Cognitive leisure activities and future risk of cognitive impairment and dementia: systematic review and meta-analysis

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Abstract

Background: As life expectancies continue to rise, modifiable lifestyle factors that may prevent cognitive decline and dementia in later life become increasingly important in order to maintain quality of life in old age.

Design: Five meta-analyses were conducted on papers identified in a systematic review. Studies were grouped according to outcomes (dementia, cognitive impairment including amnestic Mild Cognitive Impairment [aMCI], Mild Cognitive Impairment [MCI] and cognitive decline) and output (risk [RR], odds [OR], or hazard ratios [HR]).

Results: Nineteen studies met our inclusion criteria and quality assessments. Four of five meta-analyses showed significant associations between participation in cognitive leisure activities and reduced risk of cognitive impairment (OR=0.69, 95% CI: 0.56-0.85) and dementia (HR=0.58, 95% CI: 0.46-0.74; RR=0.61, 95% CI: 0.42-0.90; OR=0.78, 95% CI: 0.67-0.90). However, one pooled analysis of cognitive impairment studies did not reach significance (HR=0.85, 95% CI: 0.71-1.02). Mentally stimulating leisure activities were significantly associated with later life cognition (β=0.11, p=0.05), better memory (β=0.20, 95% CI: 0.11-0.29), speed of processing (β=0.37, 95% CI: 0.29-0.45), and executive functioning (β=0.23, 95% CI: 0.15-0.29), and less decline in overall cognition (β=-.23, p<.01), language (β=-.11, p<.05), and executive functioning (β=-.13, p<.05). Activities were also shown to reduce rate of cognitive decline (estimate = 0.03, SE = 0.01, p=0.00).

Conclusions: There is increasing evidence that participation in cognitively stimulating leisure activities may contribute to a reduction of risk of dementia and cognitive impairment in later life. Promoting involvement in such activities across lifespan could be an important focus for primary prevention strategies for governments and health services.

Key words: Cognitive impairment, cognitive activity, cognitive reserve, dementia, risk factors, leisure activities

Introduction

Ageing populations represent a great challenge to health and social care systems. Dementia is one of the most common age-related disorders, and with the number of cases expected to double every 20 years, governments worldwide are being urged to make dementia a clinical and research priority (Alzheimer's Disease International, 2009). Investigation into modifiable risk and protective factors could lead to the identification of preventative strategies or habits that people might integrate into their lifestyle (Desai *et al*., 2010). Indeed, in a recent review of population attributable risk (PAR) it was estimated that potentially modifiable risk factors may contribute to a third of cases of Alzheimer's Disease (Norton *et al*., 2014). The impact of these risk factors may be modified or mediated by interactions with other concurrent factors, and is likely to be related to the age at which exposures occur (Norton *et al*., 2013).

Participation in mentally stimulating leisure activities has emerged as a potential contributor to sustained cognitive health, exerting a protective effect against decline and dementia (Fratiglioni *et al*., 2004), as well as having other social and psychological benefits (Lennartsson *et al*., 2001). Associations between non-cognitive leisure pursuits, such as social (Marioni *et al.,* 2015) and physical (Willey *et al.,* 2016) activities and risk of cognitive decline and dementia have also been reported, but currently do not appear to be as robust as mentally stimulating activities. Maintaining cognitive health may prolong independence resulting in reduced institutionalization, reduced dependence on health and social care services, and improved quality of life (Stern *et al*., 2010).

Verghese *et al.* (2006) provide a definition of leisure activities as those which 'individuals engage in for enjoyment or well-being that are independent of work or activities of daily living'. The impact of a range of leisure pursuits, including physical (Wang *et al*. 2012), mental (Wilson *et al*., 2010), and social (Saczynski *et al*., 2006) activities has been explored, generating suggestions for possible mechanisms of action. A popular theory for the observed advantages of leisure activities is that participation can improve cognitive reserve, a function that allows neurons to communicate with increased efficiency, flexibility and adaptability as well as increasing neuronal capacity (Katzman, 1993; Tucker-Drob *et al*., 2009).

Previous reviews have investigated the potential impact of cognitively stimulating leisure activities on cognitive decline and risk of dementia in non-systematic (Stern and Munn, 2010) or non-parametric formats (Valenzuela and Sachdev, 2006). However, this review seeks to a) pool data from studies on cognitively stimulating leisure activities in a series of meta-analyses, b) assess the impact on cognition and risk of dementia in later life, and c) determine the quality of evidence.

Methods

Criteria for inclusion and exclusion of studies

Types of participants: Cognitively healthy adults (i.e. no diagnosis of impairment or dementia), aged 18 or over.

Types of activity: Unstructured leisure activities which elicit a 'mental response' from the participant (Stern and Munn, 2010). Standardized or structured activity

interventions were excluded (e.g. manual approaches, professionally delivered programs, or formal courses).

Types of studies: Quantitative studies published as English-language journal articles including randomized controlled trials (RCTs), cross-sectional studies, case-control studies and cohort studies.

Types of outcome: Scores on one or more tests of cognitive functioning, diagnosis of aMCI, MCI or dementia using standardized criteria (e.g. Diagnostic and Statistical Manual of Mental Disorders, 4th Edition [DSM-IV] (American Psychiatric Association [APA], (2000)).

Search terms

Combinations and variations of the search terms; 'dementia', 'cognitive activity', 'leisure activity', 'cognition', 'lifestyle' and 'hobbies' were selected. Studies published between 2004 and 2014 were considered. Systematic searches of PsychInfo, MEDLINE, CINAHL, EMBASE and the Web of Knowledge (Web of Science) were carried out in March 2014. A three-stage screening process was carried out: (1) titles were assessed for relevance to the search topic, and duplicates deleted, (2) abstracts were examined (referring to full text if relevance was unclear from title and abstract alone), and (3) the quality of the remaining papers after title and abstract sifts was assessed (see below for details). LY conducted the initial title sift and removal of duplicates. Title and abstract sifts were performed by LY and SZ. The reference lists of papers passing the quality control stage were reviewed to ensure no relevant papers were overlooked.

A template data collection spreadsheet was created and used by the reviewing authors to record study details and reasons for exclusion. In cases where multiple papers were based on the same cohort, papers were assessed for relevance to the review question, or use of a particular subset of the cohort not included in alternative papers. Several large projects were identified: the Kungsholmen Project (Fratiglioni *et al*., 1992), Mayo Clinic Study of Aging (MCSA) (Roberts *et al*., 2008), Bronx Aging Study (Verghese *et al*.,2003), RUSH Memory and Ageing Project (Bennett *et al*., 2005), and the Age Gene / Environment Susceptibility-Reykjavik Study (Harris *et al*., 2007). Nine studies were excluded as one of multiple papers based on the same project.

Assessing study quality

Quality was assessed using guidelines provided by the Critical Appraisal Skills Programme (CASP) Oxford UK (CASP, 2014). Specifically, checklists for cohort and case control studies were applied in the reading of papers reaching the quality assessment stage. The checklists included items assessing appropriateness of the issue investigated, recruitment, risk of bias, confounders, follow-up, results (strength of effect, precision, viability), generalisability, comparison to other available evidence, and implications. LY and SZ conducted the quality assessments independently with guidance from MO, a practicing clinician and expert in dementia research. If there were any differences in judgment of appropriateness and quality of the papers, the team reconsidered them collaboratively to reach a consensus.

Data extraction

Descriptive data from the final studies, including study sample, methods (including variables adjusted for in analyses), types of leisure activities, measures (e.g. leisure activity scales, cognition, diagnoses of cognitive impairment), and outcomes relevant to the review were summarized by the primary author (Table 2).

Analyses

Studies included in the meta-analyses were grouped by outcome (dementia, cognitive impairment including aMCI, MCI and cognitive decline) and type of output (risk [RR], odds [OR], or hazard ratios [HR]). Where necessary, ORs and RRs were calculated based on raw data from the papers so that data from several studies could be pooled for analysis. In the first instance a random effects model of meta-analysis was selected as studies varied in population and measures, hence it was expected that effect sizes would vary between studies. This model accounts for random error within studies as well as this variation in effect sizes between studies (Borenstein *et al*., 2007). Where a random effects model did not adequately reflect patterns in the data, the analysis was repeated using a fixed effects model.

Five meta-analyses were performed using data from 15 of the 19 studies. Three of the meta-analyses pooled data on the association between participation in leisure activities and risk of developing dementia, and two were focused on the association between leisure activities and cognitive decline and impairment. The remaining four studies provided other types of data including output from brain imaging tests.

Selection of data from studies

In cases where multiple models of analysis were applied to data to adjust for variables such as age and baseline cognition, the adjusted output was used for our analysis. RRs and ORs calculated by the authors of this review were based on data presented in the papers, therefore output does not take into account statistical adjustment for covariables. Where papers presented data on a range of specific leisure activities or authors created composite categories, activities or categories were included in the analyses when fulfilling the following criteria:

- Activity is common amongst the studies. To discern their frequency, the activities specified in each paper were listed and ranked according to how many studies gathered data on them. For example, reading was cited most frequently (15 studies), so data pertaining to reading would be prioritized over data for playing games (11 studies).
- Activity is predominantly cognitive in nature and requires active processing of information. For example, reading requires the use of memory, and stimulates visual and abstract thinking.

Composite categories must be specified as ‘mental’, ‘intellectual’ or ‘stimulating’, or describe an active cognitive skill (e.g. novelty seeking activities).

Results

Search results

In total, 3859 references were located across the five databases (see Figure 1). After the initial title sift and removal of duplicates, 494 papers remained. The title and abstract review yielded 92 papers which passed to the quality assessment stage. Nineteen papers were included in this review.

Included studies

Of the 19 included studies, there were 17 longitudinal cohort studies and two case control studies (Table 2). The studies were carried out in several countries: France (1), Germany (1), Iceland (1), Australia (1), Japan (1), Singapore (1), Sweden (3), China (3) and the USA (7). All participants were 46 years or older (mean = 77 years).

Participation in leisure activities and risk of dementia

Data was pooled for studies by Akbaraly *et al*. (2009) and Almeida *et al*. (2012) for the first meta-analysis (Figure 2). Pooling the results revealed an overall significant reduction in risk of dementia for those participating in stimulating activities including using computers (HR=0.58, 95% CI: 0.46-0.74,*p*=0.00).

Three studies (Paillard-Borg *et al*.,2009; Sattler *et al*., 2012; Wilson *et al*., 2007) were collated for the second meta-analysis in this set, of which Paillard-Borg *et al*., 2009 and Wilson *et al*., 2007, respectively, provided RRs as original data (RR=0.79, 95% CI:0.57-1.09; RR= 0.47, 95% CI:0.34-0.66) (Figure 2). The RR was calculated for Sattler *et al*. (2012) (RR=0.63, 95% CI: 0.28-1.39). The overall result of the meta-analysis was significant (RR=0.61, 95% CI: 0.42-0.90, *p*=0.01).

Two case control studies were included. Fritsch *et al*. (2005) found novelty seeking cognitive activities had the strongest association with this reduction in odds (OR=0.25, 95% CI: 0.15-0.41). The data from Lindstrom *et al*. (2005) was categorized as ‘intellectually stimulating’ activities (OR=0.84, 95% CI: 0.72-0.98). Both concluded that the odds of developing dementia were significantly lower for those frequently participating in leisure activities. However, despite this pattern the

random effects model was not significant. Since both studies independently had shown significant results, the analysis was repeated using a fixed effects model (OR=0.78, 95% CI: 0.67-0.90). This analysis found a significant association between participation in leisure activities and reduced risk of dementia.

Participation in leisure activities and risk of cognitive decline and impairment

ORs were calculated using data presented in papers by Geda *et al*. (2011), Li *et al*. (2013), Iwasa *et al*. (2012), Monastero *et al*. (2007), and Niti *et al*. (2008). Of the raw data available from Geda *et al.* (2011), 'reading books' was used according to the defined criteria for selection of activity / composite score data (see 'selection of data from studies'). Leisure activities were found to be significantly associated with a reduction in odds of cognitive impairment (OR=0.58, 95% CI: 0.43-0.70). The association was not significant based on data (full sample, high vs. low participation in leisure activities) from Niti *et al.* (2008) (OR=0.87, 95% CI: 0.67-1.13).

Li *et al.* (2013) performed an analysis of variance (ANOVA) between MCI and 'cognitively normal' groups, thus an OR was calculated. Complete raw data necessary to calculate the OR was only available for two cognitive activities (reading, writing), of which the data for 'reading' was used (OR= 0.54, 95% CI: 0.33-0.89) (see 'selection of data from studies').

Iwasa *et al.* (2012) and Monastero *et al.* (2007) presented ORs expressing increased odds of developing cognitive impairment. Data from the papers was taken to calculate reduction in odds (OR=0.55, 95% CI: 0.35-0.85 [Iwasa *et al.,* 2012]; OR=0.54, 95% CI:0.33-0.91 [Monastero *et al.,* 2007]) in order to be consistent with

the format of the ORs from the other papers contributing data to this meta-analysis set. Reduction in odds was significant (OR=0.69, 95% CI: 0.56-0.85, *p*=0.00) when data form the five studies was pooled.

Significant associations between participation in leisure activities and reduced risk of cognitive impairment were reported by Verghese *et al.* (2006) (HR=0.39, 95% CI: 0.25-0.61, *p*=0.00) and Wang *et al.* (2006) (HR=0.96, 95% CI: 0.93-0.99, *p*=0.01). The association did not reach significance in the study by Carlson *et al*. (2012). (HR=0.94, 95% CI: 0.85-1.037, *p*=0.22), nor when the overall HR for the studies were combined (HR=0.85, 95% CI: 0.71-1.02, *p*=0.08).

Relative Risk Reduction (RRR), Hazard Reduction & Odds Reduction

Relative risk, hazard and odds reduction percentages were calculated (Table 3) to assess the magnitude of significant protective effects. The reduction in risk of cognitive impairment or dementia associated with participation in cognitive leisure activities ranged from 4% to 75% (mean=43.36%). The analysis set including data from Geda *et al*. (2011) had the most consistent reduction effects (range = 42-46%). Effect sizes were considerably different for two of the analysis sets: (1) Fritsch *et al*. (2005) (75%) and Lindstrom *et al*. *(2005)* (16%), and (2) Carlson *et al*. (2006), Verghese *et al*. (2006) (61%), and Wang *et al*. (2012) (4%).

Tests of heterogeneity

The I^2 statistic was used as a measure of the impact of heterogeneity on the meta-analysis. Developed by Higgins & Thompson (2002), the calculation represents the proportion of total variation in estimates of treatment effects that are attributable to

differences between studies rather than sampling error within studies. The I^2 statistics produced for each meta-analysis set were interpreted according to the P value from the Chi-squared tests (ie: strength of evidence) alongside the following thresholds outlined in the Cochrane Handbook (Higgins and Green, 2008):

(i) 0-40%: may not be important

(ii) 30-60%: moderate heterogeneity

(iii) 50-90%: substantial heterogeneity

(iv) 75-100%: considerable heterogeneity

The level of heterogeneity for the meta-analysis set including Akbaraly *et al*. (2009) was potentially negligible and did not reach significance (p=0.39). Heterogeneity was 'moderate' in two of the sets; Paillard-Borg *et al*. (2009) (p=0.09) and Geda *et al*. (2011) (p=0.15). 'Substantial' heterogeneity was detected in the meta-analysis set including Carlson *et al*. (2012) (p=0.08), and highly significant (p=0.000) and 'considerable' heterogeneity was found in the meta-analysis including Fritsch *et al*. (2005).

Findings of other studies included in the review

Kåreholt *et al*. (2011) conducted a longitudinal cohort study on the association between leisure activities in mid-life and cognition in later life with 1643 participants. Mental activities (e.g. reading books, playing a musical instrument, hobby activities) were found to be significantly associated with later life cognition (β=0.11, p=0.05).

Saczynski *et al*. (2008) found that frequent participation in leisure activities was associated with better cognition; memory (β=0.20, 95% CI: 0.11-0.29), speed of processing (β=0.37, 95% CI: 0.29-0.45), and executive functioning (β=0.23, 95% CI: 0.15-0.29). In addition, participation in leisure activities was found to modify the link between white matter lesions (WML) and speed of processing (β=0.15, 95% CI: 0.01-0.30, *p*<.05).

Wang *et al*. (2013), discovered high engagement in mental activity was significantly associated with less decline in overall cognition (β=-.23, *p*<.01), language (β=-.11, *p*<.05), and executive function (β=-.13, *p*<.05).

Wilson *et al*. (2010) studied the relationship between participation in cognitive activities and rate of cognitive decline. Participation in cognitive activities did not have the same effect on those with cognitive impairment or AD at follow up as those without cognitive impairment. Rate of cognitive decline was reduced by 52% per year for each additional point on the cognitive activity scale (CAS) for those without cognitive impairment (estimate = 0.03, SE = 0.01, *p*=0.00). By contrast, rate of cognitive decline was not significantly associated with participation in cognitive activity for people with MCI (estimate = -0.02, SE = 0.02, *p*=0.30). For those with AD, for each point on the CAS, the mean rate of decline increased by 42% per year (estimate = 0.08, SE = 0.02, *p*<0.00).

Publication bias

We could not assess publication bias as there were too few studies within each grouping (i.e., meta analysis groups and other studies group), therefore there would not be sufficient power to detect true asymmetry (Higgins & Green, 2008).

Discussion

Summary of findings

This review includes five meta-analyses; three focusing on the impact of cognitively stimulating leisure activities on risk of dementia, and two on risk of cognitive impairment and decline. Participation in cognitive leisure activities consistently showed to be associated with reduced risk of dementia and cognitive impairment. This suggests that mental stimulation can have a protective effect on cognitive abilities, an association observed as early as Cicero (106 B.C.- 43 B.C.), writing that 'Old men retain their intellects well enough, if only they keep their minds active and fully employed.' Neuropsychological evidence of capacity for change, new learning, and plasticity also suggests that cultivation of an enriched cognitive environment may contribute to successful ageing (Mora *et al*., 2007).

Interpretation of findings

Ageing can be seen as a dynamic interplay of gains and losses in function, influenced not only by the physiological capacity of the brain, but also by the cognitive pragmatics of intelligence or skills learned as a result of cultural environment. Cognitive mechanics are largely contained within the pattern of growth in early life, stability in adulthood, and decline in later life (Baltes and Singer, 2001). By contrast, uptake, maintenance, and abandonment of cognitive pragmatics varies across lifespan and between individuals, according to levels of cultural exposure,

motivation to seek out opportunities for stimulation, and perhaps innate intelligence. It is thought that cognitive reserve (CR) is developed through formation and exercise of cognitive pragmatics. Multiple or well developed cognitive resources (eg: alternative neural pathways) are available should cognitive networks be damaged, meaning deficits in functioning associated with cognitive impairment and dementia are not expressed at all, or are not as profound as they might be in individuals with less CR (Scarmeas and Stern, 2003).

The selective-optimization with compensation model (SOC), posits that successful maintenance of functioning in the face of the challenge of losses is best achieved by reducing the variety of channels in which cognitive investments are made (selection) (Baltes and Baltes, 1993). Cognitive resources can then be channeled into a smaller pool of interests, in which performance is concentrated and, as a result optimized. The key then may be quality and level of investment in, rather than quantity and variety of cognitive leisure activities in later life. If evidence emerges that certain activities are more beneficial than others, we then need to discern any specific qualities that are responsible for their effectiveness, and ideally when in lifespan participation should be advised to achieve maximum benefits.

Methodological strengths and limitations

Although incidence rates were not available, an alternative analytic approach would have been to examine actual incidence rates of cognitive impairment/dementia in exposed and non-exposed groups and the absolute risk reductions. Considerable heterogeneity was detected in two of the meta-analyses. Higgins *et al*. (2003) reported that amongst 509 meta-analyses in the Cochrane Database of Systematic

Reviews, a quarter had heterogeneity of over 50%. This suggests the levels of heterogeneity observed in this review (e.g. 41%, 58.51%, 87.23%, 93.71%) are not uncommon. Additionally, the distribution of all of the findings was weighted towards a protective effect. An advantage of heterogeneity is the generalizability of findings. Whilst other associated risk factors for dementia (e.g. age, gender, vascular health) were accounted for in the models of analysis in the majority of studies, these variables may have factored into the differences detected.

There were no standardized classifications of leisure activities, making it difficult to compare studies. The most common composite categories included were 'mental', 'physical' and 'social'. Problems of collating individual activities to create composites include the fact that some leisure activities have multiple components, so it is difficult to identify a primary characteristic, which determines their classification. Furthermore, it is difficult to know how many activities within each category classification were practiced per person where overall categories were assigned. Frequency of participation was often recorded in daily, weekly, monthly, or yearly terms, then converted into an overall 'high', 'moderate' or 'low' levels. Again, the thresholds for category placement were not standardized, and so varied according to the judgment of authors. This might affect the reliability of the results.

The majority of studies included were observational studies. Whilst this methodology represents the most practical way of investigating this area, it is limited.because participants select themselves into different groups (i.e., exposed and unexposed). This methodology is also prone to bias. Sample bias was noted in some studies, such as Verghese *et al*. (2006). More positively, the populations included were

relatively ethnically diverse owing to the dispersion of locations of the studies. Due to the nature of the research, ‘survival bias’ requires consideration. A less active lifestyle is associated with higher mortality, as is lower socio-economic status (Adler and Ostrove, 1999), thus the strength of associations between participation in leisure activities and cognitive impairment may be under-estimated (Elias *et al*., 2000).

The studies acknowledge the potential risk of ‘reverse causality’ whereby low levels of participation in leisure activities may not be a cause of cognitive decline, rather an indication of experience of cognitive deficits in pre-clinical dementia (Roberts *et al*., 2008). Measures to avoid this were incorporated into the design or factored into the analysis of most studies. For example, most screened for dementia and cognitive impairment at baseline using standardized diagnostic criteria. Studies with shorter follow up periods (eg: Akbaraly *et al*., 2009) were more prone to detecting leisure behaviors attributable to pre-clinical dementia, as changes including apathy may begin to occur up to ten years prior to the development of dementia (Elias *et al*., 2000). However, in order to reduce this risk, a ‘cut off point’ was often defined, with those diagnosed with dementia at or before this time being excluded.

All of the studies identified and adjusted for confounding variables, as this was necessary for them to qualify for inclusion in this review at the quality control stage. However, some were more comprehensive than others. Age, sex / gender, education and significant co-morbidities were universally factored into analyses. Other risk factors that have been associated with dementia and cognitive impairment were considered as confounders in some studies including; vascular health, negative

health behaviors (eg: smoking, drinking), depressive symptoms, physical functioning, socio-economic status and APOE genotype.

Implications of findings

Interventions at a population level with a focus on reducing incidence may make a promising contribution to reducing future prevalence of dementia (Norton *et al*., 2013; Ritchie *et al*., 2010). Delaying the onset or progression of cognitive decline could impact incidence. Desai *et al*. (2010) estimate that even a relatively moderate delay could significantly impact incidence, as deaths are attributable to others causes before any experience of impairment. Projections of global dementia cases suggest that of the 106 million cases expected by 2050, 23 million could be averted if onset were delayed by just two years (Brookmeyer *et al*., 1998). These delays could also translate to economic savings, an estimated $10 billion over 10 years for an average one-year delay (Brookmeyer *et al*., 2007). Given the growing body of evidence that participating in cognitively stimulating leisure activities may contribute to reducing the risk of cognitive impairment in later life, promoting participation in such activities across lifespan, or at least from middle adulthood onwards, could be a worthwhile primary prevention strategy which could be used in combination with other strategies for overall maintenance of cognitive health.

Increasing awareness of the advantages of an engaged and cognitively enriching lifestyle may be achieved through public awareness campaigns, which may be led by the government, health service, voluntary organizations, or academic institutions. Desai emphasized the need for individualized cognitive fitness plans tailored to the strengths, limitations and preferences of the individual, and that these should be

integrated into daily routine as soon as possible for maximum effect (Desai, 2011). There may be an argument for encouraging cognitive leisure activities from an early age in education (Gold *et al*., 1995).

Future research

By identifying the methodological limitations of studies, systematic reviews assist research groups to design and conduct subsequent research of a higher quality. In addition, reviews can help to identify gaps in the field for further investigation. In this field there is a significant paucity of RCTs. However, this trial design may not be the most appropriate method of collecting epidemiological data owing to issues around the feasibility and ethical implications of manipulating exposure to something like leisure activities at random. The development of a standardized measure of leisure activities, with clearly defined categories and details of where individual activities should be placed; would be a useful contribution to this area of research. Placement of activities could be corroborated by both experts in the field and target populations. Further examination of specific leisure activities and differential impacts would also be valuable once a standardized scale is available. The benefits of using technology such as computers is an area of research warranting attention, since current data suggests an association with reduced risk of dementia. Given general computer use is helpful, cognitive leisure activities delivered via a computer platform may have enhanced benefits, as the content and platform are cognitively stimulating in their own right.

Conflict of interest

None

Description of authors' roles

LY and MO developed the research question for the review. MO provided supervision and guidance at all stages including the analyses. LY conducted the literature searches and initial sifting. SZ assisted LY with further sifting, assessments of the quality of studies, and meta-analyses. AS assisted with drafting the paper. SZ prepared the manuscript for publication. All authors reviewed and commented on drafts of the manuscript. All authors read and approved the final manuscript.

Acknowledgements

We would like to thank Ruth Muscat (knowledge resources librarian, University College London [UCL]) for her advice on the development of the search strategy for this review, and Dr. Shaun Scholes (research associate, epidemiology and public health, UCL) for consultation on statistical methods.

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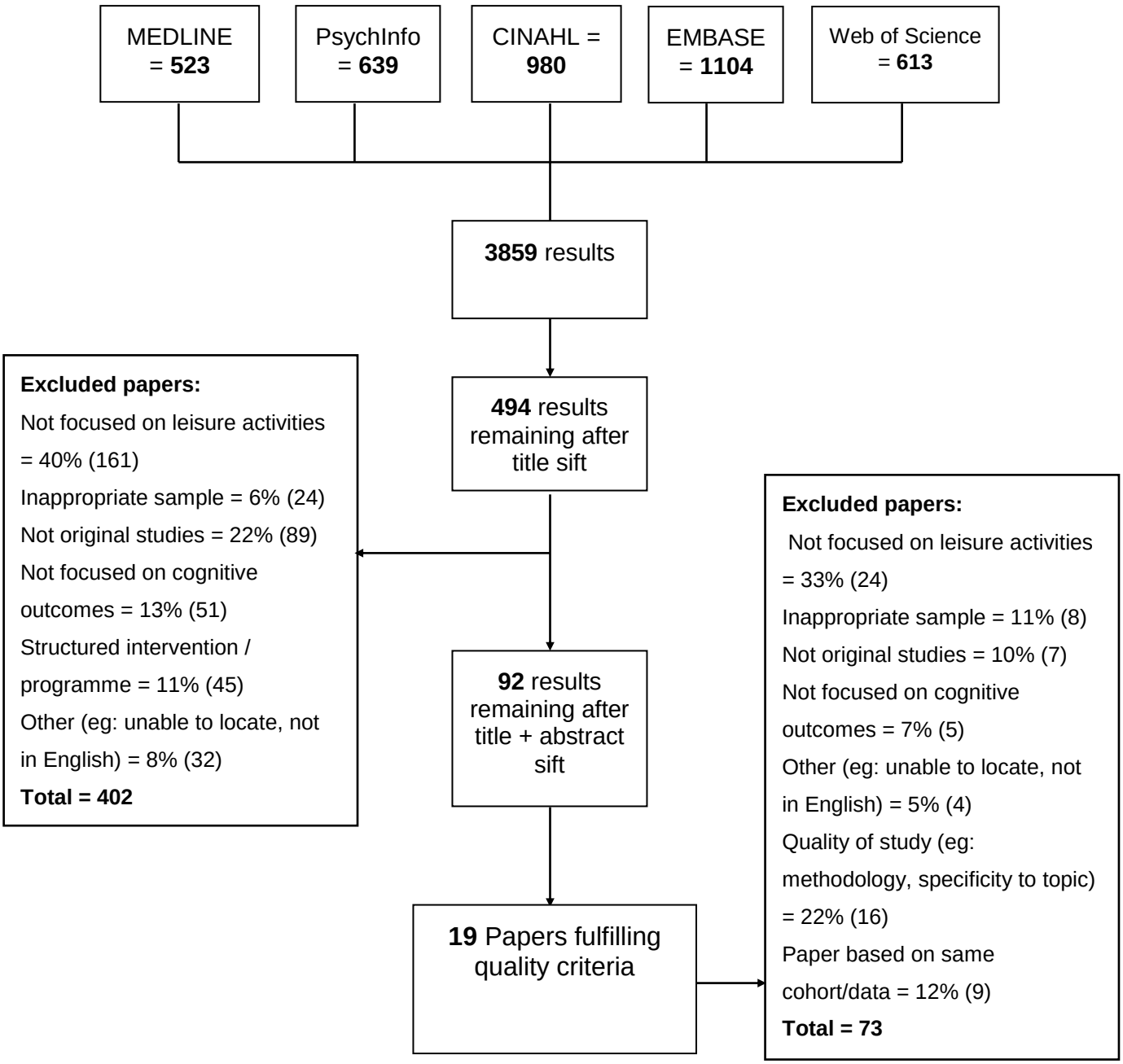

Figure 1. *Study selection*

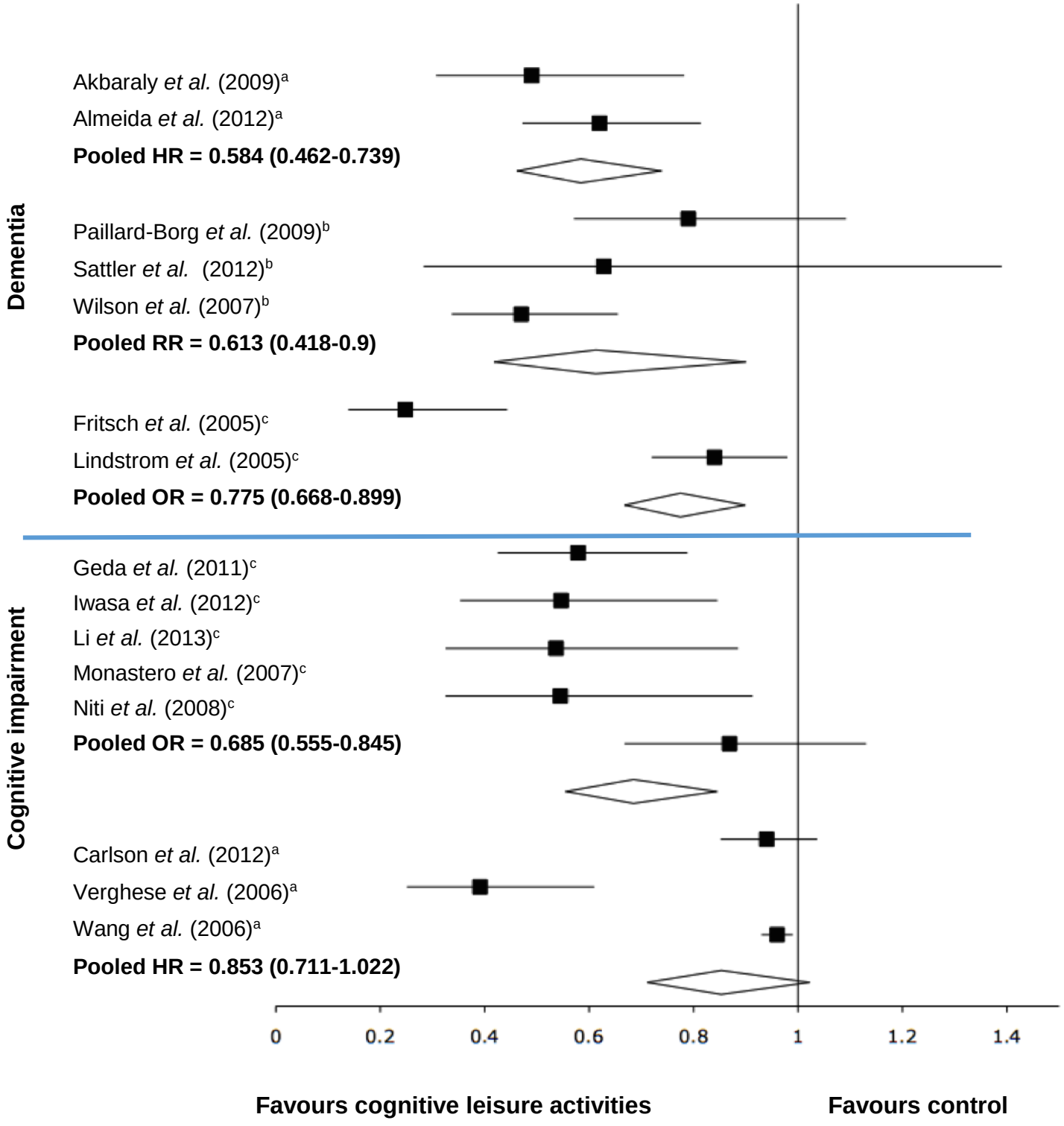

Figure 2. *Effect sizes for five meta-analyses (95% confidence intervals) including pooled values for each grouping. Output type: [a] Hazard Ratio (HR) [b] Relative Risk (RR) [c] Odds Ratio (OR).*

Table 1. *List of abbreviations*

Abbreviation	Description
AACD	Ageing Associated Cognitive Decline
AD	Alzheimer's Disease
aMCI	Amnesic Mild Cognitive Impairment
APOE	Apolipoprotein E
CAS	Cognitive Activity Scale
CASP	Critical Skills Appraisal Programme
CI	Confidence Interval
CINAHL	Cumulative Index to Nursing and Allied Health Literature
CR	Cognitive Reserve
CSID	Community Screening Interview for Dementia
CVLT	California Verbal Learning Test
DSM-III, DSM-IV	Diagnostic and Statistical Manual of Mental Disorders 3rd Edition, Diagnostic and Statistical Manual of Mental Disorders 4th Edition
DSST	Digit Symbol Substitution Test
EMBASE	Excerpta Medica dataBASE
HR	Hazard Ratio
HVLT	Hopkins Verbal Learning Test
ICD-10	International Statistical Classification of Diseases and Related Health Problems 10th Revision
MCSA	Mayo Clinic Study of Aging
MCI	Mild Cognitive Impairment
MMSE	Mini-mental State Examination
NINCDS-ADRDA	National Institute of Neurological and Communicative Disorders and Stroke–Alzheimer Disease and Related Disorders Association
NIINDS-AIREN	National Institute of Neurological Disorders and Stroke and Association Internationale pour la Recherché et l'Enseignement en Neurosciences
OR	Odds Ratio
PAR	Population Attributable Risk
RCT	Randomized Controlled Trial
RR	Risk Ratio
SDMT	Symbol Digit Modalities Test
SE	Standard Error
SOC	Selection Optimization Compensation
TMT	Trail Making Test
UCL	University College London
WML	White Matter Lesions

Table 2. *Descriptive summary of studies. Studies are grouped into their analysis sets.*

Study	Design	Sample size (*n=)*	Outcomes & diagnostic criteria	Cognitive assessment	Leisure activities	Follow up (years)	Adjusted variab
Akbaraly *et al.* (2009)	Longitudinal cohort	5506	Dementia: DSM-IV, NINCDS-ADRDA, NINDS-AIREN	MMSE	'Stimulating activities' (eg: crosswords, playing cards).	4	Age, gender, education, occup study centre, vascular risk, dep symptoms, physical functionin activities
Almeida *et al.* (2012)	Longitudinal cohort	5698	Dementia: ICD-10	MMSE	Computer use.	6 (mean)	Age, education, size of social n depression, significant co-mor cognitive function.
Paillard-Borg *et al.* (2009)	Longitudinal cohort	776	Dementia: DSM-III criteria	MMSE	Intellectual activities (eg: reading books/newspapers, writing, studying).	9	Age, gender, education, co-mo cognitive & physical functionin arrangement, depressive symp genotype.
Sattler, Toro, Schonknecht and Schroder (2012)	Longitudinal cohort	381	Dementia: AACD, NINCDS-ADRDA, NINDS-AIREN	MMSE	Cognitive activities (eg: reading books).	12	Education, socio-economic sta depression.
Wilson *et al.* (2007)	Longitudinal cohort	775	Dementia: NINCDS-ADRDA	19 tests: episodic memory (7), semantic memory (2), working memory (3), perceptual speed (5), visuo-spatial ability (2).	Seeking/processing information activities (eg: reading, games).	3.5 (mean)	Past cognitive activity, lifespan economic status, current socia activity, low baseline cognitive
Fritsch *et al*. (2005)	Case-control	264 dementia cases, 365 matched, 181 community	Dementia: NINCDS-ADRDA, DQ (dementia questionnaire)	IQ CODE Informant questionnaire on cognitive decline in the elderly (IQ CODE)	Novelty seeking activities (eg: new skill, mentally challenging activities, solving a problem).	Cross sectional	Year of birth, gender, ethnicity occupational status.

Lindstrom *et al.* (2005)	Case-control	135 AD cases 331 controls	Dementia: neuropsychological, laboratory & neurological examination	N/A	Intellectual activities (eg: reading, jigsaw puzzles, crosswords, playing music).	Cross sectional	Year of birth, gender, income,
Geda *et al.* (2011)	Longitudinal cohort	1321	Cognitive impairment: Mayo Clinic Criteria for MCI, DSM-IV, Petersen's criteria, CDR	N/A	Cognitive activities (eg: reading craft activities, computer activities).	Cross sectional	Age, gender, education, medic morbidity, depression, physica
Iwasa *et al.* (2012)	Longitudinal cohort	567	N/A	Cognitive impairment: MMSE	Hobbies (eg: gardening, watching TV, travelling, knitting, reading books)	5	Age, gender, years of educatio diseases, IADL, depressive sy smoking, hearing deficit & bas score.
Li *et al.* (2013)	Longitudinal cohort	1020	Cognitive impairment: Petersen's criteria	N/A	Reading, writing. Frequency: 'rare' or 'frequent'.	Cross sectional	Gender, martial status, dwellin monthly income, chronic disea
Monastero *et al.* (2007)	Longitudinal cohort	718	N/A	Cognitive impairment: MMSE	Mental activities (eg: reading books / newspapers, writing, studying).	3.4 (mean)	Age, gender, education, time t up, confounders for social hyp depressive symptoms, ADL di disease. Development of AD a up.
Niti *et al.* (2008)	Longitudinal cohort	1635	N/A	Cognitive impairment: MMSE	Social (eg: church, group activities, playing games), productive (eg: hobbies, preparing meals, shopping), physical activities (eg: walking, keep fit). High, medium, low participation.	1-2	Age, gender, education, smok consumption, depression, vas factors and diseases, APOE g functional status.
Carlson *et al.* (2012)	Longitudinal cohort	436	N/A	Cognitive impairment: MMSE, TMT, HVLT-R	Highly cognitively demanding activities (eg: crosswords, taking courses, drawing, singing).	9.5	Age, education, race, number diseases at baseline.
Verghese *et al.* (2006)	Longitudinal cohort	437	Cognitive impairment: DSM-III, Petersen's criteria,	Blessed Test, Wechsler IQ scales, Fuld object-memory	Cognitive activities (eg: reading, writing, crosswords, board/card games, group discussions,	5.6 (mean)	Age, gender, education, chron

				evaluation test, verbal IQ test	playing music).		
Wang *et al.* (2006)	Longitudinal cohort	5437	N/A	Cognitive impairment: MMSE	Cognitive activities (eg: board games, reading, writing, calligraphy/painting).	4.7 (mean)	Age, gender, education, occup conditions, smoking, drinking, symptoms, baseline MMSE, A participation in activities other by the questionnaire.
Kåreholt *et al.* (2011)[40]	Longitudinal cohort	1643	N/A	Cognitive impairment: MMSE	Mental activities (eg: reading books, playing music, singing)	22.8 (mean)	Age, age-square, gender, follo mobility problems, symptoms distress, employment status, e & childhood socio-economic st
Saczynski *et al.* (2008)	Longitudinal cohort	2300	Dementia: DSM-IV,	7 tests: Memory (1), speed (3), executive function (3)	Crosswords, reading, religious services, board or card games, using computer, writing letters/poems, artwork, etc.	Cross sectional	Age, gender, education, depre risk factors, diabetes, smoking genotype
Wang *et al.* (2013)	Longitudinal cohort	1463	N/A	Cognitive impairment: CSID, episodic memory (3), language (1), executive function (1).	Mental activity (eg: sewing, weaving, reading).	2.4 (mean)	Age, gender, years of schoolin status, household composition consumption, smoking, medica APOE genotype
Wilson *et al.* (2010)	Longitudinal cohort	614 controls 395 MCI 148 AD	Cognitive impairment: NINCDS-ADRDA	East Boston Story (immediate & delayed recall), SDMT, MMSE	Seeking/processing information activities (eg: TV, reading newspaper / books, games, crosswords, puzzles, museum).	12	Age, gender, ethnicity, educati cognitive activity.

Table 3. *Data for meta-analyses. RRRs calculated when data was significant. * indicates data extracted from original paper rather than calculated as part of this review*

	Study	Original data	CI	Calculated data	CI	p value	Relative reduction
Dementia							
Cohort	Akbaraly *et al.* (2009)	HR=0.49	0.31-0.79	*	*	*	51%
	Almeida *et al.* (2012)	HR=0.62	0.47-0.81	*	*	*	38%
Cohort	Paillard-Borg *et al.* (2009)	RR=0.79	0.57-1.09	*	*	*	Not significant
	Sattler, Toro, Schonknecht & Schroder (2012)	OR=0.38	0.15-0.99	RR=0.6276	0.2833-1.3904	p=0.2510	Not significant
	Wilson *et al.* (2007)	RR=0.47	0.34-0.66	*	*	*	53%
Case control	Fritsch *et al.* (2005)	OR=0.248	0.139-0.443	*	*	*	75%
	Lindstrom *et al.* (2005)	OR=0.84	0.72-0.98	*	*	*	16%
Cognitive impairment							
Cohort	Geda *et al.* (2011)	OR=0.67	0.49-0.94	0.5788	0.4251-0.7881	p=0.0005	42%
	Iwasa *et al.* (2012)	OR=1.87	1.16-3.02	OR=0.5463	0.3530-0.8455	p=0.0067	45%
	Li *et al.* (2013)	N/A	N/A	OR=0.5367	0.3253-0.8855	p=0.0149	46%
	Monastero *et al.* (2007)	OR=1.5	0.8-2.7	OR=0.5448	0.3251-0.9129	p=0.0211	46%
	Niti *et al.* (2008)	OR=0.62	0.46-0.85	OR=0.8689	0.6679-1.1305	p=0.2953	Not significant
Cohort	Carlson *et al.* (2012)	HR=0.94	0.86-1.04	*	*	*	Not significant
	Verghese *et al.* (2006)	HR=0.391	0.250-0.609	*	*	*	61%
	Wang *et al.* (2006)	HR=0.96	0.94-0.99	*	*	*	4%