only a proportion addressed face validity issues by involving the local population in development (31, 32). The remainder used clinician opinion for development or modification of scales designed in high-income countries.

Table 5. AUROC curve analysis for the IDEA-IADL questionnaire, the Lawton IADL scale and the IDEA cognitive screen

	AUROC curve (95% CI)
Lawton IADL scale	0.828 (0.751–0.906)
IDEA-IADL questionnaire	0.896 (0.842–0.951)
IDEA cognitive screen	0.846 (0.776–0.915)
Combined IDEA cognitive screen and IDEA-IADL questionnaire	0.937 (0.896–0.979)

The questionnaire worked well and had good predictive properties, both when used in isolation or together with a brief cognitive screening instrument. In a low-education, developing world, setting the increased predictive ability of cognitive screening, if combined with a functional assessment, has been noted by other authors (33). Involvement of local healthcare workers in the development of the questionnaire ensured good face validity. Furthermore, by focussing on normal social roles and activities, we hoped to minimise gender and education bias in the items included.

Internal consistency of the final questionnaire was high, indicating that all 11 items are broadly testing the same underlying trait. It could be argued that, because of such strong correlation between items, some may be redundant in the context of a single score-generating screening tool. However, the use of this tool in clinical practice needs to be considered. With increased number of IADLs assessed and explored with the informant, the tool will be more useful to healthcare staff in their overall clinical judgement than a tool that was designed to generate the most efficient statistical score. Considering this, alongside the fact that the time taken to complete the assessment is short and viable for screening use in every day clinical practice, it would seem more appropriate to include all 11 items.

We did not attempt to adjust responses to allow for the fact that some participants may not routinely engage in some of the activities included in the scale. Our main aim was to develop a screening instrument for use by non-specialist healthcare workers that would allow referral to specialist services as appropriate. We felt that a relatively straightforward scoring system would make the collection and interpretation of information relatively efficient. Further details on normal functioning could be obtained during a more detailed clinical assessment in those thought suitable for further assessment. The responsiveness of the IDEA-IADL questionnaire to changes in function will be assessed during future fieldwork.

Limitations

A potential significant selection bias was possible as participation in the study involved self or family referral to screening at a village office. Those who were physically

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Table 6. Regression analysis

	β Coefficient	Scaled β coefficient	Exp β	Significance
Logistic regression model				
Total IDEA-IADL questionnaire	−0.0138	1	0.871 (95% CI 0.822 to 0.922)	<0.001
Total IDEA cognitive screen	−0.646	4.681	0.524 (95% CI 0.371 to 0.739)	<0.001
Constant	6.915	–	–	–
Linear regression model				
Any formal education	1.466 (95% CI −1.905 to 4.838)	–	–	0.391
Male gender	1.215 (95% CI −2.239 to 4.669)	–	–	0.487
Age (years)	−0.031 (95% CI −0.204 to 0.142)	–	–	0.725
DSM-IV dementia present	−15.896 (95% CI −19.978 to −11.815)	–	–	<0.001
Constant	26.900	–	–	–

unwell or disabled were thus much less likely to attend for screening, and this could have significantly affected results since they are also more likely to perform poorly on functional assessment. To partly overcome this problem, we offered home visits for screening to patients identified as frail by village enumerators. Eleven participants were recruited in this way. Nevertheless, in this resource-limited setting, where primary healthcare coverage is very limited, such screening events are likely to be one of the most effective and sustainable methods of identifying people with cognitive impairment. As such, those included in this study are likely to be representative of one of the main groups the scale is designed to assess in normal use.

Five people achieving an IDEA cognitive screen score ≤ 9 were not seen for full clinical diagnosis. As this was a relatively small proportion of those seen, and they were missed randomly due to errors in addition on the part of research staff or contact and tracing difficulties, this is unlikely to have resulted in a substantial bias. For a further five participants, it was not possible to trace a reliable informant or informant data was incomplete. This has implications in clinical practice in that, for a small minority of people, it may not be possible to carry out a reliable functional assessment, hindering diagnosis.

Results can only be said to be representative of the community-dwelling population of Hai district. Further validation of the questionnaire in different geographical (e.g. urban and rural) and clinical (e.g. inpatients and outpatients) settings is required. As such, we are reluctant to extrapolate our findings beyond the setting it was developed and tested in. However, the IDEA-IADL questionnaire may be of use in assessing IADLs in other patient settings, in other parts of Tanzania and SSA and in other world regions.

Finally, cognitive and IADL assessments were carried out by nine separate assessors. Inter-rater reliability has yet to be established, and we cannot rule out the possibility that this may have influenced our results. Nevertheless, we have attempted to validate our tool in the setting for which it was designed, utilised by non-specialist primary healthcare workers in the community. We plan to assess the inter-rater reliability of the scale as an important next step.

Conclusions

This is the first validation of functional assessment tools for use in Tanzania and one of very few conducted in SSA. The IDEA-IADL has good internal consistency and construct validity against the gold standard DSM-IV diagnosis of dementia. It is both time and cost-efficient, it does not require a specialist healthcare background to administer, and little training is needed. It appears to represent a better functional assessment in this population than the Lawton assessment.

Authors' Contributions

Design/conception – Stella-Maria Paddick, Richard Walker, Catherine Dotchin. Literature search – Stella-Maria Paddick, Celia Collingwood, William K. Gray. Data collection – Celia Collingwood, Stella-Maria Paddick, Aloyce Kisoli, Godfrey Mbowe, Sarah Mkenda. Data analysis – William K. Gray, Celia Collingwood, Stella-Maria Paddick. Interpretation of results – Celia Collingwood, Stella-Maria Paddick, Richard Walker, Catherine Dotchin, William Gray. Writing of paper – William K. Gray, Celia Collingwood, Stella-Maria Paddick, Aloyce Kisoli, Catherine Dotchin, Richard Walker.

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Conflicts of interest and funding

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Role of the funding source

The sponsors of this study had no role in designing the study; in the collection, analysis, and interpretation of data; in the writing of the report; or in the decision to submit the paper for publication.

References

1. Prince M, Guerchet M, Prina M. Policy brief for heads of government: the global impact of dementia 2013–2050. London, UK: Alzheimer Disease International; 2013.
2. Dotchin CL, Akinyemi RO, Gray WK, Walker RW. Geriatric medicine: services and training in Africa. Age Ageing 2013; 42: 124–8.
3. Bower JH, Zenebe G. Neurologic services in the nations of Africa. Neurology 2005; 64: 412–15.
4. Saxena S, Thornicroft G, Knapp M, Whiteford H. Resources for mental health: scarcity, inequity, and inefficiency. Lancet 2007; 370: 878–89.
5. World Health Organization (2010). mhGAP Intervention Guide for mental, neurological and substance use disorders in non-specialized health settings. Geneva, Switzerland: World Health Organization.
6. Beaglehole R, Epping-Jordan J, Patel V, Chopra M, Ebrahim S, Kidd M, et al. Improving the prevention and management of chronic disease in low-income and middle-income countries: a priority for primary health care. Lancet 2008; 372: 940–9.
7. Eaton J, McCay L, Semrau M, Chatterjee S, Baingana F, Araya R, et al. Scale up of services for mental health in low-income and middle-income countries. Lancet 2011; 378: 1592–603.
8. Hall KS, Gao SJ, Emsley CL, Ogunniyi AO, Morgan O, Hendrie HC. Community screening interview for dementia (CSI 'D'); performance in five disparate study sites. Int J Geriatr Psychiatry 2000; 15: 521–31.
9. Chen CH, Mizuno T, Elston R, Kariuki MM, Hall K, Unverzagt F, et al. A comparative study to screen dementia and APOE genotypes in an ageing East African population. Neurobiol Aging 2010; 31: 732–40.
10. Prince M, Acosta D, Ferri CP, Guerra M, Huang Y, Jacob KS, et al. A brief dementia screener suitable for use by non-specialists in resource poor settings – the cross-cultural derivation and validation of the brief Community Screening Instrument for Dementia. Int J Geriatr Psychiatry 2011; 26: 899–907.
11. Gray WK, Paddick SM, Kisoli A, Dotchin CL, Longdon AR, Chaote P, et al. Development and validation of the identification and Intervention for Dementia in Elderly Africans (IDEA) study dementia screening instrument. J Geriatr Psychiatry Neurol 2014; 27: 110–18.
12. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. Gerontologist 1969; 9: 179–86.
13. Castilla-Rilo J, Lopez-Arrieta J, Bermejo-Pareja F, Ruiz M, Sanchez-Sanchez F, Trincado R. Instrumental activities of daily living in the screening of dementia in population studies: a systematic review and meta-analysis. Int J Geriatr Psychiatry 2007; 22: 829–36.
14. Hendrie HC, Lane KA, Ogunniyi A, Baiyewu O, Gureje O, Evans R, et al. The development of a semi-structured home interview (CHIF) to directly assess function in cognitively impaired elderly people in two cultures. Int Psychogeriatr 2006; 18: 653–66.
15. Longdon AR, Paddick SM, Kisoli A, Dotchin C, Gray WK, Dewhurst F, et al. The prevalence of dementia in rural Tanzania: a cross-sectional community-based study. Int J Geriatr Psychiatry 2013; 28: 728–37.
16. World Bank (2014). Data: Tanzania. Available from: http://data.worldbank.org/country/tanzania#cp_wdi [cited 20 July 2014].
17. Adult Morbidity and Mortality Project (AMMP) (2004). Policy implications of adult morbidity and mortality. Final report. Dar-es-Salaam: Tanzanian Ministry of Health.
18. American Psychiatric Association (1994). Diagnostic and statistical manual of mental disorders. 4th ed. Washington, DC: American Medical Association.
19. Winblad B, Palmer K, Kivipelto M, Jelic V, Fratiglioni L, Wahlund LO, et al. Mild cognitive impairment – beyond controversies, towards a consensus: report of the International Working Group on Mild Cognitive Impairment. J Intern Med 2004; 256: 240–6.
20. Sullivan LM, Massaro JM, D'Agostino RB, Sr. Presentation of multivariate data for clinical use: the Framingham study risk score functions. Stat Med 2004; 23: 1631–60.
21. Ramos-Cerqueira AT, Torres AR, Crepaldi AL, Oliveira NI, Scazufca M, Menezes PR, et al. Identification of dementia cases in the community: a Brazilian experience. J Am Geriatr Soc 2005; 53: 1738–42.
22. Shaji KS, Arun Kishore NR, Lal KP, Prince M. Revealing a hidden problem. An evaluation of a community dementia case-finding program from the Indian 10/66 dementia research network. Int J Geriatr Psychiatry 2002; 17: 222–5.
23. Juva K, Makela M, Erkinjuntti T, Sulkava R, Ylikoski R, Valvanne J, et al. Functional assessment scales in detecting dementia. Age Ageing 1997; 26: 393–400.
24. Barberger-Gateau P, Commenges D, Gagnon M, Letenneur L, Sauvel C, Dartigues JF. Instrumental activities of daily living as a screening tool for cognitive impairment and dementia in elderly community dwellers. J Am Geriatr Soc 1992; 40: 1129–34.
25. Iavarone A, Milan G, Vargas G, Lamenza F, De Falco C, Gallotta G, et al. Role of functional performance in diagnosis of dementia in elderly people with low educational level living in Southern Italy. Aging Clin Exp Res 2007; 19: 104–9.
26. Gold DA. An examination of instrumental activities of daily living assessment in older adults and mild cognitive impairment. J Clin Exp Neuropsychol 2012; 34: 11–34.
27. Sikkes SA, de Lange-de Klerk ES, Pijnenburg YA, Scheltens P, Uitdehaag BM. A systematic review of Instrumental Activities of Daily Living scales in dementia: room for improvement. J Neurol Neurosurg Psychiatry 2009; 80: 7–12.
28. Senanarong V, Harnphadungkit K, Prayoonwiwat N, Poungvarin N, Sivasariyanonds N, Printarakul T, et al. A new measurement of activities of daily living for Thai elderly with dementia. Int Psychogeriatr 2003; 15: 135–48.
29. Jitapunkul S, Kamolratanakul P, Ebrahim S. The meaning of activities of daily living in a Thai elderly population: development of a new index. Age Ageing 1994; 23: 97–101.
30. Umayal S, Kulathunga M, Somaratne S, Srikanth S, Kathriarachchi S, De Silva R. Validation of a functional

screening instrument for dementia in an elderly Sri Lankan population: comparison of modified Bristol and blessed activities of daily living scales. BMC Res Notes 2010; 3: 268.
31. Fillenbaum GG, Chandra V, Ganguli M, Pandav R, Gilby JE, Seaberg EC, et al. Development of an activities of daily living scale to screen for dementia in an illiterate rural older population in India. Age Ageing 1999; 28: 161–8.
32. Mathuranath PS, George A, Cherian PJ, Mathew R, Sarma PS. Instrumental activities of daily living scale for dementia screening in elderly people. Int Psychogeriatr 2005; 17: 461–74.
33. Jacinto AF, Brucki SM, Porto CS, Martins Mde A, Citero Vde A, Nitrini R. Suggested instruments for General Practitioners in countries with low schooling to screen for cognitive impairment in the elderly. Int Psychogeriatr 2014; 26: 1121–5.

21. Commentary on Key Paper 3

Development and validation of a brief functional assessment tool for dementia diagnosis in sub-Saharan Africa (the IDEA-IADL) (cohort 4b))

21.1. Overview

This paper summarises the development, pilot and community-based validation of a culturally appropriate assessment of instrumental activities of daily living (IADLs) to assist with identification of dementia in rural SSA. IADLs are extended or complex activities of daily living which tend to be affected earlier in cognitive impairment or dementia in contrast to activities of daily living (ADLs) which are more basic self-care activities such as bathing and dressing and are a measure of care needs rather than cognitive impairment. It was recognised that a brief, culture specific assessment of functional ability would be likely to improve upon cognitive screening, especially amongst those older people who were achieving lower scores on formal cognitive screening due to educational level. Since the diagnosis of dementia requires demonstration of functional impairment it was hypothesised that a culturally appropriate functional assessment tool would reduce the effect of false positive cognitive screening, especially in those with lower levels of education. Existing assessment tools frequently used in high income countries focus on activities such as medication management or management of finances, and it was felt that these activities might not be as relevant in rural SSA. This study took place in rural Hai, utilising the same community dementia screening cohort as described in Key Paper 2 for the second stage validation. Numbers of participants differ slightly from those in Key Paper 2 (cohort 4a) due to availability of complete data for inclusion in the study.

21.2. Materials and methods

Development of the IDEA-IADL

The IDEA IADL was initially developed at a workshop attended by 55 primary healthcare workers in the Hai district. These workers had roles as village based enumerators for the purposes of epidemiological research as part of the framework of the Hai DSS. Participants of this workshop, all of whom worked in rural clinics or in public health activities had previously been trained in identification of dementia and cognitive screening and assisted in the 2010 dementia prevalence study. Workshop participants were asked to list the usual social roles and activities of an older person in their setting. In order to avoid answers being biased by general frailty or old age, and to focus on activities that might have a cognitive element, participant were asked to state activities and roles that could be undertaken by any cognitively normal older person, even if they could not see

well or walk a long distance. In order to avoid influencing the discussion, no existing HIC IADL assessment tools were demonstrated. An initial list of 12 items was generated.

Initial pilot

This assessment list was piloted in a sample of 52 individuals under follow up as part of a mild cognitive impairment (MCI) follow up study as described above in cohorts 1a and 1b. In this pilot study, the IDEA IADL was administered by a research nurse blind to diagnosis. All participants subsequently underwent clinical assessment to determine diagnosis of DSM-IV dementia or MCI by Petersen consensus criteria. The cohort consisted of 28 people with normal cognition, 14 with mild cognitive impairment (MCI) and 10 with dementia. At a cut off of 23/44 sensitivity was 80%, specificity 78.6% and AUROC 0.814 (0.689-0.939). One item was removed at this point from the scale because most health workers had felt uncomfortable asking it. The IDEA-IADL scale is included here in .

Instrumental Activity of Daily Living for Elderly -IADL screen

Tathmini ya uwezo wakufanya shughuli za kila siku kwa watu wazee

Please ask each question to the relative of the patient. For each question please ask ***'can the patient do this with no difficulty'?*** Each question may score 1 – 4 points:

Tafadhali muulize ndugu/mlezi wa mgonjwa kila swali. Kwa kila swali tafadhali uliza" Je mgonjwa anaweza kufanya hivi bila shida?"

1 point :Yes, they can do this with no difficulty, no help needed/

Ndio, wanaweza kufanya hilibi la shida, hakuna msada unaohitajika

2 points: Yes with a small amount of help of assistance/

Alama 2 Ndio anaweza na msada mdogo

3 points: With much assistance

Alama 3: anahitaji msaada mkubwa

4 points: They cannot do this

Alama 4: Hawezi kufanyahili

1. Wanatoa historia kama za familia/maisha yao/matukio ya zamani They give histories i.e. of the family/ their lives/ past events	Alama Score:
2. Wanasuluhisha migogoro They settle conflicts	Alama Score:
3. Wanasaidia kazi ndogo ndogo za nyumbani They assist in small works of the home	Alama Score:
4. Wanatoa ushauri They give advice	Alama Score:
5. Wanadumisha na kufundisha mila na desturi za jamii They teach the traditions of society	Alama Score:
6. Wanachunga nyumba wakati watu wengine wakitoka They watch over the house when others are out	Alama: Score:
7. Wanatunza wajukuu They look after the grandchildren	Alama Score:
8. Wanatoa ushawishi au kubadilisha mawazo ya watu wengine kwa uzuri Persuasion, or changing people's ideas for the better	Alama: Score:
9. Wana saidia katika maswala mazito kama sherehe They preside over feasts and ceremonies	Alama: Score:
10. Wanapangia watu majukumu Delegation of responsibilities to others	Alama: Score:
11. Wana simamia haki katika familia na jamii. Wana hakikisha usawa They fight for justice within the family and the community. They ensure	Alama: Score:
Jumla ya alama Total score:	

Figure 13. Instrumental Activity of Daily Living for Elderly -IADL screen

21.3. Formal validation (Hai dementia screening programme)

Formal validation of the refined 11-item scale took place in a community sample of adults aged 65 and over who had presented as part of a widely advertised dementia screening programme in the Hai district (cohort 4b). Individuals were screened using the IDEA six-item cognitive screen by a trained primary health care worker as described in Key Paper 2. Participants were asked to attend for screening with a relative who knew them well. Following-day appointments were given for those relatives who did not attend, with home visits arranged for those relatives where attendance at the health centre was inconvenient. The IDEA-IADL was completed by the village enumerator, with the identified informant blinded to all other screening and diagnostic data. In addition, the enumerator was asked to indicate if in their opinion, the answers given and scores obtained were reliable for example in cases where the participant had identified a neighbour as the informant or it was felt a relative visited infrequently. In addition, the Lawton IADL scale, commonly used in HIC settings was also administered at the same interview, translated by members of the IDEA study team fluent in both English and Swahili and with training in dementia assessment.

Screening

A total of 455 people were screened, of whom after exclusions complete data were available for 417 people. Methodology was identical to that in Key Paper 2, in that all those scoring 9 or below (possible or probable dementia) were assessed in the second stage alongside 15% of those scoring over 9/15 selected through blindly drawing lots from a container. The second stage detailed clinical assessment for dementia, blind to the outcome of both screening tools (IDEA six-item screen and IDEA-IADL) was identical to that described in Key Paper 2.

The second stage validation cohort for this analysis included 130 people. The study diagram (describing both phases of the study) is included here in Figure 14.

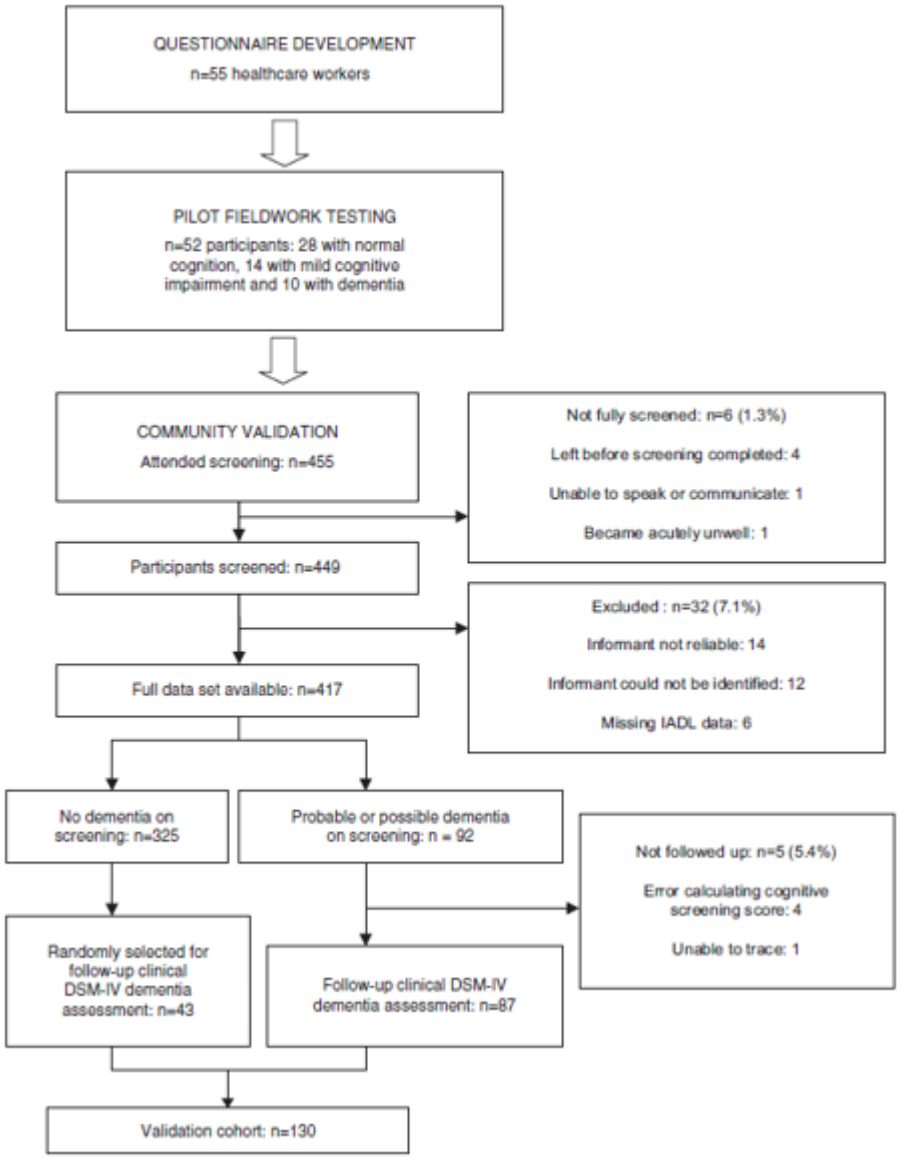


Figure 14. IDEA-IADL development flowchart

21.4. Summary of Results

The IDEA-IADL was quick to complete (median 5 minutes, IQR 3-7). Of the 130 people who underwent second stage assessment, 35 (26.9%) had dementia by DSM-IV criteria.

Used alone, the IDEA IADL had a diagnostic accuracy of 0.896 (0.842-0.951). For combination with the IDEA six-item cognitive screen, logistic regression was used to determine the weighting to give to the IDEA-IADL. Importantly, the IDEA-IADL improved upon the diagnostic accuracy of the IDEA six-item cognitive screen used alone from AUROC 0.846 (95% CI 0.776-0.915) to 0.937 (95% CI 0.896-0.979) used together with a weighting of 5 to 1 as indicated by the beta values obtained through logistic regression (see table 6, Key Paper 3).

Factor analysis indicated that only one latent variable was present with only one factor identified with an eigenvalue of over 1 and explaining 71.6% of the variance, and internal consistency as measured by Cronbach's alpha was very high (0.959).

Linear regression analysis indicated that age, gender and previous formal education were not associated with IDEA-IADL score independently of dementia diagnosis. Dementia diagnosis was independently associated with IDEA-IADL score

The IDEA IADL did not appear to have a marked ceiling effect. Of a total score of 44, median score in those without cognitive impairment was 33 (IQR 27.5-33). In those with probable dementia median score was 13 (4-30) but a wide distribution of scores was present.

21.5. Strengths and limitations of Key Paper 3

A strength of this study was the involvement of the local community in scale development, rather than attempting to translate or adapt a scale utilised in HIC settings, or to develop an assessment based on clinician opinion only. This was felt to be an appropriate strategy for an assessment tool designed to be completed by family informants rather than clinicians.

An important limitation is that the IDEA-IADL was administered blinded to the outcome of cognitive screening. Whilst this assesses criterion validity of the IDEA-IADL alone, combination with the IDEA six-item cognitive screen was done retrospectively and may not be reflective of the situation in which we might wish the scale to be used, i.e. together with cognitive screening in an individual presenting to a primary health care clinic with a relative. A further validation of both scales used together in 'real life' conditions would be useful.

Additionally, assessment inter-rater reliability was not possible to complete due to resource limitations, and these data were collected by a team of nine different health workers. Further examination of underlying variability would be important to complete.

Finally, this scale was developed for use in a particular community, specifically rural Hai, and whilst it appears likely that this scale could be used in other similar SSA settings, validity in urban settings where cultural expectations may differ, has not been established.

21.6. Outcome of Key Paper 3

This study has presented initial data on development and validation of a functional assessment based on informant history which has good criterion validity for identification of dementia when administered primary health care workers in a rural Tanzanian setting. Importantly it improves the performance of the IDEA six-item cognitive screen by improving diagnostic accuracy.

The very high level of internal consistency and identification of one underlying factor explaining most of the variance on factor analysis suggests that the scale might be shortened, as some items may be redundant. A balance needs to be struck between brevity, increasing the likelihood of use by busy clinicians and applicability and generalisability in that inclusion of a range of items increases likelihood of the scale being broadly applicable to older people. Further work will attempt to assess whether the scale could in fact be shortened.

Figure 15. Hai community dementia screening programme

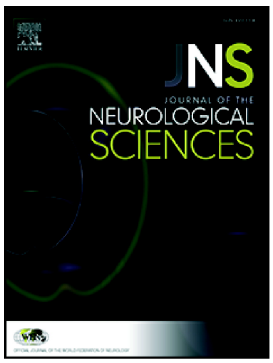
Figure 16. Completion of matchstick task during a home visit for screening

Figure 17 Hai community dementia screening programme 2

Figure 18 Hai community dementia screening programme 3

Key Paper 4

‘Identification of delirium and dementia in older medical inpatients in Tanzania. A comparison of screening and diagnostic methods’



Identification of delirium and dementia in older medical inpatients in Tanzania: A comparison of screening and diagnostic methods

S.M. Paddick, E.G. Lewis, A. Duinmaijer, J. Banks, S. Urasa, L. Tucker, A. Kisoli, J. Cletus, C. Lissu, J. Kissima, C. Dotchin, W. Gray, E. Muaketova-Ladinska, G. Cosker, R. Walker

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Identification of delirium and dementia in older medical inpatients in Tanzania: A comparison of screening and diagnostic methods

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Running head – identification of delirium in sub-Saharan Africa

Key words – Delirium, Screening, Africa, Cognition, Dementia, Confusion Assessment Method (CAM)

ABSTRACT

Background: In sub-Saharan Africa, there are no validated screening tools for delirium in older adults. This study assesses clinical utility of two instruments, the IDEA cognitive screen and the Confusion Assessment Method (CAM) for identification of delirium in older adults admitted to medical wards of a tertiary referral hospital in Tanzania.

Method: The IDEA cognitive screen and CAM were administered to a consecutive cohort of older individuals on admission to Kilimanjaro Christian Medical Centre using a blinded protocol. Consensus diagnosis for delirium was established against DSM-V criteria and dementia by DSM-IV criteria

Results: Of 507 admission assessments, 95 (18.7%) had DSM-V delirium and 95 (18.7%) had DSM-IV dementia (33 (6.5%) delirium superimposed on dementia). The CAM and IDEA cognitive screen had very good diagnostic accuracy for delirium (AUROC curve 0.94 and 0.87 respectively). However, a number of participants (10.5% and 16.4% respectively) were unable to complete these screening assessments due to reduced consciousness, or other causes of reduced verbal response and were excluded from this analysis; many of whom met DSM-V criteria for delirium. Secondary analysis suggests that selected cognitive and observational items from the CAM and IDEA cognitive screen may be as effective as the full screening tools in identifying delirium even in unresponsive patients.

C**onclusion:** Both instruments appeared useful for delirium screening in this inpatient setting, but had significant limitations. The combination of assessment items identified may form the basis of a brief, simple delirium screening tool suitable for use by non-specialist clinicians. Further development work is needed.

(250 words)

INTRODUCTION

Delirium is an acute onset syndrome of cognitive dysfunction presenting with deficits in attention, arousal and global cognition [1], highly prevalent in older hospitalised adults in high-income countries (HICs) [2]. Well-recognised adverse outcomes include cognitive decline [2-5], disability [6, 7] and increased mortality rates [3, 6].

Although prompt interventions can improve outcome [8], delirium remains under diagnosed, and may be missed in up to 50% of cases in HICs [9, 10]. Diagnosis is most challenging in some of those most at risk, such as older people and those with preexisting cognitive impairment. Use of validated screening tools improves detection rates [9, 11].and is recommended in guidelines for older hospitalised adults [12].

In sub-Saharan Africa (SSA), there are currently no validated screening tools for delirium in older people. Demographic transition has resulted in a rapidly growing older population, and recent epidemiological studies of dementia suggest a similar prevalence to that seen in HICs [13, 14]. Delirium is likely to be similarly prevalent in older adults but existing data are limited. Currently available data suggest a high rate of misdiagnosis of delirium as a psychiatric disorder and adverse outcomes [15]. A substantial diagnostic gap is suggested by the fact that the limited available studies report prevalence of 9.1-19.7% [16, 17] on clinical criteria whereas in contrast a large case-note based study of older people admitted to three large centers in SSA reported delirium prevalence of 0-2.6% [18].

This diagnostic gap may also be due to shortages of specialist clinicians with skills in cognitive assessment. Geriatricians, psychiatrists and neurologists are scarce across SSA outside large urban centers [19-21]. Cognitive assessment tools and other screening methods developed in HICs often perform poorly in SSA due to cultural differences and high levels of illiteracy amongst older adults, especially in rural areas [12]. Therefore, objective screening methods for the cognitive impairments typical of delirium, that can be used accurately by non-

specialists and are not literacy-dependent, are needed.

Our overall aim was to determine the most effective method of screening and identification of delirium in older hospitalised adults in SSA. Key objectives were: 1) Evaluate the performance of two screening instruments with potential utility for identification of delirium in this setting (the IDEA cognitive screen and Confusion Assessment Method (CAM)) against gold-standard DSM-V consensus diagnosis of delirium; and 2) Conduct a secondary analysis of all screening and assessment items to determine those most predictive of delirium and potentially useful in development of a screening method for use by non- specialists.

MATERIALS AND METHODS

Ethical approval and consent

Ethical approval was granted locally by the Kilimanjaro Christian Medical College Research and ethics committee (CRERC) and by the National Institute of Medical Research (NIMR) of Tanzania in Dar-es-Salaam. Patients were given written and verbal information about the study and its aims before gaining their informed consent. Where patients were unable to write, a thumbprint was used. If patients were admitted unconscious or lacking the capacity to consent, a close relative was asked to assent on the patient's behalf.

Setting and study participants

This study took place in the internal medicine department of Kilimanjaro Christian Medical Centre (KCMC), an 800-bed tertiary referral hospital in Northern Tanzania serving a rural population of over eight million people. Consecutive samples of individuals aged 60 and over admitted to the department from 14th January to 3rd February 2015 (pilot phase) and from 6th March 2015 to 10th July 2015 were invited to participate on admission. No substantial changes were made to the study design or data collection methods following the pilot phase and so data were combined for analysis (**Figure 1).**

Assessments

Initial clinical assessment took place wherever possible in the morning after admission, following initial review by the treating medical team. The following data were collected: background demographic data alongside physical observations; level of arousal using the Alert-Voice-Pain-Unresponsive (AVPU) scale [22] designed for use by non-specialists in routine practice and pain assessed on a visual analogue scale of 0-10 with 10 rated as most severe. Where necessary, non-literate or observational assessments (e.g. Wong-Baker Faces scale) were used and equivalent scores recorded. Data on medical diagnoses, comorbidities, risk factors and outcome were also collected and participants reassessed

every three days during admission to determine in-hospital incidence of delirium. This study relates to screening at admission only.

Clinical assessment for delirium and dementia

All patients were assessed by a research doctor with an interest in geriatrics or psychiatry (S-MP, AD, EGL or LT) assisted by a trained study nurse or clinical officer with experience of cognitive assessment in older adults, and fluent in both English and Swahili. Clinical assessments were conducted independently of, and blinded to, IDEA cognitive screen scores. Full assessment for cognitive impairment included a neurological examination, detailed standardised bedside cognitive assessment and mental state examination recorded in free text (see **Figure 1**). Where significant low mood was observed, the brief Geriatric Depression Scale (GDS) was used to identify possible depression as a possible cause of poor cognitive performance but depression or other psychiatric disorders were not the main focus of the assessment and were not routinely screened for. Assessment of potential confounders of screening tool performance including educational level and sensory impairment was also carried out (see **Figure 1)**.

Pre-existing dementia was assessed through a detailed semi-structured informant history for cognitive and functional impairment based on DSM-IV criteria previously used for dementia assessment in Tanzania and Nigeria [23]. Informants were usually close relatives and resident in the same household. All informants were asked 'is this a recent change?'. Use of a single question in identification of delirium has been validated in HICs [24].

In order to take into account possible fluctuations in presentation, a subset of participants were reviewed by a neurologist or physician to increase accuracy of diagnoses, where possible this assessment took place later the same day. This assessment took place blinded to the outcome of both screening tools to maintain objectivity. Where possible all those screen-positive on the CAM were assessed alongside 10% of screen-negative individuals, selected using a random number generator.

Consensus diagnoses of delirium and dementia

All clinical assessment data, with the exception of the IDEA cognitive screen result and CAM algorithm, were reviewed by a consultant old age psychiatrist, nurse specialist in old age psychiatry and research doctor in psychiatry (EML, GC, S-MP) for blinded consensus diagnosis of delirium by DSM-V criteria. Cases of subsyndromal or resolving delirium not meeting DSM-V criteria were recorded, but classified as 'no delirium'.

We considered it important to accurately identify dementia in order to assess screening tool performance in delirium versus cognitive impairment in general. Consensus diagnoses of dementia followed DSM-IV criteria, taking into account all available clinical information, including previous admission records where available. In cases of possible dementia not meeting DSM-IV criteria a follow-up assessment was offered for diagnostic clarification after discharge. Where necessary, due to geographical constraints, this assessment took place by telephone interview with a close relative. Dementia subtype diagnoses were made by clinical criteria where possible, but limited, partly because neuroimaging was not available at the time of the study. Other psychiatric disorders were noted where a clear clinical description of symptoms made this possible.

Identification of delirium or major cognitive impairment by treating medical team

A retrospective case note review compared consensus diagnoses of delirium with identification of delirium by the treating medical team during admission (see **Figure 1**)

Cognitive screening using the IDEA (Identification and Intervention for Dementia in Elderly Africans) cognitive screen

All consented individuals underwent bedside cognitive screening using the IDEA cognitive screen. The IDEA was developed for use by non-specialist healthcare workers to identify dementia in low-literacy populations in SSA. It has been validated for major cognitive impairment in hospital inpatient settings in Tanzania and Nigeria and outpatient and community settings in Tanzania [23, 25, 26]. Assuming basic training in a healthcare profession, minimal additional training is required to allow it to be administered

successfully. The IDEA includes assessment of orientation, delayed recall, abstract thought, category (animal) fluency and visuo-construction. The IDEA cognitive screen was administered by a study nurse or clinical officer, blinded to outcome of all other clinical assessments. On completion, the IDEA screen was immediately filed separately from other clinical data to maintain blinding of personnel conducting the other clinical assessments. Where the IDEA screen was attempted, but abandoned because of confusion or inability to understand the task, total scores were recorded as zero as the individual was assumed to have severely impaired cognition preventing successful performance on the test. Where screening was not possible due to physical illness or lowered conscious level, outcome was recorded as 'unable to complete'.

Confusion Assessment Method (CAM) screening

The CAM algorithm [27] includes the following; acute onset cognitive disturbance with fluctuation (CAM 1) *and* attention deficit (CAM 2) alongside *either* disorganised thinking (CAM 3) or abnormal arousal (CAM 4). Sensitivity and specificity for delirium by DSM-IV criteria are excellent in published meta-analyses [28] and in HIC settings the CAM is used for both delirium screening and diagnosis [29]. The CAM typically takes 10-15 minutes to complete [27] but requires a degree of training and clinical experience of cognitive assessment [30]. The CAM algorithm was completed by a junior research doctor (blinded to IDEA cognitive screen score and other clinical assessments) following detailed bedside clinical assessment (see below) and discussion with nursing staff and family members. The CAM was then filed separately to maintain blinding for clinicians completing additional assessments and consensus diagnoses (see **Figure 1**).

Where CAM assessment was considered impossible by the assessing doctor (e.g. due to limited verbal response) participants were classified 'CAM-unable' and CAM items assessable through observation scored alongside limited neurological and mental state examination and informant history.

Statistical analysis

Data were analysed using SPSS software (version 20 for windows, IBM Corp, Armonk, NY, USA). All data were non-normally distributed and therefore data were presented by median and inter-quartile range and non-parametric tests were used throughout. Diagnostic accuracy was assessed using the area under the receiver operating characteristic (AUROC) curve statistic as an overall assessment of screening performance.

Exploratory factor analysis of all screening and assessment items for delirium (IDEA six item screen and CAM items, beside cognitive tests and informant single question) was conducted to investigate latent traits within the screening items. An oblique rotation method was selected due to high correlation between variables. Factors to be extracted were determined using a scree plot. Items with the largest loadings on each factor were explored using logistic regression models with DSM-V delirium as the dependent variable. The significance level was set at 5% and two-tailed tests were used throughout.

RESULTS

Characteristics of the study cohort

During the study period there were 609 admissions (including 51 re-admissions) of individuals aged 60 and over to the internal medical department. Of these, 510 patients were recruited to the study. Reasons for exclusion were as follows: died or transferred before assessment (n = 56) refused or were unable to consent (n = 26) or could not be assessed for other reasons (n = 17) (see **Figure 1**). Three further patients were excluded from analysis due to large amounts of missing data. Thus data were available for 507 people, see **Figure 1**. The 507 admissions fully assessed and the 102 exclusions not assessed for delirium did not significantly differ in sex (X^2 (1) = 0.921, p = 0.337) or in median age (U = 24312.0, p = 0.340).

Characteristics of the study cohort are described in **Table 1**. Ninety-five people (18.7%) had delirium and 95 (18.7%) had dementia (only one of whom had previously been given a diagnosis). Of the 95 with delirium, 33 (6.5%) had delirium superimposed on dementia. There was a high prevalence of reduced arousal (20.6%). Delirium was recorded in the hospital records of 8 individuals of whom 6 met DSM-V delirium criteria (see **Table 1**).

Diagnostic accuracy of the CAM

Of the 507 people with a clinical diagnosis, 53 (10.5%) were classified as 'CAM unable'. Of the remaining 454, 89 (19.6%) were CAM positive for delirium. The overall diagnostic accuracy of the CAM was excellent (see **Table 2)**. A total of 8/53 (15.1%) of 'CAM unable' participants met DSM-V delirium criteria and overall 22/53 (41.5%) met criteria for major cognitive impairment (dementia or delirium). CAM items 2 and 3, which are more reliant on verbal response, were poorly completed, whilst almost all participants could be assessed on observation and clinical history items CAM 1 and CAM 4 (see **Table 2**). Allowing for these limitations, CAM 2 (inattention) showed the highest diagnostic accuracy.

Diagnostic accuracy of the IDEA six-item screen

The IDEA cognitive screen was attempted by 424 (83.7%) participants. Reasons for exclusions are detailed in **Figure 1**. Of those attempting the IDEA cognitive screen, 64 (15.1%) had DSM-V delirium, 73 (17.2%) had DSM-IV dementia (25 (5.9%) had delirium superimposed on dementia). A significant proportion of the 83 unable to attempt the IDEA screen met DSM-V delirium criteria (n = 31, 37.3%), DSM-IV dementia criteria (n = 22, 26.5%) or had delirium superimposed on dementia (n = 8, 9.6%). In those assessed, diagnostic accuracy of the IDEA screen for DSM-V delirium and major cognitive impairment was good, with an AUROC curve of 0.866 (0.826-0.907) for delirium and 0.874 (0.838-0.909) for major cognitive impairment. Sensitivity, specificity and predictive value are reported in **Table 2**.

Differentiation of delirium and dementia

Within the group identified with major cognitive impairment (delirium or dementia) the CAM demonstrated excellent discriminatory ability in identifying delirium from dementia. Of 134 with major cognitive impairment who completed the CAM, 87 had delirium and 47 had dementia without delirium. The CAM correctly identified 79/87 (90.8%) of those with delirium and 45/47 (93.7%) of those without delirium. Of two incorrectly classified as having delirium, both had dementia. Within this group sensitivity was 91% and specificity was 96%. CAM 2 (inattention) was the most accurate individual test when used alone (sensitivity 94%, specificity 76%). In the 103 who had major cognitive impairment and completed the IDEA cognitive screen, differential accuracy was poor, with an AUROC curve of only 0.60 (95% confidence interval (CI) 0.49-0.71) for delirium. Similarly, of those with cognitive impairment on screening (IDEA cognitive screen of 7 or below) the CAM correctly identified delirium (sensitivity 0.93, specificity 0.96). Of those with major cognitive impairment, 23/157 (14.6%) and 45/157 (28.7%) were unable to complete the CAM or attempt the IDEA cognitive screen,

limiting clinical utility. The single question 'is this a sudden change?' was only moderately useful (sensitivity 92% specificity 60%).

The role of visual impairment

We wished to investigate whether the relatively poor performance of the IDEA cognitive screen was due to uncorrected visual impairment. The IDEA screen was re-evaluated disregarding the only visually presented item (matchstick constructional praxis task). Removal of the praxis task made little difference to the overall accuracy of the IDEA for identification of delirium or major cognitive impairment [AUROC 0.871 (95% CI 0.833-0.912), 0.879 (95% CI 0.844-0.913)] respectively.

Investigation of combinations of individual CAM and IDEA cognitive screen items as predictors of delirium

All six IDEA screen items, bedside cognitive tests of orientation, attention, registration and recall, CAM items 1 and 4 and the single informant question were investigated to identify those that may be of greatest clinical utility in this setting. CAM items 2 and 3 were not evaluated due to the observed difficulties in rating these items, suggesting that they would not be suitable for screening in this setting. Exploratory factor analysis identified three factors broadly interpreted as representing learning/recall, observation/behaviour and orientation, explaining 41.9%, 9.67% and 7.5% of the variability respectively. A logistic regression model was constructed to identify those items that were significant independent predictors of delirium. The final model is shown in **Table 3** and included word recall, CAM 1, CAM 4 and sex. Nagelkerke's R^2 for the model was 0.676. Weightings were applied to the model based on the parameter estimates and these weights used to develop a crude screening tool. The tool had a higher AUROC than the IDEA cognitive screen (0.94 (95% CI 0.92 to 0.97)), and had the advantage of being much shorter. Accuracy was similar to that of the CAM, but assessment data were available for almost all participants including those rated unassessable on the full CAM. The scoring system ran from 0 to 8, with a score of ≥6 the optimal cut off for identifying those with delirium (sensitivity 0.94, specificity 0.90).

DISCUSSION

The brief delirium screen developed outperformed both the IDEA and CAM on internal validation. Our presented development and validation models demonstrated a high degree of accuracy in detection of delirium, which surpassed that of the IDEA and was similar to that of the CAM.

This increased accuracy may be due in part to its simplicity and lower reliance on clinical judgement. In our study, non-neurologists with cognitive assessment experience had difficulty in rating CAM items 2 and 3 in individuals with lowered arousal. This reduced the overall clinical utility of the CAM because a significant proportion of these 'CAM unable' individuals met DSM-V delirium criteria. Similar reductions in CAM sensitivity due to difficulties with CAM items 2 and 3 have been noted in other studies, especially where less experienced raters administered the CAM [30].

The novel delirium screening tool developed includes assessment of the following cognitive and observational elements; short term recall, altered consciousness and both acute onset and fluctuation. It does not specifically include inattention. Attentional deficits are well-recognised to differentiate delirium and dementia [31] because attention is typically affected globally and early in delirium, but only complex attention is impaired in mild to moderate Alzheimer's disease [32]. Although we identified inattention as the most accurate CAM item in terms of general diagnostic accuracy and discrimination of delirium and dementia, it was excluded from the model due to the identified difficulties with its completion. Although it could be argued that difficulty completing an item assessing attention is consistent with attentional difficulty, the fact that a large number of people who would fit into this description were recorded as unassessable suggests that inclusion of this item in a screen could lead to people being misclassified. The decision to exclude this item was, therefore, a pragmatic one, based on our desire to develop a simple and robust screening tool. Our modelled screening tool includes short term recall of a previously learned word list. This item might therefore be indirectly measuring attention (since attention is required in order to register

and retain the list) without the challenge of assessing inattention in more complex clinical assessment.

Many screening tools used for identification of delirium in HICs rely heavily on orientation, despite evidence that orientation may be unaffected in up to a quarter of older people with delirium [32]. Our tool includes items requiring registration and short-term recall rather than orientation, and may therefore have broader applicability.

Acute onset and fluctuation as reported by a carer was identified as a key element during modelling. In contrast, a positive answer to 'is this a sudden change' by an informant was only moderately useful in differentiating delirium and dementia. Previous work by our team has described a high prevalence of both vascular dementia and stroke in Tanzania [9, 10] It may be difficult for family members asked this question to separate delirium from stepwise deterioration in vascular cognitive impairment. The additional element of 'fluctuation' as well as acute change appeared to be more useful in identification of delirium in this setting.

Altered arousal is another key element of our delirium screening tool. Lowered arousal is independently associated with poor outcome and therefore these individuals are at particularly high risk, but likely to be missed by routine use of the CAM for screening by non-specialists (as lowered arousal might prevent assessment of inattention or disorganised speech).

Overall utility of the CAM

Joint practice recommendations from the European and American Delirium Associations advise that inability to cooperate with cognitive assessment for attention be rated as severe inattention, in patients able to make at least some verbal response and not in coma [33]. This was the approach followed when making DSM-V consensus diagnoses [34] but differs from that of the DSM-IV on which the CAM is based. Accurate completion of the CAM in a setting with a high prevalence of severe physiological illness is challenging and requires experience and judgement. Although the overall diagnostic accuracy of the CAM compared favourably to that reported in HIC meta-analyses (sensitivity 91% vs 82-94% and specificity

96% vs 89-99% [29, 35]), in SSA where expertise in neurology or geriatrics might be limited outside urban centres, the CAM is unlikely to be useful in routine screening. In our cohort the CAM demonstrated excellent performance in differentiating delirium and dementia in those with major cognitive impairment (delirium or dementia) and those with cognitive impairment on screening (IDEA screen ≤7). It has been recommended that the CAM be used for confirmatory assessment in those found to have cognitive impairment on initial screening [29] due to the time taken to complete the assessment and level of skill required. In this hospital setting with trained personnel including physicians and neurologists, this approach should be feasible. In rural areas (where up to 63% of people in SSA live) and without specialist staff this approach may be problematic.

Screening using the IDEA cognitive screen

Routine bedside structured cognitive assessment of older hospitalised adults at risk of delirium is recommended by existing good practice guidelines in HICs [12]. The diagnostic accuracy of the IDEA cognitive screen compared favourably to other previous validation studies [23, 26] and other commonly-used cognitive screening tests [36]. Diagnostic accuracy for major cognitive impairment (delirium and dementia) was lower than that previously reported in medical inpatients and outpatients in SSA (0.903 and 0.931 respectively) [23]. This may relate to the degree and severity of illness in this cohort.

Previous validation work took place in a small, government hospital where those who were seriously unwell were routinely transferred to tertiary services for further management.

Although the IDEA cognitive screen appeared clinically useful, a significant proportion of participants were unable to complete it. Over a third of the 83 individuals unable to attempt the IDEA screen due to lowered arousal or illness severity had DSM-V delirium and routine cognitive assessment with the IDEA screen might lead to these individuals being missed. A major finding of this study was that the IDEA cognitive screen alone did not differentiate delirium and dementia. Since only one participant had a previous dementia diagnosis, and

both delirium and dementia were highly prevalent, use of the IDEA alone would not differentiate individuals with delirium and needing urgent medical attention from those with long standing cognitive impairment. Nevertheless, it is unrealistic to expect any brief cognitive screen, including those commonly used in high-income settings, to be able to identify underlying reasons for poor screening performance.

Association with confounders

The effect of visual impairment has not previously been evaluated in performance of the IDEA screen. In this study we found that significant and uncorrected visual impairment was highly prevalent, and that significant measured visual impairment correlated with a score ≤7 on the IDEA screen (the previously validated cut-off for major cognitive impairment), independent of age, education and the presence of delirium. This is likely to be due to difficulties in completing the matchstick praxis task and indicates that this needs to be taken into account when interpreting the IDEA score. Nevertheless, disregarding the matchstick item made little difference to test accuracy despite the high prevalence of visual impairment and since visuospatial impairments are commonly found in delirium, this test appears to be clinically useful. As in previous validation studies for dementia, the IDEA did not appear educationally biased in this setting despite the literacy rate being substantially higher than in previous validation studies.

Overall utility of screening tools

Both CAM and IDEA greatly outperformed routine detection of delirium by nursing and medical staff as evidenced by mention of delirium or confusion in the medical notes. Improvement of detection rates through use of a structured screening method is well evidenced in HIC settings [11] and our findings indicate that routine delirium screening using an appropriate method is highly recommended.

Limitations

A number of limitations are acknowledged. KCMC is a tertiary referral hospital and therefore those admitted would be expected to be more seriously unwell than in other hospital

settings. Educational level was higher than that recorded in previous validation studies of the IDEA cognitive screen in the same geographical region, indicating possible differences in socio-economic status. Our cohort might therefore not be typical of other settings in Tanzania. All cognitive tests were conducted in a very busy ward environment, which could at times be noisy, and this could have impacted on performance on cognitive tests, particularly for those with sensory impairment. Nevertheless no private or quiet environment for testing was available, and this therefore represented the 'real life' conditions in which cognitive assessment would normally take place. Similarly, we deliberately included all possible patients in this study, including those who may have been dysphasic or aphasic or with lowered level of consciousness. Although this may have affected screening tool performance, this reflects the situation in which these tools would be used.

Although a subset of individuals received a second review by a specialist (neurologist or physician) on the same day, it was not possible to provide a second independent clinical review for all patients due to resource implications in this busy hospital environment. Some individuals with cognitive fluctuations may therefore have been missed.

This was not a study of dementia or depression, and therefore milder cases may have been missed, particularly in those with delirium at assessment. Only 12 GDS assessments for depression were completed, suggesting that only those with the most severe symptoms were identified during neurocognitive assessment. The effect of depression on cognitive assessment with the IDEA screen cannot therefore be commented on. Nevertheless, we were able to obtain an informant history for almost all participants, and the vast majority of participants lived with family members. As a result, cognitive impairments were likely to have been observed and commented on by family members in the history. A strength of the study was the follow-up assessments for diagnostic clarification in cases of possible dementia, reducing the possibility that cases of dementia were missed. Finally, identification of delirium by treating medical staff was assessed only through retrospective case note review and it is possible that a greater number of cases were recognised, but not identified through this process.

Conclusions

This study has evaluated the performance of a brief cognitive screening tool designed for identification of dementia (the IDEA cognitive screen) and the CAM in identification of delirium in a large tertiary referral hospital in Tanzania, with a similar presence of delirium on admission to that seen in HICs. Both tools performed well in identification of delirium, but sensitivity was reduced due to difficulty in completion of assessments by those individuals who were most severely unwell, and therefore likely to be at the greatest risk. The IDEA screen did not differentiate delirium and dementia. The CAM showed excellent diagnostic accuracy for delirium in individuals identified with cognitive impairment, but requires specialist knowledge for accurate completion. Using all relevant cognitive and behavioural assessment data collected during the study we have suggested a brief assessment for delirium designed for use by non-specialists which appears to identify delirium with a high degree of accuracy. Further development work and testing in other centres in SSA will confirm the utility of these screening items for delirium. Our findings indicate that use of a structured screening tool outperformed routine clinical assessment in identification of delirium as in previous HIC studies and routine use of a delirium screening tool in older hospitalised adults is therefore highly recommended.

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References

[1] J. Cerejeira, H. Firmino, A. Vaz-Serra, E.B. Mukaetova-Ladinska, The neuroinflammatory hypothesis of delirium, Acta neuropathologica 119(6) (2010) 737-754.
[2] S.K. Inouye, R.G. Westendorp, J.S. Saczynski, Delirium in elderly people, The Lancet 383(9920) (2014) 911-922.
[3] N. Siddiqi, A.O. House, J.D. Holmes, Occurrence and outcome of delirium in medical in-patients: a systematic literature review, Age and Ageing 35(4) (2006) 350-364.
[4] J.S. Saczynski, E.R. Marcantonio, L. Quach, T.G. Fong, A. Gross, S.K. Inouye, R.N. Jones, Cognitive trajectories after postoperative delirium, N Engl J Med 367 (2012).
[5] D.H. Davis, G. Muniz Terrera, H. Keage, T. Rahkonen, M. Oinas, F.E. Matthews, C. Cunningham, T. Polvikoski, R. Sulkava, A.M. Maclullich, C. Brayne, Delirium is a strong risk factor for dementia in the oldest-old: a population-based cohort study, Brain 135 (2012).
[6] J. Witlox, L.S. Eurelings, J.F. de Jonghe, K.J. Kalisvaart, P. Eikelenboom, W.A. Van Gool, Delirium in elderly patients and the risk of postdischarge mortality, institutionalization, and dementia: a meta-analysis, Jama 304(4) (2010) 443-451.
[7] S. O'Keeffe, J. Lavan, The Prognostic Significance of Delirium in Older Hospital Patients, Journal of the American Geriatrics Society 45(2) (1997) 174-178.
[8] M. Lundstrom, A. Edlund, S. Karlsson, B. Brannstrom, G. Bucht, Y. Gustafson, A multifactorial intervention program reduces the duration of delirium, length of hospitalization, and mortality in delirious patients, Journal of the American Geriatrics Society 53(4) (2005) 622-8.
[9] R. Walker, D. Whiting, N. Unwin, F. Mugusi, M. Swai, E. Aris, A. Jusabani, G. Kabadi, W.K. Gray, M. Lewanga, Stroke incidence in rural and urban Tanzania: a prospective, community-based study, The Lancet Neurology 9(8) (2010) 786-792.
[10] S.-M. Paddick, A. Longdon, A. Kisoli, W.K. Gray, C.L. Dotchin, A. Jusabani, A. Iqbal, J. Hughes, A. Teodorczuk, P. Chaote, The Prevalence of Dementia Subtypes in Rural Tanzania, The American Journal of Geriatric Psychiatry 22(12) (2014) 1613-1622.
[11] S.K. Inouye, M.D. Foreman, L.C. Mion, K.H. Katz, L.M. Cooney Jr, Nurses' recognition of delirium and its symptoms: comparison of nurse and researcher ratings, Archives of internal medicine 161(20) (2001) 2467-2473.
[12] J. Young, L. Murthy, M. Westby, A. Akunne, R. O'Mahony, Diagnosis, prevention, and management of delirium: summary of NICE guidance, Bmj 341 (2010) c3704.
[13] M. Guerchet, P. M'belesso, A.M. Mouanga, B. Bandzouzi, A. Tabo, D.S. Houinato, M.N. Paraïso, P. Cowppli-Bony, P. Nubukpo, V. Aboyans, J.P. Clément, J.F. Dartigues, P.M. Preux, Prevalence of Dementia in Elderly Living in Two Cities of Central Africa: The EDAC Survey, Dementia and Geriatric Cognitive Disorders 30(3) (2010) 261-268.
[14] A.R. Longdon, S.M. Paddick, A. Kisoli, C. Dotchin, W.K. Gray, F. Dewhurst, P. Chaote, A. Teodorczuk, M. Dewhurst, A.M. Jusabani, The prevalence of dementia in rural Tanzania: a cross-sectional community-based study, International journal of geriatric psychiatry 28(7) (2013) 728-737.
[15] S.-M. Paddick, R. Kalaria, E. Mukaetova-Ladinska, The prevalence and clinical manifestations of delirium in sub-Saharan Africa: A systematic review with inferences, Journal of the neurological sciences 348(1) (2015) 6-17.
[16] E. Lewis, S.M. Paddick, J. Banks, A. Duinmaijer, L. Tucker, A. Kisoli, J. Cletus, C. Lissu, C. Dotchin, W. Gray, Prevalence of Delirium in Older Medical Inpatients in Tanzania, Journal of the American Geriatrics Society 64(9) (2016).
[17] R. Uwakwe, Psychiatric morbidity in elderly patients admitted to non-psychiatric wards in a general/teaching hospital in Nigeria, International journal of geriatric psychiatry 15(4) (2000) 346-354.
[18] R.O. Akinyemi, I.M.H. Izzeldin, C. Dotchin, W.K. Gray, O. Adeniji, O.A. Seidi, J.J. Mwakisambwe, C.J. Mhina, F. Mutesi, H.Z. Msechu, K.A. Mteta, M.A.M. Ahmed, S.H.M. Hamid,

N.A.A. Abuelgasim, S.A.A. Mohamed, A.Y.O. Mohamed, F. Adesina, M. Hamzat, T. Olunuga, V.P. Maro, R. Walker, Contribution of Noncommunicable Diseases to Medical Admissions of Elderly Adults in Africa: A Prospective, Cross-Sectional Study in Nigeria, Sudan, and Tanzania, Journal of the American Geriatrics Society 62(8) (2014) 1460-1466.

[19] S. Saxena, G. Thornicroft, M. Knapp, H. Whiteford, Resources for mental health: scarcity, inequity, and inefficiency, The Lancet 370(9590) 878-889.

[20] C.L. Dotchin, R.O. Akinyemi, W.K. Gray, R.W. Walker, Geriatric medicine: services and training in Africa, Age and ageing (2012) afs119.

[21] J.H. Bower, G. Zenebe, Neurologic services in the nations of Africa, Neurology 64(3) (2005) 412-415.

[22] American College of Surgeons Committee on Trauma., Advanced trauma life support course for physicians, Committee on Trauma, American College of Surgeons 1989.

[23] S.-M. Paddick, W.K. Gray, L. Ogunjimi, O. Olakehinde, A. Kisoli, J. Kissima, G. Mbowe, S. Mkenda, C.L. Dotchin, R.W. Walker, Validation of the Identification and Intervention for Dementia in Elderly Africans (IDEA) cognitive screen in Nigeria and Tanzania, BMC geriatrics 15(1) (2015) 1.

[24] M. Sands, B. Dantoc, A. Hartshorn, C. Ryan, S. Lujic, Single question in delirium (SQiD): testing its efficacy against psychiatrist interview, the confusion assessment method and the memorial delirium assessment scale, Palliative Medicine 24(6) (2010) 561-565.

[25] W.K. Gray, S.-M. Paddick, A. Kisoli, C.L. Dotchin, A.R. Longdon, P. Chaote, M. Samuel, A.M. Jusabani, R.W. Walker, Development and validation of the identification and Intervention for Dementia in Elderly Africans (IDEA) study dementia screening instrument, Journal of geriatric psychiatry and neurology (2014) 0891988714522695.

[26] W.K. Gray, S.M. Paddick, C. Collingwood, A. Kisoli, G. Mbowe, S. Mkenda, C. Lissu, J. Rogathi, J. Kissima, R.W. Walker, Community validation of the IDEA study cognitive screen in rural Tanzania, International journal of geriatric psychiatry (2016).

[27] S.K. Inouye, C.H. Van Dyck, C.A. Alessi, S. Balkin, A.P. Siegal, R.I. Horwitz, Clarifying confusion: the confusion assessment method: a new method for detection of delirium, Annals of internal medicine 113(12) (1990) 941-948.

[28] C.L. Wong, J. Holroyd-Leduc, D.L. Simel, S.E. Straus, Does this patient have delirium?: value of bedside instruments, Jama 304(7) (2010) 779-786.

[29] L.A. Wei, M.A. Fearing, E.J. Sternberg, S.K. Inouye, The Confusion Assessment Method: A Systematic Review of Current Usage, Journal of the American Geriatrics Society 56(5) (2008) 823-830.

[30] N.A. O'Regan, D.J. Ryan, E. Boland, W. Connolly, C. McGlade, M. Leonard, J. Clare, J.A. Eustace, D. Meagher, S. Timmons, Attention! A good bedside test for delirium?, Journal of Neurology, Neurosurgery & Psychiatry (2014) jnnp-2013-307053.

[31] D.J. Meagher, M. Leonard, S. Donnelly, M. Conroy, J. Saunders, P.T. Trzepacz, A comparison of neuropsychiatric and cognitive profiles in delirium, dementia, comorbid delirium-dementia and cognitively intact controls, Journal of Neurology, Neurosurgery & Psychiatry 81(8) (2010) 876-881.

[32] D.J. MEAGHER, M. MORAN, B. RAJU, D. GIBBONS, S. DONNELLY, J. SAUNDERS, P.T. TRZEPACZ, Phenomenology of delirium, Assessment of 100 adult cases using standardised measures 190(2) (2007) 135-141.

[33] EuropeanDelirium Association, The DSM-5 criteria, level of arousal and delirium diagnosis: inclusiveness is safer, BMC medicine 12(1) (2014) 141.

[34] D.J. Meagher, A. Morandi, S.K. Inouye, W. Ely, D. Adamis, A.J. Maclullich, J.L. Rudolph, K. Neufeld, M. Leonard, G. Bellelli, Concordance between DSM-IV and DSM-5 criteria for delirium diagnosis in a pooled database of 768 prospectively evaluated patients using the delirium rating scale-revised-98, BMC medicine 12(1) (2014) 1.

[35] Q. Shi, L. Warren, G. Saposnik, J.C. Macdermid, Confusion assessment method: a systematic review and meta-analysis of diagnostic accuracy, Neuropsychiatric disease and treatment 9 (2013) 1359-70.

[36] A.J. Mitchell, D. Shukla, H.A. Ajumal, B. Stubbs, T.A. Tahir, The Mini-Mental State Examination as a diagnostic and screening test for delirium: systematic review and meta-analysis, General hospital psychiatry 36(6) (2014) 627-633.

Figure 1: Study recruitment and assessment flow chart

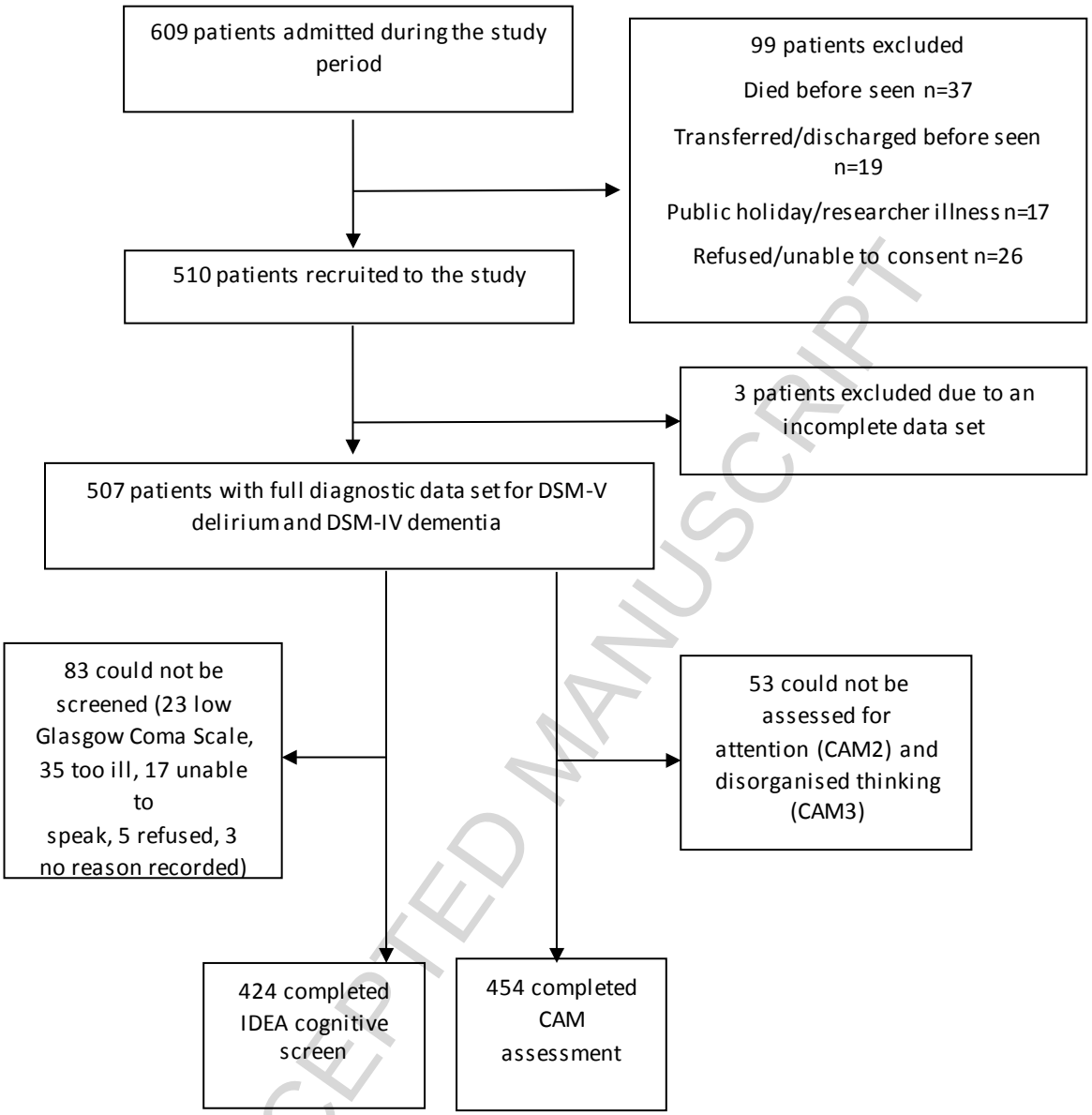

Table 1: Characteristics of the 507 patients included in the study

Full days from hospital admission to assessment	
1	415/497 (83.5%)
2	51/497 (10.3%)
3	27/497 (5.4%)
3-7	4/497 (0.8%)
Median age (IQR)	75 (67-81)
Sex	225 Females (44.4%)
Highest educational level	
Less than one year or none	96/500 (19.2%)
Some primary school	163/500 (32.6%)
Completed primary school	111/500 (22.2%)
Some secondary school	58/500 (11.6%)
Completed secondary school	34/500 (6.8%)
Tertiary education	38/500 (7.6%)
AVPU arousal	
A-Alert	400/501 (79.4%)
V-Voice	71/501 (14.1%)
P-Pain	12/501 (2.4%)
U-Unresponsive	21/501 (4.2%)
Prevalence of dementia	
Overall	95/507 (18.7%)
Males	47/282 (16.6%)
Females	48/225 (21.3%)
60-69 years	12/175 (6.86%)
70-79 years	26/173 (15.0%)
80 years and over	57/159 (35.8%)
Prevalence of delirium	
Overall	95/507 (18.7%)
Males	68/282 (24.1%)
Females	27/225 (12.0%)
60-69 years	25/175 (14.3%)
70-79 years	27/173 (15.6%)
80 years and over	43/159 (27.0%)
Prevalence of major cognitive impairment	
Overall	157/507 (30.9%)
Males	94/282 (33.3%)
Females	63/225 (28.0%)
60-69 years	31/175 (17.7%)
70-79 years	44/173 (25.4%)
80 years and over	82/159 (51.6%)
Other psychiatric diagnoses	
Depression	8 cases
Learning disability	1 case
Depression with psychosis	1 case
Cognitive impairment identified by the medical team	
Delirium	8 (6 DSM-V delirium 2 DSM-IV dementia)
Dementia	2 (1 DSM-V delirium 1 DSM-IV dementia
Cognitive/behavioural problem 'disoriented', 'aggressive'	6 (5 DSM-V delirium, 1 DSM-IV dementia)

Table 2: Diagnostic accuracy of screening tools

IDEA cognitive screen (n = 424)	**Cut-off ≤7**	**Cut-off ≤8**
DSM-V delirium	sensitivity = 0.89, specificity = 0.70, ppv = 0.35, npv = 0.97	sensitivity = 0.92, specificity = 0.64, ppv = 0.31, npv = 0.98
Major cognitive impairment	sensitivity = 0.82, specificity = 0.77, ppv = 0.56, npv = 0.92	sensitivity = 0.88, specificity = 0.71, ppv = 0.52, npv = 0.94
CAM (n = 454)		
Delirium	sensitivity = 0.91 specificity = 0.97, ppv = 0.880, npv = 0.978	
Major cognitive impairment	sensitivity = 0.53 specificity = 0.90, ppv = 0.61, npv = 0.87	
Individual CAM items		
CAM 1 (n=499) Delirium	sensitivity = 0.95, specificity = 0.85, ppv = 0.60, npv = 0.97	
CAM 2 (n=454) Delirium	sensitivity = 0.94 specificity = 0.90, ppv = 0.69, npv = 0.99	
CAM 3 (n=448) Delirium	sensitivity = 0.72 specificity = 0.96, ppv = 0.80, npv = 0.94	
CAM 4 (n=496) Delirium	sensitivity = 0.86 specificity = 0.85, ppv = 0.56, npv = 0.96	

ppv – positive predictive value,

npv – negative predictive value

Table 3: Independent predictors of DSM V delirium form screening and assessment items

	Parameter estimate	Odds ratio (95% CI)	Weight
Unable to recall any words on 10 word list	1.169	3.217 (1.291 to 8.016)	1
Positive CAM1	3.468	32.074 (11.333 to 90.776)	4
Positive CAM4	1.454	4.280 (1.869 to 9.802)	2
Male	0.957	2.604 (1.268 to 5.349)	1

Highlights

- Identification of delirium is challenging in Africa and screening tools are lacking
- The CAM and IDEA screen had clinical utility, but limitations in this setting
- A novel brief delirium screen for older inpatients is proposed for further validation

22. Commentary on Key Paper 4

Hospital validation of the IDEA for major cognitive impairment (delirium and dementia) (cohorts 5a and 5b)

22.1. Overview

This study was a repeat validation of the IDEA six item screen for delirium and for major cognitive impairment (delirium and dementia) in a large prospective consecutive cohort of older adults aged 60 and over admitted to medical inpatient wards of a tertiary referral hospital in Tanzania (KCMC) and took place between January and July 2015. The performance of the IDEA six item screen in identification of delirium was assessed as a result of the outcome of the systematic review indicating little existing data on delirium in SSA, particularly in older adults (see Background Paper 1). The aims of the study were to estimate prevalence of delirium on admission as well as prevalence of 'in hospital' delirium, to conduct a blinded validation of the Confusion Assessment Method (CAM) for delirium and the IDEA six-item screen for both delirium and major cognitive impairment (dementia and delirium) against gold standard DSM-5 delirium criteria by applied consensus. It was also intended to assess the clinical utility of serial assessment with the IDEA screen for identification of delirium in a hospital population. This study also collected data on risk factors and aetiology of delirium in this setting, alongside mortality and other outcome data. All available screening data were analysed using factor analysis and logistic regression to determine which items were most predictive of delirium in this setting. A brief combined screening tool, outperforming both the IDEA six item screen and CAM is presented following preliminary internal validation.

22.2. Materials and methods

This was a prospective cross sectional study of a consecutive sample of adults aged 60 and over admitted to medical wards of a tertiary referral hospital (KCMC). The IDEA six-item screen was administered to participants on admission by a trained study nurse or clinical officer and filed separately and not shared with the research doctor completing delirium assessments.

Clinical assessments for delirium were similar to those conducted in previous IDEA screening tool validation studies and included a mental state examination, neurological examination and detailed bedside cognitive assessment with a focus on identification of delirium. A detailed free text summary of this assessment was recorded to assist with consensus diagnosis. Detailed clinical assessments for delirium took place on admission, but after initial assessment from the treating medical team. The study diagram and summary of bedside assessments is included below in Figure 19.

The CAM algorithm was completed and filed separately in order to maintain blinding. Dementia diagnosis relied heavily on informant history, and where necessary a follow up interview post discharge to clarify the onset of symptoms and to assess cognitive and functional performance in the home environment once acute symptoms of physical illness had resolved.

Assessment for potential confounders included assessment of visual acuity using a Landholt C broken ring Logmar eye chart designed for use in illiterate populations, level of consciousness as measured by the Alert-Voice-Pain-Unresponsive (AVPU) scale and degree of physiological illness as measured by the National Early Warning Scale (NEWS) a risk grading system widely used in the UK. Other potential confounders including self-reported visual and hearing impairment, the use of sensory aids and occupational and educational background were recorded.

Baseline physical observation data were recorded, and participants felt to be too acutely unwell, in the opinion of the assessing doctor were re-assessed the following day. Where possible, participants were also reviewed for the presence of delirium symptoms by a neurologist to take into account possible fluctuations. Delirium by DSM-5 criteria was made by consensus, blinded to the outcome of the IDEA six-item screen and CAM algorithm.

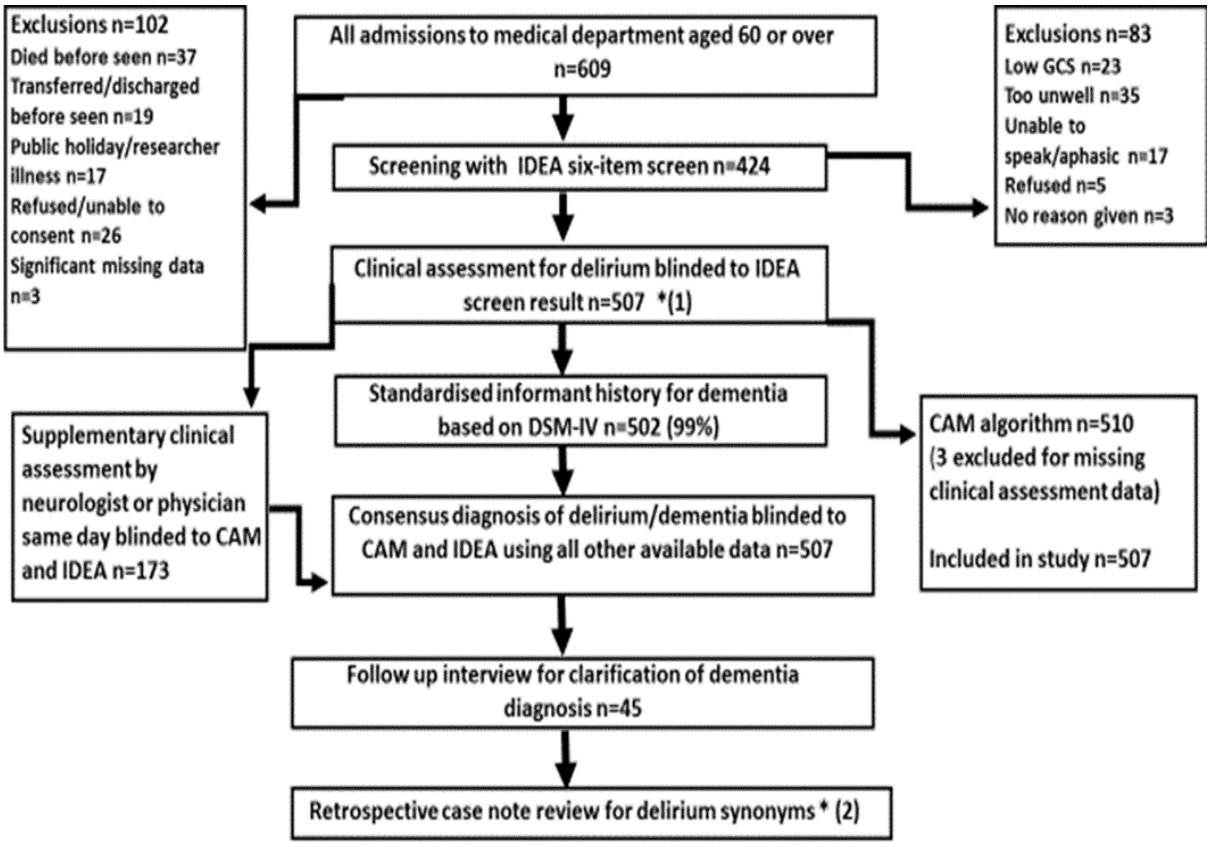

Figure 19 Delirium study flowchart and clinical diagnostic assessment

Key to figure 19* (1) **Description of assessment**

Detailed standardised bedside cognitive assessment Included : attention (days of the week backwards), registration (three market items) recall (three market items) Receptive language (three stage command)expressive language (naming, open questions about changes (environmental/political/social) specific to locality praxis (reciprocal coordination, Luria's fist/palm/side executive function/new learning (Luria's fist/palm/side sequencing Disorganisation of thought (open questions about changes (environmental/political/social) specific to locality) Orientation, time of day, place, when admitted, describe events leading up to hospital admission Confabulation, 'have you met me before'

Neurological examination (focus on vascular disease and Parkinsonism) Pronator drift, tone, power, coordination, tendon reflexes, gait (where able to stand). Where indicated, Babinski reflex glabellar tap, bradykinesia

Mental state examination General observation of appearance and behaviour Mood, reactivity, response to questions on activities enjoyed at home, hope for future Screen for delusions 'is anyone trying to trick you or doing anything bad to you?' Observation for response to unseen stimuli, distractibility

Assessment for confounders of cognitive screen performance - Visual acuity - Landholt C broken ring logmar three metre chart designed for illiterate populations. Acuity of <1.0 logmar in the best eye considered significant visual impairment. Hearing impairment - graded subjectively as mild, moderate or severe based on performance during clinical assessment.

Highest educational level - school grade literacy (ability to read and write a simple note)

Physiological illness - NEWS scale including pulse, temperature, blood pressure, respiration rate and conscious level **Conscious level** - Alert-Voice-Pain-Unresponsive (AVPU) scale Pain - 0-10 visual analogue scale

*(2) **Retrospective case note review**

Synonyms for delirium and major cognitive impairment were searched for in medical notes corresponding to the admission period during which each participant was assessed as part of this study. Synonyms included, delirium, organic mental state, organic psychosis, confusion, dementia, mental impairment, disorientation and wandering.

Development of a new delirium assessment scale

All available cognitive screening data were analysed using factor analysis and logistic regression in order to determine those items most predictive of delirium. Exploratory factor analysis of all screening and assessment items for delirium (IDEA six item screen and CAM items, beside cognitive tests and informant single question) was conducted to investigate latent traits within the screening items. An oblique rotation method was selected due to high correlation between variables. Factors to be extracted were determined using a scree plot. Items with the largest loadings on each factor were explored using logistic regression models with DSM-5 delirium as the dependent variable. Item weights were determined using parameter estimates from the final logistic regression model. Models were evaluated for diagnostic accuracy using AUROC curves.

22.3. Summary of Results

Of 507 admission assessments, 95 (18.7%) had DSM-5 delirium, 95 (18.7%) dementia and 33 (6.5%) delirium superimposed on dementia. In hospital occurrence of delirium was very low (13/362 repeat assessments (3.6%)).

Performance of the CAM for identification of delirium

Of the 507 people with a full dataset for DSM-5 delirium diagnosis, 89 (17.6%) were CAM positive, and 53 (10.5%) were classified as 'CAM unable'. In those 454 with complete CAM assessments, overall diagnostic accuracy was excellent (AUROC 0.94 (95% CI 0.904-0.977) with sensitivity and specificity of 0.91 and 0.97 respectively. Inclusion of the whole cohort with 'CAM unable' individuals classified as negative resulted in similar diagnostic accuracy but lower sensitivity (sensitivity 0.832 specificity 0.976 AUROC 0.904 (0.858-0.949). Positive (30.2) and negative likelihood ratios (0.09) were also excellent. (Diagnosis by CAM algorithm had a high level of agreement with DSM-5 diagnosis (kappa 0.827 T 18.645 sig <0.001) when those unable to complete the CAM were classified as 'no delirium' rising to (0.873 T 18.606 sig <0.001) in those able to complete the CAM.

Performance of the IDEA six-item screen

The IDEA screen identified delirium and major cognitive impairment (AUROC 0.866, 0.874 respectively) but did not differentiate these conditions. Although performance on all individual items of the IDEA screen correlated with educational level (except naming the village chairman) previous formal education and illiteracy were not significant on multivariable analysis controlling for age, gender and presence of delirium or dementia. The need to adjust scores in those without formal education has previously been investigated (in hospital and community validations of the IDEA six-item screen) and found not to be justified.

Development and internal validation of a brief combined screening tool for delirium in hospital settings

All six IDEA screen items, bedside cognitive tests of orientation, attention, registration and recall, CAM items 1 and 4 and the single informant question were investigated to identify those that may be of greatest clinical utility in this setting. CAM items 2 and 3 were not evaluated due to the observed difficulties in rating these items, suggesting that they would not be suitable for screening in this setting. Exploratory factor analysis identified three factors broadly interpreted as representing learning/recall, observation/behaviour and orientation, explaining 41.9%, 9.67% and 7.5% of the variability respectively. A logistic regression model was constructed to identify those items that were significant independent predictors of delirium. The final model is shown in Table 11. Independent predictors of DSM V delirium form screening and assessment items and included word recall, CAM 1, CAM 4 and sex. Nagelkerke's R2 for the model was 0.676.

The brief delirium screening tool had a higher AUROC than the IDEA cognitive screen (0.94 (95% CI 0.92 to 0.97)), and had the advantage of being much shorter. Accuracy was similar to that of the CAM, but assessment data were available for almost all participants including those rated unassessable on the full CAM. The scoring system ran from 0 to 8, with a score of ≥6 the optimal cut off for identifying those with delirium (sensitivity 0.94, specificity 0.90).

Table 11. Independent predictors of DSM V delirium form screening and assessment items

	Parameter estimate	Odds ratio (95% CI)	Weight
Unable to recall any words on 10 word list	1.169	3.217 (1.291 to 8.016)	1
Positive CAM1	3.468	32.074 (11.333 to 90.776)	4
Positive CAM4	1.454	4.280 (1.869 to 9.802)	2
Male	0.957	2.604 (1.268 to 5.349)	1

Table 12. Demographic data- IDEA delirium study

Full days from hospital admission to assessment	
1	415/497 (83.5%)
2	51/497 (10.3%)
3	27/497 (5.4%)
3-7	4/497 (0.8%)
Median age (IQR)	75 (67-81)
Sex	225 Females (44.4%)
Highest educational level	
Less than one year or none	96/500 (19.2%)
Some primary school	163/500 (32.6%)
Completed primary school	111/500 (22.2%)
Some secondary school	58/500 (11.6%)
Completed secondary school	34/500 (6.8%)
Tertiary education	38/500 (7.6%)
AVPU arousal	
A-Alert	400/501 (79.4%)
V-Voice	71/501 (14.1%)
P-Pain	12/501 (2.4%)
U-Unresponsive	21/501 (4.2%)
Prevalence of dementia	
Overall	95/507 (18.7%)
Males	47/282 (16.6%)
Females	48/225 (21.3%)
60-69 years	12/175 (6.86%)
70-79 years	26/173 (15.0%)
80 years and over	57/159 (35.8%)
Prevalence of delirium	
Overall	95/507 (18.7%)
Males	68/282 (24.1%)
Females	27/225 (12.0%)
60-69 years	25/175 (14.3%)
70-79 years	27/173 (15.6%)
80 years and over	43/159 (27.0%)
Prevalence of major cognitive impairment	
Overall	157/507 (30.9%)
Males	94/282 (33.3%)
Females	63/225 (28.0%)
60-69 years	31/175 (17.7%)
70-79 years	44/173 (25.4%)
80 years and over	82/159 (51.6%)
Other psychiatric diagnoses	
Depression	8 cases
Learning disability	1 case
Depression with psychosis	1 case
Cognitive impairment identified by the medical team	
Delirium	8 (6 DSM-5 delirium 2 DSM-IV dementia)
Dementia	2 (1 DSM-5 delirium 1 DSM-IV dementia
Cognitive/behavioural problem ‘disoriented’, ‘aggressive’	6 (5 DSM-5 delirium, 1 DSM-IV dementia)

Table 13. Diagnostic accuracy of screening tools –IDEA delirium study

IDEA cognitive screen (n = 424)	Cut-off ≤7	Cut-off ≤8
DSM-5 delirium	sensitivity = 0.89, specificity = 0.70, ppv = 0.35, npv = 0.97	sensitivity = 0.92, specificity = 0.64, ppv = 0.31, npv = 0.98
Major cognitive impairment	sensitivity = 0.82, specificity = 0.77, ppv = 0.56, npv = 0.92	sensitivity = 0.88, specificity = 0.71, ppv = 0.52, npv = 0.94
CAM (n = 454)		
Delirium	sensitivity = 0.91 specificity = 0.97, ppv = 0.880, npv = 0.978	
Major cognitive impairment	sensitivity = 0.53 specificity = 0.90, ppv = 0.61, npv = 0.87	
Individual CAM items		
CAM 1 (n=499) Delirium	sensitivity = 0.95, specificity = 0.85, ppv = 0.60, npv = 0.97	
CAM 2 (n=454) Delirium	sensitivity = 0.94 specificity = 0.90, ppv = 0.69, npv = 0.99	
CAM 3 (n=448) Delirium	sensitivity = 0.72 specificity = 0.96, ppv = 0.80, npv = 0.94	
CAM 4 (n=496) Delirium	sensitivity = 0.86 specificity = 0.85, ppv = 0.56, npv = 0.96	

ppv – positive predictive value,

npv – negative predictive value

Table 14. Performance of screening tools in individuals with cognitive impairment (dementia or delirium)

IDEA delirium study

	AUROC (95% CI)	Cut-off ≤7	Cut-off ≤8
IDEA cognitive screen (n = 103)			
DSM-5 delirium Cut off 3 Cut off 7 Cut off 8	0.60(0.49-0.71)	sn = 0.88 sp = 0.28 ppv = 0.59 npv = 0.65	sn = 0.91 sp = 0.19 ppv = 0.57 npv = 0.64
CAM (n = 134)			
Delirium	0.93 (0.88-0.98)	sn = 0.91 sp = 0.96 ppv = 0.98 npv = 0.85	
CAM1 (n=155)	0.82(0.75-0.90)	sn = 0.95 sp = 0.70 ppv = 0.83 npv = 0.89	
CAM2 (n=133)	0.85 (0.77-0.93)	sn = 0.94 sp = 0.76 ppv = ?? npv = ??	
CAM3(n=129)	0.76(0.68-0.85)	sn = 0.72 sp = 0.80 ppv = 0.87 npv = 0.62	
CAM4(n=151)	0.76(0.68-0.85)	sn = 0.86 sp = 0.67 ppv = 0.79 npv = 0.76	

sn – sensitivity,
sp – specificity,
ppv – positive predictive value,
npv – negative predictive value

Table 15. Performance of IDEA six-item screen core disregarding matchstick construction task

	AUROC (95% CI)	Cut-off ≤4	Cut-off ≤5
IDEA cognitive screen without matchsticks (n=424)			
DSM-5 delirium	0.86(0.82-0.90)	sn = 0.80 sp = 0.80	sn = 0.84 sp = 0.74
Cut off 4 Cut off 5		ppv = 0.39 npv = 0.96	ppv = 0.34 npv = 0.97
Major cognitive impairment	0.87 (0.84-0.91)	sn = 0.70 sp = 0.86	sn = 0.79 sp = 0.81
Cut-off 4 Cut-off 5		ppv = 0.62 npv = 0.90	ppv = 0.58 npv = 0.92

sn – sensitivity,
sp – specificity,
ppv – positive predictive value,
npv – negative predictive value

Table 16. Between group differences (Dementia, Delirium and Major Cognitive Impairment)

	No major CI (N=312)	Major CI N=112	Delirium N=64	Dementia (no delirium) N=48	Pairwise comparisons (MWU/Chi)
Age (Md, IQR)	72 (65-79)	80 (73-85)	79.5(70.25 -84.75)	81.5 (77.25-88)	**No CI vs CI** U 10145.500 z -6.592 Sig<0.001 **No CI vs delirium** U 6421.500 Z -4.502 sig <0.001 **No CI vs dementia** U 3724.000 Z -5.613 sig<0.001 **Delirium vs Dementia** U 1259.500 Z=-1.628 sig <0.104
Female, (n %)	144 (46.2%)	44 (39.3%)	17 (26.6%)	27 (56.3%)	**No CI vs CI** Chi sq. 1.575 Sig 0.209 Exact sig 0.224 **Delirium vs Dementia** Chi 13.722 (male) sig <0.001 Ex <0.001
Education =>1year, (n %)	258 (82.7%) m=2	80 (71.4%) m=3	52 (81.3%) m=2	28 (58.3%) m=1	No CI vs CI Chi Sq4.998 sig 0.025 exact sig 0.034 **Delirium vs Dementia** Chi sq. 5.974 Sig 0.15 Exact 0.22
Literacy, (n %)	250 (80.1%) m=10	75 (67%) m=4	48 (75%) m=3	27 (56.3%) m=1	**No CI vs CI** Chi Sq. 8.611 sig 0.003 Exact 0.005 Delirium vs Dementia Chi 5.170 sig 0.023 exact 0.027
Total IDEA score (Md, IQR)	11 (8-13)	4 (0-7)	3 (0-6)	5 (2-8)	**No CI vs CI** U= 4408.500 Z=-11.775 Sig<0.001 **No CI vs delirium** U=1931.500 Z=-10.198 sig <0.001 **No CI vs dementia** U=2477.000 Z=-7.491 sig<0.001 Delirium vs Dementia U=1146.500 Z=-2.318 sig 0.020
Word learning (Md, IQR)	11 (8-14)	5 (0-7)	3 (0-7)	6 (1-10)	**No CI vs CI** U=5480.000 Z=-10.807 Sig<0.001 **No CI vs delirium** U=2410.500 Z=-9.586 sig <0.001 **No CI vs dementia** U=3069.500 Z=-6.600 sig <0.001 Delirium vs Dementia U=1166.500 Z=-2.203 sig <0.028
Bridge (n,% correct)	263 (84.3%)	53 (47.3%)	29 (45.3%)	24 (50%)	No CI vs CI 59.348 sig <0.001 exact <0.001 **Delirium vs dementia** 1.288 sig 0.256 exact 0.300
Animal fluency (md, IQR)	9 (7-11) m= 71	4 (1-7) m= 25	4 (0-6.75) m= 16	4 (2-8) m=9	**No CI vs CI** U=2975.500 Z=-9.939 Sig <0.001 **No CI vs delirium** U=1394.000 Z=-8.335 sig <0.001

					No CI vs dementia U=1581.500 Z=-6.675 sig <0.001 **Delirium vs Dementia** U=809.500 Z=-1.093 sig< 0.274
Animal score (Md, IQR)	2 (1-2)	1 (0-1)	1 (0-1)	1 (0-2)	**No CI vs CI** U=7338.000 Z=-10.296 Sig <0.001 **No CI vs delirium** U=3323.500 Z=-9.708 sig<0.001 **No CI vs dementia** U=4014.500 Z=-6.180 sig,0.001 Delirium vs dementia U= 1185.000 Z=-2.228 sig 0.026
Chairman (n,% correct)	252 (80.8%)	50 (44.6%)	24 (37.5%)	26 (54.2%)	No CI vs CI 52.483 sig ,0.001 exact <0.001 **Delirium vs dementia** 5.140 sig 0.023 exact 0.034
Weekday (n, % correct)	223 (71.3%)	28 (25%)	11 (17.2%)	17 (35.4%)	No CI vs CI 73.696 sig <0.001 exact <0.001 **Delirium vs dementia** 6.693 sig 0.01 exact 0.17
Word recall(Md, IQR)	3 (1-4)	0 (0-0)	0 (0-0)	0 (0-1)	**No CI vs CI** U=6133.500 Z=-10.510 Sig <0.001 **No CI vs delirium** U=3058.000 Z=-8.959 sig<0.001 **No CI vs dementia** U=3075.500 z=-6.705 sig<0.001 Delirium vs Dementia U=1316.000 Z=-1.754 sig<0.079
Matchstick(Md, IQR)best	3 (1-3)	0 (0-2)	0 (0-2)	1 (0-3)	**No CI vs CI** U=9099.000 Z=-8.257 Sig<0.001 **No CI vs delirium** U=4647.000 Z=-7.494 sig <0.001 **No CI vs dementia** U 4452.000 Z -5.103 Sig<0.001 **Delirium vs Dementia** U 1298.000 Z -1.544 sig <0.123

22.4. Strengths and limitations of Key Paper 4

This study allowed a further evaluation of the IDEA screen in a large cohort and in a large tertiary referral hospital cohort and in a younger age group to those included in previous validation studies. Education level was also higher than that in previous validation studies. Strengths of this paper were the formal consensus panel diagnoses of delirium and dementia with follow-up assessments available to clarify diagnoses. Other strengths are the consecutive sampling, large sample size and amount of clinical information available to corroborate diagnoses. Nevertheless the tertiary referral hospital study site (KCMC) resulted in a cohort for assessment with high levels of physiological illness which may not be typical of other hospital settings in Tanzania. In this study, this issue (illness severity and high prevalence of altered consciousness) led to a relatively high proportion of individuals labelled as 'unable to assess'. KCMC is funded through a partnership between local government and a charitable foundation and user payments are required in individuals without health insurance. This is likely to have impacted on the representativeness of individuals admitted compared to those admitted to government hospitals with lower admission charges.

A major difficulty identified during this study was assessment of inattention. The use of relatively junior doctors to carry out delirium assessments resulted in a situation likely to be similar to that in routine practice, but resulted in individuals unable to answer due to illness or inability to follow commands frequently labelled as 'unable to assess' for inattention. Consensus guidelines recommend that inability to follow instructions, in individuals without coma be regarded as inattention. This was taken as the approach during formal consensus panel diagnosis and may have been the case if assessments were conducted by specialists in neurology or psychiatry. However since delirium screening would typically be carried out by non-specialists in Tanzania as in HICs I felt that this was a useful illustration of problems with use of the full CAM in this setting.

The effect of visual impairment has not previously been evaluated in performance of the IDEA screen. In this study we found that visual impairment based on measured visual acuity was highly prevalent, and that significant measured visual impairment correlated with a score </7 on the IDEA screen, independent of age, education and the presence of delirium. This is likely to be due to difficulties in completing the visuospatial task and indicates that this needs to be taken into account when interpreting the IDEA score. Nevertheless, the IDEA screen also performed well (AUROC 0.86 DSM-5 delirium and AUROC 0.87 Major cognitive impairment) when the matchstick item was disregarded indicating that removal of this item would be a reasonable step to take in a hospital setting.

Depression

This was not a study of depression, and assessments focussed only on exclusion of depression as a possible confounding factor for poor cognitive performance. The 15 item Geriatric Depression Scale (GDS) was used in a small number of participants, but depression was only assessed for if there was evidence of low mood or lack of enjoyment or reactivity on mental state examination. It is therefore likely that some cases of depression would have been missed, especially those that were less severe. This was partly due to the acute hospital setting and the fact that no validated screening tools for assessment or screening of depression in older people exist in SSA making this a challenging area. The effect of depression on IDEA screen scores cannot therefore be commented upon, however some preliminary work on the association between depression symptoms and IDEA screen scores in the community found no evidence of independent association.

Serial cognitive screening

We were not able to assess the effect of serial cognitive screening using the IDEA in detection of delirium due to a surprisingly low occurrence of in-hospital delirium (3.6% of repeat assessments). The reasons for this finding are unclear. in HICs, meta-analyses of in-hospital incidence of delirium report rates of between 11-29 on geriatric and general medical wards[111, 112] rising to 56% in those with pre-existing dementia. One reason may be the presence of a bedsider, a family member staying with the patient to provide meals and carry out basic nursing care. Existing guidelines recommend nursing by one familiar person in order to reduce disorientation in prevention of delirium and this may have had an effect[120]. Almost all individuals in this study had a bedsider, as evidenced by over 99% being able to provide an appropriate informant history for cognitive impairment. A significant number of individuals described delirium symptoms prior to admission, and the cost and geographical distance may have led to delayed presentation and therefore resolution of symptoms prior to admission.

Limitations of the IDEA six-item screen in identification of delirium

One major issue identified during the process of development of this screening method for delirium was the absence of a suitably validated method of screening for inattention. The presence of inattention was the item most predictive of delirium in the CAM algorithm (based on outcome of bedside cognitive assessment and mental state examination), and this item had good diagnostic accuracy used alone for delirium screening. Most measures of attention and concentration used in routine cognitive screening in HIC settings rely on spelling or calculation, and in this setting the lower literacy version used (days of the week backwards) also appeared correlated with educational level,

although it was difficult to separate this from presence of cognitive decline in this acute inpatient setting. Inattention was assessed clinically through both clinical assessment and in general discussion and ability to stay on the topic of the conversation and respond to commands, but this assessment strategy requires skills and experience in cognitive assessment and these assessments proved difficult in cases where individuals were significantly unwell. The IDEA does not include an item assessing attention directly, but other cognitive screening items requiring attention for completion such as word list learning, recall (because adequate encoding requires attention) and categorical fluency have shown potential as surrogate measures of attention. The inclusion of word list recall in the brief delirium screening tool developed probably reflects this.

22.5. Outcome of Key Paper 4

Our findings indicate that use of a structured screening tool outperformed routine clinical assessment in identification of delirium as in previous HIC studies. Routine use of a delirium screening tool in older hospitalised adults is therefore highly recommended.

This work completed towards development of a delirium screening method is preliminary but shows the potential of continuing to work incrementally towards creation of an integrated cognitive assessment method that can be used in both inpatient and outpatient settings.

23. Outcomes

23.1. Summary

This series of published papers outline my work towards development of an integrated cognitive assessment method designed to assist health workers in sub-Saharan Africa to identify dementia accounting for higher levels of illiteracy in some areas. Any assessment method for dementia needs to offer decision support in cases of possible delirium needing prompt medical intervention, and for this reason work on identification of delirium has been included. The overall outcome at present is a brief combined cognitive and functional assessment method for dementia in community settings.

Development of screening tools suitable for use in a low-literacy environment is complicated by the need for tools which can be used in both illiterate and literate individuals without significant floor and ceiling effects. The evidence presented indicates that although tools can be designed to be used in lower literacy settings the cognitive (and neurodevelopmental) differences between illiterate and literate individuals are such that cognitive performance cannot be expected to be equivalent. The need to make a correction to screening scores in illiterate individuals has been explored and found to be unnecessary. Indeed this approach is likely to reduce validity, particularly since lack of formal education may be a risk factor for cognitive decline and dementia. The screening tool we have developed has advantages over many of those used in HIC settings as it screens all four lobes of the brain and a wider range of cognitive functions than many similarly brief cognitive assessment tools which focus on memory and orientation only. We are therefore more likely to identify a wider range of cognitive impairments, and to successfully screen dementias other than ADD. It is important to state that we have not yet formally validated the IDEA in different dementia subtypes, partially because during the period in which these studies were completed there were no neuroimaging facilities available locally.

Examination of published literature on cognitive performance in illiterate and low-literate populations demonstrates that assessment methods such as the CSI-D, despite being used in low literacy settings, include many items which are known to be poorly answered in individuals who are illiterate. These items include abstract thought (similarities) logical memory (recall of a brief story) and a three stage command as well as items more obviously related to literacy such as drawing interlocking sentences or pentagons. Although orientation has been shown to be less affected by education than other cognitive domains, cultural background is also important in this regard, and the CSI-D includes items such as the year which may be difficult for older people in rural areas. The IDEA six-item screen appears to address these issues.

The second overall outcome is the development and internal validation of a brief screening method for identification of delirium in a hospital inpatient setting. This screening method appears to have a high degree of accuracy, and has the advantage of being brief and based on simple cognitive and behavioural observation items so it has potential for use by non-specialists in an inpatient setting. Further (and external) validation is needed in other similar settings.

The review of cognitive screening tools validated in illiterate and low-literate settings worldwide presented in Background Paper 1 demonstrates that few screening tools are adequately validated. Few have more than one good quality validation study and therefore the evidence for use of any one particular test is extremely limited. The IDEA screen was not included within this review, because at the time of completion of the literature searches, the initial validation of the IDEA had not been published. The IDEA has now been validated in inpatient, outpatient and community settings in Tanzania, inpatients in Nigeria and a separate validation has taken place for patients aged 60 and over admitted to a mission hospital in Katete, Zambia (unpublished data).

The studies presented here were conducted with very limited resources, both in terms of equipment and specialist staff. Whilst this was appropriate in that the goal was development of a screening method suitable for a resource poor setting, it meant that some data which would have been useful in informing the work were not collected. For example neuroimaging facilities were not available locally at the time the studies were carried out, meaning that dementia subtypes could not be confidently stated. Similarly increased staff resources would have allowed assessment of delirium phenomenology in more detail, with completion of a detailed assessment tool such as the DRS-98. We were also not able to conduct regular repeat cognitive assessments on individuals with delirium in order to determine the rate of resolution of symptoms as we needed to prioritise assessment of a complete consecutive admission cohort.

Table 17. Accuracy of the IDEA cognitive screening tools for dementia, delirium and major cognitive impairment in different settings

		Prevalence	AUROC	sensitivity	specificity	PPV	NPV	LR+	LR-
Major CI									
	IP 7/17 Cut off 8/15	33/97	0.917	90.9 93.9	87.5 81.3	78.9 72.1		7.3 5.0	
	OPD 7/15 Cut off 8/15	13/59	0.919	61.5 84.6	93.5 89.1	- -		9.5 7.8	
	Tertiary referral hospital	112/424 (26.4%)	0.874 (0.84-0.91)	0.821 0.875	0.766 0.712	0.558 0.521	0.923 0.941	3.511 3.033	0.233 0.176
Dementia	Community	39/153	0.855 (0.80-0.92)	59 87.2	86 67.5				
	IADL	35/130	0.896 (0.84-0.95)						
	Combined IDEA IADL	35/130	0.937 (0.896-0.979)						
	MMSE	17/60	0.805 (0.69-0.92)	0.77	0.71				
Delirium in hospital	IDEA 6 item screen Cut off 7 Cut off 8	64/424 (15.1%)	0.866 (0.826-0.907)	0.891 0.922	0.700 0.642	0.345 0.314	0.973 0.979	2.969 2.573	0.156 0.122
	CAM	89/454	0.94 (95% CI 0.904-0.977	0.91	0.97	0.880	0.978	30.199	0.093
Validation dataset	Brief delirium assessment (internal validation)	18/76 (m=1)	0.979 (0.954-1.0)	1.0	0.921	0.783	1.000	11.600	0.000
Development dataset		68/304 (4m)	0.936 (0.911-0.961)	0.926	0.826	0.606	0.975	5.333	0.089

23.2. Future work

This work has not yet addressed the issue of cognitive assessment in HIV and effective screening methods for HIV dementia and HIV-related neurocognitive impairment in this setting. I completed a study which aimed to answer this question in a cohort of individuals aged 50 and over under long term follow up at a government free-of-charge HIV clinic in march to May 2016 with further follow-up due to commence in March 2017. Data analysis is ongoing. Identification of depression is another issue needing further assessment. A study intended to identify the best method of screening for depression in older adults in this setting is in preparation and due to commence in 2017.

The work outlined in this thesis is preliminary, as independent external validation of the screening tools presented here is needed in order to avoid the shortcomings noted in the systematic review of existing cognitive screening tools presented in the introductory section (Background Paper 1)

It is hoped that the final result will be a screening method and decision-support aid for primary health care workers and hospital inpatient staff to use when assessing older people who may have cognitive impairment and accurately identify dementia in order to refer individuals for appropriate interventions, identify those who may have delirium and consider whether symptoms may be better explained by depression in order to refer appropriately.

Pilot validation of a brief community-based combined cognitive screen (including cognitive and selected functional assessment items only) is due to commence in the Hai district in 2017.

Figure 20 The IDEA study team, 2014

Key:

Front row (from left) Declare Mushi, Olaide Olakehinde, Sarah Mkenda, Adesola Ogunniyi, Stella-Maria Paddick, Godfrey Mbowe, Aloyce Kisoli

Back row (from left) Celia Collingwood, Catherine Dotchin, Akin Adebiyi, Richard Walker, Keith Gray

Key members not present, Sarah Urasa, John Kissima (Tanzania) Akeem Siwoku (Nigeria)

23.3. Selected publications not included in thesis

Paddick, S.M., Mkenda, S., Mbowe, G., Kisoli, A., Gray, W.K., Dotchin, C.L., Ternent, L., Ogunniyi, A., Kissima, J., Olakehinde, O. and Mushi, D., 2017. Cognitive stimulation therapy as a sustainable intervention for dementia in sub-Saharan Africa: feasibility and clinical efficacy using a stepped-wedge design. International psychogeriatrics, pp.1-11.

Paddick, S.M., Kisoli, A., Mkenda, S., Mbowe, G., Gray, W.K., Dotchin, C., Ogunniyi, A., Kisima, J., Olakehinde, O., Mushi, D. and Walker, R.W., 2017. Adaptation and validation of the Alzheimer's Disease Assessment Scale–Cognitive (ADAS-Cog) in a low-literacy setting in sub-Saharan Africa. Acta Neuropsychiatrica, pp.1-8.

Lewis, E., **Paddick, S.M**., Banks, J., Duinmaijer, A., Tucker, L., Kisoli, A., Cletus, J., Lissu, C., Dotchin, C., Gray, W. and Walker, R., 2016. Prevalence of Delirium in Older Medical Inpatients in Tanzania. Journal of the American Geriatrics Society, 64(9).

Paddick, S.M., Kisoli, A., Dotchin, C.L., Gray, W.K., Chaote, P., Longdon, A. and Walker, R.W., 2015. Mortality rates in community-dwelling Tanzanians with dementia and mild cognitive impairment: a 4-year follow-up study. Age and Ageing, 44 (4): 636-641

Paddick, S.M., Kisoli, A., Samuel, M., Higginson, J., Gray, W.K., Dotchin, C.L., Longdon, A.R., Teodorczuk, A., Chaote, P. and Walker, R.W., 2015. Mild cognitive impairment in rural Tanzania: Prevalence, profile, and outcomes at 4-year follow-up. The American Journal of Geriatric Psychiatry, 23(9), pp.950-959.

Paddick, S.M., Kisoli, A., Longdon, A., Dotchin, C., Gray, W.K., Chaote, P., Teodorczuk, A. and Walker, R., 2015. The prevalence and burden of behavioural and psychological symptoms of dementia in rural Tanzania. International journal of geriatric psychiatry, 30(8), pp.815-823

Hindley, G., Kissima, J., L Oates, L., **Paddick, S.M**., Kisoli, A., Brandsma, C., K Gray, W., Walker, R.W., Mushi, D. and Dotchin, C.L., 2017. The role of traditional and faith healers in the treatment of dementia in Tanzania and the potential for collaboration with allopathic healthcare services. Age and ageing, 46(1), pp.130-137

Mushi, D., Rongai, A., **Paddick, S.M**., Dotchin, C., Mtuya, C. and Walker, R., 2014. Social representation and practices related to dementia in Hai District of Tanzania. BMC public health, 14(1), p.260.

24.References

1. Prince M, Bryce R, Albanese E, Wimo A, Ribeiro W, Ferri CP. The global prevalence of dementia: a systematic review and metaanalysis. *Alzheimer's & Dementia* 2013; **9**(1): 63-75. e2.
2. Wimo A, Jönsson L, Bond J, Prince M, Winblad B. The worldwide economic impact of dementia 2010. *Alzheimer's & Dementia* 2013; **9**(1): 1-11.e3.
3. Olayinka OO, Mbuyi NN. Epidemiology of dementia among the elderly in sub-Saharan Africa. *International Journal of Alzheimer's Disease* 2014; **2014**.
4. Ogunniyi AO, Osuntokun BO, Lekwauwa UB, Falope ZF. Rarity of dementia (by DSM-III-R) in an urban community in Nigeria. *East African Medical Journal* 1992; **69**(2): 64-8.
5. Osuntokun BO, Adeuja AOG, Schoenberg BS, et al. Neurological disorders in Nigerian Africans: A community-based study. *Acta neurologica Scandinavica* 1987; **75**(1): 13-21.
6. Hendrie HC, Osuntokun BO, Hall KS, et al. Prevalence of Alzheimer's disease and dementia in two communities: Nigerian Africans and African Americans. *The American journal of psychiatry* 1995; **152**(10): 1485-92.
7. Ogunniyi A, Baiyewu O, Gureje O, et al. Epidemiology of dementia in Nigeria: results from the Indianapolis-Ibadan study. *European journal of neurology : the official journal of the European Federation of Neurological Societies* 2000; **7**(5): 485-90.
8. Yusuf AJ, Baiyewu O, Sheikh TL, Shehu AU. Prevalence of dementia and dementia subtypes among community-dwelling elderly people in northern Nigeria. *Int Psychogeriatr* 2011; **23**(3): 379-86.
9. Longdon AR, Paddick SM, Kisoli A, et al. The prevalence of dementia in rural Tanzania: a cross-sectional community-based study. *Int J Geriatr Psychiatry* 2013; **28**(7): 728-37.
10. Guerchet M, M'Belesso P, Mouanga AM, et al. Prevalence of dementia in elderly living in two cities of Central Africa: the EDAC survey. *Dementia and geriatric cognitive disorders* 2010; **30**(3): 261-8.
11. Clausen T, Romoren TI, Ferreira M, Kristensen P, Ingstad B, Holmboe-Ottesen G. Chronic diseases and health inequalities in older persons in Botswana (southern Africa): a national survey. *Journal of Nutrition, Health & Aging* 2005; **9**(6): 455-61.
12. Guerchet M, Houinato D, Paraiso MN, et al. Cognitive impairment and dementia in elderly people living in rural Benin, west Africa. *Dement Geriatr Cogn Disord* 2009; **27**(1): 34-41.
13. Gureje O, Ogunniyi A, Kola L. The profile and impact of probable dementia in a sub-Saharan African community: Results from the Ibadan Study of Aging. *J Psychosom Res* 2006; **61**(3): 327-33.
14. Kowal P, Chatterji S, Naidoo N, et al. Data resource profile: the World Health Organization Study on global AGEing and adult health (SAGE). *International journal of epidemiology* 2012; **41**(6): 1639-49.
15. Beaglehole R, Bonita R, Horton R, et al. Priority actions for the non-communicable disease crisis. *The Lancet* 2011; **377**(9775): 1438-47.
16. Chen C-H, Mizuno T, Elston R, et al. A comparative study to screen dementia and APOE genotypes in an ageing East African population. *Neurobiology of aging* 2010; **31**(5): 732-40.
17. Gureje O, Ogunniyi A, Baiyewu O, et al. APOE ε4 is not associated with Alzheimer's disease in elderly Nigerians. *Annals of neurology* 2006; **59**(1): 182-5.
18. Osuntokun BO, Sahota A, Ogunniyi A, et al. Lack of an association between apolipoprotein E ϵ4 and Alzheimer's disease in elderly Nigerians. *Annals of neurology* 1995; **38**(3): 463-5.
19. Paddick S-M, Mkenda S, Mbowe G, et al. Cognitive stimulation therapy (CST) as a sustainable intervention for dementia in low-resource settings: Results of a controlled trial in rural tanzania. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association* 2015; **11**(7): P322.
20. Ogunniyi A, Gureje O, Baiyewu O, et al. Profile of dementia in a Nigerian community--types, pattern of impairment, and severity rating. *Journal of the National Medical Association* 1997; **89**(6): 392-6.

21. Uwakwe R. Psychiatric morbidity in elderly patients admitted to non-psychiatric wards in a general/teaching hospital in Nigeria. *International Journal of Geriatric Psychiatry* 2000; **15**(4): 346-54.
22. Baiyewu O, Unverzagt F, Ogunniyi A, et al. Cognitive impairment in community-dwelling older Nigerians: clinical correlates and stability of diagnosis. *European Journal of Neurology* 2002; **9**(6): 573-80.
23. Ochayi B, Thacher T. Risk factors for dementia in central Nigeria. *Aging and Mental Health* 2006; **10**(6): 616-20.
24. Uwakwe R, Ibeh CC, Modebe AI, et al. The Epidemiology of Dependence in Older People in Nigeria: Prevalence, Determinants, Informal Care, and Health Service Utilization. A 10/66 Dementia Research Group Cross-Sectional Survey. *Journal of the American Geriatrics Society* 2009; **57**(9): 1620-7.
25. Guerchet M, M'belesso P, Mouanga AM, et al. Prevalence of Dementia in Elderly Living in Two Cities of Central Africa: The EDAC Survey. *Dementia and Geriatric Cognitive Disorders* 2010; **30**(3): 261-8.
26. Paraïso MN, Guerchet M, Saizonou J, et al. Prevalence of dementia among elderly people living in Cotonou, an urban area of Benin (West Africa). *Neuroepidemiology* 2011; **36**(4): 245-51.
27. Paddick S-M, Longdon A, Kisoli A, et al. The Prevalence of Dementia Subtypes in Rural Tanzania. *The American Journal of Geriatric Psychiatry* 2014; **22**(12): 1613-22.
28. Baiyewu O, Adeyemi JD, Ogunniyi A. Psychiatric disorders in Nigerian nursing home residents. *International journal of geriatric psychiatry* 1997; **12**(12): 1146-50.
29. Napon C, Traore I, Niakara A, Ouango G, Kabra A, Kabore J. Dementias in sub-Saharan Africa Clinical and Etiological Aspects in Hospital Environment in Ouagadogou (Burkina Faso). *African Journal of the Neurological Sciences* 2009; **28**(1).
30. Ramlall S, Chipps J, Pillay BJ, Bhigjee AI. Mild cognitive impairment and dementia in a heterogeneous elderly population: prevalence and risk profile. *African journal of psychiatry* 2013; **16**(6).
31. Coume M, Toure K, Thiam MH, et al. [Estimate of the prevalence of cognitive impairment in an elderly population of the health center of Senegalese national retirement institution]. *Geriatrie et psychologie neuropsychiatrie du vieillissement* 2012; **10**(1): 39-46.
32. TourÉ K, CoumÉ M, Ndiaye NND, et al. The test of Senegal: a valid and reliable screening tool to assess for dementia in a Senegalese elderly population

African Journal of Neurological Sciences 2008; **27**(1): 4.
33. Yusuf A, Maitama H, Amedu M, Sheikh T, Ahmed M, Mbibu H. Male urinary incontinence and dementia in Zaria, Nigeria. *West African journal of medicine* 2012; **32**(4): 263-6.
34. Gnonlonfoun DD, Adjien C, Ossou-Nguiet PM, et al. Prevalence of Dementia and Its Associated Factors in Cotonou Teaching Hospital, Benin. *Advances in Alzheimer's Disease* 2014; **2014**.
35. Prince M, Acosta D, Chiu H, Scazufca M, Varghese M. Dementia diagnosis in developing countries: a cross-cultural validation study. *The Lancet* 2003; **361**(9361): 909-17.
36. Sosa AL, Albanese E, Prince M, et al. Population normative data for the 10/66 Dementia Research Group cognitive test battery from Latin America, India and China: a cross-sectional survey. *Bmc Neurology* 2009; **9**(1): 1.
37. Hall KS, Gao S, Emsley CL, Ogunniyi AO, Morgan O, Hendrie HC. Community screening interview for dementia (CSI 'D'); performance in five disparate study sites. *Int J Geriatr Psychiatry* 2000; **15**(6): 521-31.
38. Prince M. Dementia in developing countries. A consensus statement from the 10/66 Dementia Research Group. *International Journal of Geriatric Psychiatry* 2000; **15**(1): 14-20.
39. Prince M. Methodological issues for population-based research into dementia in developing countries. A position paper from the 10/66 Dementia Research Group. *International journal of geriatric psychiatry* 2000; **15**(1): 21-30.

40. Uwakwe R. Psychiatric morbidity in elderly patients admitted to non-psychiatric wards in a general/teaching hospital in Nigeria. *International journal of geriatric psychiatry* 2000; **15**(4): 346-54.
41. Shulman KI, Herrmann N, Brodaty H, et al. IPA survey of brief cognitive screening instruments. *International Psychogeriatrics* 2006; **18**(02): 281-94.
42. Lang L, Clifford A, Wei L, et al. Prevalence and determinants of undetected dementia in the community: a systematic literature review and a meta-analysis. *BMJ open* 2017; **7**(2): e011146.
43. Yokomizo JE, Simon SS, de Campos Bottino CM. Cognitive screening for dementia in primary care: a systematic review. *International Psychogeriatrics* 2014; **26**(11): 1783-804.
44. Saxena S, Thornicroft G, Knapp M, Whiteford H. Resources for mental health: scarcity, inequity, and inefficiency. *The Lancet*; **370**(9590): 878-89.
45. Dotchin CL, Akinyemi RO, Gray WK, Walker RW. Geriatric medicine: services and training in Africa. *Age and ageing* 2012: afs119.
46. Bower JH, Zenebe G. Neurologic services in the nations of Africa. *Neurology* 2005; **64**(3): 412-5.
47. Organization WH. mhGAP intervention guide for mental, neurological and substance use disorders in non-specialized health settings: mental health Gap Action Programme (mhGAP): Geneva: World Health Organization; 2010.
48. Shaji K, Arun Kishore N, Lal KP, Prince M. Revealing a hidden problem. An evaluation of a community dementia case-finding program from the Indian 10/66 dementia research network. *International Journal of Geriatric Psychiatry* 2002; **17**(3): 222-5.
49. Ramos-Cerqueira ATA, Torres AR, Crepaldi AL, et al. Identification of dementia cases in the community: a Brazilian experience. *Journal of the American Geriatrics Society* 2005; **53**(10): 1738-42.
50. UNESCO. Education data 2015. 2015 ed. Quebec, Canada: UNESCO; 2015.
51. Chandra V, Ganguli M, Ratcliff G, et al. Practical issues in cognitive screening of elderly illiterate populations in developing countries. The Indo-US Cross-National Dementia Epidemiology Study. *Aging-Clinical & Experimental Research* 1998; **10**(5): 349-57.
52. Ostrosky-Solis F, Ardila A, Rosselli M, Lopez-Arango G, Uriel-Mendoza V. Neuropsychological test performance in illiterate subjects. *Archives of Clinical Neuropsychology* 1998; **13**(7): 645-60.
53. Ardila A, Rosselli M, Rosas P. Neuropsychological assessment in illiterates: Visuospatial and memory abilities. *Brain and cognition* 1989; **11**(2): 147-66.
54. Ostrosky-Solís F, Ardila A, Rosselli M. NEUROPSI: A brief neuropsychological test battery in Spanish with norms by age and educational level. *Journal of the international Neuropsychological Society* 1999; **5**(5): 413-33.
55. Rosselli M, Ardila A, Rosas P. Neuropsychological assessment in illiterates: II. Language and praxic abilities. *Brain and Cognition* 1990; **12**(2): 281-96.
56. Scazufca M, Almeida O, Vallada H, Tasse W, Menezes P. Limitations of the Mini-Mental State Examination for screening dementia in a community with low socioeconomic status. *Eur Arch Psychiatry Clin Neurosci* 2009; **259**(1): 8-15.
57. Castro-Caldas A, Reis A, Guerreiro M. Neuropsychological aspects of illiteracy. *Neuropsychological rehabilitation* 1997; **7**(4): 327-38.
58. Reis A, Guerreiro M, Petersson KM. A sociodemographic and neuropsychological characterization of an illiterate population. *Applied Neuropsychology* 2003; **10**(4): 191-204.
59. Nitrini R, Caramelli P, Herrera Junior E, et al. Performance of illiterate and literate nondemented elderly subjects in two tests of long-term memory. *Journal of the International Neuropsychological Society : JINS* 2004; **10**(4): 634-8.
60. Kosmidis MH, Tsapkini K, Folia V, Vlahou CH, Kiosseoglou G. Semantic and phonological processing in illiteracy. *Journal of the International Neuropsychological Society* 2004; **10**(06): 818-27.

61. Castro-Caldas A, Petersson KM, Reis A, Stone-Elander S, Ingvar M. The illiterate brain. Learning to read and write during childhood influences the functional organization of the adult brain. *Brain* 1998; **121**(6): 1053-63.
62. Da Silva CG, Petersson KM, Faísca L, Ingvar M, Reis A. The effects of literacy and education on the quantitative and qualitative aspects of semantic verbal fluency. *Journal of clinical and experimental neuropsychology* 2004; **26**(2): 266-77.
63. Petersson KM, Reis A, Ingvar M. Cognitive processing in literate and illiterate subjects: A review of some recent behavioral and functional neuroimaging data. *Scandinavian journal of psychology* 2001; **42**(3): 251-67.
64. Nitrini R, Caramelli P, Herrera Jr E, Charchat-Fichman H, Porto CS. Performance in Luria's fist-edge-palm test according to educational level. *Cognitive and behavioral neurology* 2005; **18**(4): 211-4.
65. Ardila A, Bertolucci PH, Braga LW, et al. Illiteracy: the neuropsychology of cognition without reading. *Archives of Clinical Neuropsychology* 2010; **25**(8): 689-712.
66. Reis A, Petersson KM, Castro-Caldas A, Ingvar M. Formal schooling influences two-but not three-dimensional naming skills. *Brain and cognition* 2001; **47**(3): 397-411.
67. de Paula JJ, Costa MV, Bocardi MB, Cortezzi M, De Moraes EN, Malloy-Diniz LF. The Stick Design Test on the assessment of older adults with low formal education: evidences of construct, criterion-related and ecological validity. *International Psychogeriatrics* 2013; **25**(12): 2057-65.
68. Matute E, Leal F, Zarabozo D, Robles A, Cedillo C. Does literacy have an effect on stick construction tasks? *Journal of the International Neuropsychological Society* 2000; **6**(06): 668-72.
69. Ostrosky-Solís F, García MA, Pérez M. Can learning to read and write change the brain organization? An electrophysiological study. *International Journal of Psychology* 2004; **39**(1): 27-35.
70. Lecours A, Mehler J, Parente MA, et al. Illiteracy and brain damage 3: A contribution to the study of speech and language disorders in illiterates with unilateral brain damage (initial testing). *Neuropsychologia* 1988; **26**(4): 575-89.
71. Coppens P, Parente M, Lecours A. Aphasia in illiterate individuals. *Aphasia in atypical populations* 1998: 175-202.
72. Castro-Caldas A, Miranda PC, Carmo I, et al. Influence of learning to read and write on the morphology of the corpus callosum. *European Journal of Neurology* 1999; **6**(1): 23-8.
73. Carreiras M, Seghier ML, Baquero S, et al. An anatomical signature for literacy. *Nature* 2009; **461**(7266): 983-6.
74. Castro-Caldas A. Targeting regions of interest for the study of the illiterate brain. *International Journal of Psychology* 2004; **39**(1): 5-17.
75. Brucki SMD. Illiteracy and dementia. *Dementia & Neuropsychologia* 2010; **4**(3): 153-7.
76. Goody J, Cole M, Scribner S. Writing and formal operations: A case study among the Vai. *Africa* 1977; **47**(03): 289-304.
77. Scribner S, Cole M. Literacy without schooling: Testing for intellectual effects. *Harvard Educational Review* 1978; **48**(4): 448-61.
78. Scazufca M, Menezes PR, Vallada HP, et al. High prevalence of dementia among older adults from poor socioeconomic backgrounds in Sao Paulo, Brazil. *International Psychogeriatrics* 2008; **20**(02): 394-405.
79. Whalley LJ, Deary IJ, Appleton CL, Starr JM. Cognitive reserve and the neurobiology of cognitive aging. *Ageing research reviews* 2004; **3**(4): 369-82.
80. Fratiglioni L, Wang HX. Brain reserve hypothesis in dementia. *Journal of Alzheimer's disease : JAD* 2007; **12**(1): 11-22.
81. Valenzuela MJ, Sachdev P. Brain reserve and dementia: a systematic review. *Psychological medicine* 2006; **36**(4): 441-54.

82. Prince M, Acosta D, Ferri CP, et al. Dementia incidence and mortality in middle-income countries, and associations with indicators of cognitive reserve: a 10/66 Dementia Research Group population-based cohort study. *Lancet* 2012; **380**(9836): 50-8.
83. Murray AD, Staff RT, McNeil CJ, et al. The balance between cognitive reserve and brain imaging biomarkers of cerebrovascular and Alzheimer's diseases. *Brain : a journal of neurology* 2011; **134**(Pt 12): 3687-96.
84. Mortimer JA, Snowdon DA, Markesbery WR. Head circumference, education and risk of dementia: findings from the Nun Study. *Journal of clinical and experimental neuropsychology* 2003; **25**(5): 671-9.
85. Meng X, D'Arcy C. Education and dementia in the context of the cognitive reserve hypothesis: a systematic review with meta-analyses and qualitative analyses. *PLoS One* 2012; **7**(6): e38268.
86. Mortimer JA, Snowdon DA, Markesbery WR. Head circumference, education and risk of dementia: findings from the Nun Study. *Journal of Clinical and experimental Neuropsychology* 2003; **25**(5): 671-9.
87. Whalley L, Starr J, Athawes R, Hunter D, Pattie A, Deary I. Childhood mental ability and dementia. *Neurology* 2000; **55**(10): 1455-9.
88. Deary IJ, Whiteman MC, Starr JM, Whalley LJ, Fox HC. The impact of childhood intelligence on later life: following up the Scottish mental surveys of 1932 and 1947. *Journal of personality and social psychology* 2004; **86**(1): 130.
89. Letenneur L, Launer LJ, Andersen K, et al. Education and the risk for Alzheimer's disease: sex makes a difference. EURODEM pooled analyses. EURODEM Incidence Research Group. *American journal of epidemiology* 2000; **151**(11): 1064-71.
90. Cobb JL, Wolf PA, Au R, White R, D'Agostino RB. The effect of education on the incidence of dementia and Alzheimer's disease in the Framingham Study. *Neurology* 1995; **45**(9): 1707-12.
91. Lindsay J, Laurin D, Verreault R, et al. Risk factors for Alzheimer's disease: a prospective analysis from the Canadian Study of Health and Aging. *American journal of epidemiology* 2002; **156**(5): 445-53.
92. Stern Y, Gurland B, Tatemichi TK, Tang MX, Wilder D, Mayeux R. Influence of education and occupation on the incidence of Alzheimer's disease. *JAMA : the journal of the American Medical Association* 1994; **271**(13): 1004-10.
93. Caamano-Isorna F, Corral M, Montes-Martinez A, Takkouche B. Education and dementia: a meta-analytic study. *Neuroepidemiology* 2006; **26**(4): 226-32.
94. Yusuf AJ, Baiyewu O, Sheikh TL, Shehu AU. Prevalence of dementia and dementia subtypes among community-dwelling elderly people in northern Nigeria. *International Psychogeriatrics* 2011; **23**(03): 379-86.
95. Kraemer HC, Moritz DJ, Yesavage J. Adjusting Mini-Mental State Examination Scores for Age and Educational Level to Screen for Dementia: Correcting Bias or Reducing Validity? *International Psychogeriatrics* 1998; **10**(01): 43-51.
96. Kalaria RN, Maestre GE, Arizaga R, et al. Alzheimer's disease and vascular dementia in developing countries: prevalence, management, and risk factors. *Lancet Neurol* 2008; **7**(9): 812-26.
97. Ikeda M, Hokoishi K, Maki N, et al. Increased prevalence of vascular dementia in Japan A community-based epidemiological study. *Neurology* 2001; **57**(5): 839-44.
98. Jorm AF. Cross-national comparisons of the occurrence of Alzheimer's and vascular dementias. *European archives of psychiatry and clinical neuroscience* 1991; **240**(4-5): 218-22.
99. Sekita A, Ninomiya T, Tanizaki Y, et al. Trends in prevalence of Alzheimer's disease and vascular dementia in a Japanese community: the Hisayama Study. *Acta Psychiatrica Scandinavica* 2010; **122**(4): 319-25.
100. Catindig J-AS, Venketasubramanian N, Ikram MK, Chen C. Epidemiology of dementia in Asia: insights on prevalence, trends and novel risk factors. *Journal of the neurological sciences* 2012; **321**(1): 11-6.

101. Adebayo P, Ajani A, Adeniji O, Akinyemi R. Neuropsychiatric and Parkinsonian manifestations of dementia: A case report in a Nigerian woman, 2013.
102. Cullen B, O'Neill B, Evans JJ, Coen RF, Lawlor BA. A review of screening tests for cognitive impairment. *Journal of Neurology, Neurosurgery & Psychiatry* 2007; **78**(8): 790-9.
103. Tsoi KF, Chan JC, Hirai HW, Wong SS, Kwok TY. Cognitive tests to detect dementia: A systematic review and meta-analysis. *JAMA Internal Medicine* 2015; **175**(9): 1450-8.
104. Fillenbaum GG, Chandra V, Ganguli M, et al. Development of an activities of daily living scale to screen for dementia in an illiterate rural older population in India. *Age Ageing* 1999; **28**(2): 161-8.
105. Hendrie HC, Lane KA, Ogunniyi A, et al. The development of a semi-structured home interview (CHIF) to directly assess function in cognitively impaired elderly people in two cultures. *Int Psychogeriatr* 2006; **18**(4): 653-66.
106. Jitapunkul S, Kamolratanakul P, Ebrahim S. The meaning of activities of daily living in a Thai elderly population: development of a new index. *Age Ageing* 1994; **23**(2): 97-101.
107. Mathuranath PS, George A, Cherian PJ, Mathew R, Sarma PS. Instrumental activities of daily living scale for dementia screening in elderly people. *Int Psychogeriatr* 2005; **17**(3): 461-74.
108. Senanarong V, Harnphadungkit K, Prayoonwiwat N, et al. A new measurement of activities of daily living for Thai elderly with dementia. *Int Psychogeriatr* 2003; **15**(2): 135-48.
109. Umayal S, Kulathunga M, Somaratne S, Srikanth S, Kathriarachchi S, De Silva R. Validation of a functional screening instrument for dementia in an elderly sri lankan population: comparison of modified bristol and blessed activities of daily living scales. *BMC Res Notes* 2010; **3**: 268.
110. Cerejeira J, Firmino H, Vaz-Serra A, Mukaetova-Ladinska EB. The neuroinflammatory hypothesis of delirium. *Acta neuropathologica* 2010; **119**(6): 737-54.
111. Inouye SK, Westendorp RG, Saczynski JS. Delirium in elderly people. *The Lancet* 2014; **383**(9920): 911-22.
112. Siddiqi N, House AO, Holmes JD. Occurrence and outcome of delirium in medical in-patients: a systematic literature review. *Age and Ageing* 2006; **35**(4): 350-64.
113. Saczynski JS, Marcantonio ER, Quach L, et al. Cognitive trajectories after postoperative delirium. *N Engl J Med* 2012; **367**.
114. Davis DH, Muniz Terrera G, Keage H, et al. Delirium is a strong risk factor for dementia in the oldest-old: a population-based cohort study. *Brain* 2012; **135**.
115. Witlox J, Eurelings LS, de Jonghe JF, Kalisvaart KJ, Eikelenboom P, Van Gool WA. Delirium in elderly patients and the risk of postdischarge mortality, institutionalization, and dementia: a meta-analysis. *Jama* 2010; **304**(4): 443-51.
116. O'Keeffe S, Lavan J. The Prognostic Significance of Delirium in Older Hospital Patients. *Journal of the American Geriatrics Society* 1997; **45**(2): 174-8.
117. Lundstrom M, Edlund A, Karlsson S, Brannstrom B, Bucht G, Gustafson Y. A multifactorial intervention program reduces the duration of delirium, length of hospitalization, and mortality in delirious patients. *Journal of the American Geriatrics Society* 2005; **53**(4): 622-8.
118. Walker R, Whiting D, Unwin N, et al. Stroke incidence in rural and urban Tanzania: a prospective, community-based study. *The Lancet Neurology* 2010; **9**(8): 786-92.
119. Inouye SK, Foreman MD, Mion LC, Katz KH, Cooney Jr LM. Nurses' recognition of delirium and its symptoms: comparison of nurse and researcher ratings. *Archives of internal medicine* 2001; **161**(20): 2467-73.
120. Lewis E, Paddick SM, Banks J, et al. Prevalence of Delirium in Older Medical Inpatients in Tanzania. *Journal of the American Geriatrics Society* 2016; **64**(9).
121. Paddick S-M, Kalaria R, Mukaetova-Ladinska E. The prevalence and clinical manifestations of delirium in sub-Saharan Africa: A systematic review with inferences. *Journal of the neurological sciences* 2015; **348**(1): 6-17.

Evaluation of the IDEA (Identification and Interventions for Dementia in Elderly Africans) brief cognitive screening tool for identification of delirium in older hospitalised adults in Tanzania

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Background and Aims

In sub-Saharan Africa (SSA), there are no validated screening tools for delirium in older adults(1), despite the known vulnerability of this group to delirium and the associated adverse outcomes(2,3).

The IDEA brief cognitive assessment has previously been validated for dementia and major cognitive impairment in low literacy settings in Tanzania and Nigeria (4). This study aims to assess the effectiveness of this brief assessment in identification of delirium in older hospitalised adults when compared to a widely validated assessment method for delirium diagnosis, the confusion assessment method (CAM).

Method

Consecutive individuals aged 60 and over were screened on admission to medical wards of a tertiary referral hospital in Northern Tanzania using the IDEA brief cognitive assessment. All participants were subsequently assessed by a research doctor using the CAM alongside bedside cognitive assessment, neurological examination and informant history, blinded to the outcome of cognitive screening. Delirium was defined as a positive CAM score. Dementia and other diagnoses were defined according to DSM-V criteria.

Interim Results

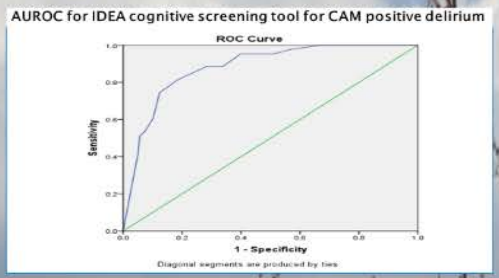
Initial results are available for 233 individuals (38.1% female) assessed using the CAM. Of these, 12 were unable to complete the cognitive screen due to reduced consciousness level and were excluded. Complete data were therefore available for 221 individuals.

Prevalence of delirium on admission was 43/221 and of major cognitive impairment (dementia or delirium) 64/221. AUROC was 0.882 (95% CI 0.831-0.933) for delirium improving to 0.903 (95% CI 0.860-0.946) for major cognitive impairment (dementia or delirium).

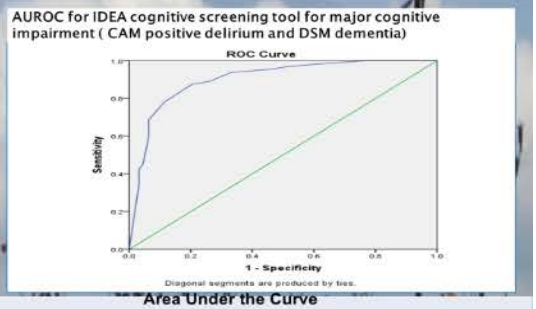
Conclusion

Provisional results indicate that the IDEA brief cognitive assessment was effective in screening for delirium in this setting. Data collection is ongoing with follow up and confirmation of dementia diagnoses due to be completed in November 2015. Further analysis on completion of the study and evaluation of the IDEA brief cognitive assessment against DSM-V diagnosis of delirium by a specialist are awaited

AUROC for IDEA cognitive screening tool for CAM positive delirium



AUROC for IDEA cognitive screening tool for major cognitive impairment (CAM positive delirium and DSM dementia)



IDEA total/15

Area Under the Curve

Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95%CI Lower Bound	Asymptotic 95%CI Upper Bound
.882	.026	.000	.831	.933

a. Under the nonparametric assumption
b. Null hypothesis: true area = 0.5

IDEA total/15

Area Under the Curve

Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95%CI Lower Bound	Asymptotic 95%CI Upper Bound
.903	.022	.000	.860	.946

a. Under the nonparametric assumption
b. Null hypothesis: true area = 0.5

REFERENCES

[1] Paddick SM, Kalaria R, Muekatova-Ladinska E. Delirium in sub-Saharan Africa, a review with inferences. Journal of the Neurological Sciences; 2015, 348(1-2), 6-17.
[2] Inouye SK. Delirium in older persons. The New England journal of medicine. 2006; 354:1157-65.
[3] O'Mahony R, Murthy L, Akunne A, Young J. Synopsis of the National Institute for Health and Clinical Excellence guideline for prevention of delirium. Annals of internal medicine. 2011;154:746-51.
[4] Gray WK, Paddick SM, Kisoli A, Dotchin CL, Longdon AR, Chaote P, et al. Development and Validation of the Identification and Intervention for Dementia in Elderly Africans (IDEA) Study Dementia Screening Instrument. Journal of geriatric psychiatry and neurology. 2014;27:110-8.

Prevalence of delirium in older hospitalised adults in Tanzania.

The IDEA (Identification and Interventions for Dementia in Elderly Africans) study.

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Background and Aims

Delirium is a serious condition known to commonly affect older adults in high-income countries (HICs)[1]. Prompt diagnosis and identification of those at risk is vital to reduce mortality and improve outcome[2]. In sub-Saharan Africa (SSA), little is currently known of the prevalence or causes of delirium[3]. To date, only one study has reported prevalence in older adults in SSA, despite the known vulnerability of this group to delirium and the associated adverse outcomes [4]. The population of SSA is ageing rapidly as a result of demographic transition, and recent studies report dementia prevalence similar to that in HICs[5]. A major issue is lack of validated screening tools for delirium relevant to this setting[3].

We aimed to identify the prevalence of delirium in 100 consecutive new inpatient medical admissions aged 65 and over in a Government hospital in Tanzania. This study took place as part of the IDEA (Identification and Interventions for Dementia in Elderly Africans) study.

Method

All eligible and consenting participants were screened for cognitive impairment using the IDEA brief cognitive screening tool, previously validated for dementia in SSA [6]. All participants were subsequently assessed by a research doctor. This assessment included the Confusion Assessment Method (CAM) alongside cognitive assessment, neurological examination and informant history and background demographic data including educational level. DSM-IV and ICD-10 criteria were used for dementia and delirium diagnosis.

Results

Demographic data for the inpatient sample are presented below. There were no significant differences in age or educational background between those with and without major cognitive impairment.

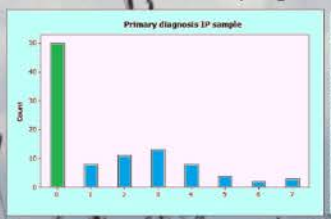
Inpatient	Major CI	No major CI	Significance of difference
Number of patients	33	64	
Median age (IQR)	78 (72.5 to 90)	75.5 (70.25 to 81)	U = 846.0, z = -1.601, p = 0.109
Number of females	14 (42.4%)	37 (57.8%)	χ^2 = 2.068, p = 0.150
Level of education	None: 15 (45.5%) Some: 17 (51.5%) Not known 1 (3.0%)	None: 22 (34.4%) Some: 42 (65.6%)	χ^2 = 1.407, p = 0.236

Results

Three patients were excluded because they did not fully complete the assessment before discharge. Of the remaining 97 patients, 17 (17.53%) met criteria for delirium when assessed. Of these, 10 (10.31%) had a history suggestive of dementia with superimposed delirium. The AUROC for the IDEA cognitive screening tool in identification of major cognitive impairment (delirium or dementia) was 0.903 (95% CI 0.84-0.965) with a sensitivity of 90.9 % and sensitivity of 87.5% at a cut-off of 7/15. False positives on screening included two cases of sub-syndromal delirium, two dysphasic/aphasic patients post-stroke and one patient with reduced conscious level.

Conclusion

Delirium was common in this group of hospitalised older adults in Tanzania, but prevalence was lower than that reported in high income country studies. Our prevalence estimate of delirium may be a conservative one, since patients were assessed only once during hospital admission. A further study of delirium prevalence at admission and during hospital stay is now in progress. The IDEA screening tool appeared effective in identifying delirium in this group and further validation is in progress.



Key
0 – normal cognition,
1– MCI,
2– dementia,
3 –delirium,
4 – dementia and delirium,
5– DSM IV depression,
6 – other psychiatric disorder,
7 – aphasic or medically unwell

REFERENCES
1] Inouye SK. Delirium in older persons. The New England journal of medicine. 2006;354:1157-65.
[2] O'Mahony R, Murthy L, Akunne A, Young J. Synopsis of the National Institute for Health and Clinical Excellence guideline for prevention of delirium. Annals of internal medicine. 2011;154:746-51.
[3] Paddick SM, Kalaria R, Muekatova-Ladinska E. Delirium in sub-Saharan Africa, a review with inferences. Journal of the Neurological Sciences. 2015; 348(1-2), 6-17.
[4] Uwakwe R. Psychiatric morbidity in elderly patients admitted to non-psychiatric wards in a general/teaching hospital in Nigeria. International journal of geriatric psychiatry. 2000;15 346-54.
[5] George-Carey R, Adeloye D, Chan KY, Paul A, Kolcic I, Campbell H, et al. An estimate of the prevalence of dementia in Africa: A systematic analysis. Journal of global health. 2012;2 020401.
[6] Gray WK, Paddick SM, Kisoli A, Dotchin CL, Longdon AR, Chaote P, et al. Development and Validation of the Identification and Intervention for Dementia in Elderly Africans (IDEA) Study Dementia Screening Instrument. Journal of geriatric psychiatry and neurology. 2014;27 110-8.

UTILITY OF THE MINI-MENTAL STATE EXAMINATION (MMSE) FOR IDENTIFICATION OF DEMENTIA IN A LOW-LITERACY SETTING IN RURAL TANZANIA

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Background and Aims

The most commonly used cognitive screening test for older adults worldwide is the mini-mental state examination (MMSE) [1]. The population of sub-Saharan Africa is ageing rapidly as a result of demographic transition, and recent studies report dementia prevalence similar to that in high-income countries[2]. Validated screening tools for dementia are therefore required. The MMSE remains the most commonly used test even in low-income countries [3], despite known limitations in lower educational settings [4, 5]. This study aimed to assess utility of the MMSE in identification of dementia in a low-literacy setting in rural Tanzania

Setting

The Hai district is on the slopes of Mount Kilimanjaro. This area has been a demographic surveillance site (DSS) for over 20 years. Most of this rural population are subsistence farmers, with some growing cash crops such as coffee. Most older people have never lived outside the district, and most live within an extended family.

Method

Sixty older adults aged 70 and over underwent full assessment for cognitive impairment and dementia as part of a mild cognitive impairment (MCI) follow up study. A minimally adapted version of the MMSE was administered to all participants by a research nurse unaware of the outcome of the assessment. Adaptations included minor changes to orientation and recall items for the settings, and inclusion of a Swahili phrase for repetition. MCI was diagnosed using international consensus criteria[6], and dementia by DSM-IV criteria[7].

Results

The sample included 17 people with dementia, with 29 with MCI and 14 with normal cognition. Overall educational level was low with 4/17, 7/29 and 7/14 having ever attended formal school respectively. Median MMSE score was 12 (IQR 4.5) in dementia, 15 (IQR 5) in MCI and 19.5 (IQR 3.75) in normal cognition. Removal of all literacy-dependent items did not significantly change scores. AUROC for dementia was 0.805 (0.69-0.92) and 0.796 (0.69-0.91) after literacy-dependent items were removed.

Conclusion

The MMSE did not perform well as a screening instrument for dementia in this setting, even after removal of all literacy-dependent items. A well-validated alternative is urgently needed.

*=missing	Dementia n=17	MCI N=29	Normal cognition N=14
Age (med, IQR)	81.0 (16.50) *=1	85.0 (10.0)	80.00 (14.0)
Female (n, %)	11 (64.71)	19 (65.52)	11 (78.57)
Ever attended formal school (n, %)	4 (23.53)	10 (34.48)	7 (50.0)
Years of education (med, IQR)	0.00 (1.00)	0.00 (3.00)	0.50 (4.0)
Self-reported basic literacy (n, %)	4 (23.53)	7 (24.14)	7 (50.0)
Minimally adapted MMSE total score (med, IQR)	12.00 (4.50)	15.0 (5.0)	19.50 (3.75)
MMSE total disregarding literacy and numeracy based items /22	12.00 (4.50)	14.0 (4.0)	19.00 (2.5)

MMSE Subset scores *=missing	Dementia	MCI	Normal Cognition
MMSE orientation/10	4.00 (3.00)	6.00 (2.0)	8.00 (2.5)
MMSE registration/3	3.00 (1.00)	3.00 (0.0)	3.00 (0.0)
MMSE recall/3	0.00 (1.00)	1.00 (2.0)	2.00 (0.0)
MMSE commands/3	2.00 (2.50)	2.00 (2.0)	2.00 (1.25)
MMSE naming/2	2.00 (0.00)	2.00 (0.0)	2.00 (0.0)
MMSE writing/1	0.00 (0.00)	0.00 (0.0) *=4	0.00 (0.0) *=1
MMSE written command/1	0.00 (0.00) *=1	0.00 (1.0)	0.00 (1.0)
MMSE copying/1	0.00 (0.00) *=4	0.00 (0.0) *=4	0.00 (0.0) *=1
MMSE attention and concentration (calculation)/5	0.00 (0.00)	0.00 (0.0)	0.00 (1.0)
MMSE repetition/1	1.00 (0.00)	1.00 (0.0)	1.00 (0.0)








REFERENCES

[1] Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. Journal of psychiatric research. 1975.12:189–98.

[2] George-Carey R, Adeloye D, Chan KY, Paul A, Kolcic I, Campbell H, et al. An estimate of the prevalence of dementia in Africa: A systematic analysis. Journal of global health. 2012.2:020401.

[3] Mitchell AJ, Malladi S. Screening and case finding tools for the detection of dementia. Part I: evidence-based meta-analysis of multidomain tests. The American journal of geriatric psychiatry : official journal of the American Association for Geriatric Psychiatry. 2010.18:759–82.

[4] Scazufca M, Almeida O, Vallada H, Tasse W, Menezes P. Limitations of the Mini-Mental State Examination for screening dementia in a community with low socioeconomic status. Eur Arch Psychiatry Clin Neurosci. 2009.259:8–15.

[5] Crum RM, Anthony JC, Bassett SS, Folstein MF. Population-based norms for the mini-mental state examination by age and educational level. JAMA : the journal of the American Medical Association. 1993.269:2386–91.

[6] Petersen RC, Smith GE, Waring SC, Ivnik RJ, Tangalos EG, Kokmen E. Mild cognitive impairment: clinical characterization and outcome. Archives of neurology. 1999.56:303–8.

[7] American Psychiatric Association (2000). Diagnostic and statistical manual of mental disorders (4th ed., Text Revision). Washington, DC: Author.