Pontifícia Universidade Católica
do Rio de Janeiro

Vitória Florêncio Velloso

Designing a Cognitive Stimulation Protocol for Cognitively Healthy Older Adults

Dissertação de Mestrado

Dissertação apresentada como requisito parcial para obtenção do grau de Mestre pelo Programa de Pós-Graduação em Psicologia (Psicologia Clínica) do Departamento de Psicologia da PUC-Rio.

Orientador: Prof. Daniel Correa Mograbi

Rio de Janeiro,
Fevereiro de 2024.

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Abstract

Velloso, Vitória Florêncio; Mograbi, Daniel Correa (Advisor). **Designing a Cognitive Stimulation Protocol for Cognitively Healthy Older Adults**. Rio de Janeiro, 2024. 115p. Dissertação de Mestrado – Departamento de Psicologia, Pontifícia Universidade Católica do Rio de Janeiro.

Changes in the demographic profile of the population represent one of the main challenges in developing regions, such as Brazil. Increases in life expectancy also lead to a high prevalence of neurodegenerative diseases such as dementia, with economic and social impacts. These data highlight the urgent need for the development of evidence-based and validated proposals for maintaining cognitive health in older adults, with cost-effectiveness and broad applicability in healthcare systems. Thus, this study aimed to provide evidence to guide the development of a new program for maintaining cognitive health in healthy older adults, based on a systematic meta-review and focus group analysis. Both contributions further endorse the need for expanded investigations into cognitive stimulation interventions for healthy older adults, corroborating prevailing gaps in the literature and echoing the demand from the target population.

Key-words: Healthy Aging; Cognitive Reserve; Health Preventive Services; Cognitive Stimulation

Resumo

Velloso, Vitória Florêncio; Mograbi, Daniel Correa. **Construção de um Protocolo de Estimulação Cognitiva para Idosos Cognitivamente Saudáveis**. Rio de Janeiro, 2024. 115p. Dissertação de Mestrado – Departamento de Psicologia, Pontifícia Universidade Católica do Rio de Janeiro.

Mudanças no perfil demográfico da população representam um dos principais desafios em regiões em desenvolvimento, como é o caso do Brasil. Aumentos na expectativa de vida também levam a uma alta prevalência de doenças neurodegenerativas como a demência, com impactos econômicos e sociais. Estes dados ressaltam a necessidade urgente do desenvolvimento de propostas baseadas em evidências e validadas para a manutenção da saúde cognitiva em idosos, com bom custo-benefício e de larga aplicabilidade nos sistemas de saúde. Desta forma, este estudo buscou fornecer evidências para guiar a construção de um novo programa para manutenção da saúde cognitiva em idosos saudáveis, a partir de uma meta-revisão sistemática e da condução de grupos focais. Ambas as contribuições ressaltaram a necessidade de ampliar investigações sobre intervenções de estimulação cognitiva para idosos saudáveis, de acordo com as lacunas predominantes na literatura e a demanda da população-alvo.

Palavras-chave: Envelhecimento Saudável; Reserva Cognitiva; Serviços Preventivos em Saúde; Estimulação Cognitiva.

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1. THEORETICAL BACKGROUND

1.1 AN AGING POPULATION

The global population aged 65 years or older is projected to exceed 1.6 billion by 2050, with individuals in this age group expected to live approximately 20 additional years (United Nations, 2022). These demographic shifts present significant challenges (He et al., 2015), particularly in developing regions like Brazil (Miranda et al., 2016). The Economic Commission for Latin America and the Caribbean (ECLAC, 2022) has reported that this region is experiencing faster aging compared to other parts of the world. Currently, Brazil is home to over 32 million people aged 60 and above (IBGE, 2018; IBGE, 2022). Furthermore, the rapid decline in fertility rates is expected to lead to older individuals outnumbering children and adolescents in Brazil's population by 2030 (ECLAC, 2022).

Aging is characterized by the gradual decline of essential physiological functions necessary for survival and fertility over time, induced by the accumulation of damage in response to various stressors (Gilbert, 2000; Guo et al., 2022). The majority of individuals with at least one chronic condition or multimorbidity are typically between 60 and 79 years old, with projections suggesting a significant increase in this demographic group aged over 80 years from 2020 to 2050 (Ansah & Chiu, 2023). Therefore, this increase in life expectancy contributes to a growing prevalence of chronic and neurodegenerative diseases, which have substantial consequences.

Common conditions prevalent in older age, such as cardiovascular diseases, hypertension, cancer, osteoarthritis, diabetes mellitus, osteoporosis, dementia, depression, and multimorbidity pose a significant economic and psychological burden on patients, their families, and society at large (de Magalhães et al., 2017; Jaul & Barron, 2017). Moreover, lower-income individuals, facing heightened susceptibility to infectious diseases due to

limited access to protection and treatment, also experience reduced resilience against chronic diseases (Gao et al., 2021; Strulik & Grossmann, 2024).

1.2 COGNITIVE AGING AND PREVENTATIVE CARE

The normal cognitive aging process is associated with decline in certain cognitive abilities, such as processing speed and some aspects of memory, language, visuospatial function, and executive functions (Harada et al., 2013). Age-related changes in cognitive function vary greatly among individuals across all cognitive domains, with some functions showing greater susceptibility to aging effects than others (Glisky, 2007). These changes are small and should not result in functional impairment (Harada et al., 2013). However, aging also increases the risk of developing major cognitive disorders, with greater impacts on daily functioning (Cao et al., 2020).

Emerging as one of the major sources of disability and dependence among older adults, dementia is the seventh leading cause of death worldwide (World Health Organization, 2023). According to the World Health Organization (WHO), about 55 million people currently suffer from dementia, with more than 60% of them living in low- and middle-income countries (World Health Organization, 2023). Characteristic symptoms include memory loss, disorientation, impairments in comprehension and thinking, reductions in the ability to calculate, judge, learn and communicate as well as changes in mood, behavior, or motivation (World Health Organization, 2019).

This context leads to a profound social and economic challenge, impacting the healthcare and pension systems, as well as having detrimental effects on caregivers (Ferretti et al., 2018; World Health Organization, 2022). Estimated global annual costs in 2019 were 1.3 trillion dollars, with projections for costs to reach 2.8 trillion dollars in 20 years (World Health Organization, 2022). The financial burden falls heavily on the patient's family: an average of

11 hours of dementia care per day affects caregivers' employment capacity, particularly for low-income families (Carvalho & Neri, 2019).

Currently, there is no cure for dementia, and the effectiveness of treatments is limited (Disalvo et al., 2016; Preuss et al., 2016; Sanders & Rajagopal, 2020; Veroniki et al., 2022). Protective factors for cognitive health, supported by existing evidence, include cognitive activity (Deckers et al., 2014), education (El-Metwally et al., 2019; Lekoubou et al., 2014; Ribeiro et al., 2022), reducing sedentary behavior through moderate to vigorous physical activity (Falck et al., 2016) and engaging in social interactions (Navipour et al., 2019; McGrattan et al., 2021). Although the World Alzheimer Report 2023 advocates continuous learning for cognitive health (Long et al., 2023), there is no structured protocol that can be recommended for preventing cognitive decline in older adults.

1.3 GAPS IN THE EVIDENCE BASE

Cognitive interventions are usually classified as cognitive stimulation (CS), cognitive training (CT) or cognitive rehabilitation (CR) (Clare & Woods, 2004; Mlinac et al., 2022). CS involves engagement in a range of activities and discussions, CT refers to guided practices on a set of standard tasks, and CR identifies and works towards achieving goals that are relevant to everyday functioning (Clare & Woods, 2004; Mlinac et al., 2022).

Anti-aging science offers considerable commercial prospects due to its substantial potential for financial benefits (de Magalhães et al., 2017). Furthermore, the cognitive assessment and training market is expected to reach USD 11.4 billion by 2025 (Market Research Report, 2020), leading to an influx of cognitive training apps. Despite the appeal of equating brain training with other forms of personal 'fitness' (Wade, 2018), the rapid expansion of this market has outpaced the evidence supporting these interventions.

Lumosity serves as a pertinent example of a company that targeted older Americans concerned about age-related cognitive decline. They did so through advertisements claiming

that their games could prevent dementia and Alzheimer's disease. Consequently, the company agreed to pay $2 million to settle Federal Trade Commission charges, which included making these claims without "competent and reliable scientific evidence" (Federal Trade Commission, 2016). Additionally, the charges involved other false claims made for different target audiences.

Although there is some evidence suggesting that commercial cognitive training can enhance cognitive performance on tests, the presence of clinically significant outcomes is still lacking sufficient evidence (Bonnechère et al., 2020). In fact, establishing widely accessible cognitive programs remains challenging due to the scarcity of high-quality evidence and the heterogeneity in reported findings (Gavelin et al., 2020). A comprehensive meta-review encompassing cognitive interventions for healthy older adults without restrictions is needed to enhance comparability between current methods.

1.4 OBJECTIVE

The objective of this study was to provide evidence that could guide the development of a structured program for maintaining cognitive health in healthy older adults, based on a systematic meta-review (study 1) and a framework analysis of focus groups (study 2). Individual studies were carried out with the following specific objectives:

Study 1 – To assess the effectiveness and feasibility of simple and combined cognitive interventions for cognitively healthy older adults.

Study 2 – To explore the demand for, facilitators of, and barriers to implementing a cognitive stimulation protocol for healthy older adults within the context of Brazil.

2. ARTICLE SECTION

2.1 ARTICLE 1

VELLOSO, V. F., LATGÉ-TOVAR, S., BOMILCAR, I., MOGRABI, C. D. Cognitive interventions for healthy older adults: A systematic meta-review

Cognitive interventions for healthy older adults: A systematic meta-review

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Abstract

Objectives: With increasing global life expectancy, cognitive interventions hold promise in mitigating cognitive decline and fostering healthy aging. Despite the demand for reliable alternatives, comprehensive analyses of existing evidence have been lacking. This study aims to assess the effectiveness and feasibility of simple and combined cognitive interventions for cognitively healthy older adults. **Method:** Systematic meta-review, selecting articles from four databases: PubMed, Web of Science, Embase, and Cochrane Library. Quality assessment carried out with AMSTAR2. Findings were summarized and discussed narratively. **Results:** Thirty-four articles were included, with 18 meta-analyses and 16 qualitative systematic reviews. In total, there were 33 reviews addressing cognitive training, 3 covering cognitive stimulation, and 1 approaching multicomponent interventions. Most reviews had critically low quality. **Conclusions:** The prevailing evidence supports cognitive training. Continued research into cognitive stimulation and multicomponent protocols is encouraged. Longer follow-ups are important for identifying combined and clinically significant results. Rigorous risk of bias and quality assessment is necessary to enhance the evidence base.

Key-words: healthy aging; dementia; cognitive interventions.

Introduction

Life expectancy is increasing worldwide (Gauthier et al., 2022), with the world population aged 65 years or over being projected to reach 994 million by 2030 and 1.6 billion by 2050 (United Nations Department of Economic and Social Affairs, Population Division, 2022). By this year, the World Population Prospects 2022 suggests that there will be more than twice as many persons over this age as children under 5 years old worldwide, and a 65-year-old individual is expected to live for approximately 20 more years (United Nations Department of Economic and Social Affairs, Population Division, 2022). This new demographic configuration requires societies to adapt, promoting new health and social care policies to provide for the older population, preparing for the changes that lie ahead.

With the increase in life expectancy, the prevalence of major neurocognitive disorders should follow a corresponding progression (Ferri et al., 2005; Prince et al., 2013). The global prevalence of dementia in adults over 50 years old is estimated at 6.97% (Cao et al., 2020), with 153 million people expected to be living with dementia worldwide by 2050 (GBD 2019 Dementia Forecasting Collaborators, 2022). The annual global cost of dementia in 2019 was 1.3 trillion USD, with approximately half of these costs being attributable to care provided by family members and close friends (World Health Organization, 2023). Large costs of healthcare needs often impact the families of people living with dementia (PlwD) and their ability to work, particularly affecting the economy and social care in low-income countries (Carvalho & Neri, 2019).

Albeit complex, reducing age-specific risk for dementia is feasible, given changes in development and lifestyle (Langa, 2015). For example, increases in education in early life and decreases in hypertension, smoking, and diabetes across the life span have protective value (Prince et al., 2015). Recent findings suggest that cognitive activities may help reduce

the risk of dementia and enhance late-life cognition, potentially contributing to cognitive maintenance (Livingston et al., 2020).

Also, there is considerable variability between individuals regarding the susceptibility to both age-related and pathological brain changes for which cognitive reserve may be one of the factors responsible (Stern, 2012). Epidemiological evidence suggests that life experiences, even in later life, can contribute to cognitive reserve (Stern, 2012). Interventions for healthy older adults (H.O.A.) that seek to improve functional and cognitive abilities might be useful to slow age-related cognitive decline and prolong healthy aging (Stern, 2012).

Cognitive interventions are usually classified as cognitive stimulation (CS), cognitive training (CT) or cognitive rehabilitation (CR) (Clare & Woods, 2004; Mlinac et al., 2022). CS involves engagement in a range of activities and discussions, typically in a group, aimed at the general enhancement of cognitive and social functioning (Clare & Woods, 2004; Mlinac et al., 2022). CT refers to guided practices on a set of standard tasks designed to reflect particular cognitive functions (Clare & Woods, 2004; Mlinac et al., 2022). CR employs a biopsychosocial approach to identify and work towards achieving treatment goals that are relevant to everyday functioning (Clare & Woods, 2004; Mlinac et al., 2022).

The World Alzheimer Report 2023 recommends that people keep learning (Long et al., 2023), but it does not cite any structured protocol that can be strongly recommended for the prevention of cognitive decline in healthy older adults (for PwD, Cognitive Stimulation Therapy is recommended; Spector et al., 2003; Gauthier et al., 2022). Despite the demand for a reliable intervention and the diversity of empirical studies and systematic reviews for specific types of intervention, there have been few attempts to do a broad analysis of actual evidence. Gavelin et al. (2020) conducted a recent overview, but included only simple CS or CT interventions, excluding combined or other arrangements. Considering this, the current systematic meta-review investigates the effectiveness and feasibility of simple and combined

cognitive interventions designed for cognitively healthy older adults, based on the available scientific literature.

Methods

Literature search

Reviewed articles were selected according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA; Page et al., 2021) guidelines and the systematic review protocol was registered in PROSPERO (CRD42023387917). Each search term was systematically searched on the PubMed, Web of Science, Embase and Cochrane Library databases, considering articles published until the 21st of November 2022.

The following keywords were used: (("cognitive stimulation") OR ("cognitive training")) AND (("older adults") OR (elderly)) AND (((((((dementia) OR ("cognitive decline")) OR (AD)) OR (Alzheimer*)) OR (MCI)) OR ("cognitive impairment")) OR ("neurocognitive disorder*")) AND ((systematic reviews) OR (meta-analysis)).

Study selection

This systematic meta-review includes peer-reviewed systematic reviews and meta-analyses with cognitive, affective and/or functional outcomes. Eligible studies met the following criteria: psychosocial interventions for cognitively healthy older adults, with an average age greater than or equal to 50 years old. We accepted any definition of “healthy older adults” established by the review authors.

We initially planned to include only studies with an average age greater than 60 years. However, as we observed that some studies considered participants over 50 years old as healthy older adults, to conduct a comprehensive overview, these articles were not excluded. Systematic reviews and meta-analyses including studies with healthy older adults and clinical groups, or with healthy older adults and other age groups, were included only if the data of

our population of interest (cognitively healthy older adults) could be sorted from other populations and had at least 3 studies with healthy older adults included in the review.

Publications were excluded if: (1) focused on any special clinical group (dementia, diabetes, HIV, frailty, orthopedic surgeries, etc.) or (2) other ages; (3) did not include psychosocial interventions, (4) were not systematic reviews/meta-analysis, (5) no cognitive, affective or functional data from healthy participants was available, (6) were not peer reviewed articles (e.g. conference papers, protocols, etc.) or (7) not written in english. Figure 1 displays the process of study identification. A list of studies excluded by full text screening is available on Supplementary material A.

Data extraction

The study was carried out using the Rayyan software (Ouzzani et al., 2016). Two authors (V.V. and S.L.T.) independently screened abstracts for inclusion, blinded by the software. Disagreements were resolved independently by a third author (I.B.). Full-text screening was carried out with the same method among authors, in independent spreadsheets.

From selected studies, the following information was extracted: authors, year of publication, type of intervention, number of studies included, study design, sample size and mean age, intervention and session duration and frequency, outcome domains, relevant findings and quality/risk of bias assessment. Data were extracted independently by two authors (V.V. and S.L.T.) and disagreements were resolved by comparing observations and reaching a consensus. Results were summarized and discussed narratively.

We classified the studies by intervention type (e.g., CT, CS, meditation practices, multicomponent interventions) according to definitions established in primary systematic reviews. In addition, practices were highlighted when associated with physical exercises (done simultaneously (dual tasks) or subsequently (one followed by the other) or carried out

separately in multicomponent interventions). Multicomponent interventions that also had nutritional, medical, and occupational monitoring were also accepted.

Primary reviews that included only cognitive training interventions carried out on a computer or digital device were classified as "computerized cognitive training". If any type of cognitive training was allowed, including paper and pencil or digital activities, we classified it as "cognitive training" without additional elucidation.

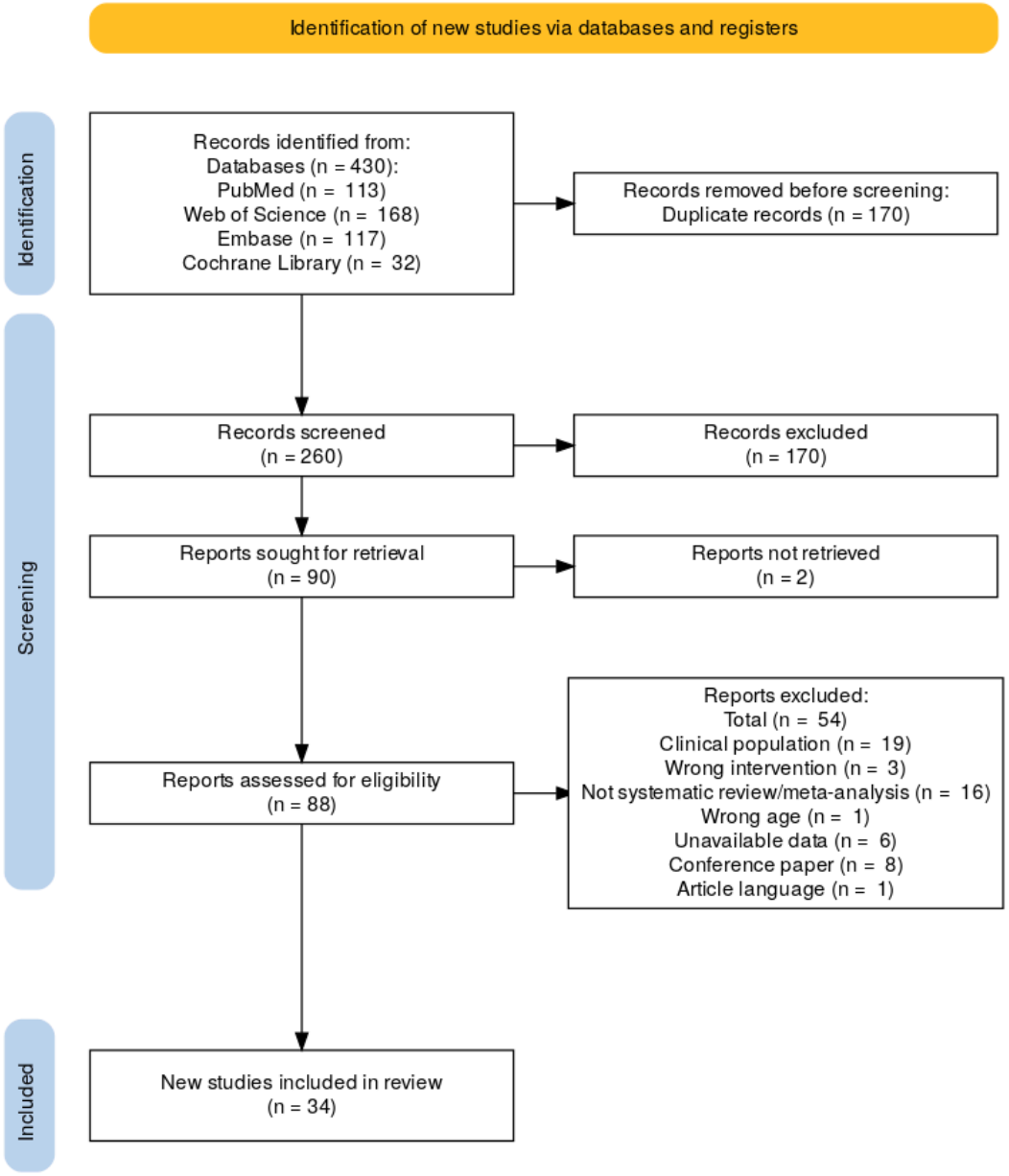

Figure 1: PRISMA flowchart of study identification, screening, assessment of eligibility and inclusion for synthesis.

Risk of bias (quality) assessment

The quality assessment was carried out with the AMSTAR2 tool (Shea et al., 2017), designed specifically for assessing the quality of systematic reviews and meta-analyses. Initially, it was planned to also use the criteria proposed by Kmet et al. (2004), but we observed that the majority of items would only be suitable for evaluating empirical studies.

The following were classified as critical appraisal questions, determining the overall confidence level of each study: (1) "Did the review authors use a comprehensive literature search strategy?", (2) "Did the review authors describe the included studies in adequate detail?", (3) "Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?", (4) "If meta-analysis was performed, did the review authors use appropriate methods for statistical combination of results?", (5) "If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?", (6) "Did the review authors account for RoB in individual studies when interpreting/discussing the results of the review?", (7) "Did the review authors provide a satisfactory explanation for and discussion of any heterogeneity observed in the results of the review?".

A partial yes was considered as "yes" for the purpose of overall confidence classification. Results for each quality criteria and overall confidence ratings across included reviews are available on Figure 2 and Figure 3. Complete AMSTAR 2 checklist (Shea et al., 2017), a description of quality criteria and the scheme for interpreting weaknesses detected in critical and non-critical items are available in Supplementary material B.

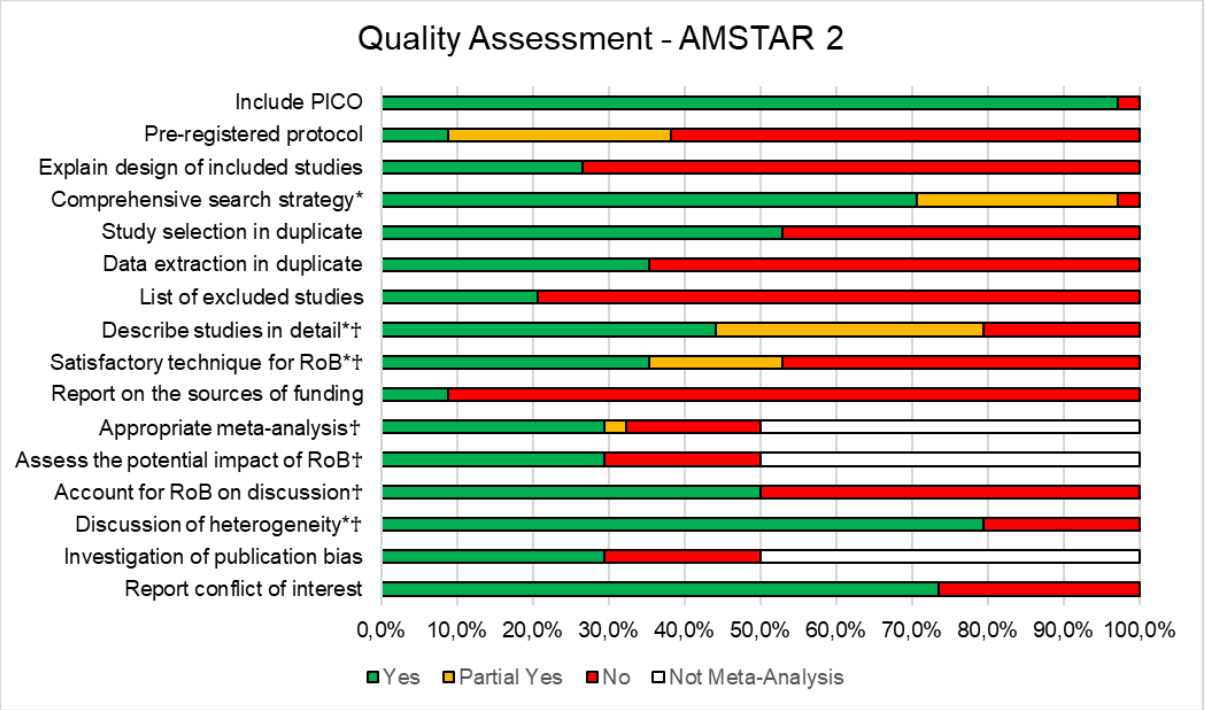

Figure 2: Results for each quality criteria across included reviews.

*Critical domains for qualitative reviews

† Critical domains for meta-analysis

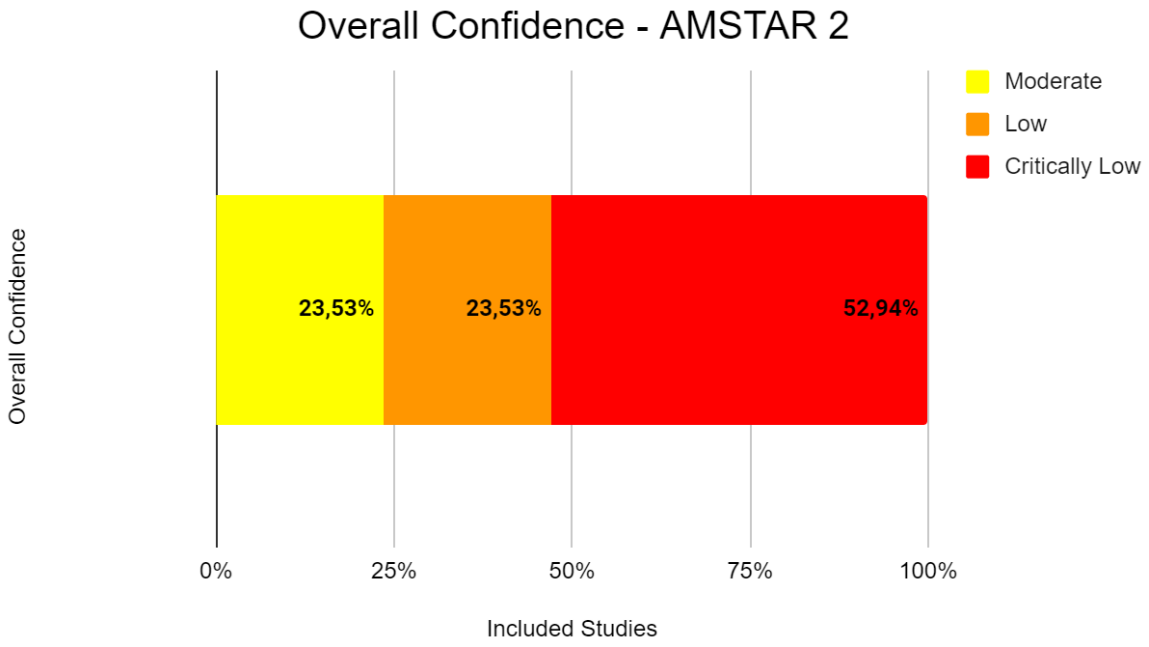

Figure 3: Overall confidence ratings across included reviews

Results

Thirty-four articles were included, with 18 meta-analyses and 16 qualitative systematic reviews. More than half (20) of the studies also accepted clinical populations. In these cases, data was extracted if (1) clinical trials only included healthy participants or (2) separated meta-data for healthy populations were available. Twenty-five articles reported the mean population age, of which 20 were between 70 and 80 years. None of them had an average of less than 60 or more than 80 years. The largest sample size was 8732 (Mendonça et al., 2022) and the smallest was 163 (ten Brinke et al., 2017). Twenty studies included only randomized clinical trials (RCT) study designs.

Most of the studies did not fully describe settings. The majority of reviews included studies with passive (P.C.) and/or active (A.C.) control groups. Lauenroth & Kim (2016) reported active, passive, or other intervention controls. Ten Brinke (2017), Alnajjarr (2019), and Mendonça (2022) informed active, passive or no control. Fan & Wong (2019) included studies with active, passive, or unclear controls.

Most reviews (18) had critically low quality. Only six reviews (23.5%) had at least moderate quality, and none were classified as high quality. The main critical flaws were unsatisfactory techniques and insufficient discussion for risk of bias (RoB) assessment and outcomes. A full description of instruments and results for risk of bias/ quality assessment carried out in each systematic review is available in Supplementary material C.

Almost all studies included PICO (Population, Intervention, Context and Outcome measures; Schardt et al., 2007) descriptions, did a comprehensive search strategy, discussed possible sources of heterogeneity and reported potential conflicts of interest. Results for individual quality domains and overall confidence across reviews are reported in Figures 2 and 3. Detailed assessment for individual reviews is available in Supplementary material B.

Findings were divided by type of intervention and reported below (for characteristics of the included studies, see Table 1, Table 2 and Table 3).

Cognitive training

Findings from meta-analyses

In total, there were 16 meta-analyses structured on CT. Out of these, 6 included any form of CT (Papp et al., 2009; Valenzuela & Sachdev , 2009; Martin et al.; 2011; Kelly al., 2014, Mewborn et al., 2017; Nguyen et al. 2021), 4 focused only on computerized CT (Lampit et al., 2014; Webb et al., 2018; Basak et al., 2020; Gates et al., 2021), 3 investigated combined CT and physical exercise (PE) (Bruderer-Hofstetter et al., 2018; Guo et al., 2020; Gavelin et al., 2021), 2 compared CT with PE interventions (Hindin & Zelinski., 2012, Karr et al.; 2014), and 1 included both CS or CT or mixed CS plus CT (Yun & Ryu, 2022).

Most (13) studies selected only RCT. Also, 2 included any pre- and post-test design with a control group (Hindin & Zelinski., 2012; Nguyen et al. 2021) and 1 included any type of clinical trial (Karr et al, 2014). Between 7 to 161 studies were included in each meta-analysis, with a sample size between 670 and 13797 participants and a mean age of 72.2 years. In these studies, CT (applied with or without other interventions) programs had a duration between 1 to 96 weeks, with a range of 6 to 240 minutes for each session, and less than 1 to 10 sessions per week. Sample size and intervention characteristics were not described separately in Yun & Ryu (2022).

Overall, studies found small to large effects for processing speed (Kelly al., 2014; Lampit et al., 2014; Webb et al., 2018; Nguyen et al. 2021), very small to small effect for global cognitive function (Papp et al., 2009; Kelly al., 2014; Lampit et al., 2014; Mewborn et al., 2017; Bruderer-Hofstetter et al., 2018; Webb et al., 2018; Basak et al., 2020; Gates et al., 2021; Gavelin et al., 2021; Yun & Ryu., 2022) and executive functions (Hindin & Zelinski., 2012; Karr et al., 2014; Kelly al., 2014; Guo et al., 2020) and mixed findings for memory.

Kelly et al. (2014) found moderate to large ESs for executive functions and reported that effects of transfer and maintenance of intervention were most commonly reported with at least 10 adaptive training sessions and a long-term follow-up. Findings for specific subtypes of CT or comparisons are reported below.

Computerized cognitive training

Four meta-analyses focused exclusively on CT interventions that were performed on digital devices (Lampit et al., 2014; Webb et al., 2018; Basak et al., 2020; Gates et al., 2021) and had RCT as the study design. Webb et al. (2018) used the same dataset as Lampit et al. (2014), categorizing cognitive outcomes differently. Between 8 to 161 studies were included in each meta-analysis, with a sample size between 1183 and 13797 and a mean age of 71.6 years. In these studies, CT had an intervention duration of 1 to 26 weeks, with a range of 10 to 120 minutes for each session and 1 to 7 sessions per week.

Overall, studies found a small effect of computerized CT on overall cognition. Lampit et al. (2014) and Webb et al. (2018) found moderate effects on processing speed and small effects on visuospatial abilities. Different from Lampit et al. (2014), Webb et al. (2018) found a small effect of computerized CT on executive functions analyzing the same dataset. Some evidence of improvement in different aspects of memory (Lampit et al., 2014; Webb et al, 2018; Gates et al., 2021). Mixed and inconclusive findings for other cognitive domains. Basak et al. (2020) found larger effect sizes for near transfer in studies with lower educational levels and with less cognitive outcomes.

Cognitive training combined with physical exercise

In total, there were 3 meta-analyses structured on combined CT and PE (Bruderer-Hofstetter et al., 2018; Guo et al., 2020; Gavelin et al., 2021), performed simultaneously or subsequently. All selected only RCT as the study design. Between 11 to 27 studies were included in each meta-analysis, with a sample size of between 670 and 2620 and a mean age

of 72.2 years. Combined CT and PE had an intervention duration of 4 to 24 weeks, with 15 to 150 minutes for each session and 1 to 10 sessions per week.

Studies reported a small effect of combined interventions for overall cognitive (Bruderer-Hofstetter et al., 2018; Gavelin et al., 2021) and executive functions (Karr et al., 2014; Guo et al., 2020) in comparison with controls.

Cognitive training compared with physical exercise

In total, there were 2 meta-analyses focused on comparing CT with PE interventions (Hindin & Zelinski., 2012; Karr et al., 2014). Hindin & Zelinski (2012) included 42 studies with pre- and post-test design and a control group, with a sample size of 3781 and a mean age of 69.2 years (CT: 69.9; PE: 67.9).

Karr et al. (2014) included 27 studies with any type of clinical trial, with a sample size of 2013 (CT: 1061; PE: 1038) and a mean age of 73.6 years (CT: 72.3; PE: 74.9). CT had an intervention duration of 2 to 96 weeks, with a range of 15 to 240 minutes for each session, and less than 1 to 5 sessions per week. PE had an intervention duration of 8 to 52 weeks, with a range of 30 to 120 minutes for each session and 1 to 5 sessions per week.

Karr et al. (2014) found a small and significant effect only for CT in overall executive functions. The larger effect for narrow EF outcomes was for problem-solving. Hindin & Zelinski (2012) analyzed aerobic physical interventions along more cognitive outcomes and found a small effect both for aerobic exercise and CT on untrained domains - far transfer for reaction time, memory and executive functions - with a better study quality associated with larger Ess.

Table 1: Systematic reviews and meta-analysis about cognitive training interventions

Main Author (Year)	Studies Included (*n*)	Study Design	Sample Size (mean age)	Intervention and Session Duration and Frequency	Outcome Domains	Review Outcome
Meta - analyses						
Papp (2009)	10	RCT	4009 (74.1)	6 - 90 weeks; 30 - 180 min/sess; 1 - 5 sess/week	GC, WM/Divided Att., Inhibition, Planning/CF, PS, RT/Motor Speed, Mem., VSA, ADLs	Small effect of PS interventions on overall cognition; very small for all cognitive interventions across all outcomes, and for Mem., Reas. and multimodal interventions; similar effects with A.C. and P.C. I^2: n/c
Valenzuela & Sachdev (2009)	7	RCT	6339 (NR)	5 - 30 weeks; 60 - 90 min/sess; 1 - 4 sess/week	Att., EF, Mem., Verbal Learning, VSA	Large effect size compared with P.C.; RCTs with follow-up > 2 years had similar E.S. as shorter follow-ups (sensitivity analysis) I^2: n/c
Martin (2011)	NR	RCT	NR (NR)	n.f.d.	Mem.	Better mem. score than P.C. but not than A.C. I^2. n.f.d.
Hindin & Zelinski (2012)	42 CT: 25 PE: 17	pre- post-test with C.G.	2765 (69.9)	2 - 12 weeks	EF, Choice RT, Mem.	Small effect on untrained cognitive tasks. Better study quality linked with E.S.s. I^2: n/c

Karr (2014)	27	clinical trial	1061 (72,3)	4 - 96 weeks; 15 - 240 min/sess; < 1 - 5 sess/week	EF (Att., VF, WM, Inhibition, Problem-Solving)	Significant effect for EF. I^2: n.f.d.
Kelly (2014)[1]	23	RCT	5037 (54 - 99)	2 - 96 weeks; 15 - 120 min/sess; 1 - 5 sess/week	GC, EF (Att., WM, VF, Reas., PS), Mem., SCP, Daily Function	Compared to A.C., moderate (WM; I^2: 84%) to large (PS; I^2: 75%) effects for EF, moderate E.S. for recognition (I^2: 0%), small ES for cognitive function (I^2: 0%). Compared to P.C., small ES for subjective Mem. (I^2: 13%); mixed findings for different types of mem. Transfer and maintenance linked with adaptive training (≥ 10 sess and a long-term follow-up).
Lampit (2014)	51	RCT	4885 (70.8)	2 - 16 weeks; 15 - 120 min/sess; 1 - 7 sess/week	GC, Att., EF, WM, PS, Mem., VSA	Small ES on overall cognition (I^2: 29.9%), nonverbal Mem. (I^2: 24.5%), WM (I^2: 45.6%) and VSA (I^2: 42.7%). Moderate ES on PS (I^2: 84.5%). Very small ES for verbal Mem. (I^2: 50.1%). No effect for EF (I^2: 31.8%) and Att. (I^2: 62.9%). Home-based less effective than group training, and > 3 sess/week was ineffective versus ≤ 3.

Mewborn (2017)	48	RCT	3718 (77.0)	1 - 90 weeks; 6 - 180 min/sess; 1 - 7 sess/week	GC, Att., EF, WM, PS, Reas., Mem., Lang., VSA	Small effect on overall cognition relative to A.C. and P.C. (I^2: 57%).
Bruderer--Hofstetter (2018)	11	RCT	670 (71.5)	4 - 24 weeks; 20 - 90 min/sess; 1 - 3 sess/week	GC, Att., EF, Mem., IADLs, Percep. Motor Function	Effective for overall cognition (I^2: 4%); best ranked: aerobic exercise (interval) + CT (Israel method).
Webb (2018)	51	RCT	4885 (70.8)	2 - 16 weeks; 15 - 120 min/sess; 1 - 7 sess/week	EF, STM, PS, Fluid Reas., Long-Term Storage/Retrieval, VSA	Differences from Lampit et al. (2014). Moderate effect for PS (I^2: 87.3%). Small ES for VSA (I^2: 15.4%), ES (I^2: 24.0%), long-term storage and retrieval (I^2: 67.0%) and STM (I^2: 44.6 %). No effects for fluid Reas. (I^2: 61.1%).
Basak (2020)	161 single:94 multi:67	RCT	total: 13797 single:8612 multi: 5185 (70.3)	single: 1 - 12 multi: 1 - 90 weeks	GC, EF, PS, Reas., Mem., Lang., Daily Function	Small net gain on overall cognition (I^2: 82.3%), for single (I^2: 84.0%) or multicomponent training (I^2: 82.3%), and for near (I^2: 85.4%) and far (I^2: 82.3%) transfer. Larger ES for near transfer, lower educational level and fewer outcomes.

Gates (2020)	8	RCT	1183 (74.5)	12 - 26 weeks; 10 - 90 min/sess; 1 - 3 sess/week	GC, Att., EF, WM, PS, VF, Episodic Mem., QoL/ Well-Being	Small effect on global cognition compared to A.C. (after 3 months) (I^2: 0%), and on episodic Mem. compared to P.C. (after 6 months) (I^2: n/a).
Guo (2020)	14	RCT	1012 (71.8)	7 - 24 weeks; 15 - 150 min/sess; 1 - 10 sess/week	EF: Complex EF, Inhibition, Shifting	Small effect for EF (I^2: 23.3%).
Gavelin (2021)	27	RCT	2620 (73.4)	4 - 24 weeks; 15 - 105 min/sess; 1 - 6 sess/week	GC, EF, WM, STM, PS, Fluid Reas., Long-Term Mem., Visual Process.	Small effect for overall cognition ($\tau 2$: 4.94).
Nguyen (2021)	37	pre- post-test with C.G.	2511 (71.2)	2 - 16 weeks; 10 - 90 min/sess; 1.3 - 7.5 sess/total	Att., EF, PS, Fluid Intelligence, Lang., Mem., VSA, Daily Function	After adjusting for publication bias, only small E.S. for PS remained significant (I^2: 69.2%).
Yun & Ryu (2022)	29	RCT	n.f.d. (70.6)	n.f.d.	GC, ADLs, IADLs, QoL, Depr.	Small effect for overall cognition. (I^2: 29.3)

Systematic Reviews						
Kueider (2012)	38	pre- post-test design	Total: 3205 (50 - 96); CCT: 1835 (52 - 96); NS: 1043 (51 - 87); VG: 327 (50 - 86)	CCT: 2 - 68 weeks; 15 - 240 min/sess; 1 - 7 sess/week. NS: 3 - 12 weeks; 20 - 120 min/sess; 1 - 5 sess/week. VG: 4 - 11 weeks; 60 - 90 min/sess; 1 - 5 sess/week	GC, Att., EF, WM, PS, RT, Mem., VSA.	Overall, improvement on trained domain. PS and RT outcomes: larger median ESs. Classic CT and neuropsychological softwares: large median ES for processing speed. Videogames: moderate median ES. Both CT and videogames: moderate median ES for RT.
Reijnders (2013)[1,2]	13	RCT	1432 (69.7)	2 - 12 weeks; 20 - 120 min/sess; 2 - 5 sess/week	GC, Att., EF, WM, PS, Reas., Mem., SCP, Percep., Daily Function, Mood	Some efficacy in improving Mem., EF, PS, Att., fluid intelligence, subjective and overall cognition. No generalization for daily functioning.
Law (2014)	3	RCT, NRCT	480 (71.8)	8 - 48 weeks; 40 - 150 min/sess (CT: 40 - 90; PE: 45 - 150); 1 - 3 (CT: 1 - 2; PE: 1 - 3) sess/week	GC, EF, Mem., Episodic Mem., SCP, Somatic Function, Daily Function, Mood, Apathy, Relationships	Mixed findings for GC and Mem.

Lauenroth (2016)	13	clinical trial	883 (74.1)	4-30 weeks (simul.); 8-30 (subs.) // 30-60 (simul.); PE: 30-60 + CT: 10-90 (subs.); 1 - 5 (simul.)// PE: 1 - 4 + CT: 1 - 5 (subs.)	GC, Att., EF, WM, RT, Inhibition, Mem., Lang., Calculation, VSA, Praxis, ADLs	Most studies reported post-intervention improvements in trained cognitive functions.
Mowszowski (2016)	13	RCT, quasi-RCT	4120 (70)	2 - 16 weeks; 52.5 - 90 min/sess; 1 - 2 sess/week	WM, CF, Inhibition, Reas., Planning, Phonemic VF, Problem-Solving, IADLs, Daily Function	Most studies with moderate to large E.S., focusing on inductive Reas. Evidence of sustained benefits and far transfer.
Butler (2017)	6	RCT	4357 (n.f.d.)	2 - 24 weeks; 20 - 120 min/sess; 1 - 5 sess/week	Att., EF, PS, VF, Reas., Problem-Solving, Mem., Lang., VSA, ADLs, IADLs, Daily Function	Moderate-strength evidence of improvement on the domain trained. Results driven by 1 large trial.

Shah (2017)	Total: 26 quasi-RCT /RCT: 18 follow-up: 8	RCT, quasi-RCT, follow-up	5381 (50 - 95)	3 - 24 weeks; 15 - 75 min/sess; 2 - 5sess/week	GC, Att., EF, WM, CF, PS, RT, Reas., Problem-Solving, Mem., Lang., VSA, SCP, Praxis, Speech-in-Noise Percep., IADLs., Daily Function, HRQoL, Well-Being	Near transfer for the domain trained (programs with level I and II evidence). Improvement in PS (level II). Far transfer for IADLS and HRQoL only in > 5 years follow-up (level I) and well-being (level III). Twelve out of 19 studies were conducted/funded by the program's company.
ten Brinke (2017)	6	RCT, quasi-exp.	163 (69.7)	1 - 17 weeks; 30 - 60 min/sess; 3 - 6 sess/week	GC, EF, WM, PS, RT, Reas., Mem.	Inconclusive results because most studies have no control group.
Alnajjar (2019)	15	pre- post-test design	3199 (57 - 84)	4 - 32 weeks; 20 - 60 min/sess; 1 - 5 sess/week.	GC, Att., EF, WM, PS, RT, Reas., Controlled Process., Problem-Solving, Mem., Lang., Spatial Navigation, ADLs, Well-Being, Depr.	Inconclusive results due to mixed findings and study designs.

Fan & Wong (2019)	9	RCT	6554 (71.0)	10 - 36 sessions	GC, WM, PS, Reas., Mem., VSA, IADLs	IADLs improved. Evidence of improvement for GC, and for Mem. and Reas. in domain specific interventions (near transfer)
Nguyen (2019)	20	pre- post-test with C.G.	635 (69.4)	4 - 24 weeks; 15 - 90 min/sess; 1 - 5 sess/week	GC, Att., EF, WM, CF, Inhibition, PS, RT, Reas., Dual-Task, Multi-task, Mem., VSA	Trained cognitive tasks improved, with mixed findings for untrained tasks.
Marr (2020)	7	RCT, NRCT	1319 (70.0)	2 - 16 weeks; 30 - 90 min/sess; 1 - 3 sess/week	EF, WM, Reas., Divergent Thinking, Mem.	Some evidence of efficacy for EF, Reas. and Mem.
Masurovsky (2020)	19	RCT	n.f.d. (n.f.d.)	n.f.d.	Att., PS, Cognitive Control, Mem., Lang., Visuospatial construction	12 of 19 studies had near transfer. None which had significant effect for far transfer (6) measured expectations, and only 1 included A.C.
Dhir (2021)	5	pre- post-test with C.G.	193 (n.f.d.)	n.f.d.	Inhibition	Only one study reached significance, with large ES for simultaneous combined training on inhibition.

Intzandt (2021)	38 CT: 12 PE: 26	RCT. quasi-exp.	Total: 1677 CT: 607 (68.1) PE: 1070 (68.5)	CT: 2 - 24 week; 45 - 120 min/sess; 1 - 5 sess/week PE: 6 -135 weeks; 10 - 90 min/sess; 1 - 7 sess/week	Att., EF, WM, VF, PS, Reas., Mem.	Most studies reported significant effects on at least one measure of cognitive functioning, especially memory.
Webb (2021)	5	pre- post-test design	1687 (72.2)	2 - 6 weeks; 30 - 120 min/sess; 1 - 3 sess/week	WM, PS, Mem. (objective and subjective)	Inconclusive results due to mixed findings and study designs.
Mendonça (2022)	13	cohort	8732 (n.f.d.)	3 - 140 weeks; 45 - 120 min/sess; 1 - 2 sess/week	Mem. (episodic)	All studies found significant results for episodic memory.

Table 1: Systematic reviews and meta-analysis about cognitive training interventions. n/a: not applicable; n/c: not calculated; n.f.d.: not fully described. ADLs: activities of daily living; Att.: attention; CF: cognitive flexibility; Depr.: depression; EF: executive functions; GC: global cognition; HRQoL: health-related quality of life; IADLs: instrumental activities of daily living; Lang.: language; Mem.: memory; Percep.: perception; Process.: processing; PS: processing speed; QoL: quality of life; Reas.: reasoning; RT: reaction time; SCP: subjective cognitive performance; STM: short-term memory; VF: verbal fluency; VSA: visuospatial ability; WM: working memory.
[1]Reijnders et al. (2013) and Kelly al. (2014) presented results for both CS and CT; for ease of interpretation, those results are presented separately on tables 1 and 2.
[2] 1 Clinical study non-RCT was included, but poorly described with no quality evaluation. Therefore, we did not include these results.

Findings from systematic reviews

In total, there were 17 qualitative systematic reviews structured on CT. Out of these, 8 included any form of CT (Reijnders et al., 2013; Mowszowski et al., 2016; Butler et al., 2017; Fan & Wong, 2019; Nguyen et al., 2019; Marr et al., 2020; Dhir et al., 2021; Webb et al., 2021; Mendonça et al., 2022), 5 focused only on computerized CT (Kueider et al., 2012; Shah et al., 2017; ten Brinke et al., 2017; Alnajjar et al., 2019; Masurovsky, 2020), 3 investigated combined CT and physical exercise (PE) (Law et al., 2014; Lauenroth et al., 2016; Dhir et al., 2021), and 1 compared CT with PE interventions (Intzandt et al., 2021).

Four studies selected only RCT as the study design (Reijnders et al., 2013; Butler et al., 2017; Fan & Wong, 2019; Masurovsky, 2020), 4 included any pre- and post-test design with a control group (Kueider et al., 2012; Alnajjar et al., 2019; Nguyen et al., 2019; Dhir et al., 2021), 2 included RCT and quasi-experimental studies (ten Brinke et al., 2017; Intzandt et al., 2021), 1 included any pre- and post-test design with or without a control group (Webb et al., 2021), 1 included RCT and non-randomized clinical trials (Law et al.,2014), 1 included any type of clinical trial (Lauenroth et al., 2016), 1 included RCTs and quasi-RCTs (Mowszowski et al., 2016), 1 included RCTs, quasi-RCTs and follow-up studies (Shah et al., 2017), 1 included RCTs and non-RCTs (Marr et al., 2020) and 1 included only cohort studies (Mendonça et al., 2022).

Between 3 to 38 studies were included in each analysis, with a sample size between 163 and 8732 participants and a mean age of 70.4 years. In these studies, CT programs (applied with or without other interventions) had a duration of between 1 to 240 weeks, with a range of 15 to 240 minutes for each session and less than 1 to 7 sessions per week. Butler et al. (2017) and Mendonça et al. (2022) did not fully describe population age separately for H.O.A. Fan & Wong (2019) did not fully describe intervention characteristics. Masurovsky (2020) and Dhir et al. (2021) did not fully describe neither sample nor intervention characteristics.

Kueider et al. (2012), Shah et al. (2017) and Alnajjar et al. (2019) did not describe average age.

Overall, studies have found some efficacy in improvement for trained domains (Lauenroth et al., 2016; Shah et al., 2017; Butler et al., 2017; Fan & Wong, 2019; Nguyen et al., 2019; Masurovsky, 2020), memory (Reijnders et al., 2013; Shah et al., 2017; Butler et al., 2017; Fan & Wong, 2019; Marr et al., 2020; Intzandt et al., 2021; Webb et al., 2021; Mendonça et al., 2022), reasoning/fluid intelligence (Reijnders et al., 2013; Mowszowski et al., 2016; Shah et al., 2017; Butler et al., 2017; Fan & Wong, 2019; Marr et al., 2020), executive functions (Reijnders et al., 2013; Butler et al., 2017; Marr et al., 2020), attention (Reijnders et al., 2013; Shah et al., 2017; Butler et al., 2017), processing speed (Kueider et al., 2012; Shah et al., 2017; Butler et al., 2017) and global cognition (Reijnders et al., 2013; Fan & Wong, 2019). Mixed results for daily functioning (Reijnders et al., 2013; Fan & Wong, 2019).

Findings for specific subtypes of CT or comparison are reported below.

Computerized cognitive training

In total, 5 qualitative analyses focused exclusively on CT interventions that were performed on digital devices (Kueider et al., 2012; Shah et al., 2017; ten Brinke et al., 2017; Alnajjar et al., 2019; Masurovsky, 2020). Two studies included any pre- and post-test design (Kueider et al., 2012; Alnajjar et al., 2019), 1 included RCTs and quasi-experimental trials (ten Brinke et al., 2017), 1 included RCTs, quasi-RCTs and follow-up studies (Shah et al., 2017), and 1 included only RCTs (Masurovsky, 2020).

Between 6 to 38 studies were included in each analysis, with a sample size of between 163 to 5381 participants and average ages between 50 to 96 years. Among these, computerized CT interventions had a duration between 1 to 68 weeks, with 15 to 240 minutes for each session,

and 1 to 7 sessions per week. Masurovsky (2020) did not fully describe the sample and intervention characteristics. Only ten Brinke et al. (2017) described the mean sample age.

Overall, there was some evidence of post-intervention improvement in trained cognitive domains (Kueider et al.,2012; Shah et al., 2017; Masurovsky, 2020). Kueider et al. (2012) found moderate to large effects in classical CT, neuropsychological software (NS), and video games (VG) for processing speed, and moderate effects of CT and VG for reaction time. Masurovsky (2020) reported that none of the included studies (published between 2016-2018) that found effects for far transfer have measured participants' expectations, and only one used active control. Shah et al. (2017) found good quality evidence of far transfer for IADLS and HRQoL only in > 5 years of follow-up.

Cognitive training combined with physical exercise

Three qualitative systematic reviews were structured on combined CT and PE (Law et al., 2014; Lauenroth et al., 2016; Dhir et al., 2021), performed both simultaneously (simul.) or subsequently (subs.). Law et al. (2014) selected RCT and non-randomized clinical trials as the study design and included 3 studies, with a sample size of 480 and a mean age of 71.6 years. Combined CT and PE performed subsequently had an intervention duration of 8 to 48 weeks, and a session duration of 40 to 150 minutes (CT) + 45 to 150 minutes of PE. Frequency varied from 1 to 2 CT sessions plus 1 to 3 PE sessions per week.

Lauenroth et al. (2016) selected RCT and clinical trials as the study design and included 13 studies (simul.: 7; subs.: 6) with a sample size of 883 (simul.: 308; subs.: 575) and a mean age of 74.1 years (simul.: 72.5; subs.: 75.6). Combined CT and PE had an intervention duration of 4 to 30 weeks (simul.: 4 - 25; subs.: 8 - 30). Session duration varied within 30 to 60 minutes of CT and PE performed simultaneously, or within 10 to 90 minutes of CT plus

30 to 60 minutes of PE performed subsequently. Frequency varied from 1 to 5 days of simultaneous training per week, or 1 to 5 CT sessions plus 1 to 4 PE sessions per week.

Dhir et al. (2021) included any pre/post test with the control group but did not fully describe neither sample nor intervention characteristics. They did a meta-analysis, but separate meta-analytic data for healthy older adults was unavailable.

Most studies included in Lauenroth et al. (2016) reported post-intervention improvements at least in the trained cognitive function. Law et al. (2014) and Dhir et al. (2021) had limited findings given the small number of studies included for the population of interest.

Cognitive Stimulation

Findings from meta-analysis

There was 1 meta-analysis structured on cognitive stimulation (CS) which included RCTs analyzing CT, CS and mixed interventions of CS with CT (Yun & Ryu., 2022). The authors included 11 CS studies and 1 study with a mixed intervention using CS and CT. They found a small effect with substantial heterogeneity for overall cognitive functioning and did not describe sample sizes or intervention characteristics separately for H.O.A or CS studies.

Findings from systematic reviews

There were 2 qualitative reviews structured on CS (Reijnders et al., 2013; Kelly al., 2014), which included 16 RCTs. CS interventions had a duration between 4 to 96 weeks, with 30 to 240 minutes for each session, and less than 1 to 4 sessions per week. Reijnders et al. (2013) found 8 CS studies, including 1088 participants with 73.7 years of age on average. Kelly et al. (2014) found 8 CS studies, including 905 participants with 60 to 93 years of age. Both reviews reported mixed findings for cognitive outcomes.

Main Author (Year)	Studies Included (*n*)	Study Design	Sample Size (mean age)	Intervention and Session Duration and Frequency	Outcome Domains	Review Outcome
Meta - analyses						
Yun & Ryu (2022)	12	RCT	n.f.d. (70.6)	n.f.d.	GC, ADLs, IADLs, QoL, Depr.	Small effect on overall cognitive function. I^2: 65.2
Systematic Reviews						
Reijnders (2013)[1, 2]	8	RCT	1088 (73.7)	4 - 96 weeks; 30 - 240 min/sess; < 1 - 4 sess/week	Att., EF, WM, PS, Reas., Mem., SCP, Praxis, IADLs, Daily Function	Mixed findings for all cognitive outcomes.
Kelly (2014)[1]	8	RCT	905 (60 - 93)	4 - 51 weeks; 30 - 240 min/sess; < 1 - 3 sess/week	GC, EF, Mem., SCP	Mixed findings for all cognitive outcomes. No effect for subjective cognitive function. No trial that included follow-up assessments reported maintenance of intervention effects.

Table 2: Systematic reviews analyzing cognitive stimulation interventions. ADLs: activities of daily living; Att.: attention; Depr.: depression; EF: executive functions; GC: global cognition; IADLs: instrumental activities of daily living; Mem.: memory; PS: processing speed; QoL: quality of life; Reas.: reasoning; SCP: subjective cognitive performance; WM: working memory.

[1]Reijnders et al. (2013) and Kelly al. (2014) presented results for both CS and CT; for ease of interpretation, those results are presented separately on tables 1 and 2.

Main Author (Year)	Studies Included (*n*)	Study Design	Sample Size (mean age)	Intervention and Session Duration and Frequency	Outcome Domains	Review Outcome
Kim (2022)	6	RCT	1102 (74.8)	6 - 24 weeks; 20 - 150 min/sess; < 1 - 2 sess/week.	GC, ADLs, IADLs, HRQoL, Adaptative Strategies, Falls Efficacy, Depr., Anxiety, Confidence on Daily Tasks, Fear of Falling, Loneliness.	Some evidence of efficacy of occupational + physical therapy and cognitive-behavioral therapy + baduanjin qigong on ADLs and IADLs; mixed findings for multicomponent CT.

Table 3: Systematic review analyzing multicomponent interventions. ADLs: activities of daily living; Depr.: depression; GC: global cognition; HRQoL: health-related quality of life; IADLs: instrumental activities of daily living.

Multicomponent Interventions

Also, there was 1 qualitative review structured on multicomponent interventions, defined by the authors as “multicomponent approaches that combine two or more intervention strategies” (Kim et al., 2022, p.2). Six RCTs were included. The sample size was of 1102 and the mean age was 74.8 years. Multicomponent programs had a duration between 6 to 24 weeks, with 20 to 150 minutes for each session, and less than 1 to 2 sessions per week. Results underlined some efficacy of occupational plus physical therapy, and cognitive-behavioral therapy plus Baduanjin qigong, on ADLs and IADLs. Mixed findings for CT multicomponent interventions – diverse types of CT associated - on IADL outcomes.

Discussion

This meta-review summarizes existing evidence regarding cognitive training, cognitive stimulation, combined and multicomponent protocols aimed at preventing or reducing cognitive decline in HOA. The most frequent flaws in the available knowledge were revealed through a rigorous quality assessment. Meta-analyses and narrative reviews were analyzed separately, contributing to a comprehensive understanding of the field.

Results indicated CT interventions as the most promising ones, considering the number of included studies and corresponding effect sizes. Results from meta-analysis reviews suggested larger CT effects for speed of processing, which was found to be a predictor for functional decline or high-functioning cognitive aging (Wahl et al., 2010; Ticha et al., 2023). However, vast heterogeneity of effect sizes suggests important mediators need to be further investigated.

An important issue in relation to CT is the capacity to generalize the skills acquired, namely transfer (Sala et al., 2019). Overall, qualitative systematic reviews provided more evidence for near transfer. The distinction between near and far transfer as described by Barnett & Ceci (2002) is not simple, but generally signifies the generalization of skills in similar domains/tasks, and the transfer of skills in domains/tasks that are not or very weakly related to each other. One example of far transfer is the effect on everyday functioning.

However, effects on everyday functioning - which are clinically significant - were under-investigated. The best evidence of far transfer could be observed only some years after training (Shah et al., 2017), which represents cognitive decline prevention instead of an actual improvement. The fact that most studies only examined immediate effects suggests a systematic bias. According to the evidence collected, near transfer could have an immediate impact, which could potentially prevent cognitive decline years later.

Two reviews examined commercial computerized cognitive training. Shah et al. (2017) and Nguyen (2021) observed improvements in processing speed but highlighted the lack of direct evidence supporting clinically significant outcomes. Shah et al. (2017) noted near transfer effects in most trials, with some indication of far transfer effects at least 5 years post-training, albeit based on data from only one commercial program. The fast expansion of this market (Market Research Report, 2020) has outpaced the evidence supporting these interventions.

A vast diversity of intervention durations, session durations and frequencies were presented. Based on the included meta-analyses, an effective pattern seems to include adaptive training with 10 sessions or more (Kelly et al., 2014), delivered less than 3 times a week in groups (Lampit et al., 2014). The findings are in line with the cognitive training employed in the FINGER study, the first long-term RCT to demonstrate the efficacy of multidomain lifestyle interventions in reducing cognitive decline among older adults at a higher risk of dementia (Ngandu et al., 2015; Rosenberg et al., 2019). The computer-based training took place for two 6-month periods, during which participants attended 72 sessions of the adaptive CT program, three times a week (Kivipelto et al., 2013).

Nonetheless, a program with a slightly different population had different conclusions. In an analysis published by Andrieu et al. (2017), they investigated the effects of a multidomain intervention and polyunsaturated fatty acids supplementation, either alone or in combination. CT consisted of 12 group sessions lasting 60 minutes each, with reasoning and memory training. In the first month, there were two sessions per week, while in the second month, there was only one session per week. Over the course of 3 years, there were no significant effects on cognitive decline in elderly people with memory complaints.

In addition, there was limited evidence for further benefits when combining cognitive training with physical activity. Small improvement was found for combined interventions, CT and PA when compared with each other. This is consistent with a recent meta-analysis which

found no significant differences between combined interventions and cognitive activity alone (Gheysen et al., 2018). However, physical activity has been largely recognized to improve a myriad of health outcomes, prevent several chronic medical conditions, enhance mobility and cognition, and promote independent functioning (Penedo & Dahn, 2005; Warburton & Bredin, 2017; Eckstrom et al., 2020).

Moreover, it influences cognitive functions and neuronal mechanisms that are most at risk of age-related changes, such as attention, executive functions and episodic memory (Blanchet et al., 2018) being associated with a reduced risk of developing cognitive impairment (Erickson et al., 2019). Physical activity even prevents the progression of cognitive deficits and/or improves psychological well-being in people with diagnosed mild cognitive impairment or dementia (Blanchet et al., 2018; Du et al., 2018; Nuzum et al., 2020).

Considering the vast evidence of the benefits of physical activity for a number of health outcomes, the lack of findings in the current review may indicate a ceiling effect of interventions on short-term outcomes. All included reviews analyzing interventions combining or comparing PA and CT only considered immediate post-intervention effects. A future review that examines combined interventions and considers long-term outcomes could possibly aid in elucidating this question. On the other hand, the heterogeneity of the combined arrangements may be concealing the effect of the most effective models, which could be addressed by expanding evidence with further moderator analysis.

For cognitive stimulation and multicomponent interventions, it was not possible to find a shared effect. This can be attributed to the vast heterogeneity of stimulation interventions developed and the relatively small number of studies included in each analysis. Alternatively, it could be that the majority of already designed protocols did not include the appropriate features for stimulating cognitive plasticity in the healthy population. Gómez-Soria et al. (2023) carried out a systematic review and meta-analysis about cognitive stimulation and

found improvements in general cognitive functioning for healthy older adults. However, this review included only two studies for this subgroup analysis, combining effects of different tests and follow-ups.

The lack of evidence for CS effects on H.O.A. contrasts with the actual guidance for people with established cognitive decline. World Alzheimer Report 2022 recommends Cognitive Stimulation Therapy (CST; Spector et al., 2003) as a best practice to improve cognitive function in people with mild to moderate dementia (Gauthier et al., 2022). Beyond the cognitive gains, CST is recognized to be cost effective and was shown to be feasible in low-resource settings (Gauthier et al., 2022). It is possible that a CS protocol that complies with specific appropriate principles could be advantageous for the healthy population according to this literature. Given the multiple possibilities that the term 'cognitive stimulation' can encompass, it could be that the most effective protocol has yet to be created.

Expanding the number of studies on CS and multicomponent interventions is necessary to draw a more comprehensive panorama in the future. For example, physical activity that is either linked to or separate from cognitive interventions, despite limited current evidence, may be used as well. Future research can be carried out in an exploratory manner by applying different theoretical principles to achieve this purpose.

The main limitations of this meta-review were the quality and risk of bias of included studies. However, this was due to a previous limitation of the reviews included here, suggesting an intrinsic and systemic limitation of the actual state of art of this field. Future investigations should select a proper method for assessing risk of bias (RoB) and provide a satisfactory discussion of its implications. Another potential limitation was the vast range of interventions and methodologies included, which may have led to high heterogeneity and difficulty to summarize results. The broad inclusion criteria provided a wide perspective about the field

but may have limited comparability between results. This limitation was addressed by providing separate results.

In conclusion, the current evidence supports CT activities more decisively, with at least 10 adaptive sessions delivered less than three times weekly in group meetings and encourages ongoing research into CS and multicomponent protocols. Nevertheless, the issue related to the transfer of effects for clinical outcomes remains under-investigated, with urgent need for its examination on both short and long-term. Longer follow-ups seem to be a key issue to find combined and clinically significant results. Rigorous risk of bias and quality assessment is necessary to improve current evidence on cognitive interventions.

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Supplementary Material A - List of studies excluded by full text screening

Title	Author (year)	Exclusion Reason
Advances in Non-Pharmacological Interventions for Subjective Cognitive Decline: A Systematic Review and Meta-Analysis	Sheng et al. (2020)	Clinical population
Aerobic exercise to improve cognitive function in older people without known cognitive impairment	Young et al. (2015)	Wrong intervention
Aging Mindfully to Minimize Cognitive Decline	Kurth et al. (2017)	Not systematic review/meta-analysis
A systematic review of language and communication intervention research delivered in groups to older adults living in care homes	Davis et al. (2022)	Clinical population
Closed-loop rehabilitation of age-related cognitive disorders	Mishra & Gazzaley (2014)	Not systematic review/meta-analysis
Cognition-Oriented Treatments for Older Adults: a Systematic Overview of Systematic Reviews	Gavelin et al. (2020)	Not systematic review/meta-analysis
Cognitive and memory training in adults at risk of dementia: A Systematic Review	Gates et al. (2011)	Clinical population
Cognitive interventions for healthy older adults: A systematic review	Kelly et al. (2014)	Conference paper
Cognitive plasticity in older adults: Effects of cognitive training and physical exercise	Bherer (2015)	Not systematic review/meta-analysis

Cognitive stimulation and cognitive results in older adults: A systematic review and meta-analysis	Gómez-Soria et al. (2023)	Clinical population
Cognitive stimulation for healthy older adults through computer-based programs: a review of the literature	Rosell et al. (2018)	Not systematic review/meta-analysis
Cognitive stimulation in the workplace, plasma proteins, and risk of dementia: Three analyses of population cohort studies	Kivimäki et al. (2021)	Not systematic review/meta-analysis
Cognitive stimulation to improve cognitive functioning in people with dementia	Woods et al. (2012)	Clinical population
Cognitive Training for Older Adults: What Works?	Lenze & Bowie (2018)	Not systematic review/meta-analysis
Cognitive training for persons with mild cognitive impairment	Belleville (2008)	Not systematic review/meta-analysis
Computerised cognitive training for preventing dementia in people with mild cognitive impairment	Gates et al. (2019)	Clinical population
Computerized cognitive training interventions to improve neuropsychological outcomes: evidence and future directions	Howren, Vander Weg, Wolinsky (2014)	Not systematic review/meta-analysis
Convergence and divergence across meta-analyses studying computerised cognitive training in older adults	Leung et al. (2017)	Conference paper
Design of controls in trials of computerised cognitive training is ineffectual: A meta-analysis in healthy older adults	Hallock et al. (2017)	Conference paper
Dissecting the anatomy of computerised cognitive training: Systematic review and meta-analysis of rCts in older adults	Lampit, Hallock, Valenzuela (2013)	Conference paper

Do cognitive interventions improve general cognition in dementia? A meta-analysis and meta-regression	Huntley et al. (2015)	Clinical population
Effectiveness of cognitive interventions for adult surgical patients after general anaesthesia to improve cognitive functioning: A systematic review	Bowden et al. (2022)	Clinical population
Effects of Combined Physical Activity and Cognitive Training on Cognitive Function in Older Adults with Subjective Cognitive Decline: A Systematic Review and Meta-Analysis of Randomized Controlled Trials	Sun et al. (2021)	Clinical population
Effects of sustained cognitive activity on white matter microstructure and cognitive outcomes in healthy middle-aged adults: A systematic review	McPhee, Downey, Stough (2019)	Unavailable data
Efficacy of lifestyle and psychosocial interventions in reducing cognitive decline in older people: Systematic review	Whitty et al. (2020)	Unavailable data
Exercise interventions for older adults: A systematic review of meta-analyses	Di Lorito et al. (2021)	Not systematic review/meta-analysis
Factors and predictors of cognitive impairment in the elderly: A synopsis and comment on "Systematic Review: Factors associated with risk for and possible prevention of cognitive decline in later life"	Buscemi, Steglitz, Spring (2012)	Not systematic review/meta-analysis
Feasibility of remotely supervised transcranial direct current stimulation and cognitive remediation: A systematic review	Gough et al. (2020)	Clinical population
Functional brain changes associated with cognitive training in healthy older adults: A preliminary ALE meta-analysis	Duda & Sweet (2020)	Unavailable data
Guidelines for prevention and treatment of cognitive impairment in the elderly	Brodziak et al. (2015)	Not systematic review/meta-analysis

Healthy Cognitive Aging and Dementia Prevention	Smith (2016)	Not systematic review/meta-analysis
Individually modifiable risk factors to ameliorate cognitive aging: a systematic review and meta-analysis	Lehert et al. (2015)	Unavailable data
Information and communication technologies for the improvement of cognitive function in healthy older adults: a systematic review protocol	Pastells-Peiro et al. (2021)	Not systematic review/meta-analysis
Interventions for subjective cognitive decline: systematic review and meta-analysis	Bhome et al. (2018)	Clinical population
Investigating heterogeneity across clinical trials to guide clinical implementation of cognitive training	Lampit (2018)	Conference paper
Multi‐domain interventions for the prevention of dementia and cognitive decline	Hafdi, Hoevenaar-Blom, Richard (2021)	Wrong intervention
Nonpharmacological enhancement of cognitive function in Parkinson's disease: A systematic review	Hindle et al. (2013)	Clinical population
Nonpharmacological therapies in Alzheimer's disease: a systematic review of efficacy	Olazarán et al. (2010)	Clinical population
Planning and optimising a digital intervention to protect older adults' cognitive health	Essery et al. (2021)	Not systematic review/meta-analysis
Preserving prospective memory in daily life: A systematic review and meta-analysis of mnemonic strategy, cognitive training, external memory aid, and combination interventions	Jones, Benge, Scullin (2021)	Wrong age

Systematic review: factors associated with risk for and possible prevention of cognitive decline in later life	Plassman et al. (2010)	Unavailable data
Systematic review of the effectiveness of non-pharmacological interventions to improve quality of life of people with dementia	Cooper et al. (2012)	Clinical population
The application of technology to improve cognition in older adults: A review and suggestions for future directions	Leung et al. (2022)	Not systematic review/meta-analysis
The effect of computerized cognitive training on the improvement of cognitive functions of cognitively healthy elderly	Zeleníková et al. (2022)	Article language
The effects of aerobic exercise and transcranial direct current stimulation on cognitive function in older adults with and without cognitive impairment: A systematic review and meta-analysis	Talar et al. (2022)	Wrong intervention
The Effects of Cognitive Training on Brain Network Activity and Connectivity in Aging and Neurodegenerative Diseases: a Systematic Review	van Balkom et al. (2020)	Unavailable data
The effects of interventions to enhance cognitive and physical functions in older people with cognitive frailty: a systematic review and meta-analysis	Tam et al. (2022)	Clinical population
The Effects of Multi-Domain Interventions on Cognition: A Systematic Review	Ahn et al. (2022)	Clinical population
The potential effects of meditation on age-related cognitive decline: a systematic review	Gard, Holzel, Lazar (2014)	Clinical population
UFOV cognitive training enhances IADL and reduces dementia risk: How do we move the field of behavioral interventions forward	Edwards & Green (2018)	Conference paper

Visual art therapy as an option to tackle cognitive decline and the associated psychological symptoms among older adults: A systematic review and meta-analysis	Masika, Yu, Li (2019)	Conference paper
Working memory training in healthy elderly: A meta-analysis	Racine, Plourde, Simard (2017)	Conference paper
The Effectiveness of e-Health Solutions for Aging With Cognitive Impairment: A Systematic Review	Dequanter et al. (2021)	Clinical population
Can HIV-associated neurocognitive disorder (HAND) be treated with computerized cognitive training? Evidence from a systematic review	Vance et al. (2018)	Clinical population

Supplementary Table 1: List of studies excluded by full text screening.

Note: a study could be ineligible for multiple reasons but appear only once in this table.

Supplementary Material B - Quality assessment (AMSTAR 2)

	Quality Criteria (AMSTAR 2)
1	Did the research questions and inclusion criteria for the review include the components of PICO?
2	Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?
3	Did the review authors explain their selection of the study designs for inclusion in the review?
4	Did the review authors use a comprehensive literature search strategy?*
5	Did the review authors perform study selection in duplicate?
6	Did the review authors perform data extraction in duplicate?
7	Did the review authors provide a list of excluded studies and justify the exclusions?
8	Did the review authors describe the included studies in adequate detail?*†
9	Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?*†
10	Did the review authors report on the sources of funding for the studies included in the review?
11	If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?†
12	If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?†
13	Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?*†

14	Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?*†
15	If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?
16	Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?

Supplementary Table 2: Questions for each quality criteria proposed by AMSTAR 2 (Shea et al., 2017).

*Critical domains for qualitative reviews.

† Critical domains for meta-analysis.

Overall Confidence Classification	**Scheme for interpreting weaknesses detected in critical and non-critical item**
High	No or one non-critical weakness: the systematic review provides an accurate and comprehensive summary of the results of the available studies that address the question of interest
Moderate	More than one non-critical weakness: the systematic review has more than one weakness but no critical flaws. It may provide an accurate summary of the results of the available studies that were included in the review
Low	One critical flaw with or without non-critical weaknesses: the review has a critical flaw and may not provide an accurate and comprehensive summary of the available studies that address the question of interest
Critically Low	More than one critical flaw with or without non-critical weaknesses: the review has more than one critical flaw and should not be relied on to provide an accurate and comprehensive summary of the available studies

Supplementary Table 3: Scheme for interpreting overall confidence of each study using AMSTAR 2 (Shea et al., 2017).

Quality Criteria	1	2	3	4*	5	6	7	8*†	9*†	10	11†	12†	13†	14*†	15	16	Overall Confidence
Papp et al. (2009)	2	R	R	2	R	R	R	Y	R	R	R	R	R	R	R	R	Critically Low
Valenzuela & Sachdev (2009)	2	R	R	2	R	R	R	Y	R	R	R	R	R	R	R	R	Critically Low
Martin et al. (2011)	2	2	R	2	2	2	2	2	Y	R	2	R	R	2	R	R	Critically Low
Hindin & Zelinski (2012)	2	R	R	Y	R	R	R	R	R	R	R	2	2	2	R	2	Critically Low
Kueider et al. (2012)	2	R	R	2	R	R	R	R	R	R			R	2		2	Critically Low
Reijnders et al. (2013)	R	R	R	2	R	2	R	2	R	R			2	2		2	Low
Karr et al. (2014)	2	R	R	2	R	2	2	R	R	R	R	2	2	2	R	2	Critically Low
Kelly et al. (2014)	2	Y	R	2	2	2	2	Y	2	R	2	R	R	R	R	2	Critically Low
Lampit et al. (2014)	2	Y	2	Y	2	2	R	2	2	R	2	2	R	2	2	2	Low
Law et al. (2014)	2	R	R	2	2	R	2	2	2	R			R	2		2	Low
Lauenroth et al. (2016)	2	R	R	2	2	2	R	Y	R	R			R	2		2	Critically Low
Mowszowski et al. (2016)	2	R	R	2	R	R	R	2	R	R			R	2		2	Low
Butler et al. (2017)	2	Y	R	2	2	R	R	2	2	2			2	2		2	Moderate
Mewborn et al. (2017)	2	Y	2	2	R	R	R	2	2	R	2	2	2	2	2	R	Moderate
Shah et al. (2017)	2	R	2	Y	2	R	R	2	R	2			2	R		R	Critically Low
ten Brinke et al. (2017)	2	R	R	Y	R	2	R	2	R	R			2	2		2	Low
Bruderer-Hofstetter et al. (2018)	2	Y	R	2	2	2	R	2	2	R	2	R	2	2	R	R	Low
Webb et al. (2018)	2	Y	2	Y	2	2	R	2	2	R	2	R	R	2	2	R	Critically Low
Alnajjar et al. (2019)	2	R	R	2	R	R	R	Y	R	R			R	R		2	Critically Low
Fan & Wong (2019)	2	Y	R	2	R	R	R	2	R	R			R	2		2	Critically Low
Nguyen et al. (2019)	2	R	2	2	2	R	R	Y	Y	R			R	2		2	Low
Basak et al. (2020)	2	2	R	2	R	R	2	2	Y	R	2	2	2	2	2	R	Moderate
Guo et al. (2020)	2	R	R	2	R	R	R	Y	2	R	2	2	2	2	2	2	Moderate
Marr et al. (2020)	2	Y	R	2	R	R	R	Y	Y	R			2	2		2	Moderate
Masurovsky (2020)	2	R	R	R	R	R	R	Y	R	R			R	R		2	Critically Low
Dhir et al. (2021)	2	R	R	2	2	R	R	R	R	R	R	R	R	2	2	2	Critically Low
Gates et al. (2021)	2	2	R	2	2	2	2	2	2	2	2	2	2	2	2	2	Moderate
Gavelin et al. (2021)	2	Y	2	2	2	2	2	Y	2	R	2	2	2	2	2	2	Moderate
Intzandt et al. (2021)	2	R	2	2	2	2	R	R	R	R			2	2		R	Critically Low
Nguyen et al. (2021)	2	R	2	Y	2	R	R	R	Y	R	Y	2	2	2	2	2	Low
Webb et al. (2021)	2	Y	R	2	2	R	R	2	R	R			R	2		2	Critically Low
Kim et al. (2022)	2	R	R	Y	2	R	R	Y	2	R			R	R		2	Critically Low
Mendonça et al. (2022)	2	R	R	Y	R	R	R	Y	Y	R			2	2		2	Moderate
Yun & Ryu (2022)	2	R	2	Y	2	R	R	R	2	R	R	2	2	2	2	2	Critically Low

Supplementary Table 4: Results for each quality criteria and overall confidence of included studies according to the evaluation performed with AMSTAR 2.

*Critical domains for qualitative reviews.

†Critical domains for meta-analysis.

AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non- randomised studies of healthcare interventions, or both

1. Did the research questions and inclusion criteria for the review include the components of PICO?

For Yes:
- ☐ Population
- ☐ Intervention
- ☐ Comparator group
- ☐ Outcome

Optional (recommended)
- ☐ Timeframe for follow-up

☐ Yes
☐ No

2. Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review and did the report justify any significant deviations from the protocol?

For Partial Yes:
The authors state that they had a written protocol or guide that included ALL the following:
- ☐ review question(s)
- ☐ a search strategy
- ☐ inclusion/exclusion criteria
- ☐ a risk of bias assessment

For Yes:
As for partial yes, plus the protocol should be registered and should also have specified:
- ☐ a meta-analysis/synthesis plan, if appropriate, *and*
- ☐ a plan for investigating causes of heterogeneity
- ☐ justification for any deviations from the protocol

☐ Yes
☐ Partial Yes
☐ No

3. Did the review authors explain their selection of the study designs for inclusion in the review?

For Yes, the review should satisfy ONE of the following:
- ☐ *Explanation for* including only RCTs
- ☐ OR *Explanation for* including only NRSI
- ☐ OR *Explanation for* including both RCTs and NRSI

☐ Yes
☐ No

4. Did the review authors use a comprehensive literature search strategy?

For Partial Yes (all the following):
- ☐ searched at least 2 databases (relevant to research question)
- ☐ provided key word and/or search strategy
- ☐ justified publication restrictions (e.g. language)

For Yes, should also have (all the following):
- ☐ searched the reference lists / bibliographies of included studies
- ☐ searched trial/study registries
- ☐ included/consulted content experts in the field
- ☐ where relevant, searched for grey literature
- ☐ conducted search within 24 months of completion of the review

☐ Yes
☐ Partial Yes
☐ No

5. Did the review authors perform study selection in duplicate?

For Yes, either ONE of the following:
- ☐ at least two reviewers independently agreed on selection of eligible studies and achieved consensus on which studies to include
- ☐ OR two reviewers selected a sample of eligible studies and achieved good agreement (at least 80 percent), with the remainder selected by one reviewer.

☐ Yes
☐ No

AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non- randomised studies of healthcare interventions, or both

6. Did the review authors perform data extraction in duplicate?

For Yes, either ONE of the following:
- ☐ at least two reviewers achieved consensus on which data to extract from included studies
- ☐ OR two reviewers extracted data from a sample of eligible studies and achieved good agreement (at least 80 percent), with the remainder extracted by one reviewer.

☐ Yes
☐ No

7. Did the review authors provide a list of excluded studies and justify the exclusions?

For Partial Yes:
- ☐ provided a list of all potentially relevant studies that were read in full-text form but excluded from the review

For Yes, must also have:
- ☐ Justified the exclusion from the review of each potentially relevant study

☐ Yes
☐ Partial Yes
☐ No

8. Did the review authors describe the included studies in adequate detail?

For Partial Yes (ALL the following):
- ☐ described populations
- ☐ described interventions
- ☐ described comparators
- ☐ described outcomes
- ☐ described research designs

For Yes, should also have ALL the following:
- ☐ described population in detail
- ☐ described intervention in detail (including doses where relevant)
- ☐ described comparator in detail (including doses where relevant)
- ☐ described study's setting
- ☐ timeframe for follow-up

☐ Yes
☐ Partial Yes
☐ No

9. Did the review authors use a satisfactory technique for assessing the risk of bias (RoB) in individual studies that were included in the review?

RCTs

For Partial Yes, must have assessed RoB from
- ☐ unconcealed allocation, *and*
- ☐ lack of blinding of patients and assessors when assessing outcomes (unnecessary for objective outcomes such as all-cause mortality)

For Yes, must also have assessed RoB from:
- ☐ allocation sequence that was not truly random, *and*
- ☐ selection of the reported result from among multiple measurements or analyses of a specified outcome

☐ Yes
☐ Partial Yes
☐ No
☐ Includes only NRSI

NRSI

For Partial Yes, must have assessed RoB:
- ☐ from confounding, *and*
- ☐ from selection bias

For Yes, must also have assessed RoB:
- ☐ methods used to ascertain exposures and outcomes, *and*
- ☐ selection of the reported result from among multiple measurements or analyses of a specified outcome

☐ Yes
☐ Partial Yes
☐ No
☐ Includes only RCTs

10. Did the review authors report o n the sources of funding for the studies included in this review?

For Yes
- ☐ Must have reported on the sources of funding for individual studies included in the review. Note: Reporting that the reviewers looked for this information but it was not reported by study authors also qualifies

☐ Yes
☐ No

AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non- randomised studies of healthcare interventions, or both

11. If meta-analysis was performed did the review authors use appropriate methods for statistical combination of results?

RCTs

For Yes:

- ☐ The authors justified combining the data in a meta-analysis
  - ☐ AND they used an appropriate weighted technique to combine study results and adjusted for heterogeneity if present.
  - ☐ AND investigated the causes of any heterogeneity

☐ Yes
☐ No
☐ No meta-analysis conducted

For NRSI

For Yes:

- ☐ The authors justified combining the data in a meta-analysis
  - ☐ AND they used an appropriate weighted technique to combine study results, adjusting for heterogeneity if present
  - ☐ AND they statistically combined effect estimates from NRSI that were adjusted for confounding, rather than combining raw data, or justified combining raw data when adjusted effect estimates were not available
  - ☐ AND they reported separate summary estimates for RCTs and NRSI separately when both were included in the review

☐ Yes
☐ No
☐ No meta-analysis conducted

12. If meta-analysis was performed, did the review authors assess the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis?

For Yes:

- ☐ included only low risk of bias RCTs
- ☐ OR, if the pooled estimate was based on RCTs and/or NRSI at variable RoB, the authors performed analyses to investigate possible impact of RoB on summary estimates of effect.

☐ Yes
☐ No
☐ No meta-analysis conducted

13. Did the review authors account for RoB in individual studies when interpreting/ discussing the results of the review?

For Yes:

- ☐ included only low risk of bias RCTs
- ☐ OR, if RCTs with moderate or high RoB, or NRSI were included the review provided a discussion of the likely impact of RoB on the results

☐ Yes
☐ No

14. Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review?

For Yes:

- ☐ There was no significant heterogeneity in the results
- ☐ OR if heterogeneity was present the authors performed an investigation of sources of any heterogeneity in the results and discussed the impact of this on the results of the review

☐ Yes
☐ No

15. If they performed quantitative synthesis did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review?

For Yes:

- ☐ performed graphical or statistical tests for publication bias and discussed the likelihood and magnitude of impact of publication bias

☐ Yes
☐ No
☐ No meta-analysis conducted

AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non- randomised studies of healthcare interventions, or both

16. Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?	
For Yes: ☐ The authors reported no competing interests OR ☐ The authors described their funding sources and how they managed potential conflicts of interest	☐ Yes ☐ No

Supplementary Figure 1: Complete AMSTAR 2 Checklist (Shea et al., 2017).

Note: We made an adaptation on question four. For "partial yes", language was not considered in the evaluation of justified publication restrictions. For "yes", the first and last items were the only ones that were considered.

Supplementary Material C - Risk of bias/ quality assessment used in included reviews

Main Author, Year	Risk of Bias/ Quality Assessment Instrument	Risk of Bias/ Quality Assessment of the Included Studies
Papp et al. (2009)	Items from a modified SASQI (Sitzer et al., 2006) + items from Jadad et al.(1996)	Most studies attended to at least half of the criteria
Valenzuela & Sachdev (2009)	CONSORT 2001 reporting criteria	Only three studies met minimum CONSORT criteria. Low quality of trial report.
Martin et al. (2011)	Cochrane Reviewers' Handbook (Higgins et al., 2008)	Most studies had intermediate quality.
Hindin & Zelinski. (2012)	5-point scale adapted from Papp et al. (2009)	Most studies had good quality.
Kueider et al. (2012)	None	-
Reijnders et al. (2013)	CONSORT 2010 for RCTs (Schulz et al., 2010)	Less than 50% of the items from the instrument were reported.
Karr et al. (2014)	PEDro scale (Maher et al., 2003)	Most studies had good quality; one study had fair quality.
Kelly al. (2014)	RoB 1 (Higgins et al., 2011)	Most studies had unclear risk of bias in at least some domains.
Lampit et al. (2014)	RoB 1 (Higgins et al., 2011) and PEDro scale (Maher et al., 2003)	Most studies had high risk of bias and good quality
Law et al. (2014)	13-item checklist based on Delphi list (Verhagen et al., 1998), PEDro scale (Maher et al., 2003), and the "Design-specific criteria to assess for risk of bias" by AHRQ (Viswanathan et al., 2012)	All studies had moderate quality.
Lauenroth et al. (2016)	PEDro scale (Maher et al., 2003)	Most studies had moderate to high quality.
Mowszowski et al.	Shorted PEDro scale (Maher et al., 2003)	Most studies had moderate to high quality.

(2016)		
Mewborn et al. (2017)	RoB 1 (Higgins et al., 2011)	Most studies had uncertain risk of bias in at least some domains.
Shah et al. (2017)	PEDro scale (Maher et al., 2003)	Most studies classified as high or moderate, and no studies classified as poor quality.
ten Brinke et al. (2017)	PEDro scale (Maher et al., 2003) + 3 items	Half of the studies had moderate to high quality.
Bruderer-Hofstetter et al. (2018)	RoB 1 (Higgins et al., 2011)	Most studies had uncertain risk of bias.
Butler et al. (2017)	AHRQ guidance (Viswanathan et al., 2012)	Trials with low or medium risk of bias.
Webb et al. (2018)	RoB 1 (Higgins et al., 2011) and PEDro scale (Maher et al., 2003)	Risk of bias effect was investigated in Lampit et al. (2014) analysis and did not moderate Ess, therefore, it was not included here.
Alnajjar et al. (2019)	Modified Delphi list (Verhagen et al., 1998).	Most studies attended to at least half of the criteria, except for three.
Fan & Wong (2019)	PEDro scale (Maher et al., 2003)	Not reported.
Nguyen et al. (2019)	RoB 1 (Higgins et al., 2011)	Overall risk was low or unclear for each source of bias, but most studies had high or uncertain risk of bias in some domains.
Basak et al. (2020)	PEDro scale (Maher et al., 2003)	Average PEDro score with good quality.
Guo et al. (2020)	Delphi modified list	Most studies had medium methodological quality, and the other were high quality.
Marr et al. (2020)	RoB 1 (Higgins et al., 2011)	Most studies had high risk of bias.
Masurovsky (2020)	None	-
Dhir et al. (2021)	RoB 1 (Higgins et al., 2019)	Most trials at low or unclear risk of bias.
Gates et al. (2021)	RoB 1 (Higgins et al., 2011)	Included studies had moderate risk of bias.
Gavelin et al. (2021)	RoB 2 (Sterne et al., 2019)	Most studies had low or some concern for risk of bias.

Intzandt et al. (2021)	Cochrane Reviewers' Handbook (Higgins 2008)	Most studies had uncertain risk of bias due to lack of information.
Nguyen et al. (2021)	Rob 1 (Higgins et al., 2011)	60% of studies had low risk of bias; 40% had a high risk.
Webb et al. (2021)	RoB 1 (Higgins et al., 2011)	Most of the studies had low risk of bias in most of the domains.
Kim et al. (2022)	RoB 1 (Higgins et al., 2011)	Most studies had high or unclear risk of bias in at least some domains.
Mendonça et al. (2022)	Newcastle Ottawa Scale (Wells et al., 2013).	Most studies classified as high quality.
Yun & Ryu (2022)	RoB 2 (Sterne et al., 2019)	Most studies had some concern for overall bias.

Supplementary Table 5: Instruments and results for risk of bias/ quality assessment carried out in each systematic review.

2.2 ARTICLE 2

VELLOSO, V. F., HERRERA, V., BOMILCAR, I., ALMEIDA, J., MOGRABI, C. D. Assessing Demand, Facilitators, and Barriers of a Cognitive Stimulation Intervention for Healthy Older Adults

Assessing Demand, Facilitators, and Barriers of a Cognitive Stimulation Intervention for Healthy Older Adults

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Abstract

Objectives: With rising life expectancy and declining birth rates, a global demographic shift towards an aging population is evident. While major health organizations recommend cognitive stimulation and education to reduce cognitive decline, there lacks a standardized protocol for implementation in health services. **Method:** Focus groups involving older adults, their families, health professionals and researchers on aging (n = 33) were conducted. The data, recorded and transcribed, were then analyzed using Framework Analysis. **Results:** Five main themes ('Demand', 'Facilitators', 'Barriers', 'Targets for stimulation', 'Expected outcomes') and 23 sub themes emerged regarding the implementation of a cognitive stimulation protocol for healthy older adults in Brazil. Stakeholders acknowledged the demand and emphasized the importance of social interaction and attractive presentation. They discussed multifaceted barriers, and numerous stimulation targets indicated the need for general cognitive stimulation. Primary indicators of intervention success included enhanced mood, social engagement, functionality, and cognitive health preservation. **Conclusions:** Future interventions should prioritize engaging promotional materials, targeted designs, and group activities to enhance social support networks and cognitive health.

Key-words: active aging; healthy aging; Brazilian population; cognitive stimulation.

Introduction

As life expectancy increases and birth rates decrease, humanity undergoes a significant demographic transition that is characterized by an increasingly older population (He et al., 2015). Projections from the United Nations (2022) suggest that the global populace aged 65 years or older will surpass 1.6 billion and live 20 additional years by 2050. In response to these changes, the Madrid International Plan of Action on Ageing (2002) highlights the significance of promoting health and well-being throughout life, ensuring universal and equitable access to health-care services, training caregivers and health professionals and addressing the mental health needs of older persons (United Nations, 2002). One of the recommended actions is the designing of early interventions to prevent or delay the onset of disease and disability (United Nations, 2002).

Alzheimer's disease and other forms of dementia are the second most prevalent cause of disability in the 80 to 84 age group and the leading cause of disability for people aged 85 and over (ECLAC, 2022). The World Alzheimer Report 2023 recommends that people keep learning (Long et al., 2023), though it does not cite any structured protocol that can be strongly recommended for the prevention of cognitive decline in older adults (for PwD, Cognitive Stimulation Therapy is recommended; Spector et al., 2003; Gauthier et al., 2022). Major health organizations recommend cognitive stimulation and/or education as an option for maintaining brain health and mitigating cognitive decline, but it seems that not every activity will provide the same cognitive benefits (Krivanek et al., 2021). In fact, establishing widely accessible cognitive programs is a challenge due to scarcity of high-quality evidence and heterogeneity in reported findings (Gavelin et al., 2020).

Furthermore, cognitive interventions, largely originating from high-income European nations (Yun & Ryu, 2022), reflect a broader trend of low and middle-income countries (LMICs) being underrepresented in health research (Woods et al., 2023). Highlighting this issue, the

Economic Commission for Latin America and the Caribbean (ECLAC, 2022) has noted a pronounced fast aging trend in the region, surpassing European paces. Consequently, there remains a pressing need to develop interventions that are not only effective, but also culturally designed for the specific needs of developing nations and feasible for large-scale implementation on LMICs' health systems.

When developing new alternatives to improve health and healthcare, one of the key steps is to involve stakeholders, including those who will deliver, use, and benefit from the intervention (O'Cathain et al., 2019). Engaging stakeholders allows for adjustments to be made to better align with their needs and preferences, consequently enhancing the feasibility, quality, and relevance of the study (Maurer et al., 2022). Utilizing focus groups enables researchers to gain a comprehensive understanding of stakeholders' perspectives and to identify potential issues related to demand and acceptability of interventions (Krueger & Casey, 2015). By delving into stakeholders' perceptions, comprehension, and valuation of the questions posed, different models can be designed and empirically verified subsequently (Krueger & Casey, 2015).

In light of the aforementioned considerations, this study aims to explore the demand for, facilitators of, and barriers to implementing a cognitive stimulation protocol for healthy older adults within the context of a Latin American LMIC, specifically Brazil. To achieve this, focus groups were conducted with stakeholders using semi-structured interviews. Framework Analysis, developed by Ritchie and Spencer (1994), was selected as a qualitative data analysis method specifically tailored for applied policy research. It involves a systematic process that enables the reconsideration and refinement of ideas, made accessible through the documentation of the analytical process.

The objectives were to ascertain: (1) the existence of demand for such an intervention, (2) factors that could enhance its efficacy and feasibility, (3) potential barriers to implementation,

(4) target areas for stimulation and (5) the population's expectations regarding the most important outcomes for program success.

Methods

Semi-structured interviews were conducted to assess the demands, facilitators and barriers for the implementation of a cognitive stimulation protocol for healthy older adults in the Brazilian context. The main characteristics of the intervention to be developed were also discussed. Two complementary formats of focus groups were used: face-to-face and remote.

Recruitment

The community was invited to participate in focus groups through an open invitation, which included social media outreach and pamphlets. Furthermore, a day center was contacted to interview its health professionals and users.

Procedure

Focus groups were audio-recorded and were then transcribed verbatim. Nine focus groups were conducted with healthy older adults living in community (n = 9), their relatives (n = 2), and multidisciplinary health professionals including psychologists, nutritionists, physical educators, physiotherapists, caregivers and researchers (n = 22). Each group was attended by at least two members of the research team, one of whom took on the role as facilitator and led the group discussion (V.V. or I.B.), while the others observed the group and made notes to supplement the audio data collected (V.V. or J.A.). The interview schedule was developed in a semi-structured style, guided by a series of predetermined focus points (Table1). A brief description of the research project and the principles of cognitive stimulation was given. The participants discussed the feasibility and the demand for the planned intervention, including opinions about the modality, frequency of sessions, duration and structure for each session,

duration of intervention, group size and composition, settings, possible activities, targets for stimulation and expected outcomes. Each group lasted approximately 90 minutes in total.

Focus points of the semi-structured interviews
Barriers and facilitators for psychosocial programs that aim to prevent cognitive decline
Relevance of the approach
Frequency, duration, setting, mode of delivery, group size, infrastructure, qualified professionals
Adequacy of activities
Target audience
Target cognitive domains
Validation of outcomes

Table 1: Focus points of the semi-structured interviews

Analyses

The analysis of the transcripts followed a systematic approach known as Framework Analysis (Ritchie & Spencer, 1994), consisting of five steps: (1) Familiarization, (2) Thematic framework identification, (3) Coding, (4) Charting and (5) Interpretation. No analysis software was employed throughout the process. Initially, two researchers (V.V. and V.H.) read all the transcripts to discern broad themes. These themes were gathered and refined to create a comprehensive coding key that covers both broad themes and sub-themes. The transcripts were later categorized and charted accordingly. Lastly, a mapping and interpretation process was then performed to determine factors that will guide the design of a cognitive stimulation intervention for healthy older adults in Brazil.

Ethics

The research project was approved by the research ethics committee of the Catholic University of Petrópolis (UCP/RJ; project ref: 64677022.7.0000.5281).

Themes	Sub-themes
Demand	Is there a demand? Reasons
Facilitators	Naming Publicizing and instruction Intervention's structure Activities Accessibility Partnerships Finances Interest Familiarity with the service Outcomes
Barriers	Naming Publicizing and instruction Intervention's structure Activities Accessibility Partnerships Finances Interest Recognition and/or prioritization of demand Screening for healthy older adults
Targets for stimulation	Targets for stimulation
Expected Outcomes	Participation Improved mood Socialization Cognitive health Functionality maintenance Quality of life Learning new things

Table 2: Themes and sub-themes identified across focus groups.

Results

Nine focus group sessions were held, including 33 participants. The greatest difficulties in organizing the groups were reaching the target audience and reconciling schedules. Most of

the sample preferred to participate remotely, including the target audience. Only two groups occurred in person, with professionals and users of a day center that performs cognitive stimulation work.

Five themes and 23 sub-themes were identified consistently across the interviews (Table 2). Of these, 8 sub-themes were identified as both facilitators and barriers. Illustrative quotes are provided for each sub-theme on tables 3 to 7.

Theme 1: Demand

Is there a demand for this type of program? Illustrative quotes can be seen in table 3.

Is there a demand?

The initial inquiry was regarding the demand for this type of program. Most responses were positive. However, some participants expressed that not all older adults would be interested in participating, and it is dependent on the program's development.

Reasons

When asked about the reasons for this demand, respondents cited the interest in maintaining cognitive health and the lack of evidence about current cognitive preventive strategies.

Theme 2: Facilitators

Factors that can help with program implementation, performance, and maintenance. Illustrative quotes can be seen in table 4.

Naming

When using terms related to good health and high functionality, such as active aging and stimulation, naming was mentioned as a facilitator.

Publicizing and instruction

Some respondents suggested that the dissemination strategies should focus on the preventive results, while others suggested focusing on the positive experience of meeting people and participating.

Intervention's structure

In regard to the intervention's structure, participation in groups was quoted as a significant facilitator. According to the preference of each possible participant, the modality (online or in person) was also cited as a key factor in the success of the program.

Activities

The moments of social interaction, such as snacks and walks, were the activities that most piqued the public's interest.

Accessibility

Places that are prepared with accessible distance, paths, and movement should facilitate face-to-face participation. Online access would be easier for those with good technological skills by avoiding barriers on the route.

Partnerships

Partnerships with existing groups of older adults, public managers, and private institutions were mentioned as potential catalysts for implementation.

Finances

Facilitators for the financial aspects of the program included the low cost of materials, the opportunity to reduce public costs, and the possibility of entering a market niche.

Interest

According to the respondents, the prior interest of certain individuals in maintaining its functionality and the use of strategies to increase participants' interest during sessions can be of great value in attracting and keeping the target audience.

Familiarity

Familiarity was deemed a great facilitator. Prior familiarity with other types of activity groups, professionals involved, or other cognitive activities can facilitate joining. Over time, the target audience's familiarity with the developed program could lead to an increase in

adherence.

Outcomes

The interviewees believe that the benefits that participants receive (or anticipate receiving) from the program will have an impact on their motivation to stay.

Theme 1: Demand	
	"So, I think it is super valid and it is very urgent this need to have a protocol for healthy older adults, those who do not yet have a diagnosis or who may not even have, but who want to prevent themselves."
1.1 Is there a demand?	"I think it depends a lot on the profile of the elderly, okay? And so, what he wants, right? Because I've done stimulation, I've already started stimulation in an elderly person who it was actually more the daughter [...] who wanted her father to do the stimulation, okay? So, I couldn't give much time to the stimulation because I didn't notice his interest so much and he didn't see much purpose [...] he wasn't feeling the need. Another case, an old man [...] who is still working and wants to keep working. So, he has a purpose, right?"
	"Not many protocols have been studied for non-drug interventions for healthy older adults. We have many courses and many teams that do cognitive stimulation or cognitive activities in order to delay or prevent cognitive decline, or some cognitive issue. However, I see that there is not so much care in being a protocol and having studies that effectively show the evidence of these interventions, right? And then when we have a population that's getting older and older, we have an increase in the elderly population here in Brazil and around the world, I think that becomes even more relevant and necessary."
1.2 Reasons?	"What is unanimous for everyone, the biggest fear we have is becoming dependent, mentally incapable. [...] Everyone's just afraid... including a friend of eighty-nine who went to the meeting, she said 'my great fear is to be mentally dependent, because I will not be able… I will no longer be my owner', she spoke in these terms. So I think it is also a great interest, there is a great interest within people like me, for example, who are elderly but I am fully active, and live alone [...] but I am afraid too, I am afraid of the day I will need my children to come here for me to enter the internet, that my children come here for me to do income tax, that my children come here, anyway, to help me do some installation, and then for worse, because it always gets worse, the truth is this. Even when there is no Alzheimer's."

Table 3: Illustrative quotes for every sub-theme in theme 1.

Theme 2: Facilitators	
2.1 Naming	“What could be more attractive is a group for active aging, so that the older adults remain active. Active in every way: you take care of your body, you take care of your appearance, you take care of your bank account, you can take care of your mind [...] bring reality to now, bring attention to now” “I find the term stimulation that you use also much more interesting, flashy, say, than intervention. Intervention, I don’t know if for everyone but for me it has a kind of imperious connotation. And I really like this... cognitive stimulation, I liked it. I found it very interesting.”
2.2 Publicizing and instruction	“Convince not only for health. 'You go because you need to, because you depend on it'... no! 'Come on, because it’s good, you will make friends, you will interact', so I guess you have to talk to convince.” "And let it be clear that it is also preventive. I think it is also very cool. As an old woman I love preventive activities, whatever it is. [...] For head, body, skin, anything. For general health. Prevention is great."
2.3 Intervention's Structure	"Nowadays I’ve been so lazy to do things myself. I end up 'pushing with my belly' and I won’t. If you can do something where there’s someone else you know or that you’re going to meet people, it’s motivating. [...] So this idea of the project being group activities, I think it's motivating." "Online works for some types of stimulation proposal, not all, right? Depends a lot on what will be applied, I believe. The level of activity, the level of demand in their performance. But it works a lot for some active older adults, and they even prefer it. There are many seniors who like the online, right? And there are others... I say most— at least here, is a lot of face-to-face, right? —do not adhere to online."
2.4 Activities	“I sometimes prepare a lot of stuff, get there and I can’t do anything but a conversation circle. They want to talk! And then I want to go to the activity and they’re like, 'no, but this is already the activity!'. And then I let this playful activity flow. Because what he needs is to talk, is someone who is interested in what he says. So, when he comes back to this group, it decreases his functional losses.” "People like to have a snack after the activity [...] each one takes some junk food, always. And then they’re just sitting there talking to each other and having fun. 'But mom, so you go for it [...]'. It’s a social event too.”

2.5 Accessibility	"It would also have to be a place that had accessibility. Not to make people have to go upstairs, downstairs, climb, none of that. And I think it's good that there's also an ease of access for driving there. For example, cars can come in and leave the person. Can't be anything too complicated, because it gets hard, right? It's hard." "If you have a good online class that flows, but you start to see that twice a week would be the best, I think it works great. Because he's at home, so it's even easier. And he doesn't have the difficulty of the journey, or sometimes having to get in the way of sleep..."
2.6 Partnerships	"I keep thinking about... I don't know, some partnerships with the health departments, with, uh... I don't know, ministry, I don't know. I keep thinking... for example, nowadays we have a protocol of evaluation of functionality for the older adults, very well established and that seems to me also came from the university and was gaining space increasingly within the public sector as a base of work. Nowadays you can no longer think about treating an elderly person without functionality evaluation" To implement, maybe the beginning should be looking for groups that are already constituted, right? [...] Given that they already have a habit of going somewhere and doing some activity, I think it would be more effective for implementation in a group that has already been formed."
2.7 Finances	"My major experience is in public service. So, in this industry, I think the facilitator, or the biggest draw would be some way to prove financial impact. You know? Some way to prove that reducing or delaying cases of greater dependence and dysautonomia, you can reduce costs. [...] you generate proof, or at least a formula that says it will have a positive financial impact and that the investment is low. It's important to consider this because these are not significant appliances or equipment. You don't need a huge structure when talking about it. It's people and, of course, resources there, games and such. Even if it involves purchasing technology, like software, I think it's cheaper. " "In the private sector [...] I think you have to really appeal to the issue of prevention in general. In the same way that those who work in aesthetics, physical activity, physical preparation, hair, and the silver market today appeal in this way. [...] You prevent yourself, you dress younger, you are up to date with trends, but are you taking care of your cognitive aging? Are you taking care of what will keep you active longer? Because in fact, the person can be wheelchair-bound, bedridden, and have optimal cognition. In the private market, I think there is a growing trend towards marketing the gray market, also known as the silver market."

2.8 Interest	"As I already had a family history [of Alzheimer's Disease], my mother as I said. In this case I would already come [...] for this reason, understood? Because I've had history in the family, it was my mother as I told you." "Just have the will, have the curiosity, something you were called... 'Oh, I'm going there', 'ah, I liked it, I'll stay', 'Cool, tomorrow will have more new things'"
2.9 Familiarity	"If you take older adults who may already be participating in some kind of group, it makes it easier, right? Or, I don't know, groups that do some physical activity. Or groups that, I don't know, church groups, whatever. Because he's more motivated to leave the house and join a group. I think it makes it easier than to imagine that maybe an elderly person who is quieter, let's say so... maybe you will want to join this group, right?" "I imagine that the more society has access to this type of work, the more mobilized it will be, and the more stimulated it will be to work and understand what we are doing. That is to make your mind exercise, right? Make your mind work, in a preventive way. In a way that brings you physical benefits, right? "
2.10 Outcomes	"What would this stimulation bring to benefit, right? What would be good. Because always the person will need motivation, right? So, what am I going to do from this group, what's going to benefit me, right?" "What will they receive [...] when they check the opportunity of the program, the improvement that their elderly [...] will verify that their elderly, they will be supported and cared for, right? And the elderly who will often arrive, how they get here, suspicious, right? He will have the opportunity to know, right? To check that he will be well taken care of. Often the best care is in this program than at home [...] heard, not mistreated, more cherished, right?"

Table 4: Illustrative quotes for every sub-theme in theme 2.

Theme 3: Barriers

Factors that can hinder the implementation, performance and maintenance of the program.

Illustrative quotes can be seen in table 5.

Naming

When using terms related to health treatments and diseases, such as therapy and intervention,

naming was mentioned as a barrier. Moreover, the term "healthy older adults" may inhibit the participation of cognitively healthy people who have some issue of physical health.

Publicizing and instruction

Respondents recommended that dissemination strategies steer clear of the natural and pathological damage associated with aging, as well as direct references to terms like 'elderly'. In addition, there was disagreement about the utilization of digital media to reach the intended audience.

Intervention's structure

Excessive duration and frequency of the intervention were perceived as barriers due to potential conflicts with other activities of the participants. For older adults who lack autonomy in the use of digital technologies, the remote mode was perceived as an obstacle.

Activities

Activities that are not acceptable include those that are infantile, based on very recent references, have only one possible answer, are excessively difficult, can cause embarrassment or require skills that the person lacks. It was noted that predicting the negative effects of an activity is not always possible, and the team needs to be prepared to handle these situations.

Accessibility

The most significant hindrances to face-to-face participation are large displacements, inadequate transportation, urban insecurity, and disregard for older citizens' rights. Large and heterogeneous groups can make it difficult to plan activities that are accessible to all.

Partnerships

The lack of specialized private agents who are interested in working with this target audience and the complexity of public agencies, make it difficult to establish partnerships for implementation.

Finances

The biggest financial challenge is finding a balance between the program's need to generate profit and the financial reality of elderly retirees.

Recognition and/or prioritization of demand

Even though there is a demand, it is often not recognized or prioritized by the target audience or the agents who can meet it.

Interest

The interviewees pointed out that the target audience's lack of interest, either due to lack of demand recognition or stigma surrounding psychosocial programs, can act as a significant obstacle to its implementation.

Screening for healthy older adults

Finding and screening healthy older adults for the program is a barrier in itself, as they often decline during the program or retain some cognitive abilities but not others. Furthermore, a significant number of older individuals are already experiencing the long-term consequences of an unhealthy lifestyle.

Theme 3: Barriers	
3.1 Naming	"I don’t really like talking about healthy but active seniors [...] because it can restrict or inhibit the participation of people who... 'If I have cancer, I may have good cognition but I’m not healthy, I’m not eligible for that group,' you know? Or 'if I have a physical disability or whatever, I can’t join this group because I’m not healthy'." “Avoid using the term therapy, which has a negative resemblance.”
3.2 Publicizing and instruction	"And I see resistance [...] I went to deliver pamphlets, and I was almost beaten. Right? I was very... I had a very negative view when I delivered the pamphlets inviting them to gain health. Because they saw the 'elderly', and then I saw in my propaganda that I was completely wrong." "In regard to the media, we are currently using digital media as a means of providing more information. But it turns out that not all individuals in this age group consume digital information."

3.3 Intervention's Structure	"I also do not know what the idea of the frequency of the program is [...] Because I realized that some seniors don't want to commit to going there, maybe two or three times a week. [...] It's very uncommon to find an older adult who is not involved in any other activities. [...] So maybe that could be a barrier. [...] It typically takes an hour and a half or two… anything longer than that is already too exhausting [...] and even when you finish it in an hour and a half or two, you need to take a fifteen-minute break." "Because when you have to ask his son to call or give him his cell phone to enter, that autonomy that we want him to maintain is lost. And then he gets frustrated, he gets sad. Even though he is an older adult who will schedule, who does the shopping, does everything at home, who has the cognitive preserved, but who has no affinity with technology."
3.4 Activities	"It is important to avoid activities that infantilize, right? Nothing with childish traits. I also think it is important to avoid activities that have very current elements, right? Or that depends, for example, on the person having a greater motor development ... right? Use… that he can't use a phone or tablet. So make cultural references to their time and don't bring too much that might cause a sense of strangeness, right? Or overload these people. " "Activities that were one-way or difficult in a large group."
3.5 Accessibility	"This place would be crawling with people if we had the means to transport them. One of the things that stopped us immediately, and we had a lot of difficulty, was precisely this displacement. Why? Why? Because of insecurity, the elderly feel insecure when they have to move. 'Ah, but there's a ticket, there's a gratuity'. Not always, because the driver does not want to carry him and passes straight through. That was one of the things we heard. 'Ah, if there was a shuttle bus...'[...] Because of violence to the elderly, they fear violence. They are fragile. So, the transport that is unsafe, the roads, the buses… the older adult gets on the bus and the driver starts. When he goes up, when it stops, he already feels shy to use gratuity [...] So transport is a deterrent at first. It's the first". "A difficulty that we had, as the groups were heterogeneous... so sometimes there was someone with difficulty hearing, with difficulty of visual acuity. So, we had to think of several ways to serve everyone the same way [...] Because that was a big difficulty. Sometimes we would play a video, then we would have to have a radio or cell phone for a lady who had difficulty hearing. Then, groups of people who were highly educated and illiterate people. So, we had to think about the same activity, how to make it possible. One would talk, another would draw, one would write. So it took a lot of care from the team so that people wouldn't feel inferior, and it wouldn't interfere with adherence."

	"Because the people I looked for [...] when I said that my focus could be the older adults, or cognitive training and so on, they said: 'no, but we work with children.', 'no, but we work with adolescents and adults'. I stated, 'Let's add to the clinic, alright? Let's work with the older adults, okay? '. And so immediately everyone said 'no' to me."
3.6 Partnerships	"Here [...] it belongs to the state government [...] And the family clinic that makes the recommendations, it is the city hall. They are different government agencies, right? [...] this is even a difficulty in this exchange, right? It is very difficult, because it is a government agency... and often the mayor is from one party, the governor is from another party. [...] There are those difficulties, right?"
	"And in the private sector [...] there is the question of the manager thinking about money. And not only money, but profit. So, for you to sell a project like this, it's not just about how interesting it is. You have to see if it will be worth it financially, if you will make a profit [...] I do not think it is easy to sell this product."
3.7 Finances	"Because in retirement you start to earn less, understand? You spend... sometimes some people even in their old age have to help their family, grandchildren, and children. In addition to being already retired, there is no way you have an extra job. In fact, retirement even reduces your salaries. And sometimes you still have to help your grandchildren. [...] So, the lack of money is a complex issue. I think it impacts a lot. "
	"I see a lot of resistance because they are still very active, and they do not see themselves with the demand to do preventive work [...] I see, before the seventies, a lot of resistance. Especially on the male side."
3.8 Recognition and/or prioritization of demand	"I had never paid attention to the fact that the population is aging very fast, and that this will become increasingly common, right? So, I feel a general ignorance about the subject. I graduated [...] in 2010 and so... nothing about this area, nothing about the health of older adults, except something like this... in social psychology, the vision of the elderly in society. Now, something related to diseases, something related to treatment, something related to prevention... nothing, nothing. So, I find it quite challenging that it comes."

	"The difference between male and female elderly seeking cognitive development is brutal, right? And global health, especially mental, right? In the assisted living homes, there was a proportion of 80% of women to 20% of men, when this proportion was generous"
3.9 Interest	"Not generalizing, but I believe that the acceptance of being able to do something to benefit, even not presenting any kind of commitment or difficulty [...] which is to reach these groups, without even having a reason to be there, but only understanding that it's for another kind of factor, right? So, I believe that is really coming to this activity without having a greater stimulus, a greater motivation or some kind of referral. Maybe in that sense. At least in my experience it's a lot like that, right? The person needs to have a justification sometimes. He doesn't understand much about how it can do well or that involving you might make it easier to prevent it in that sense. "
3.10 Screening for healthy older adults	"There are elderly who initially before work, you think his cognition is ok. After starting the work, it becomes apparent that there are axes within it that are not. It seemed like it was initially, but then it wasn't [...] Cognition will have different axes, right? Cognition will have different axes, right? It will have different focuses and then, at first, you say 'no, his cognition is preserved'. But when you create a working relationship, you will notice that his cognitive abilities are not so preserved at some points. "It's an audience that, in their old age, doesn't have time for that. They exhausted themselves at work, and I saw many people with a life of finalization. For working too hard, right? For not obeying the deadlines… which should be a prescription, leisure, vacation, holiday, hours! Hours of mental leisure, so you can clear your brain, good sleep, identify your quality of life in life. How did you get through your life? You're not gonna pay that bill just in the end, you're gonna pay a lifetime bill, right?"

Table 5: Illustrative quotes for every sub-theme in theme 3.

Theme 4: Targets for stimulation

What would be the most important targets to stimulate and/or measure in this type of program? Responders quoted 14 targets, including: global cognition, attention, memory, reasoning, executive functions, speed of processing, language, orientation, subjective cognitive performance, ADLs and IADLs, social skills, behavior, mood, self-awareness. See table 6.

Theme 4: Targets for stimulation	
4.1 **Targets for stimulation**	Global Cognition Attention Memory Reasoning Executive Functions Speed of processing Language Orientation Subjective Cognitive Performance ADLs and IADLs Social skills Behavior Mood Self-awareness

Table 6: Stimulation targets identified in theme 4.

Theme 5: Expected Outcomes

The benefits and outcomes that respondents want to see at the end of the program. Illustrative quotes can be seen in table 7.

Participation

It is pointed out that people's constant and enjoyable participation is a benefit in itself.

Improved mood

Mood improvement was highlighted as a major outcome, both for itself and its importance in protecting cognition.

Socialization

The expansion of opportunities for socialization, development of new relationships and partnerships, and strengthening of support networks was highlighted as a beneficial outcome for both the older adults and the social circle around them.

Cognitive health

It was mentioned that properly demonstrating the maintenance of cognitive health is important for the intended social impact.

Functionality maintenance

It was pointed out that maintaining functionality and autonomy for daily activities is a desirable outcome.

Quality of life

The respondents stated that they would like to achieve a better quality of life as a result.

Learning new things

According to the interviewees, it is expected to learn new things and listen to different points of view.

Theme 5: Expected Outcomes	
5.1 Participation	"First of all, I think the first thing is the presence of people. Right? Right? If we're discussing how hard it is to bring people in, if they keep up and sustain it, it's a great sign of success."
	“Look, I confess that at the moment what is giving me pleasure is to participate [...] the pleasure of being there contributing, for me is already positive [...] I’m happy to contribute, you know? And not necessarily having to assess whether this increased or not, for example, my memory capacity, etc."
5.2 Improved mood	“So, what I see that can influence in a very positive way an elderly person is the work with mood. That’s what I say about mood disorders. [...] And I believe that stimulation plays a significant role in even the self-esteem of the elderly. Because elderly people sometimes feel depressed or give up when they start to lose their ability to do certain things. And if he already has a tendency or history that makes him vulnerable to the installation of dementia, this can also be a risk factor. So, I imagine that focusing on this would be highly interesting for a preventive group for the older population”
	"I think I would say that it was worth it, if this activity ultimately made me a happier person. For me, it all comes down to this. Will the person get better, will the family get better? If you have learned this, that, that other thing... that in itself is a means. But for me, the purpose of human life is to be happy, to overcome obstacles, and to evolve. I feel like I’m better, so it was worth it."

5.3 Socialization	"And I think it even creates opportunities, new opportunities, even for people to put themselves in another way in society. For example, one who does one activity and wants to continue working, generating income, together with the other... so it's creating an ecosystem, let's say, when you offer this and you're... and everything works, and people have access, this ecosystem of learning, cognitive stimulation, it's going back to society." "More experiential contact with people, meeting people... it is very difficult for you to meet people at our age, right? [...] It's just family members, and the family doesn't have these commitments because it's almost an obligation, right? [...] Something more spontaneous is missing. And go out, do things with company, have a motivation to go out and find people"
5.4 Cognitive health	" [...] I think it's important to have a study of evidence as well, that it would be a stimulation that has a visible effect of protection and prevention, right? [...] Because I think that in order to have this social effect, it would have to be something that has evidence that actually influences that, right?" "I think if you preserve cognition, the rest is a consequence. I think that by preserving cognition, the individual will have the discernment to make the right decisions, which will lead to an excellent quality of life."
5.5 Functionality maintenance	"Helping me carry out the activities we have to… for life everyone has to fulfill, right?" "I think to preserve maximum autonomy and independence, right? Knowing that we have a decline even in healthy older adults."
5.6 Quality of life	"These activities would all bring me global well-being." "The result I would expect would be a lot about how much quality of life was gained there."
5.7 Learning new things	"I want to do, I want to learn something, I want to have an exchange, right? I'd like to express myself and get something good from you, right? That I can enjoy if I add to my life." "When you come out of your bubble, you start to see things, you create new things, your way of thinking changes about everything"

Table 7: Illustrative quotes for every sub-theme in theme 5.

Discussion

Summary of the results

The present study aims to assess the demand and feasibility of a preventive cognitive stimulation program in Brazil by comprehending the potential barriers, facilitators, expectations and required characteristics for its implementation and effectiveness. The program's different model possibilities led to numerous questions about facilitators, barriers, and stimulation targets, as well as varied expectations about possible results. Indeed, five themes (i.e. Demand, Facilitators, Barriers, Targets for stimulation and Expected Outcomes) and twenty-three sub-themes were identified consistently across the interviews.

Interpretation of findings

There was an agreement among health professionals, researchers, older adults and their families that there is demand for this type of cognitive stimulating program. This is a significant contribution to the literature, as no other studies have previously explored this demand from the personal perspective of the target audience. Although there is evidence that cognitive interventions can improve cognition and mood (Piccirilli et al., 2019; Yun & Ryu, 2022), respondents cited a current lack of access to a reliable intervention. However, it should be noted that the older population has a variety of profiles and interests, based on individual differences like age, gender, culture and ethnicity, socio-economic status, work, literacy, health and functional status, family structure, sexual orientation and gender identity (Peck, 2019). The fact that there is a demand from respondents does not mean that everyone is interested.

Both facilitators and barriers were identified for naming, publicizing and instruction, the intervention's structure, activities, accessibility, partnerships, finances and interest, depending on their features. Other facilitators were familiarity and recognized good outcomes. Strategies that prioritize personal development and positive emotions while also being compatible with

the participant's daily life appear to be the most desirable. However, these recommendations could also apply to group interventions based on leisure activities, which also have the potential to protect cognitive health (Litwin et al., 2016; Grimaud et al., 2017; Gardner et al., 2020; Su et al., 2022). To show advantages over these strategies, the cognitive stimulation program needs to show greater benefits of health, finance, or applicability in public policies.

A main barrier is that mentioning cognitive decline or disease can lead to public disinterest, even in the context of prevention. Consistent with the literature on the search for mental health services in general, stigma, high costs, and negative perceptions of mental health services appear to be central obstacles for older adults (Usra Elshaikh et al., 2023). Moreover, it seems that any design option of the program will hinder the access of some part of the population, whether face-to-face or online, with activities that are either very easy or very difficult. For example, although in-person was more indicated for the program in general, most people preferred to participate online for the interviews because of the required route. A program with guidelines that can be adapted to different groups within the older population could potentially solve this issue.

Other barriers were recognition and/ or prioritization of demand and screening for healthy older adults, both linked to the health worker/participant relationship. A gap has been found between the services provided and the needs of older adults, which is evident in the lack of participation (Srivarathan et al., 2019). The perception of functional decline as an inevitable part of aging processes and the notion of services being neither accessible nor acceptable in the context of complex health and psychosocial needs were both reasons for this (Srivarathan et al., 2019). The significance of trust, proximity, and presence was underlined by health care professionals who work to improve the acceptability and accessibility of health promotion services (Srivarathan et al., 2019), which is in accordance with the facilitators found in the present study.

While global cognition, memory and attention were frequently mentioned, we did not find a consensus on best targets for stimulation. This is consistent with the typical definition of cognitive stimulation, aimed at general enhancement of cognitive and social functioning (Clare & Woods, 2004; Mlinac et al., 2022). Interviewees had a higher degree of certainty about their expected results, demonstrating greater certainty about the end than the means. The expected outcomes were linked and interrelated, including participation, enhanced mood, socialization, cognitive health, functional maintenance, quality of life, and learning new things. The factors that influence effectiveness cannot be properly evaluated without achieving the first step, which is to guarantee the expressive participation of the population.

It is remarkable that socialization appeared both as a desirable activity and as an expected result of stimulation. Cognitive health, functionality maintenance and enhanced mood appeared both as targets of stimulation and as expected results. In interpreting these facts, it seems that there is a desire for group activities to strengthen social networks, maintain cognitive health, enhance mood, and preserve autonomy. Silva et al. (2021) analyzed the evidence for this in a systematic review, highlighting the positive outcomes of cognitive interventions on quality of life and reducing depressive symptoms in elderly and mature adults without dementia or depression. In addition, Sommerlad et al. (2023) collected observational evidence suggesting that a lower level of engagement in social activities is linked to a greater relative risk of dementia (Sommerlad et al., 2023). Initial evidence was found by the authors that group social interventions can improve cognition, but there is no evidence regarding dementia prevention, and interventions that have had an effect on cognition may not continue to delay or prevent dementia (Sommerlad et al., 2023).

Limitations

Focus groups have their own set of limitations, including the possibility of bias and manipulation by leading or dominating participants and difficulties in distinguishing between

individual and group views, generalizing the results from the small focus group to the larger population, and having a truly representative sample (Gundumogula, 2020). Although we found a great demand for this type of intervention, it is possible that only people who already believed in this demand accepted to participate in the interviews. Furthermore, we were unable to create a profile of who would be more interested or would be better served by this demand, which would have improved the necessary information to select the ideal intervention characteristics.

Conclusion

The need for a preventive cognitive stimulation program in Brazil was highlighted by older adults, their families, and health professionals, who expressed the lack of evidence-based options for those looking to maintain cognitive health. In order to include and engage the population of interest and potential partnerships, new interventions must focus on developing attractive promotional materials and targeted intervention design. Group activities for global cognitive stimulation, whether conducted online or in person, seem to be crucial for enhancing social support networks, boosting mood, and maintaining cognitive health and functionality. Those results will be further investigated in a pilot study that will follow.

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Conflict of Interest

There is no conflict of interest declared by the authors.

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3. GENERAL DISCUSSION

In response to the challenges posed by an aging population and the resulting increase in neurodegenerative diseases, this study aims to provide evidence to guide the development of a structured program focused on preserving cognition in healthy older adults. First, a systematic meta-review of current literature on both simple and combined cognitive-based interventions was carried out. Afterwards, focus groups involving stakeholders were conducted to assess the demand for, identify facilitators of, and uncover barriers to implementing a cognitive stimulation protocol for healthy older adults in Brazil. Additionally, the study tries to explore the necessary characteristics for successful implementation.

The systematic meta-review examined 34 articles, comprising 33 reviews on cognitive training, 3 on cognitive stimulation, and 1 on multicomponent interventions. While cognitive training was predominantly supported, there was a noticeable dearth of evidence on cognitive stimulation and multicomponent interventions. In contrast to Gavelin et al.'s (2020) systematic overview, the present study conducts a more comprehensive review by including combined and multicomponent programs. Furthermore, this study is more specific, focusing solely on data pertaining to cognitively healthy older adults. Both studies employed the same quality analysis tool, revealing a prevalent critically low quality and indicating a consistent evidence gap in the field. Additionally, both studies observed that interventions primarily influenced outcomes of objective tests, lacking evidence to suggest clinical value even for cognitive training.

The qualitative analysis included 33 stakeholders participating in nine focus groups. The framework analysis revealed that these groups addressed five main themes (‘Demand’, ‘Facilitators’, ‘Barriers’, ‘Targets for stimulation’, and ‘Expected outcomes’) and 23 sub-themes. Stakeholders, including older adults, their families, health professionals, and researchers, highlighted the necessity for a preventive cognitive stimulation program in Brazil

due to the lack of evidence-based options for maintaining cognitive health. They emphasized the importance of social interaction and attractive presentation, discussed multifaceted barriers, and identified various stimulation targets, highlighting the need for general cognitive stimulation. Key indicators of intervention success included improved mood, social engagement, functionality, and preservation of cognitive health. However, it is noteworthy that many of the facilitators mentioned may also be applicable to group interventions centered around leisure activities, which are recognized for their potential in protect cognitive health (Litwin et al., 2016; Grimaud et al., 2017; Gardner et al., 2020; Su et al., 2022). Further research is warranted to provide more specific guidance in this regard.

Together, the systematic meta-review and the qualitative analysis offer valuable insights into the current status and future trajectories of cognitive interventions for healthy older adults. Notably, the meta-review delineated a predominant focus on cognitive training in 33 out of 34 studies, indicating a notable deficiency in evidence pertaining to cognitive stimulation and multicomponent interventions. This discrepancy underscores an open question in existing research, a gap that the qualitative study was able to address. This initiative marks the first phase of developing and assessing a novel cognitive stimulation protocol tailored to mitigate cognitive decline risks in older adults. Employing framework analysis is important in this context as a best practice for intervention research (O'Cathain et al., 2019; Maurer et al., 2022). The meta-review's identification of a dearth in clinically validated outcomes resonates with the focus groups' findings, wherein stakeholders emphasized outcomes intricately linked with daily life activities. Both contributions further endorse the need for expanded investigations into cognitive stimulation interventions for healthy older adults, corroborating prevailing gaps in the literature and echoing the demand from the target population.

The principal limitations of this study encompass those previously delineated for each individual study. In the systematic meta-review, constraints were observed, including the critically low quality of the included reviews and the extensive range of interventions and methodologies, potentially impeding comparability between outcomes. The Framework analysis encountered inherent limitations associated with focus groups, such as susceptibility to bias and manipulation by dominant participants, challenges in discerning individual perspectives within group dynamics, the generalizability of findings, and the difficulty in securing a truly representative sample (Gundumogula, 2020). Moreover, limitations were encountered regarding participant bias in accepting interview invitations, as well as challenges in developing a comprehensive profile of individuals predisposed to be more receptive to the intervention.

The objective of this study was to provide evidence for informing the development of a novel program aimed at preserving cognitive health in older adults. Despite the wealth of evidence gathered, notable gaps persist. The challenge in determining the most effective cognitive intervention for maintaining cognitive health emerged from the disparate quantity of studies, limiting comparability. Moreover, delineating specific characteristics of the proposed cognitive stimulation intervention (e.g., modality, frequency, duration) proved complex and dependent upon the specific target group of older adults, precluding the formulation of general guidelines. While the identification of a prioritized group of older adults could have mitigated this limitation, establishing such a profile was unfeasible. Additionally, the focus group study exclusively included participants from Brazil, thereby limiting the generalizability of findings to other populations.

In terms of clinical implications, the current literature predominantly supports cognitive training activities, particularly favoring 10 adaptive sessions delivered less than three times weekly in group settings. However, the issue concerning the transfer of effects to clinical

outcomes remains inadequately explored, warranting urgent investigation across short and long-term durations. From the perspective of the target audience, there is a notable interest in exploring interventions involving group activities for comprehensive cognitive stimulation to strengthen social networks, sustain cognitive health, improve mood, and maintain autonomy. The necessity for a preventive cognitive stimulation program in Brazil was underscored by older adults, their families, researchers and health professionals, who emphasized the importance of developing appealing promotional materials and tailored intervention strategies. Those results will be further investigated in a pilot study that will follow.

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