

Cognitive Reserve and Cognitive Function in Healthy Older People: A Meta-Analysis

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Abstract

The associations between proxy measures of cognitive reserve (CR) and cognition vary across studies and cognitive domains. This meta-analysis aimed to assess the relationship between CR and cognition in multiple domains (memory, executive function, visuospatial ability, and language). CR was considered in terms of three key proxy measures - educational level, occupational status, and engagement in cognitively-stimulating activities – individually and in combination. One-hundred and thirty-five studies representing 128,328 participants were included. Of these, 109 used a measure of education, 19 used a measure of occupation, 31 used a measure of participation in cognitively-stimulating activities, and six used a combination of these. All three proxy measures had a modest positive association with cognition; occupational status and cognitive activities showed the most variation across cognitive domains. This supports the view that the commonly-used proxy measures of CR share an underlying process but that each additionally provides a unique contribution to CR.

Key words:

Occupational status; education; cognitively-stimulating leisure activities; memory; executive function; visuospatial ability; language.

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Cognitive Reserve and Cognitive Function in Healthy Older People: A Meta-Analysis

The concept of cognitive reserve (CR) was developed to explain the repeated finding that the amount of observed brain pathology or damage does not always correspond with the clinical presentation of an associated condition. In some older people, despite the presence of considerable brain pathology, there may be no clinically-observable signs or symptoms of disease (Mortimer, Snowden, & Markesbery, 2003). Stern (2002) proposed that CR is “the ability to optimize or maximize performance through differential recruitment of brain networks, which perhaps reflect the use of alternate cognitive strategies” (p. 451). More recently, Stern (2009) noted that CR is relevant not just to the onset of dementia but also to normal ageing, as it may allow individuals to cope more effectively with typical age-related brain changes.

Both active and passive models of reserve have been outlined. The passive model is often referred to as ‘brain reserve’ while the active model is commonly referred to as ‘cognitive reserve’ (see Stern, 2002; 2006; 2009 for thorough reviews). The passive model of brain reserve refers to the relationship between greater brain size or neuronal count and the ability to sustain more pathology before a clinical impairment is observed (Stern, 2009). In contrast, the active model of CR focuses on the role of experiences such as education, occupation and participation in cognitively-stimulating leisure activities, suggesting that higher levels of education, engagement in more complex occupations, and participation in more cognitively-stimulating leisure activities may provide a buffer against the effects of brain damage or pathology, helping the individual to cope by enlisting compensatory processes (Stern, 2009). CR has also been referred to as ‘behavioural brain reserve’ by some researchers (e.g. Valenzuela & Sachdev, 2006a; 2006b), as it is suggested that certain behaviours or experiences lead to increased reserve. In this meta-analysis the term ‘cognitive reserve’ will be employed as it is the more frequently-used of these two terms describing

active reserve. The lifestyle factors underpinning CR are potentially amenable to modification and hence, in principle, they could provide a basis for preventive intervention (Tucker & Stern, 2011). As CR cannot be directly measured, it is commonly indexed by those experiences and activities thought to increase it. The most commonly-used proxy measures are educational level, occupational status and engagement in cognitively-stimulating leisure activities. Cognitively-stimulating activities are those leisure pursuits that involve cognitive effort, such as reading, attending further education classes, doing crosswords or Sudoku, or playing games such as bridge etc. (see Aartsen, Smits, van Tilburg, Knipscheer, & Deeg, 2002; Mousavi-Nasab, Kormi-Nouri, & Nilsson, 2014; Wilson et al., 1999 for descriptions of what constitutes cognitive activity). A number of cross-sectional studies have observed a relationship between the most common indicators of CR and cognitive function in generally healthy older people but, as will be discussed below, there are variations in these findings, as well as methodological issues relating to the way in which CR has been assessed.

Cross-sectional results have varied across studies examining the relationship between educational level as a proxy measure of CR and aspects of cognitive function in older people. These results have ranged from a strong correlation between education and measures of memory (e.g. Angel, Fay, Bouazzaoui, Baudouin, & Isingrini, 2010; Arbuckle, Gold, & Andres, 1986; Lee, Lee, & Yang, 2012) to a weak correlation between education and executive function (e.g. Jefferson et al., 2011; Lee et al., 2012; Mueller, Raymond, & Yochim, 2013); suggesting that the relationship of this proxy measure with cognitive function differs according to the cognitive domain assessed. Educational level itself has also been assessed using various methods in different studies; for example, indices include years of education (Albert & Teresi, 1999), levels of education categorised into multiple groups ranging from no formal education to greater than 12 years (Mathuranath et al., 2007), and categories yielded by dichotomising education into lower and higher levels (Van Exel et al.,

2001). The main difficulty with employing education as a proxy measure of CR is that the nature, intensity and content of education differ across nationalities and social groups. Indeed, it has been suggested that literacy may be a better indicator of educational attainment (e.g. Manly, Schupf, Tang, & Stern, 2005; Manly, Touradji, Tang, & Stern, 2003). However, assessing literacy is also not without complications; for instance, performance may be influenced by dyslexia and other learning difficulties. Due to the relative ease of obtaining details about the extent of education, educational level is still more commonly-used than literacy in assessing educational attainment, and therefore educational level was the proxy measure selected for consideration in this meta-analysis.

Similarly, studies evaluating the relationship between occupational status as a proxy measure of CR and cognitive function in later life have yielded findings ranging from a weak correlation with memory (e.g. Fritsch et al., 2007; Leung et al., 2010) to a moderate correlation with executive function (e.g. Foubert-Samier et al., 2012). These findings suggest that the relationship of this proxy measure with cognitive function also varies by domain. Occupational status is also reported in a number of different ways; for example, Forstmeier and Maercker (2008) classified occupational status into motivational abilities and cognitive abilities, while Correa Ribeiro, Lopes, and Lourenco (2013) coded occupations according to their complexity with data, people, and things.

It has been noted that engagement in cognitively-stimulating leisure activities provides a strong contribution to CR, with physical and social activities playing a smaller role in relation to late life cognitive function (Marioni, van den Hout, Valenzuela, Brayne, & Matthews, 2012); hence cognitively-stimulating activities and their relationship to cognitive function are considered as a proxy measure of CR in this meta-analysis. Discrepancies between findings on the nature of this relationship can also be seen in relation to different domains of cognitive function, with small, non-significant correlations between engagement

in cognitively-stimulating leisure activities and memory (e.g. Lin, Friedman, Quinn, Chen, & Mapstone, 2012; Murphy & O'Leary, 2009) but moderate correlations between this proxy measure and executive function (e.g. Eskes et al., 2010; Lin et al., 2012; Newson & Kemps, 2005). A further issue arises in that a variety of measures to assess these activities, from details of the diversity and duration of current activities (Eskes et al., 2010) to scores on questionnaires about cognitive activities across the lifespan such as that developed by Wilson, Barnes, and Bennett (2003), have been employed.

It has been suggested that using only one proxy measure of CR does not provide a complete picture, as CR is a fluid construct resulting from a combination of experiences and activities over the course of an individual's life (Nucci, Mapelli, & Mondini, 2011; Richards & Deary, 2005; Richards & Sacker, 2003; Sánchez Rodríguez, Torrellas, Martin, & Fernandez, 2011; Stern, 2009; Tucker & Stern 2011; Whalley, Dick, & McNeill, 2006). It is doubtful whether one proxy alone constitutes a complete measure of CR, given that CR is derived from a combination of experiences and exposures across the lifespan. A number of measures combine these factors to give an index of an individual's overall CR, such as the Lifetime of Experiences Questionnaire (LEQ; Valenzuela & Sachdev, 2007) and the Cognitive Reserve Index Questionnaire (CRIQ; Nucci et al., 2011), which may help in standardising the assessment of CR across studies. A fourth indicator of CR which has been considered by some is verbal IQ. However, this was not included as a proxy measure of CR in this meta-analysis as measures of verbal ability are frequently used as measures of cognition rather than as a proxy measure of CR (e.g. Anstey, Hofer, & Luszcz, 2003; Parisi, Stine-Morrow, Noh, & Morrow, 2009; Welsh-Bohmer et al., 2009).

The fluidity of CR suggests that it could be difficult to assess fully in younger people who have yet to obtain the effects of occupational status across their working lives. Hence it is more salient to focus on people over the age of 60 who have had the opportunity to build

their CR through education, occupation, and engagement in cognitively-stimulating activities over a number of years.

In summary, many cross-sectional studies assess proxy measures of CR, in particular educational level, occupational status, and/or participation in cognitively-stimulating leisure activities, and their relationship with cognitive function yet there is some discrepancy in the results and with regard to the patterns of association with different cognitive domains.

Discrepancies in the way in which CR is indexed could account for some of the variance in findings and make synthesising the available information difficult; an indication of how each of the most commonly-used proxy measures of CR, and those measures which combine these proxies are related to cognitive function is needed. Furthermore, it is currently unclear how these proxy measures relate to different domains of cognition in a non-clinical population.

To date there is no meta-analysis or systematic review available that summarises the relationships between multiple proxy measures of CR and performance in different cognitive domains in healthy older people. Previous reviews of CR have tended to focus on the association between proxy measures of CR and incidence of dementia or take a narrative approach rather than a systematic review of the topic (e.g. La Rue, 2010; Richards & Deary, 2005; Scarmeas & Stern, 2003; Stern, 2002; 2006; 2009). Other reviews have focused only on a single proxy measure of CR and overall cognitive function (e.g. Bielak, 2010; Then et al., 2014). These reviews have generally reported that a reduction in the risk of dementia and better cognitive function are associated with greater educational level, occupational status and engagement in cognitively stimulating leisure activities. The present review aims to address the gap in the literature via meta-analytic methods which avoid the bias associated with narrative reviews (Lyman & Kuderer, 2005). While it is now widely accepted that life experiences such as educational level, occupational status and participation in cognitively-stimulating leisure activities are associated with cognitive function, this meta-analysis adds to

the literature by considering multiple proxy measures of CR and examining their association with cognitive function in different domains. It is becoming increasingly common for studies to consider the role of CR in healthy ageing, and yet no cohesive quantitative report on these studies is currently available. Specifically, this meta-analysis set out to assess how the different proxy measures of CR are employed by researchers, whether single proxy measures or combinations of these, and what the similarities and differences between these proxy measures and their associations with cognitive function in healthy older people are. The focus here is solely on cross-sectional studies assessing the relationship between proxy measures of CR and cognitive function, as previous reviews have considered the association between CR and both cognitive decline and incidence of dementia (Valenzuela & Sachdev, 2006a; 2006b). These reviews found a beneficial effect of the life experiences associated with CR, in that higher levels of these experiences resulted in less cognitive decline and reduced incidence of dementia. However, neither of these reviews considered cross-sectional studies of CR and cognitive function in different cognitive domains in healthy older people.

In this meta-analysis we set out to review and synthesise the information on the most common proxy measures of CR, namely educational level, occupational status, and engagement in cognitively-stimulating leisure activities, and their relationship with different domains of cognitive function, in generally healthy people aged over 60 years who do not have cognitive impairment or dementia. This age group was selected since individuals over 60 have had time to build CR across their life and the cognitive decline sometimes associated with ageing may begin to present itself, resulting in more variability in cognitive function within these individuals (Salthouse, 2009).

The specific aim of this meta-analysis was to collate the results of existing literature to answer the following research questions:

1. What are the similarities and differences in the relationships of each individual proxy measure of CR, specifically educational level, occupational status, engagement in cognitively-stimulating activities, and of indices which combine these proxies into a single measure, with cognitive function in healthy older people?
2. Do the nature and strength of these relationships differ across different domains of cognitive function?

Method

Literature search strategy

In order to identify studies investigating the relationship between cognitive function and CR, assessed using one of the key proxy measures or a combination of CR proxy measures, a search was conducted of the electronic databases ScienceDirect, PubMed, PsycInfo, and CINAHL on 21/11/2014. Each database was searched for (a) ‘cognitive OR cognition OR memory OR executive OR visuospatial OR language OR reserve OR lifetime’ in the title. The results of this search were then cross-matched with (b) ‘‘cognitive reserve’’ OR ‘‘brain reserve’’ OR education* OR occupation* OR activit* OR leisure OR literacy’ AND (c) ‘old* OR later life OR elder* OR aged OR aging OR ageing OR nondemented’ in the title, abstract, or keywords. The reference sections of included studies were searched for additional papers not identified in the initial search.

Inclusion and exclusion criteria

Studies were included if (a) at least 80% of participants were aged over 60 or the information for those aged over 60 was reported separately, (b) a proxy measure of CR, specifically educational level, occupational status, cognitively-stimulating leisure activities,

or a combination of these was used, and (c) a cross-sectional outcome measure of cognitive function was reported.

Studies were excluded if (a) more than 20% of the sample consisted of people with a neurological disorder or a disorder which may affect cognitive functioning (e.g. dementia, multiple sclerosis, Parkinson's disease, HIV, or traumatic brain injury), (b) an outcome of dementia or mild cognitive impairment incidence was used, or participants were grouped into those with or without cognitive impairment, as this does not allow for assessment of cognitive function as a continuous variable in generally healthy people, or (c) the authors reported a biological or pathological proxy measure or outcome only.

Procedure

A summary of the procedure for selecting studies for inclusion can be seen in Figure 1. The searches identified 15,742 titles of which 10,330 were unique. The titles were evaluated in relation to the inclusion criteria by the lead author and those clearly unrelated to later life (e.g. related to children, animals, autism, or dyslexia) were excluded. The remainder (>50%) were screened by a second reviewer. The two reviewers achieved 99% agreement on inclusion/exclusion and where there was disagreement the title was retained for abstract screening. At this point 9,710 articles were discarded as they did not meet the inclusion criteria; the primary reasons were that these studies focused solely on animals, children, or clinical populations. Six hundred and twenty abstracts were then evaluated by two reviewers working independently. The reviewers achieved 81% agreement on inclusion/exclusion with disagreements discussed and full text retrieved when agreement could not be reached. After abstract screening 275 articles were discarded as they did not meet inclusion criteria; the primary reason was that these studies used no measure of either the required CR proxy measures or cognitive function. The full texts of the remaining 345 articles were retrieved

and the method and results sections evaluated against the inclusion criteria. This process yielded 128 articles, including four PhD theses, which satisfied the inclusion criteria and provided statistical information that could be included in the meta-analysis. Authors of eight of these studies were contacted to request additional statistical information, but only three responded. As a result, conservative estimates of the p -values given in the studies were used to calculate an effect size for four of these studies; for instance where $p < .05$ was reported, the p value .049 was used (Brewster et. al., 2014; Le Carrett et al., 2003; Rexroth et al., 2014; Welsh-Bohmer et al., 2009). Morgan, Marsiske, and Whitfield (2007) provided a range of correlation values for the relationship between educational level and cognitive function, consequently the lowest value was taken to provide a conservative estimate of the effect size. Additionally, it was not possible to contact the authors of one article which reported only statistically significant correlation values (Denny & Thissen, 1983). In this instance a value of zero was used for the non-significant associations.

The 217 studies rejected at this stage were primarily excluded for the following reasons: they reported results for dementia/cognitive impairment outcomes or clinical samples ($k = 19$); they reported longitudinal research only ($k = 50$); more than 20% of the sample were aged under 60 ($k = 54$); the study did not include a required CR proxy measure, objective cognitive function outcome, or report specific results ($k = 42$); or it was not possible to retrieve the full text (three book chapters, one PhD thesis, and two journal articles). Multiple reports from the sample were dealt with in the following ways. Decisions on which study to include were based on the sample size, with those with a greater sample size reported, or on the number of cognitive domains assessed. For example the study by Ganguli and colleagues (2010) was included as they reported the association between education and five cognitive domains from the Monongahela-Youghiogheny Healthy Aging Team study for 1,413 participants while that by Snitz and colleagues (2009) was excluded as

they reported two cognitive domains for 1,866 participants from the same sample. When reports from the same sample provided separate analyses relating to different proxy measures all the relevant reports were included. For example, Hultsch, Hammer, and Small (1993) and Zahodne and colleagues (2011) both utilised data from the Victoria Longitudinal Study reporting engagement in cognitively-stimulating activities and education respectively and their association with cognitive function; therefore they were both included in the analyses for the separate proxy measures. The Supplementary Table includes information on the samples for each study reported by the authors of that study and gives a complete list of the included studies, the proxy measure of CR used, and the cognitive domains assessed. Searching the reference sections of the included studies yielded seven additional studies which satisfied the inclusion criteria and provided appropriate statistical information

(Figure 1 around here)

Effect sizes for the relationship between the relevant proxy measure of CR and the cognitive function domain calculated from the statistical information provided for each individual study are presented in the Supplementary Table. The r effect size was utilised in this meta-analysis to represent the strength of the associations and is interpreted in respect to Cohen (1992). Studies were grouped according to the proxy measure of CR used, whether this was educational level, occupational status, engagement in cognitively-stimulating activities, or a combination of these. When a study used more than one CR proxy measure, it was listed in all relevant groups.

Measures assessing cognitive function were grouped into different domains using criteria provided by Lezak (1995) and on descriptions given by the studies which had utilised the measure. The Supplementary Table provides details of the specific tests and cognitive

domains employed in each study. Cognitive screening measures commonly used with older people, including the Mini-Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975) and the Telephone Inventory for Cognitive Status (TICS; Welsh, Breitner, & Magruder-Habib, 1993), were grouped together to give an indication of the relationship between proxy measures of CR and continuous scores on these measures. The memory domain included tests of episodic, logical, and semantic memory. Working memory was analysed separately as it has been considered as relating to both memory and executive function (Lezak, 1995). The executive function domain comprised specific tests measuring aspects of executive function including processing speed, attention and verbal fluency (Lezak, 1995; Martyr & Clare, 2012). Visuospatial ability encompassed tests relating to visual search, figure copying, and line orientation. While Raven's Progressive Matrices (Raven, 1960) were incorporated into composite scores for visuospatial ability by two studies (Aiken-Morgan, Sims, & Whitfield, 2010; Jefferson et al., 2011) it has more commonly been described as a measure of fluid intelligence or general cognitive ability (e.g. Aartsen et al., 2002; Luszcz, 1992; Staff, Murray, Deary, & Whalley, 2004). Therefore, this measure was included in overall cognitive function analyses only. While a number of studies used the Spot-the-Word test (Baddeley, Emslie, & Nimmo-Smith, 1993) as a measure of language ability this was not included in this analysis as it is commonly used to assess verbal intelligence and it is not sensitive to age-related cognitive decline. The National Adult Reading Test (NART; Nelson, 1982) was excluded for the same reasons. Where studies had used confirmatory factor analysis to combine tests into specific domains, these domains were accepted as employed in the original study (e.g. Kaplan et al., 2009; Zahodne et al., 2011). To assess the associations between the proxy measures of CR and general cognitive function all the tests of cognitive function were then grouped under each proxy measure to give an indication of these relationships. Forest Plot Viewer (Boyles, Harris, Rooney, & Thayer,

2011) was used to create a forest plot which provides a visual representation of the weight of each effect size and allows for a comparison between the effects of the individual CR proxy measures in relation to each included cognitive domain.

Statistical Analysis

The Comprehensive Meta-Analysis 2 (Borenstein, Hedges, Higgins, & Rothstein, 2005) software package was used to convert the individual correlation coefficients presented in the included studies into combined r effect sizes. This software uses Fisher's Z transformations and also calculates average z -scores, p values, 95% confidence intervals for the collective effect sizes, indices of between-study heterogeneity, and Rosenthal's fail-safe N for each analysis with three or more included studies. Between-study heterogeneity was assessed using an index of inconsistency (I^2 ; Higgins, Thompson, Deeks, & Altman, 2003). The I^2 statistic gives a percentage indicating the degree of heterogeneity in relation to total variation in observed effects and is not sensitive to the effect size or the number of studies included (Borenstein, Hedges, Higgins, & Rothstein, 2009). The fail-safe N provides the number of missing studies with a mean effect of zero that if added to the analysis would yield a statistically non-significant overall effect (Borenstein et al., 2005). It has been suggested that a fail-safe N can give an indication of the stability of the analyses where stability is indicated when the fail-safe $N = 5k + 10$ (Carson, Schriesheim, & Kinicki, 1990). Where t or F statistics, mean scores, or p values were reported, the program converted these to the r effect size. The r effect size makes use of the correlation coefficient to allow for evaluations of the relationship between two continuous variables in a number of studies (Borenstein et al., 2009). Standardised betas were converted to r effect sizes using the formula reported by Peterson & Brown (2005). A random effects model was used to calculate the effect size as the included studies were heterogeneous in their methods of assessing CR and cognitive

function (DerSimonian & Laird, 1986). The random effects model allows for differences in the true effect size between studies (Borenstein et al., 2009). Holm-Bonferroni corrections were applied in the case of multiple analyses utilising each proxy of CR. These corrections were used to reduce the likelihood of making the errors associated with standard Bonferroni corrections, errors such as finding a significant association when one does not exist (Nakagawa, 2004).

Analyses were carried out to assess the relationship of each of the three most common proxy measures of CR, and combinations of these proxy measures, with the different domains of cognitive function, including cognitive screening measures, memory, executive function, visuospatial abilities, and language. Additional analyses assessed the relationship of all the measures of cognitive function employed in order to give an indication of the proxy measure's relationship with overall cognitive function. Studies reporting the relationship of cognitive function to more than one proxy measure of CR were included in the relevant analyses for each proxy. For those studies which included more than one outcome for a given cognitive domain or for multiple domains when they were analysed together, the Comprehensive Meta-Analysis 2 software program was instructed to average the within-study correlations to correct for violations of independence, so that all available data could be included in the analysis. Where more than 10 studies were included in the analysis a meta-regression was conducted to assess whether age was a moderator of the association between the CR proxy measure and cognition.

Results

The search identified 135 studies with a total of 128,238 unique participants. Of these, 109 used a measure of education ($n = 111,683$), 19 used a measure of occupational status ($n = 18,167$), 31 used a measure of participation in cognitively-stimulating leisure activities ($n =$

24,554), and six studies used composites of the key proxy measures of CR ($n = 2,799$). Of the studies evaluating educational level, 57 studies used years of education, 16 dichotomised educational levels into low and high, and 36 classified education into different levels. Of the studies evaluating occupational status, 15 used the individual's primary occupation, 3 the last occupation held, and 1 the participant's highest obtained occupation. A number of different classification systems were employed to grade the occupation for its complexity (see Supplementary Table). Of the studies evaluating engagement in cognitively-stimulating activities, 24 gave an indication of participation in the given activities currently or within the last year, five gave an indication of participation across the lifespan, and two assessed participation in cognitive activities earlier in life only (adolescence and mid-life). Of the studies evaluating composites of the proxy measures of CR, four combined the three proxy measures of CR considered in this meta-analysis and two combined education and occupation. The Supplementary Table gives further details of the various ways in which each proxy measure was operationalized in the studies.

As can be seen in Tables 1a-d, heterogeneity ranged from low to high for the analyses, and this is further discussed below in relation to each set of analyses. The levels of heterogeneity observed indicate that the included studies differed substantially in their variance, which supported the use of the random effects model.

(Table 1a-1d around here)

Figure 2 shows the effect sizes and associated confidence intervals for the relationship between the individual and combined proxy measures of CR and the domains of cognitive function assessed. This forest plot demonstrates that the largest confidence intervals were found in relationships between education and language ability and engagement in

cognitively-stimulating activities and cognitive screening measures, visuospatial ability, and language. Overall, none of the confidence intervals passed below zero indicating generally consistent positive associations between the proxy measures of CR and performance across different cognitive domains.

(Figure 2 around here)

Educational level and cognitive function

The relationship of educational level with cognition were assessed in relation to cognitive screening measures, memory, working memory, executive function, visuospatial ability, language, and a combination of all the tests of cognition employed (see Table 1a). Twelve studies combined a number of different tests into a measure of global cognitive function. These studies were included in the analysis of overall cognitive function and educational level but could not be analysed within any of the specific domains.

The random effects meta-analysis in Table 1a indicated that the estimated effect sizes for the relationship of education with all the cognitive domains were significant, though small to medium. All the results remained significant after Holm-Bonferroni corrections were applied. The fail-safe N_s indicate that a substantial number of additional studies would be required to reduce the estimated effect size to non-significant indicating good stability of the results. There was, however, a high level of heterogeneity in all of the domains, particularly for screening measures, language, and overall cognition. The high levels of heterogeneity could be due to the variation in the associations reported in the different studies, the differences in sample sizes (e.g. Unverzagt et al. (1996) report a strong association between the MMSE and education with a sample size of 83, while Schmand et al. (1997) report a weak association between the MMSE and education with a sample size of 4,051), and, the

vast number of different measures of cognitive function included in the analysis of the association between education and overall cognitive function. Age was found to be a significant moderator for the association between education and screening measures ($z = -3.13, p = .002$), working memory ($z = -5.23, p < .001$), executive function ($z = -6.30, p < .001$), language ($z = -7.56, p < .001$), and overall cognition ($z = -3.32, p = .001$) but not for memory or visuospatial ability. This indicates that age did not moderate the association between education and performance in these two cognitive domains.

Occupational status and cognitive function

The relationships between occupational status and cognitive screening measures, two separate domains of cognitive function (memory and executive function) and overall cognitive function were assessed (see Table 1b). One study assessed the association between occupational status and working memory (Leung et al. 2010), reporting a small association between the two variables ($r = .11$). One study assessed the association between occupational status and visuospatial ability (Finkel, Andel, Gatz, & Pedersen, 2009), reporting a small association between the two variables ($r = .20$). Six studies gave a score for general cognitive function on the basis of several tests. These studies were only included in the analysis of the overall relationship of occupational status with all the tests of cognitive function. The strongest estimated effects were shown for the screening measures and overall cognitive function, with occupation having a close to moderate association with these outcomes. All other analyses, while significant, showed small associations between occupation and the cognitive domains. The fail-safe Ns indicate that a large number of additional studies would be required to make the association between screening measures and overall cognition and occupation non-significant. Smaller but still stable fail-safe Ns were found for memory and executive function, which is to be expected given the small estimated effect size for these two

domains. All the analyses showed a high index of heterogeneity, indicating considerable variance between studies and supporting the use of the random effect model. Age was found to be a significant moderator for the association between occupation and overall cognition ($z = -2.05, p = .041$) which was the only occupational status analysis with more than 10 included studies.

Cognitively-stimulating leisure activities and cognitive function

Engagement in cognitively-stimulating leisure activities was assessed in relation to screening measures, memory, working memory, executive function, visuospatial ability, and language and to overall cognitive functioning (see Table 1c). Seven studies which combined a number of different tests into a measure of global cognitive function were only included in the analyses assessing cognitive function in general. The estimated effect sizes for the relationships between engagement in cognitively-stimulating leisure activities and screening measures, executive function, and overall cognitive function were moderate while the other associations were small, especially for working memory. All the associations remained significant after Holm-Bonferroni corrections were applied. The association between engagement in cognitively-stimulating leisure activities and visuospatial ability should be viewed tentatively due to the small number of studies available for inclusion in this analysis. The fail-safe N s indicated that a large number of studies would be required to bring the estimated effect size for memory, executive function, and general cognitive function below significance. However, the fail-safe N for the association between working memory and engagement in cognitively-stimulating activities indicates that the significance of this result is not stable; although, this is to be expected given the magnitude of the estimated effect size. Levels of heterogeneity were generally lower than those for education and occupation, although heterogeneity remained high for cognitively-stimulating leisure activities and

screening measures, memory, language, and overall cognition. This indicates a high level of variance between the studies, supporting the use of the random effects model. Age was found to be a significant moderator for the association between engagement in cognitively-stimulating activities and overall cognition ($z = -3.47, p < .001$) but not for memory or executive function. This indicates that age did not moderate the association between education and performance in these two cognitive domains.

Composites of cognitive reserve proxy measures and cognitive function

Composites of CR proxy measures were assessed in relation to screening measures, executive function, and overall cognitive function (see Table 1d). Only one study assessed a composite measure of CR and memory (Opdebeeck, Nelis, Quinn, & Clare, 2014), reporting a moderate association between the two variables ($r = .344$). The estimated effect sizes for the associations of the two individual domains and overall cognitive function with the composite CR proxy measures were moderate and remained significant after Holm-Bonferroni corrections were applied. The fail-safe N for screening measures was small which is to be expected given that only three studies were included in this analysis, while for executive function and overall cognitive function it was adequate given the small number of studies included and both indicated stability in the results. Levels of heterogeneity were low for instruments which combined different proxy measures of CR and their association with screening measures but were high with overall cognitive function, supporting the use of the random effects model.

Discussion

This random effects meta-analytic study aimed to investigate the relationship of the three most commonly-used proxy measures of CR - educational level, occupational status, and

engagement in cognitively-stimulating leisure activities - and measures which combine these proxy measures with a number of cognitive domains in later life. To the best of our knowledge this meta-analysis is the first to synthesise the available cross-sectional statistical information from studies investigating these relationships in a healthy population.

The first aim of this meta-analysis was to investigate the similarities and differences in the associations of educational level, occupational status, engagement in cognitively-stimulating activities, and measures which combine these proxy measures of CR with cognitive function in later life. The meta-analyses showed positive significant relationships between overall cognitive function and the three individual and combined proxy measures of CR. There were moderate associations between measures which combined the proxy measures of CR and education and cognitive function and small associations between engagement in cognitively-stimulating leisure activities and occupational status and cognition. Overall, the results are consistent with the findings of previous reviews and studies which showed a modest association of individual and combined CR proxy measures with reduced cognitive decline and incidence of dementia (Marioni et al., 2012; Valenzuela, Brayne, Sachdev, Wilcock, & Matthews, 2011; Valenzuela & Sachdev, 2006a; 2006b; 2007). Previous studies have shown large variations in the relationships between educational level, occupational status, and engagement in cognitively-stimulating leisure activities and cognitive function (e.g. Barnes, Tager, Satariano, & Yaffe, 2004; Ferreira, Owen, Mohan, Corbett, & Ballard, 2015; Fritsch et al., 2007; Smart, Gow, & Deary, 2014; Smits, van Rijsselt, Jonker, & Deeg, 1995). One explanation for this variability between studies may be due to the variations in the measures used to assess these proxy measures of CR, for example current versus past participation in cognitively-stimulating leisure activities (Fritsch et al., 2007; Smits et al., 1995). The results of this meta-analysis indicate that the three proxy

measures of CR and measures which combine these are positively associated with cognitive function in later life.

The second aim of this meta-analysis was to address whether the strength of these relationships differ across different domains of cognitive function. Measures which combined different proxy measures of CR and educational level showed the smallest variation in their relationships with different domains of cognitive function. All these relationships were positive, with moderate or marginally below moderate estimated effect sizes, and statistically significant. Both higher educational level alone and in combination with more complex occupational experience, and greater participation in cognitively-stimulating activities were related to better performance on cognitive tests in all the domains assessed. The relationships between the different cognitive domains and occupational status and engagement in cognitively-stimulating leisure activities had greater levels of variability with estimated effect sizes ranging from negligible to close to moderate. This could have been due to the greater variations in how these proxy measures were assessed, which meant that the studies included in the meta-analyses differed more widely in their results than the combined CR proxy measures and educational level studies. However, it could also suggest that these proxy measures differ in their association with cognitive function on the basis of the domain assessed. Until there is a standard method for classifying occupational status used across a number of studies, and agreement as to whether current activity levels or activity across the lifetime are crucial for building CR, it will be difficult to assess the true nature of these relationships. It should also be noted that each of the individual CR proxy measures assess experiences that are salient at different time points across the lifespan, with the majority of education primarily experienced early in life, occupational benefits in mid-life, and engagement in cognitively-stimulating activities predominantly experienced in late-life. It is probable that early life experiences are closely related to the quality of later experiences, for

example, it is probable that educational level is related to occupational status. Therefore, the individual proxy measures may not be fully orthogonal. Measures which combine the different CR proxy measures go some way to overcoming these issues. The similarities and differences in the patterns of association between the individual and combined proxy measures of CR and function across cognitive domains in later life is consistent with the suggestion that experiences across the lifespan affect cognitive function in combination as well as individually. Indeed, the findings suggest that a combination of experiences across the lifespan increases CR and may partly explain the differences in cognition observed (Nucci et al., 2011; Sánchez Rodríguez et al., 2011; Stern, 2009; Tucker & Stern, 2011).

The small to moderate effect sizes found in this meta-analysis should be considered a conservative estimate of the relationships between the different proxy measures of CR and the included domains of cognitive function. The findings may have been affected by the differences in the methods used for each proxy measure of CR and the different neuropsychological tests adopted. In a number of studies correlation coefficients were not provided and the available statistics had to be converted to correlation coefficients, with conservative estimates taken in certain studies (Brewster et al., 2014; Morgan et al., 2007; Le Carrett et al., 2003; Rexroth et al., 2014; Welsh-Bohmer et al., 2009); these should be viewed as estimates of the relevant effect sizes and may have reduced the size of the effects. This is especially true where the *p*-value and sample size had to be used as a gross estimate of the effect size as it is probable that the association was under-estimated in those studies with a large sample size due to the conservative effect size estimated by the meta-analysis software, two of these studies had a sample size of over 500 and two had a sample size of over 1,000. However, including these studies, even with conservative estimates, is less of a limitation than excluding them. There may also be some non-independence of the analyses for the different proxy measures in that 25 studies reported that given cognitive domains were

associated with more than one proxy measure of CR and cognition. However, this may add further weight to the argument that the different proxy measures of CR are differently associated with cognition (Wilson et al., 2003). Given that age was a significant moderator of a number of the associations between the CR proxy measures and cognitive function, it is possible that age plays a role in the associations. However, it should be noted that the associations with age are likely to be confounded by cohort effects. In addition, cohort effects may account for some of the variance in associations of the different CR proxy measures with cognitive function in that other confounders associated with different cohorts such as ethnicity, generational differences, or area of residence may account for differing levels of the variance in cognitive function explained by CR proxy measures; however, it was not possible to control for this potential confound.

This meta-analysis was limited to published articles and PhD theses. Consequently there may be a bias toward studies which found a relationship between the proxy measures of CR and cognitive function. However, it should be noted that a number of studies provided statistically non-significant findings which were included in the analyses (e.g. Diehl et al., 1995; Eskes et al., 2010; Jefferson et al., 2011; van Hooren et al., 2007). Additionally, the fail-safe N_s suggest that for the majority of analyses a large number of non-significant, unpublished studies would be required to reduce the estimated effect size to non-significance. A common criticism of meta-analytic studies is that they ignore differences across the included studies (Boronstein et al., 2009). This may be an issue here, in that the proxy measures of CR are assessed in a variety of ways; however, combining studies makes it possible to address broader questions and with larger samples than can usually be obtained by individual studies. Additionally, there were large differences between the sample sizes in the included studies, but the random effects meta-analysis accounts for these differences;

therefore studies with large effect sizes but small samples are unlikely to have biased the results (e.g. Angel et al., 2010; Foubert-Samier et al., 2012; Unverzagt et al., 1996).

It should be noted that while all the estimated effect sizes of the associations were significant, the relationships between engagement in cognitively-stimulating activities and working memory was very small and those of occupational status and all the individual domains assessed except for screening measures were small. This indicates that these proxy measures may show a weaker relationship with certain domains than educational level or measures which combine these proxies, although not with cognitive function overall; however, the number of studies included in these analyses were small so this conclusion may change as more studies investigate this relationship. One of the major limitations with assessing these relationships relates to the varying ways in which CR is indexed in different studies for occupational status and engagement in stimulating leisure activities. This can be noted in the high levels of heterogeneity generally seen in these analyses and could partly explain the variability seen between individual studies. Additionally, activities other than those usually included in measures of leisure activities may be classed as cognitively-stimulating, such as those undertaken in a work environment, and this may confound the associations between cognitively-stimulating leisure activities and cognitive function when this CR proxy measure is taken alone. Little can be done to rectify this until a general consensus on how to assess CR is reached. Until then, studies that use a single proxy measure to indicate CR may be better described simply as focusing on the relationship between that proxy measure, for example educational level, and cognitive function, rather than reflecting CR *per se*.

When considering the idea that CR is associated with better cognitive functioning in later life, it is important to note that we cannot be certain about the causal direction of this relationship. As Salthouse (2006) argues, the associations may be due to preserved

differentiation, with the observed variations in cognitive function reflecting innate abilities rather than lifetime experiences. However there are no known reasons not to engage in experiences and activities that are stimulating and enjoyable (Salthouse, 2006). Indeed, engaging in the cognitively-stimulating life experiences thought to increase CR has been shown to enhance levels of cognitive functioning in later life and slow cognitive ageing (Hertzog, Kramer, Wilson, & Lindenberger, 2008). Other researchers have also noted that exposure to stimulating life experiences may enhance cognitive ability throughout the lifespan (Rutter, 1985; Richards & Sacker, 2003; Schaie, 1996).

The similarities and differences in the associations between the proxy measures considered here and cognitive function across different domains supports the theory that CR is based on a lifetime of exposures (Nucci et al., 2011; Richards & Deary, 2005; Richards & Sacker, 2003; Sánchez Rodríguez et al., 2011; Stern, 2009; Tucker & Stern 2011; Whalley et al., 2006). As such, when assessing CR without measures of pathology multiple life experiences should be taken into account. Measures specifically designed to assess the experiences associated with CR, which give an overall score taking account of different life periods and experiences, could help standardise the assessment of the relationship between CR and cognitive function. For example, the LEQ (Valenzuela & Sachdev, 2007; Valenzuela et al., 2013) uses a weighting system to give equal importance to education, occupational status and participation in cognitively-stimulating leisure activities in building CR across the lifespan and provides a score which combines these experiences in different periods of life. The CRIq (Nucci et al., 2011) is another measure specifically designed to assess the experiences associated with CR. The CRIq also attempts to incorporate the influence of educational level, occupational status, and engagement in cognitively-stimulating, social, and physical leisure activities. While the CRIq incorporates three distinct sections which can be combined to give an overall score, the sections are not weighted to allow for an even

contribution of these experiences to CR as is the case with the LEQ. As these proxy measures have similar relationships with cognitive function there is likely to be significant overlap between them; it would seem prudent to give them equal weighting in their contribution to an overall score indexing CR. The results from the construction of the CRIq indicate that the three most commonly-used proxy measures are only moderately linked (Nucci et al., 2011). Indeed, Wilson and colleagues (2003) noted that there may be different patterns of association between cognitive function and educational level and engagement in cognitively-stimulating activities. These findings all support the view that the commonly-used proxy measures of CR – educational level, occupational status, and engagement in cognitively-stimulating activities - share an underlying process but that each additionally provides a unique contribution to an individual's CR.

This meta-analytic study of the relationship between the three most commonly-used proxy measures of CR and cognitive function supports the supposition that indices of CR are related to cognitive function in a number of different domains, although the associations found were modest. The results are consistent with the recent suggestion that a standardised index of CR which encompasses multiple proxy measures is required to more comprehensively investigate the relationship between this concept and cognitive function in healthy and clinical populations. Future research should employ measures such as the LEQ or the CRIq which gives an indication of CR based on a lifetime of exposures in order to more accurately assess the relationship between CR and cognitive function. A further understanding of this relationship would aid in establishing which lifestyle changes could help delay cognitive decline and the onset of dementia.

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A full reference list of studies included in the meta-analysis is available in online supplementary material.

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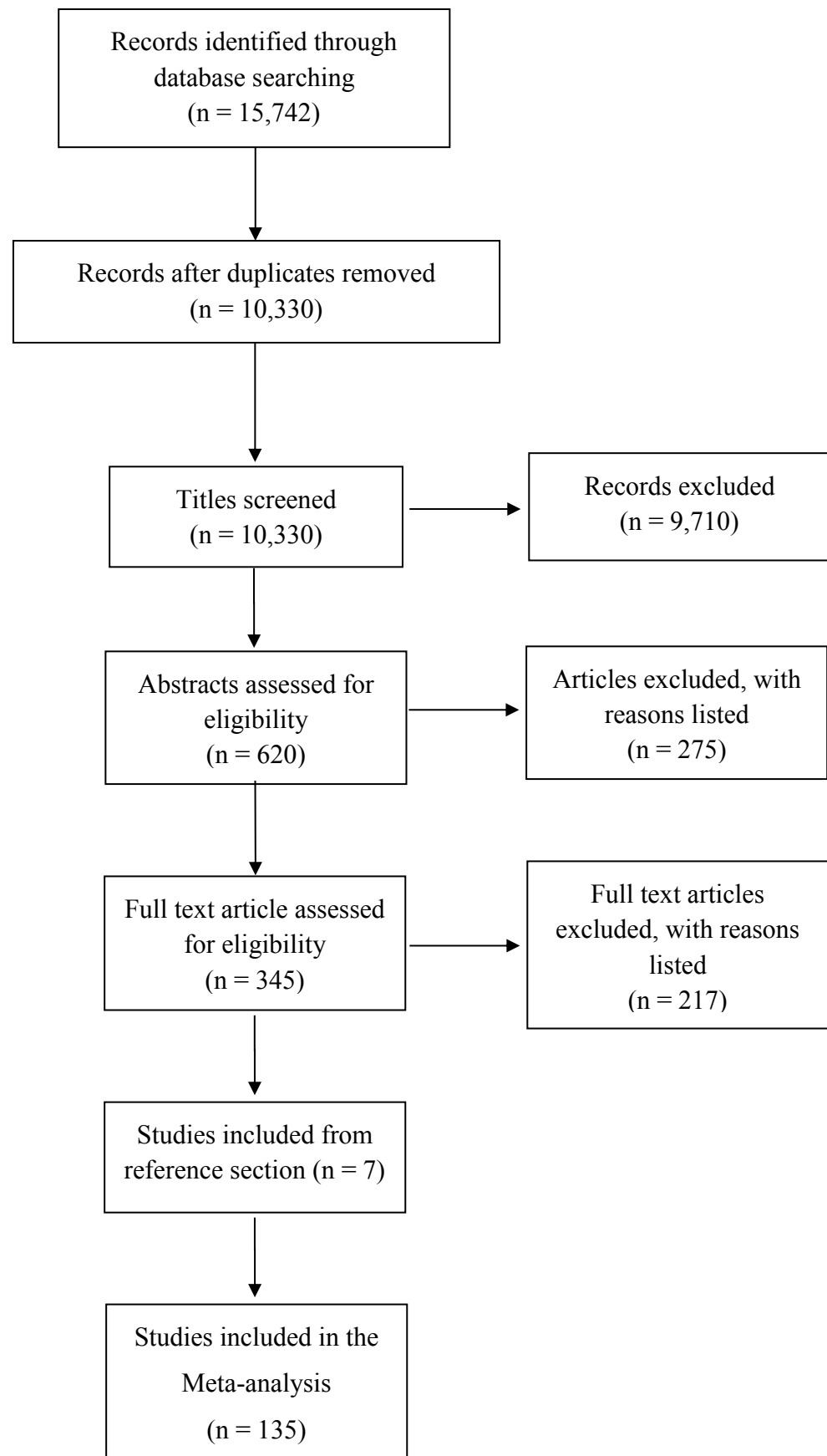


Figure 1. Study selection process

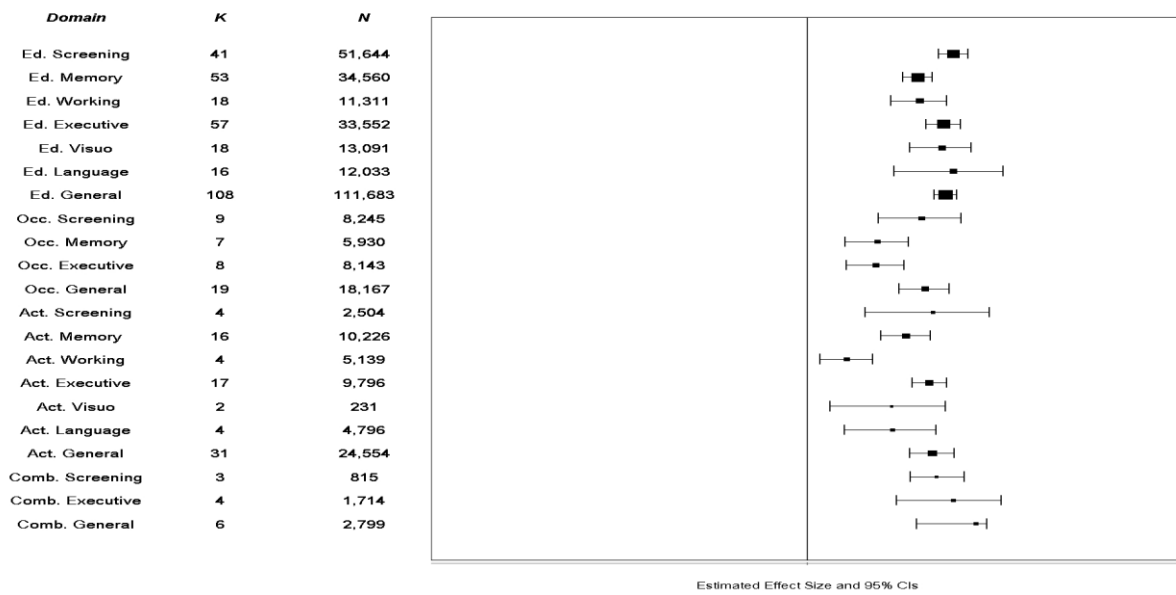


Figure 2. Forest plot of the effect sizes for each cognitive reserve proxy measure and each cognitive domain.

Figure 2 Note: Ed., educational level; Occ., occupational status; Act., cognitively-stimulating leisure activities; comb., combined cognitive reserve proxy measures; screening, cognitive status screening measures; Executive, executive function; Visuo., visuospatial abilities; General, overall cognitive function.

Table 1. Results of the meta-analyses

Table 1a. Results for the meta-analyses of the associations between educational level and cognitive function

Note: screening, cognitive status screening measures; Executive, executive function; visuospatial abilities; General, overall cognitive function. P

Cognitive domain	Studies	n	Effect size	95% CIs	Z	p	Heterogeneity				
							Q	Df(Q)	p	I-squared	Fail safe N
Screening	41	51,644	.314	.278-.349	16.10	<.001	1091.88	60	<.001	94.51	13,640
Memory	53	34,560	.230	.196-.263	13.12	<.001	466.89	55	<.001	88.22	6,640
Working	18	11,311	.235	.169-.298	6.84	<.001	191.63	18	<.001	90.61	1,996
Executive	57	33,552	.291	.249-.331	13.15	<.001	838.41	60	<.001	92.84	9,839
Visuospatial	18	13,091	.287	.212-.358	7.26	<.001	333.06	18	<.001	94.60	4,735
Language	16	12,033	.314	.177-.440	4.35	<.001	832.14	15	<.001	98.20	4,265
General	108	111,683	.295	.268-.322	20.25	<.001	2835.12	133	<.001	95.31	18,415

values in bold are significant at the 5% level after Holm-Bonferroni corrections were applied.

Table 1b. Results for the meta-analyses of the associations between occupational status and cognitive function

Cognitive domain	Studies	n	Effect size	95% CIs	Z	p	Heterogeneity				
							Q	Df(Q)	p	I-squared	Fail safe N
Screening	9	8,245	.239	.142-.332	4.72	< .001	144.40	8	< .001	94.46	991
Memory	7	5,930	.141	.073-.208	4.05	< .001	35.15	6	< .001	82.93	163
Executive	8	8,143	.138	.076-.199	4.35	< .001	41.95	6	< .001	85.70	215
General	19	18,167	.247	.187-.304	7.90	< .001	284.18	18	< .001	93.66	4,371

Note: screening, cognitive status screening measures; Executive, executive function; visuospatial abilities; General, overall cognitive function. p values in bold are significant at the 5% level after Holm-Bonferroni corrections were applied.

Table 1c. Results for the meta-analyses of the associations between engagement in cognitively-stimulating leisure activities and cognitive function

Cognitive domain	Studies	n	Effect size	95% CIs	Z	p	Heterogeneity				
							Q	Df(Q)	p	I-squared	Fail safe N
Screening	4	2,504	.265	.115-.403	3.41	.001	44.91	3	<.000	93.32	167
Memory	16	10,226	.204	.148-.259	6.96	<.001	98.37	15	<.000	84.75	1,131
Working	4	5,139	.077	.024-.130	2.85	.004	6.87	3	.076	56.30	18
Executive	17	9,796	.257	.217-.297	12.16	<.001	61.61	17	<.001	72.41	2,542
Visuospatial	2	231	.172	.043-.295	2.61	.009	0.09	1	.762	0	N/A
Language	4	4,796	.174	.072-.272	3.34	.001	19.11	3	<.001	84.30	73
General	31	24,554	.264	.212-.315	9.51	<.001	496.33	31	<.001	93.75	10,151

Note: screening, cognitive status screening measures; Executive, executive function; visuospatial abilities; General, overall cognitive function. p values in bold are significant at the 5% level after Holm-Bonferroni corrections were applied.

Table 1d. Results for the meta-analyses of the associations between measures which combined proxy measures of cognitive reserve and cognitive function

Cognitive domain	Studies	n	Effect size	95% CIs	Z	p	Heterogeneity				
							Q	Df(Q)	p	I-squared	Fail safe N
Screening	3	815	.274	.213-.340	8.09	<.001	1.17	2	.557	0	41
Executive	4	1,714	.314	.182-.435	4.51	<.001	7.58	3	.059	60.40	85
General	6	2,799	.315	.227-.398	6.70	<.001	17.32	5	.006	71.13	335

Note: screening, cognitive status screening measures; Executive, executive function; visuospatial abilities; General, overall cognitive function. p values in bold are significant at the 5% level after Holm-Bonferroni corrections were applied.

Supplementary material: Supplementary Table and references for studies included in the meta-analyses

Supplementary Table: Studies included in the meta-analysis with demographic, proxy measure, and cognitive outcome details

Authors	Participants and demographic details	Proxy measure of cognitive reserve	Cognitive outcomes and correlations
<i>Educational level</i>			
Aartsen et al. (2002)	3,107 (mean age = 68.7) from the Longitudinal Aging Study Amsterdam (LASA)	Education in years	Screening measure (MMSE, $r = .30$), memory (immediate recall, $r = .220$), executive function (Coding Task – processing speed, $r = .40$), and general cognition (RPM, $r = .34$)
Acevedo et al. (2007)	89 (mean age = 74.56, SD = 4.7)	Education categorised as 3-8 years, 9-12 years, and 13-23 years	Memory (Logical memory and visual reproduction immediate and delayed, $r = .445$), working memory (DS forward, $r = .330$), executive function (Trails B, Similarities, category fluency, phonemic fluency (FAS), $r = .401$), language (BNT), $r = .33$), and visuospatial ability (copying a figure, $r = .196$)

Aiken-Morgan et al. (2010)	449 (mean age = 67.31) from the Baltimore Study of Black Aging	Education in years	Screening measure (MMSE, $r = .36$), memory (CVLT), $r = .249$), working memory (DS Forward, $r = .24$), executive function (DS Backward, $r = .26$), and visuospatial ability which was included in overall cognition only (RPM and Card Rotation Test, $r = .24$)
Al Hazzouri et al. (2011)	7,042 (mean age = 70.6) from the Sacramento Area Latino Study (SALSA) and Mexican Health and Aging Study (MHAS)	Education in years	General cognition (short-term verbal recall, $r = .09$)
Albert & Teresi (1999)	161 participants (mean age = 75.4, SD = 7.3)	Education in years	Screening measure (MMSE, $r = .21$)
Alvarado et al. (2002)	557 (aged 65-89) from the Aging in Leganes Study	Education categorised as literate (no formal education), 1-3 years formal education, primary or more	General cognition (time orientation, space orientation, personal information, naming test, immediate &

			delayed recall (6 objects), and logical memory (short story recall), $r = .148$)
Andel et al. (2015)	810 (mean age = 83) from the Swedish Level of Living Survey and Swedish Panel Study of Living Condition of the Oldest Old (SWEOLD)	Education in years	Screening measure (MMSE, $r = .08$)
Angel et al. (2010)	28 (mean age = 66.5, SD = 6.44)	Education dichotomised into lower (< 10 yrs.) and higher (> 10 yrs.)	Memory (word recall completion, $r = .531$ and accuracy, $r = .419$)
Anstey et al. (2003)	1,823 (mean age = 77.7, SD = 6.56) participants from the	Education in years	Memory (symbol, picture, and word recall, $r = .226$) and executive function (DSST, $r = .331$)

	Australian Longitudinal Study of Aging (ALSA)		
Arbuckle et al. (1986)	285 (median age = 71.6)	Education in years	Memory (index comprising free recall (of 9 words), DS forward, and correct factual and inferential answers (10 multiple choice Qs. based on short story), $r = .46$)
Ardila et al. (2000)	250 aged 66-85	Education categorised as 1-4 years, 5-9 years, and 10+ years	Memory (recall of words and semi-complex figure, cueing, and recognition, $r = .195$), executive function (DS backward, visual detection, 20 minus 3, similarities, calculation, and sequences, and semantic and phonemic fluency, $r = .331$) visuospatial ability (copy of a figure, $r = .287$), and language (naming, repetition, and comprehension, $r = .121$). All subtests of NEUROPSI

Ashley (2008) (PhD thesis)	63 (mean age = 77.3)	Education in years	Executive function (choice reaction time, $r = .07$) and general cognition (word recall, letter series, and DSST, $r = .28$)
Barnes et al. (2004)	664 (mean age = 76) from Sonoma, California	Education in years	Screening measure (MMSE, $r = .34$), memory (CVLT, $r = .245$), and executive function (TMT-B, Stroop, and DSST, $r = .30-.36$)
Barnes et al. (2006)	108 (mean age = 72.6)	Education in years	General cognition (includes MMSE, memory (East Boston Story), perceptual speed (SDMT) and working memory (DS Backward), $r = .580$)
Barnes et al. (2011)	6,158 65+ from the Chicago Health and Aging Project (CHAP)	Education in years	General cognition (includes MMSE, memory (East Boston Story), perceptual speed (SDMT) and working memory (DS Backward), $r = .117$)
Beatty et al. (2003)	634 aged 64-94 from the Oklahoma Longitudinal	Education categorised as 8 th grade or less, some high school,	Memory (immediate and delayed, $r = .208$), executive function (attention, $r = .293$), language ($r = .206$),

	Assessment of Health Outcomes of Mature Adults (OAKLAHOMA)	GED, high school graduate, some college, or postgraduate	visuospatial ability ($r = .205$), and general cognition (all the subtests of the RBANS used, $r = .295$)
Capitani et al. (1996)	220 aged 56-85	Education dichotomised into low (mean years = 4.78-5.41) and high education (mean years = 13.07-13.62)	Memory (SRT and Block Tapping Learning, 56-70 year olds, $r = .21$ and 71-85 year olds, $r = .21$), executive function (semantic verbal fluency, 56-70 year olds, $r = .18$ and 71-85 year olds, $r = .18$), and general cognition (RPM, 56-70 year olds, $r = .18$ and 71-85 year olds, $r = .19$)
Carmelli et al. (1995)	522 (mean age = 64)	Education in years	Screening measure (Iowa Screening Battery, $r = .29$ and MMSE, $r = .30$)
Christensen et.al (1996)	703-852 participants aged 70-89 from Canberra and Quanbeyan	Education in years	Screening measure (MMSE, $r = .35$, $n = 852$) and memory (word and address recall, $r = .21$, $n = 703$)

Christensen et al. (2009)	472 aged 60-64 (mean age = 62.6, SD = 1.4) from Personality and Total Health (PATH) Through Life study	Education categorised as 0-12 years, 13 years, 14-15 years, 16+ years	Memory (immediate and delayed recall, $r = .21$) and executive function (SLMT, $r = .25$)
Christofolletti et al. (2007)	116 (mean age = 73.6)	Education categorised as 0, 1-4, 5-8, 9-11, >11	Memory (incidental, immediate and delayed recall, and recognition, $r = .301$), executive function (verbal fluency and clock drawing, $r = .695-.733$), and language (naming, $r = -.564$)
Constantinidou et al. (2012)	359 (mean age = 74.64, SD = 3.97)	Education categorised as 0-4 years, 5-9 years, and \geq to 10 years	Executive function (Trials-B, SDMT, and animal fluency, $r = .312-.483$), visuospatial ability (Trails-A and word finding, $r = .333$), and language (Peabody Picture Vocabulary Test and BNT, $r = .365$)
Correa-Ribeiro et al. (2013)	624 aged 65+	Education categorised as illiterate, 1-4 years, 5-8 years, 9-12 years, and \geq 13 years	Screening measure (MMSE, $r = .264-.402$)

Davey et al. (2013)	244 aged 98-108	Education in years	Screening measure (MMSE, $r = .36$), memory (FOME recall and recognition, $r = .09$), and executive function (COWAT, Similarities, and the Behavioural Dyscontrol Test, $r = .26$)
de Araújo Carvalho et al. (2009)	333 (mean age = 68)	Education in years	Language (oral comprehension, $r = .74$)
de Oliveira-Wachholz et al. (2011)	67 aged 60-75	Education categorised as 1-4 years, 5-8 years, and 9 or more years	Screening measure (MMSE, $r = .37$), memory (incidental memory and immediate and delayed recall, $r = .15$), working memory (DS forward, $r = .05$), executive function (clock drawing, DS backward, verbal fluency, $r = .25-.35$), and language (naming, $r = 0$, all at ceiling)
de Souza-Talarico et al. (2007)	40 (mean age = 72)	Education in years	Working memory (DS forward, $r = .28$) and executive function (DS backward, $r = .41$)

Denny & Thissen (1983)	115 men (mean age = 71.16, SD = 7.97)	Education in years	Executive function (Block Design and Twenty Questions Task, $r = .14$), language (vocabulary, $r = .42$), and general cognition (Twenty Questions Task, classification, and vocabulary, $r = .33$)
Diehl et al. (1995)	62 (Mean age = 76.4)	Education in years	Working memory (DS forward, $r = .05$), executive function (processing speed, $r = -.04$), and general cognition (Rey figure type test and recognising synonyms, $r = .17-.30$)
Dorbath et al. (2013)	64 (mean age = 68.05)	Education dichotomised into lower (< 14 years) and higher (> 18 years)	Executive function (focus switching task, cost $r = .19$, accuracy $r = .31$)
Duff et al. (2013)	576 (mean age = 68.1)	Education in years	Screening measure (TICS, $r = .21$)

Elias et al. (1997)	1,002 aged 65-88 from the Framingham Heart Study	Education categorised as 5-8 years, 9-11 years, 12 years, and >12 years	Memory (logical memory and paired associates, $r = .31$), working memory (DS forward, $r = .27$), executive function (DS backward, $r = .30$), and visuospatial ability (reproduction, $r = .28$)
Ferreira et al. (2015)	3,515 aged 65+	Education categorised as none, primary school (to age 11), secondary school, (to age 16) further education: A levels (to age 18 years), technical/vocational, university degree, postgraduate or professional qualification	Memory (Paired Associate Learning, $r = .02$), working memory (DS forward and spatial search task, $r = .07$), and language (grammatical reasoning, $r = .15$)
Fillenbaum et al. (1988)	1,637 aged 60+	Education in years	Screening measure (MMSE, $r = .45$)
Fisk et al. (1995)	361 (mean age = 73.8) From Canadian Sample of Health and Aging (Nova Scotia sample)	Education in years	Screening measure (Halifax Mental Status Scale, $r = .35$)

Foubert-Samier et al. (2012)	331 (mean age = 76.1, SD = 3.9) from the Three Cities Cohort (3C)	Education level categorised as 5 levels from primary school without a diploma to university level	Verbal fluency (IST, $r = .235$)
Fournet et al. (2012)	445 aged 55-85	Education categorised as < 8 years, 8-12 years, and 13 years	Memory (recall of words, locations, and patterns, $r = .282$) and working memory (word and location span, $r = .337$)
Fritsch et al. (2007)	349 (mean age = 74.8, SD = 1)	Education in years	Screening measure (TICS-M, $r = .23$), memory (WMS-R Logical Memory test, $r = .24$) and executive function (timed months of the year backwards and verbal fluency, $r = .17$)
Ganguli et al. (2010)	1413 (mean = 77.6) from the Monongahela-Youghiogheny Healthy	Education categorised as less than high school, high school	Memory (WMS-R Logical Memory (immediate and delayed recall), WMS-R Visual Reproduction (immediate and delayed recall), and 3-trial FOME with Semantic Interference, $r = .17$), executive function

Aging Team (MYHAT) study		graduate, and more than high school	(TMT-B, clock drawing, and phonemic verbal fluency, $r = .12$), language (BNT, verbal fluency categories, and Indiana State Token Test, $r = .20$), and visuospatial ability ($r = .20$)
Giogkaraki et al. (2013)	383 (mean age = 73.33)	Education in years	Memory (HVLT and WMS-R Logical Memory Story A immediate and delayed recall, $r = .32$), executive function (TMT-B, SDMT, category fluency, phonemic fluency, $r = .36-.56$), and visuospatial ability (TMT-A, $r = .35$)
Giordano et al. (2012)	288 (mean age = 73.5)	Education in years	Screening measure (MMSE, $r = -.01$), memory (immediate and delayed prose memory and memory with interference at 10 and 30 seconds, $r = .33$), working memory (DS forward, $r = .06$), executive function (TMT-B and clock drawing, $r = .21-.28$), and

			visuospatial ability (copying overlapping figure and TMT-A, $r = .24$)
Glymour et al. (2005)	5,726 aged 70+ from the AHEAD study	Education categorised as <12 years, 12 years, or >12 years	General cognition (composite of TICS and delayed recall, $r = .29$)
Gonzalez et al. (2013)	8,833 (mean age = 73.9) from the Health and Retirement Study (HRS)	Education in years	Screening measure (abbreviated TICS, $r = .44$)
Hashimoto et al. (2006)	155 aged 70 +	Education categorised as 6 years, 8 years and ≥ 10 years	Executive function (TMT-B, $r = .23$) and visuospatial ability (TMT-A, $r = .25$)
Hassing et al. (1998)	80 aged 90+	Education in years	Screening measure (MMSE, $r = .32$) and memory (word and object recall immediate and delayed, $r = .21$)
Hill, Whalin et al. (1995)	253 (mean age = 84.1, SD = 5.06)	Education in years	Memory (recall, $r = .25$)

Ho & Chan (2005)	204 (mean age = 68.33, SD = 7.41)	Education in years	General cognition (Chinese version of the Mattis Dementia Rating Scale, $r = .52$)
Inouye et al. (1993)	1,182 aged 70-79 from the MacArthur Foundation Research Network on Successful Aging	Education categorised as 0-7 years, 8-12 years, and >12 years	Memory (delayed recall and recognition, $r = .11$), executive function (abstraction, $r = .55$), language (naming, $r = .34$, and visuospatial ability (copying, $r = .36$))
Inzelberg et al. (2007)	260 (mean age = 72.4)	Education categorised as 0-4 years, 5-8 years, and >8 years	Screening measure (MMSE, $r = .56$)
Jefferson et al. (2011)	951 participants aged 54-100	Education scored from 0 (no formal education) to 30 (multiple advanced degrees)	Memory (WMS-R Logical Memory Story A, East Boston Story, word list learning, BNT and verbal fluency, $r = .15$), working memory (WMS-R Digit Span, Digit Ordering, $r = .14$), executive function (SDMT, number comparison, Stroop Color-Word, $r = .08$), visuospatial ability which was included in overall cognition only (line orientation and RPM, $r = .27$), and

			global cognition (z-score average from all domains, $r = .19$)
Kaplan et al. (2009)	95 participants (aged 75-90)	Education in years	Memory (RBANS List Recall, List Learning, and Semantic Fluency, $r = .21$), executive function (CalCAP sequential RT, RBANS Coding, and Stroop Color-Word, $r = .29$), and visuospatial skills (RBANS Figure Copy, Line Orientation, Trail Making Test B, Picture Naming, $r = .31$)
Kempler et al. (1998)	317 aged 54 -99	Education dichotomised as 0-8 years and 9+ years	Executive function (Category fluency, $r = .20$)
Kesse-Guyot et al. (2013)	3083 participants (mean age = 65.4, SD = 4.6) from the Supplementation with Vitamins and Mineral	Education categorised as primary, secondary, or university	Global cognition(word recall, verbal fluency, forward and backward digit span, and alternate trail-making test scores were converted into T scores and combined, $r = .37$)

Antioxidants (SU.VI.MAX)

study

Kilander et al. (1997)	504 men aged 69-74 from Uppsala Health Survey	Education categorised as low (elementary school/6-7 years), medium (secondary school), and high (university studies)	General cognition (mean z score of 13 tests to assess audio–verbal and visuospatial short term memory, learning and retention, processing speed and set-shifting capacity, $r = .40$)
Kim et al. (2011)	3157 (mean age = 72.3) from the Korean Longitudinal Study of Aging (KLoSA)	Education in years	Screening measure (Korean MMSE, $r = .48$)
Lang et al. (2008)	2,397 aged 70+ from English Longitudinal Study of Ageing (ELSA)	Education categorised as age at which left school ($\leq 14, 15, 16, 17, 18, \geq 19$)	General cognition (mean z score of 6 tests assessing orientation, immediate and delayed memory, prospective memory, verbal fluency, and attention and processing speed, $r = .27$)

Le Carrett et al. (2003)	1,022 (mean age =72.97) from Personnes Agées Quid study (PAQUID)	Education categorised as 0-5 years, 6-9 years, 10-12 years, and 12+ years	Screening measure (MMSE, $r = .10$)
Lee, Lee, & Yang (2012)	50 aged 60+	Education dichotomised as low (mean = 8.52 years) and high (mean = 13.32 years)	Memory (recall and recognition, $r = .53$) and executive function (DS backward, $r = .17$)
Leggett et al. (2013)	489 (mean age = 69)	Education categorised as none, primary school, lower secondary school, upper secondary or vocational, college or higher	Screening measure (MMSE, $r = .39$)
Leung et al. (2010)	512 (mean age = 74.5, SD = 7.1)	Education in years	Screening measure (Chinese MMSE and ADAS-Cog, r = .44 and .45), memory (word learning and delayed recall, $r = .34$), working memory (DS forward, $r = .26$,

			and executive function (DS backward and category fluency, $r = .23-.47$)
Li et al. (2013)	52 aged 60+	Education dichotomised into low (mean = 9.71 years) and high (mean = 15.79 years)	Working memory (DS forward, $r = .30$) and executive function (DSST, Stroop, Plus-Minus Shifting Task, and information updating (memory paradigm), $r = .34$)
Lin et al. (2007)	58 aged 60+	Education in years	Executive function (HSCT Part A, Monotone Counting Test, word fluency, category score and perseveration errors in a modified WCST, Stroop interference, HSCT Part B, raw score, profile score, and number of rule-breaks in a modified version of the Six Elements Test (SET), $r = .50$)
Linderberger & Baltes (1997)	516 (mean age = 84.9, SD = 8.7) from the Berlin Aging Study (BASE)	Education in years	General cognition (perceptual speed (Digit Letter, DSST, and Identical Pictured); reasoning (Figural Analogies, Letter Series, and Practical Problems); memory (Activity Recall, Memory for Text, and Paired

			Associates); knowledge (Practical Knowledge, Spot-a-Word, and Vocabulary); and verbal fluency (Animals and Letter S), $r = .39$)
Luszcz (1992)	119 (mean age = 71.6)	Education in years	Screening measure (MMSE, $r = .34$), memory (prose recall immediate and delayed, symbol recall, $r = .21$), executive function (DSST completion time and correct at 90 seconds, $r = .29$, and general cognition (RPM, $r = .14$)
Mangione et al. (1993)	472 aged 65+	Education categorised as <8 th grade, some high school, high school graduate, some college, college graduate, some postgraduate, and postgraduate degree.	Screening measure (TICS, $r = .58$)

Mathuranath et al. (2007)	488 (mean age = 68.5)	Education categorised as no formal education, 1-4 years, 5-8 years, 9-12 years, and > 12 years	Screening measure (Malayalam ACE and MMSE, $r = .35$)
Matioli et al. (2008)	83 (mean age of 71.4)	Education categorised as 1-4 years, 5-8 years, and > 8 years	Screening measure (MMSE, $r = .26$), memory (delayed recall, $r = .07$), and executive function (clock drawing and animal fluency, $r = .27-.41$)
Maurer (2011)	3,069 aged 60+ from SABE	Education in years	Screening measure (MMSE, $r = .19 - .50$)
McCarty et al. (1982)	172 aged 63-97 from Duke longitudinal study of aging	Education in years	Memory (logical memory immediate and delayed and Associate Learning, $r = .45$) and visuospatial ability (copying, $r = .50$)
Mejia et al. (1998)	60 (mean age = 69.66)	Education in years	Memory (WMS Associative Learning and Logical Memory and AMSET, $r = .15$) and executive function (WCST and phonemic and semantic verbal fluency, $r = .11-.15$)

Milan et al. (2004)	226 (mean age = 70.1)	Education categorised as none, 1-5 years, 6-10 years, >10 years	Screening measure (MMSE, $r = .47$)
Mitrushina et al. (1989)	156 (mean = 70.7 years)	Education in years	Language (Vocabulary scaled score from WAIS, $r = .29$)
Morgan et al. (2007)	162 (mean age = 73.7)	Education in years	Screening measure (MMSE, $r = .24$), memory (Rey AVLT, Hopkins VLT-R, RBMT I short story recall, $r = .24$), executive function (DSST, finding A's, identical pictures, $r = .24$).
Mousavi-Nasab et al. (2014)	794 (mean age = 74.12, SD = 7.1) form baseline of the Betula project	Education in years	Memory (recall and recognition, $r = .29$)
Mueller et al. (2013)	44 (mean age = 75.3)	Education in years	Memory (CVLT, $r = .35$) and executive function (TMT-B and D-KEFS 20 Question Subtest, $r = .17$)

Mulgrew et al. (1999)	1360 aged 60+ from San Luis Valley Health and Aging Study	Education in years	Screening measure (MMSE, $r = .18$)
Mungas et al. (2005) (Al Hazzouri et al. (2011) included for general cognition for the same dataset)	497 (mean age = 70.9, SD = 7.5) from SALSA and Woodland	Education in years	Memory (word list and spatial configuration learning, $r = .34$), working memory (verbal attention span, $r = .53$), executive function (conceptual thinking, $r = .59$), language (object naming, picture association, comprehension, and verbal expression, $r = .65$), and visuospatial ability (pattern recognition and spatial localization, $r = .50$)
Murayama et al. (2013)	118 (mean age = 69)	Education in years	Memory (verbal and visual immediate and delayed recall, $r = .19$)

Murphy & O'Leary (2009)	99 aged 60-83	Education dichotomised into lower (less than 12 yrs.) and higher (greater than 12 yrs.)	Memory (Immediate and delayed recall of the CERAD, $r = .16 - .27$)
Murden et al. (1991)	94 of 358 included aged 70-99	Education dichotomised into high (9 th grade or higher) and low (8 th grade or lower)	Screening measure (MMSE, $r = -.15-.43$)
O'Connor et al. (1989)	1,822 aged 75+ from Cambridge 75+ study	Education dichotomised into low (left school before 15) and high (left school at 15 or older)	Screening measure (MMSE, $r = .06$)
O'Shea et al. (2014)	3,484 (mean age = 76.07, SD = 6.4) from Washington Heights/Hamilton Heights Inwood Columbia Aging Project (WHICAP)	Education in years	Memory (SRT and BVRT, $r = .31$), executive function (Similarities from WAIS-R, nonverbal reasoning, verbal fluency (COWAT), and category fluency, $r = .40$), language (BNT, repetition, and auditory comprehension, $r = .57$), and visuospatial ability

			(Rosen Drawing Test and multiple choice matching of figures from the BVRT, $r = .50$)
Parisi et al. (2009)	189 (mean age = 72.9, SD = 8.2)	Education in years	Working memory (letter-number sequencing, $r = .14$), executive function (Letter and Pattern Comparison, Finding As, Identical Pictures, Letter Sets, Figure Classification, Everyday Problem Solving, Substitutes Uses, Ornamentation, and Opposites Test, Alternate Uses, Word Associations, and FAS, $r = .21$), and general cognition (composite of tests, $r = .21$)
Paula et al. (2013)	60 (mean age = 74.08, SD = 6.51)	Education in years	Executive function (verbal fluency, $r = .51$)
Pedersen et al. (1996)	580 (mean = 66.3, SD = 7.6)	Education categorised as from the Swedish Adoption/Twin Study of Aging (STATSA)	Screening measure (MMSE, $r = .16-.21$) and general cognition (Synonyms, Figure Logic, Block Design, and Figure Identification, $r = .30-.41$)

		school, junior college, and university	
Petersen et al. (1992)	161 with mean age = 79.8 (SD = 7.6)	Education in years	Memory (SRT and Rey AVLT immediate and delayed recall and WMS-R, $r = .188$) and executive function (DS backward, $r = .03$)
Plassman et al. (1995)	930 (mean age = 66.63)	Education in years	Screening measure (TICS-M, $r = .41$)
Plumet et al. (2005)	49 aged 60-69, 44 aged 70+	Education dichotomised into 7-11 years and ≥ 12 years	Executive function (Card Sorting Task and semantic verbal fluency, $r = .22 - .37$)
Portin et al. (1995)	389 aged 62	Education dichotomised into primary schooling or (up to 6 years) less and more than primary schooling	Memory (object memory and Paired Word Associates, $r = .06-.07$), working memory (DS forward, $r = .29$), executive function (Digit Symbol, Block Design, Similarities, and months backward, $r = .30-.36$), and visuospatial ability (TMT-A, $r = .15-.32$)

Puccioni & Vallesi (2012a)	17 (mean age = 73)	Education in years	Executive function (Stroop, $r = .33$)
Puccioni & Vallesi 2 (2012b)	23 (mean age = 71)	Education in years	Executive function (Stroop, $r = .63$)
Rexroth et al. (2014)	2,782 (mean = 73.6, SD = 5.9) from baseline of the Advanced Cognitive Training for Independent and Vital Elderly (ACTIVE) study	Education categorised as <12 years, 12 years, 13-15 years, and >15 years	Memory (RVLT, HVLT, and RBMT short story recall, $r = .10$) and executive function (Letter Sets, Letter Series Sets, Word Series Test, and Useful Field of View Tasks 2-4, $r = .07$)
Ritchie et al. (2013)	1628 aged 70 and 80 from the Lothian 1921 and 1936 Birth Cohorts	Education in years	Executive function (processing speed, $r = .11 - .17$)

Scherr et al. (1988)	3,564 – 3603 (varies by analysis) aged 65+ from the East Boston Study	Education categorised as some elementary, some high school, and some college	Memory (short story immediate recall, $r = .06$) and executive function (DS backward, $r = .07$)
Schmand et al. (1997)	4,051 (mean age = 75.4, SD = 5.7) from the Amsterdam Study of the Elderly (AMSTEL)	Education dichotomised into low (incomplete primary – general intermediate education) and high (intermediate vocational to university education)	Screening measure (MMSE, $r = .20$)
Senanarong et al. (2001)	3,177 aged 60+	Education in years	Screening measure (Thai MMSE, $r = .47$)
Smits et al. (1995)	115 aged 55-89	Education in years	Memory (Twelve Words Test immediate and delayed recall and Everyday Memory Test, $r = .25$), executive function (Coding Task, $r = .39$), and general cognition (RPM, $r = .36$)

Then et al. (2014)	422 (mean age = 71) from Leipzig Research Centre for Civilization Diseases	Education categorised as high (third level), medium (secondary), and low (primary)	Screening measure (MMSE, $r = .08$)
Unverzagt et al. (1996)	83 (mean age = 74.6, SD = 7.1)	Education in years	Screening measure (MMSE, $r = .65$), memory (word list learning, delayed recall, and recognition, $r = .53$), executive function (Constructional Praxis and category fluency, $r = .47-.63$), and language (BNT, $r = .65$)
Van der Linden et al. (1997)	48 aged 60 - 80	Education dichotomised as low (maximum 12 years) and high (minimum 12 years)	Memory (free and cued recall, $r = .51-.59$)
van Exel et al. (2001)	446 aged 85+ from the Leiden 85-plus Study	Education dichotomised as low (primary or <6 years) and high (more than primary or >6 years)	Memory (word list immediate and delayed, $r = 0$) and executive function (Stroop, $r = .30$)

van Hooren et al. (2007)	576 aged 65-81 from the Maastricht Aging Study (MAAS)	Education categorised as low (elementary and lower vocational), medium (intermediate secondary or vocational), high (higher secondary, vocational, university, and scientific)	Memory (VVLT, $r = .08$) and executive function (Stroop, Concept Shifting Task, and verbal fluency, $r = .19-.20$)
Vaughan et al. (2014)	393 (mean age = 81.21, SD = 4.26) from the Women's Health Initiative Study	Education in years	General cognition (combination of TICS, category verbal fluency, TMT-B, and DS Backward, $r = .16$)
Welsh-Bohmer et al. (2009)	507 age 66+ from the Cache study	Education in years	Memory (word list learning and delayed, WMS Logical Memory and BVRT immediate and delayed, $r = .09$), executive function (TMT-B, category fluency, Constructional Praxis, COWAT, and SDMT, $r = .18-.29$), language (BNT, $r = .09$), and visuospatial ability (TMT-A, $r = .09$)

Wiederholt et al. (1993)	1,692 aged 55-94 from the Rancho Bernardo study	Education dichotomised into less than college or college	Screening measure (MMSE, $r = .34$), memory (Bushke SRT and visual reproduction immediate and delayed, $r = .22$), executive function (TMT-B and category fluency, $r = .26$), visuospatial ability (copying, $r = .21$), and general cognition (2 items from the Blessed Information-Memory-Concentration Test, $r = .36$)
Yao et al. (2009)	1,000 (mean = 71.34 years, SD = 7.10) from Changsha City Study	Education in years	Screening measure (MMSE, $r = .17$)
Zahodne et al. (2011)	1,014 participants aged 54-95 (mean age = 68.8, SD = 6.8)	Education in years	Memory (sentence construction and span test, and immediate recall of 2 word lists and 2 short stories, $r = .24 - .31$), executive function (lexical decision and sentence verification, $r = .15$ and verbal fluency - 3 written tests from the Kit of Factor Referenced Cognitive Tests – controlled associates, opposites and figures of speech, $r = .41$). All standardised to z scores

Zahodne et al. (2014)	487 (mean age = 69.6, SD = 8.8) from the National Institute of Health (NIH) Toolbox norming study	Education in years	Memory (Picture Sequence Memory, $r = .11$), working memory (List Sorting, $r = .33$), and executive function (Flanker Inhibitory Control, Dimensional Change Card Sort and speed of Pattern Comparison, $r = .38$)
Zhou et al. (2014)	172 (mean age = 67.17 – 67.66)	Education dichotomised as lower (<6 years) and higher (7-12 years)	Screening measure (MoCA and MMSE, $r = .51$)
Zimmerman et al. (2012)	549 (mean age = 79.7, SD = 5.0) from the Einstein Aging Study (EAS)	Education dichotomised as lower (≥ 12 years) and higher (≥ 13 years)	Memory (SRT, $r = .04$), working memory (DS forward, $r = .07$), executive function (TMT-B, DS backward, and phonemic and category fluency, $r = .15-.20$), and visuospatial ability (TMT-A, $r = .04$)

Occupational Status

Alvarado et al. (2002)	557 aged 65-89 from the Aging in Leganes Study	Main occupation categorised into nine categories from farm workers to white-collar workers	General cognition (time orientation, space orientation, personal information, naming test, immediate and
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			delayed recall (6 objects), and logical memory (short story recall), $r = .27$)
Andel et al. (2015)	810 (mean age = 83) from the Swedish Level of Living Survey and Swedish Panel Study of Living Condition of the Oldest Old (SWEOLD)	Complexity of work with data and people in main occupation as classified by 1970 US census.	Screening measure (MMSE, $r = .26-.33$)
Correa-Ribeiro et al. (2013)	624 aged 65+	Complexity of work with data and people in main occupation as classified by 1970 US census.	Screening measure (MMSE, $r = .08$)
Finkel et al. (2009)	565 (mean age = 64.3)	Complexity of work with data and people in main occupation as classified by 1970 US census	Memory (DS, Picture Memory, and Names & Faces, $r = .19-.25$), executive function (Symbol Digit and Figure Identification, $r = .19$), and visuospatial ability

			(Figure Logic, Block Design, and Card Rotation, $r = .28-.32$)
Forstmeier & Maercker (2008)	147 aged 60-94	Main Occupation as classified by O*Net to indicate motivational and cognitive abilities	Global cognition score (comprised of memory (WAIS-III DS Forward and Backward), verbal fluency (animal naming), and executive function (Stroop Color-Word Test and WAIS-III Digit-Symbol Substitution Test), $r = .13 - .20$)
Foubert-Samier et al. (2012)	331 (mean age = 76.1, SD = 3.9)	Main occupation level as classified into 10 levels according to the International Classification of Occupations (1988)	Verbal fluency (IST of verbal semantic fluency, $r = .30$)
Frisoni et al. (1993)	524 aged over 70	Main occupation classified into 6 categories from white collar workers to housewives	Screening measure (MMSE, $r = .49$)

Fritsch et al. (2007)	349 (mean age = 74.8, SD = 1)	Main occupation mental demands assessed using the US department of Labour's Dictionary of Occupations (DOT)	Screening measure (TICS-M, $r = .04$), memory (WMS-R Logical Memory test, $r = .09$), and executive function (timed months of the year backwards and verbal fluency (animal naming), $r = .10-.11$)
Gow, Avlund & Mortensen (2012)	425 at age 60 from Glostrup 1914 Cohort	Intellectual challenge of current or last held occupation assessed at age 60 based on questionnaire responses.	General cognition (comprising Digit Symbol, Block Design, DS, and Picture Completion from the WAIS, $r = .33$)
Kesse-Guyot et al. (2013)	3083 (mean age = 65.4, SD = 4.6) from the Supplementation with Vitamins and Mineral Antioxidants (SU.VI.MAX) study	Main occupation categorised as homemaker, manual worker, or blue- or white-collar worker	Global cognition(word recall, verbal fluency, forward and backward digit span, and alternate trail-making test scores were converted into T scores and combined, $r = .33$)

Le Carrett et al. (2003)	1,022 (mean age =72.97) from Personnes Agées Quid study (PAQUID)	Main occupation categorised into seven categories from farm/domestic workers to intellectual professions	Screening measure (MMSE, $r = .06$), memory (BVRT and Paired Associates, $r = .05-.08$), executive function (Similarities, DSST, and verbal fluency (IST), $r = 0-$.06)
Leung et al. (2010)	512 (mean age = 74.5, SD = 7.1)	Main Occupation categorised into five categories from unskilled labourer to professional/company director	Screening measure (Chinese MMSE and ADAS-Cog, r = .19-.26 and), memory (word learning and delayed recall, $r = .14$), working memory (DS forward, $r = .11$), and executive function (DS backward and category fluency, $r = .08-.23$)
Linderberger & Baltes (1997)	516 (mean age = 84.9, SD = 8.7) from Berlin Aging Study (BASE)	Occupational prestige of last job held based on German occupational prestige rating	General cognition (perceptual speed (Digit Letter, DSST, and Identical Pictured); reasoning (Figural Analogies, Letter Series, and Practical Problems); memory (Activity Recall, Memory for Text, and Paired Associates); knowledge (Practical Knowledge, Spot-a-

Word, and Vocabulary); and verbal fluency (Animals and Letter S), $r = .41$)

Mangione et al. (1993)	472 aged 65+	Main occupation categorised as service, skilled, and farm workers to management or professionals	Screening measure (TICS, $r = .39$)
Potter et al. (2006)	3,880 (mean age = 65.83, SD = 2.74) from Duke Twins Study of Aging	Main occupation characterised using factor analysis of DOT work characteristics to assess complexity, their factor of general intellect which included positive loading for complexity with data and people, reasoning, language, mathematics aptitude, and greater time spent	Screening measure (TICS-M, $r = .31$)

Scherr et al. (1988)	3,564 – 3603 varies by analysis (aged 65+) from East Boston Study	Main occupation rated according to Duncan's socioeconomic index score	Memory (short story immediate recall, $r = .06-.08$) and executive function (DS backward, $r = .06$)
Smart et al. (2014)	1,066 (mean age = 69.6, SD = 0.8) from 1936 Lothian Birth Cohort	Complexity of work with data and people in main occupation as classified by 1970 US census	Memory (WMS-III – Logical Memory (immediate and delayed), Spatial Span (forward and backward), and Verbal Paired Associated (immediate and delayed recall), $r = .22-.28$), executive function (Symbol Search, Digit Symbol, inspection time, and simple and choice reaction time, $r = .25-.27$), and general cognition (WAIS-III – Letter-Number Sequencing, Matrix Reasoning, Block Design, Digit Symbol, DS Backward, & Symbol Search, $r = .32-.36$)
Staff et al. (2004)	99 aged 79	Occupation (highest obtained) as classified by the UK's Office of Population Statistics (1990)	Memory (AVLT, $r = .15$) and general cognition (RPM, $r = .28$)

Then et al. (2014)	1,468 aged 60 -79 from the Leipzig Research Centre for Civilization Diseases	Occupational mental demands before retirement classed as high, medium or low determined using O*NET descriptor variables of “Cognitive Activities” at work	Screening measure (MMSE, $r = .21$), executive function (TMT-B, verbal fluency, $r = .14-.15$)
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Cognitively-stimulating leisure activities

Andel et al. (2015)	810 (mean age = 83) from the Swedish Level of Living Survey and Swedish Panel Study of Living Condition of the Oldest Old (SWEOLD)	Cognitive activities in mid-life (e.g. how often they read books or went to the theatre)	Screening measure (MMSE, $r = .28$)
Arbuckle et al. (1986)	285 (median age = 71.6)	Current cognitive activity (rated for degree of intellectual effort by 10 graduate students)	Memory (index comprising free recall (of 9 words), forward digit span, and correct factual and inferential

			answers (10 multiple choice Qs. based on short story), $r = .49$)
Ashley (2008)	63 (mean age = 77.3)	Current cognitive activity assessed by Activity Questionnaire (Hultsch et al., 1999)	Executive function (choice reaction time, $r = .25$) and general cognition (word recall, letter series, and DSST, $r = .28$)
Barnes et al. (2006)	108 (mean age = 72.6)	Participation in cognitively demanding activities at age 6 (3 items), age 12 (6 items), 18 (6 items), age 40 (5 items) and currently (5 items) from daily to once a year or less.	General cognition (includes MMSE, memory (East Boston Story), perceptual speed (SDMT) and working memory (DS Backward), $r = .21$)
Brand (2003) Dissertation	94 (mean age = 72.17)	Current cognitive activity - Frequency of crossword puzzles, reading frequency, and amount	Memory (CVLT, $r = .04-.32$)

		read. Assessed with a mental exercise survey	
Brewster et al. (2014)	333 aged 60+ from UC Davis Aging Diversity Cohort	Current cognitive activity and at age 40 assessed by the Life Experiences and Activities Form (LEAF)	Memory (word list learning, $r = .05-.14$) and executive function (category and phonemic fluency, DS backward, visual-span backward, and list sorting, $r = .05-.15$)
Eskes et al. (2010)	42 (mean age = 65.1) All female	Current cognitive activity questionnaire calculated total no of activities (diversity) and total time spent in activities (duration)	Memory (Bushke SRT, Medical Complex of Georgia Complex Figures Test, $r = -.02 - .39$), executive function (DSMT and D-KEFS Color-Word Interference Test, Auditory Consonant Trigrams Test, D-KEFS Card Sorting Test, and verbal fluency, $r = 0 - .46$), language (D-KEFS verbal fluency C-Score and WASI vocabulary, $r = -.01 - .49$), visuospatial ability (WASI Matrix Reasoning and Benton Line Orientation, $r = .05 - .30$), , and global

			cognition score which comprised all tests ($r = .01 - .49$).
Ferreira et al. (2015)	3,515 aged 65+	Current cognitive activity – participation in four different activities (e.g. crosswords)	Memory (paired associate learning, $r = .05-.11$), working memory (DS forward and spatial search task, $r = .01-.15$), and language (grammatical reasoning, $r = .03-.11$)
Foubert-Samier et al. (2012)	331 (mean age = 76.1, SD = 3.9)	A self-administered questionnaire to assess participation in leisure activities in mid-life and currently. The measure comprised 30 activities, 17 of which related to cognitively stimulating activities. Only the analyses of these 17 are included here.	Verbal fluency (IST, $r = .40$)

Fritsch et al. (2007)	349 (mean age = 74.8, SD = 1)	Participation in mental, physical and social activities in high school. Only mental activities included.	Screening measure (TICS-M, $r = .18$), memory (WMS-R Logical Memory test, $r = .13$), and executive function (timed months of the year backwards and animal verbal fluency, $r = .11-.27$)
Gallucci et al. (2009)	668 aged 70+ from the Treviso Longeva Study	Current reading activity (none vs reading newspapers or novels)	Screening measure (MMSE, $r = .46$)
Gilhooly et al. (2007)	145 (mean = 78.19)	Cognitive activities in the last year, e.g. reading, playing chess or cards	Executive function (DSST, $r = .26$)
Gow, Avlund, & Mortensen (2014)	576 aged 75 from Glostrup 1914 Cohort	Current cognitive activity in 17 activities (e.g. going to theatre, travel, adult education)	Executive function (Digit Symbol and DS backward, $r = .16-.28$)

Gow, Corley et al. (2012)	778 (mean age = 69.5) from the 1936 Lothian Birth Cohort	Current cognitive activity – questionnaire combined both social and leisure (e.g. reading and visits to friends/family)	Memory (Logical Memory immediate and delayed recall, Spatial Span, Verbal Paired Associates immediate and delayed recall, $r = .21$) and executive function (Symbol Search, Digit Symbol, choice reaction time, inspection time, simple reaction time, $r = .19$)
Hill, Whalin et al. (1995)	253 aged 75-96 (mean age = 84.1, SD = 5.06)	Current cognitive activity – frequency of activities (e.g. attending concerts and adult education classes)	Memory (immediate, organised, and cued recall, $r = .21-.33$)
Ho & Chan (2005)	204 (mean age = 68.33, SD = 7.41)	Current cognitive activity measured on a 9 point scale from never to everyday (e.g. reading, attending classes)	General cognition (Chinese version of the Mattis Dementia Rating Scale, $r = .59$)

Hultsch et al. (1993)	484 (mean age = 69.2) from Victoria Longitudinal Study	Current cognitive activity with 16 items pertaining to integrative information processing, 25 to novel information processing, and 4 regarding physical activity	Memory (immediate word list and prose recall, $r = .18-.26$), working memory (word span, $r = .14$), executive function (semantic processing speed and verbal fluency, $r = .22-.27$), and language (naming, $r = .21$)
Jefferson et al. (2011)	951 aged 54-100	Cognitive activity - early-, mid-, and late-life cognitive activities were measured using the CAS, a structured questionnaire assessing the frequency of participation in specific cognitive activities (Wilson et al. 2007).	Memory (WMS-R Logical Memory Story A, East Boston Story, word list learning, BNT and verbal fluency, $r = .08-.17$) working memory (WMS-R Digit Span, Digit Ordering, $r = .08-.17$), executive function (SDMT, number comparison, Stroop Color-Word, $r = .14-.38$), visuospatial ability which was included in overall cognition only (line orientation and RPM, $r = .08-.17$), and global cognition (z-score average from all domains, $r = .11-.27$)

Lin et al. (2012)	342 aged 60-84 from MINDUS	Current cognitive activity – frequency of participation in activities (e.g. reading, playing games)	Memory (word list immediate and delayed, $r = .13$) and executive function (DS backward, category fluency, Number Series, and Backward Counting, $r =$.35)
Mueller et al. (2013)	44 (mean age = 75.3)	Current cognitive activity assessed as frequent activity (FA), higher cognitive load activity (HC), and activity maintenance (AM, decrease during the past year)	Memory (CVLT, $r = .28-.37$) and executive function (D-KEFS 20 Question Subtest, $r = .22-.31$)
Murphy & O’Leary (2009)	99 aged 60-83	Current cognitive activity as measured by the number of hours spent in activities daily.	Memory (immediate and delayed recall from the CERAD, $r = .01 - .10$)

Newson & Kemps (2005)	755 (Mean age at time 1 = 77.4) from the Australian Longitudinal Study of Aging (ALSA)	Current cognitive activity as measured by the Adelaide Activities Profile	Memory (incidental recall, $r = .24$), executive function (WAIS-R DSST and verbal fluency, $r = .24$ - .28), and language (picture naming, $r = .22$),
Parisi et al. (2009)	189 (mean age = 72.9, SD = 8.2)	Current cognitive activity assessed as literacy, competitive leisure, travel, and mathematical/ accounting activities	Working memory (Letter-Number Sequencing, $r =$.07-.25), executive function (Letter and Pattern Comparison, Finding As, Identical Pictures, Letter Sets, Figure Classification, Everyday Problem Solving, Substitutes Uses, Ornamentation, and Opposites Test, Alternate Uses, Word Associations, and FAS, $r = -.09$ -.33), visuospatial ability (Card Rotation and Hidden Patterns, $r = -.01$ -.37), and general cognition (combines tests, $r = -.11$ -.33)

Parslow et al. (2006)	2,522 aged 60-64 from the Personality and Total Health (PATH) Through Life study	Cognitive activity undertaken in past 6 months assessed by RIASEC activity questionnaire	Executive function (SDMT, $r = .19-.26$)
Saczynski et al. (2008)	1,787 (mean age = 75.7) from the Age, Gene/Environment Susceptibility Study (AGES-Reykjavik)	Current cognitive activity assessed by participation in 10 activities (e.g. playing games, attending a performance)	Memory (CVLT, $r = .25$) and executive function (DS backward, Cantab Spatial Working Memory Test, and Stroop – Word-Color Interference, $r = .28-.42$)
Sheres (2002) Thesis	77 (mean = 77.8, SD = 4.7)	Current cognitive activity – frequency of activity (e.g. reading, playing bridge or chess)	General cognition (Block Design and Matrix Reasoning from WASI, $r = .26$)
Smits et al. (1995)	115 aged 55-89	Current cognitive activity – frequency of socio-cultural activities (e.g. visiting a museum)	Memory (Twelve Words Test immediate and delayed recall and Everyday Memory Test, $r = .21-.39$), executive function (Coding Task, $r = .50$), and general cognition (RPM, $r = .44$)

Vaughan et al. (2014)	393 (mean age = 81.21, SD = 4.26) from the Women's Health Initiative Study	Cognitive activities over the prior 12 months measured using the CAS, a structured questionnaire assessing the frequency of participation in specific cognitive activities (Wilson et al. 1999).	General cognition (combination of TICS, category verbal fluency, TMT-B, and DS Backward, $r = .30$)
Vemuri et al. (2014)	1,995 (mean age = 78.9) from the Mayo Clinic Study of Aging (MCSA)	Mid- and late life cognitive activity (participation in 10 items)	General cognition (average of z-transformation from 4 domains – executive function (TMT-B, DSST, category fluency), language (BNT), memory (WMS_R Logical Memory-II, Visual Reproduction-II, and AVLT – all delayed recall), $r = .22$)
Wilson et al. (1999)	6,162 participants (mean age = 75, SD = 7.2) from baseline of Chicago Health and Aging Project (CHAP)	Current cognitive activity – frequency of participation in 7 areas, e.g. listening to radio, reading, or playing games, rated for cognitive intensity involved.	Memory (immediate and delayed recall of orally presented story), executive function (SDMT) and global cognition (summary measure using z scores from each of the 4 tests, $r = .04 - .54$)

Wirth et al. (2014)	92 aged 60-90 from the Berkley Aging Cohort (BAC)	Participation in cognitively demanding activities at age 6 (3 items), age 12 (6 items), 18 (6 items), age 40 (5 items) and currently (5 items) from daily to once a year or less	Global cognition (comprises episodic memory – CVLT, Logical Memory recall of story A and B, and Visual Reproduction delayed recall and recognition, and executive function – Stroop Test, COWAT, TMT-B, and Digit Symbol Coding Test, $r = .09-.21$)
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Combined Measures

Gonzales (2013)	90 participants (mean age = 75.98, SD = 7.05)	Lifetime of Experiences Questionnaire (Valenzuela & Sachdev, 2007)	Screening measure (MMSE, $r = .19$)
Opdebeeck et al. (2014)	236 (mean age = 70.86, SD = 7.66)	Lifetime of Experiences Questionnaire	Screening measure (MoCA, $r = .32$), memory (RBMT short story recall immediate and delayed, $r = .33-.36$), and executive function (verbal fluency (FAS), $r = .38$)

Puccioni & Vallesi (2012a)	17 (mean age = 73)	Cognitive Reserve Index questionnaire (CRIq)	Executive function (Stroop, $r = .42$)
Puccioni & Vallesi 2 (2012b)	23 (mean age = 71)	Cognitive Reserve Index questionnaire (CRIq)	Executive function (Stroop, $r = .45$)
Then et al. (2014)	1,438 aged 60 -79 from the Leipzig Research Centre for Civilization Diseases	Education/occupation combined	Screening measure (MMSE, $r = .27$) and executive function (TMT-B, verbal fluency, $r = .21-.23$)
Vemuri et al. (2014)	1,995 (mean age = 78.9) from Mayo Clinic Study of Aging (MCSA)	Education/occupation combined	General cognition (average of z-transformation from 4 domains – executive function (TMT-B, DSST, category fluency), language (BNT), memory (WMS-R Logical Memory-II, Visual Reproduction-II, and AVLT – all delayed recall), $r = .38$)

Note: MMSE, Mini Mental State Exam; RPM, Raven's Progressive Matrices; DS, digit span; BNT, Boston Naming Test; CVLT, California Verbal Learning Test; DSST, digit symbol substitution test; TMT, Trail Making Test; SDMT, symbol digit modalities test; RBANS, Repeatable Battery for the Assessment of Neuropsychological Status; SRT, Selective Reminding Test; SLMT, symbol letter modalities test; FOME, Fuld Object Memory Evaluation; COWAT,

Controlled Oral Word Association Test; TICS-M, Telephone Inventory for Cognitive Status - Modified; IST, Isaac's Set Test of verbal fluency; WMS-R, Wechsler Memory Scale - Revised; HVLTL, Hopkin's Verbal Learning Test; CalCAP, California Computerised Assessment Battery; ADAS-Cog, Alzheimer's Disease Assessment Scale cognitive subtest; HSCT, Hayling Sentence Completion Test; WCST, Wisconsin Card Sorting Task; ACE, Addenbrooke's Cognitive Examination; AMSET, Associative Memory with Semantic Enhancement; VVLT, visual verbal learning test; AVLTL, auditory verbal learning test; VLT-R, Verbal Learning Test- Revised; RBMT, Rivermead Behavioural Memory Test; CERAD, Consortium to Establish a Registry for Alzheimer's disease Neuropsychological Battery; D-KEFS, Delis-Kaplan Executive Function System; WASI, Wechsler Abbreviated Scale of Intelligence; BVRT, Benton Visual Retention Test

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