



Language and Communication Interventions in People with Alzheimer's Disease: A Systematic Review

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Abstract: Although language impairment is frequently observed in patients with Alzheimer's disease (pwAD), targeted language rehabilitation is often overlooked. The present study reviews published evidence on the impact of language training, either alone or in combination with cognitive training, on cognitive outcomes in pwAD. A systematic search of PubMed, Google Scholar, and Cochrane was carried out, including studies published from inception to November 2023. A total of eight research articles (four randomized controlled trials and four observational studies) met the inclusion criteria: six assessed language training combined with cognitive training and two evaluated language rehabilitation alone. Regarding language and non-language (mainly memory, attention, and executive functions) outcomes, there was a consensus among studies that language rehabilitation (alone or in combination with cognitive training) yields positive results. Some of the articles also explored the impact on patients' and their caregivers' quality of life, with all but one showing improvement. Consequently, the combination of language and cognitive training leads to improvements across various cognitive domains. However, limited evidence supports the value of sole language rehabilitation. This conclusion is influenced by heterogeneity among studies (different types and duration of interventions, small participant sets, various assessment tools), and, thus, further research is warranted.

Keywords: language training; communication rehabilitation; Alzheimer's disease

1. Introduction

Alzheimer's disease (AD) and other major neurocognitive disorders represent important public health concerns. According to the National Institute of Neurological and Communicative Disorders and Stroke and Alzheimer's Disease and Related Disorders Association (NINCDS ADRDA) [1] and the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) [2] criteria, AD diagnosis cannot be determined by laboratory tests; structural, and functional imaging techniques, along with clinical and neuropsychological testing, are of utmost importance. The clinical picture includes progressive impairment of memory - other cognitive and language functions [3].

In greater detail, non-language - cognitive manifestations include deterioration of episodic memory, semantic memory, working memory, executive function, and visuospatial skills [4,5]. Of note, language impairment is often underestimated [6]. Nevertheless, language deficits occur early in AD compared to other cognitive domains, and performance



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Copyright: © 2024 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https:// creativecommons.org/licenses/by/ 4.0/). on verbal fluency tasks serves as an important screening procedure and diagnostic criterion [7,8]. This language decline appears to be hierarchical in nature, with the language forms learned last in the sequence of language development deteriorating first [9]. Early stages are characterized by anomia [10], repetitions, and periphrasis; aphasic-like language occurs at later disease stages [11]. Semantic errors (e.g., difficulty finding the right word, poor vocabulary) are frequent [5,12], and semantic [13] and letter fluency [14] problems can be identified. The domain of syntax consists of acceptable sentences regarding simple, common, and automated forms, but grammatical and syntactic difficulties emerge in more complex structures at early stages [12,15]; sentence comprehension deficits vary with the degree of dementia severity [16]. At mild-to-moderate stages, morphosyntactic production and comprehension impairments are evident both on word [17,18] and sentence levels [19,20]. Finally, phonology is the most well-preserved language domain in AD [9], although the production of phonemic paraphasias and neologisms is not rare [21].

Neuropsychological assessment plays a critical role in characterizing cognitive and language deficits associated with AD [22]. Language is a multiscale system that we use to decode symbols (word, sign, or other forms of linguistic labels) to convey or comprehend a message, and to apply the appropriate grammatical and syntactical rules. However, the literature shows a close relationship between language brain networks and other aspects of cognition, suggesting a difficulty in assessing and treating it in isolation [23]. Clinicians can evaluate the elements of language function via conversational and spontaneous speech, naming exercises, comprehension tasks (such as giving specific commands to the patient), repetition, reading, and writing [24].

To date, many pharmacological therapies have been explored but have failed to achieve satisfactory outcomes regarding language and cognitive impairments [25]. Non-pharmacological strategies, however, have been found effective in improving or at least maintaining the concurrent level of handicap [26,27]. In greater detail, cognitive rehabilitation (including activities for language improvement), physical exercise, music therapy, behavioral and psychological interventions, occupational therapy, complementary and alternative medicine (such as acupuncture therapy), and new technologies (non-invasive brain stimulation, assistive technology and domotics, virtual reality, gaming, and telemedicine) have demonstrated respectable results [28,29].

It appears that most researchers have focused on cognitive interventions, which may or may not include language rehabilitation, and have involved patients with various types of dementia [30–33]. Notably, the most structured cognitive therapy programs emphasize on memory [34]. There is limited understanding of interventions specifically aiming to improve language and communication deficits in people with Alzheimer's disease (pwAD).

In view of the aforementioned gaps in the literature, we conducted a systematic review to summarize evidence from studies implementing language and communication interventions for pwAD. In particular, the present systematic review aimed to (a) explore the effectiveness of language and communication interventions on pwAD and (b) determine which language and cognitive skills benefit more from these interventions.

2. Materials and Methods

The current report followed the PRISMA guidelines for reporting systematic reviews (Appendix A) [35]. It was not pre-registered on an online database prior to its conduction. Each step of the process (literature search, study selection, data extraction, quality evaluation) was performed by two authors (N.D. and A.N.). Discrepancies were resolved by a third author (I.L.). Inter-rater reliability was not statistically established due to the lack of an exact number of items assessed—it was determined only with respect to quality evaluation. Among the 20 in total assessed items (5 per study, 4 studies) only one discrepancy was resolved by the third author. Nineteen in twenty items (95%) were scored similarly.

2.1. Search Strategy

An extensive literature search was conducted in PubMed, Google Scholar, and CEN-TRAL. The following search terms were used (entered as free words): (a) "language training" and "Alzheimer" and (b) "Alzheimer" and "language rehabilitation" and "communication training". The final literature search was performed on the 30 November 2023. The initial search yielded a total of 1.538 studies published up to 30 November 2023. In specific, 1296 studies were derived from PubMed, 120 studies from Google Scholar (search terms only in title), and 149 studies from CENTRAL.

2.2. Data Extraction

The following data were extracted from the retrieved studies: author, year of publication, number of participants, AD stage, targeted domains through the intervention, study design, outcome measures, duration and frequency of the intervention, and outcomes.

2.3. Eligibility Criteria

The following eligibility criteria were considered: (1) use of language and communication training, (2) inclusion of participants with AD -exclusively, (3) availability of pre- and post-intervention cognitive data, and (4) inclusion of at least 5 participants in the language rehabilitation arm. Studies were excluded if they: (1) lacked pre- or post-intervention cognitive data, (2) involved different kinds of interventions (e.g., physical training, cognitive training without language training, and so on), (3) included participants with other neurological conditions (e.g., stroke, Parkinson's), (4) were not original research articles (e.g., review articles, meta-analyses). Furthermore, language restriction criteria were applied; only articles published in English were considered for eligibility. Conclusions were based on randomized controlled studies (RCTs). Due to the small number of retrieved articles, the findings of observational studies are also narrated. Further information on the procedure of selection of eligible studies is presented in Figure 1 [35].

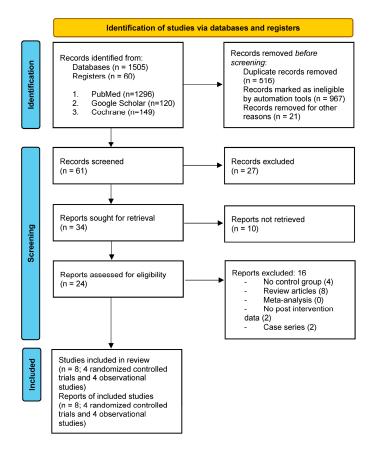


Figure 1. Prisma 2020 Flow Diagram.

2.4. Risk of Bias Assessment Tool

Risk of bias was assessed using the Risk of Bias (RoB) Cochrane tool for Systematic Reviews of interventions. Five methodological domains were appraised: (1) randomization process (allocation sequence generation, allocation concealment, baseline between group differences), (2) deviations from intended interventions (blinding of participants, blinding of personnel, appropriate analysis), (3) missing outcome data (data availability, reasons for missing data), (4) measurement of outcomes (method of measurement for both groups) and (5) selective reporting (prespecified protocol, multiple analyses). Each item was rated as of "low risk of bias", "high risk of bias", or "some concerns" based on methodological features and reporting of the retrieved studies (Figure 2).

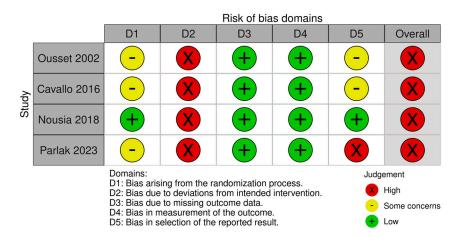


Figure 2. Risk of bias (RoB) of included studies [36–39].

3. Results

3.1. Study Characteristics

Study characteristics are in Table 1. One study was conducted in France [36], one in United Kingdom (UK) [40], two in Italy [37,41], one in Spain [42], one in Greece [38], one in India [43], and one in Turkey [39]. Sample sizes ranged from 8 to 80 participants: in total, 272 AD patients were included, 183 of which were in the "training group" (TG) and 89 were in the "control group" (CG).

Table 1. General information of the retrieved studies.

| Study | Country | Groups | Participants per Group | Intervention |
|---------------------------------------|-----------------|-----------------|--|---|
| Ousset et al. (2002) [36] | France | AD ¹ | 8 LT ² group 8 OT ³ group | (LT ²) Naming sessions presented on a computer |
| Noonan et al. (2012) [40] | United Kingdtom | AD ¹ | 8 | Naming sessions |
| Spitonelli et al. (2013) [41] | Italy | AD ¹ | 11 | Tasks were presented by either paper and pencil or by a computer |
| Cavallo et al. (2016) [37] | Italy | AD ¹ | 40 TG ⁴ 40 CG ⁵ | Rehabilitative software Brainer1 |
| Martínez-Moreno et al. (2016) [42] | Spain | AD ¹ | 60 | At the Outpatients Clinics in the Day Hospital (pen and paper tasks) |
| Nousia et al. (2018) [38] | Greece | AD ¹ | 25 TG ⁴ 25 CG ⁵ | 1st part = 30 min. computer-based intervention 2nd part = 30 min. exercises with paper and pencil |
| Bajpai et al. (2020) [43] | India | AD ¹ | 15 | AD 1 : tasks with a trained caregiver |
| Parlak et al. (2023) [39] | Turkey | AD ¹ | 16 TG ⁴ 16 CG ⁵ | Computer-supported application (software) at home |

 1 AD = Alzheimer's disease; 2 LT = Lexical Therapy; 3 OT = Occupational Therapy, 4 TG = training group; 5 CG = control group.

The patients' characteristics are in Table 2. TG included 183 individuals: 70 males and 105 females, while CG consisted of 89 participants: 30 males and 68 females [36–39,41–43]. The study by Noonan et al. [40] did not provide any information about the gender of the participants.

| Table 2. Den | nographics of | f study participant | ts of the retrieved | l studies. |
|--------------|---------------|---------------------|---------------------|------------|
|--------------|---------------|---------------------|---------------------|------------|

| Study | N ¹ | AD ² Type | Diagnostic Criteria | CDR ³ | GDS ⁴ Mean (±SD) | Gender (Males/Total) | Age in Years [Mean (SD ⁵)] | Education in Years [Mean (SD ⁵)] | Pharmacological Treatment |
|---|---|--|---|------------------|--------------------------------|-------------------------|--|--|--|
| Ousset et al. | 8 AD ² (LT ⁶) | Probable | NINCDS- | - | _ | 5/8 | 67.7 ± 12.9 | - | Cholinergic |
| (2002) [36] | 8 AD ² (OT ⁷) | AD ² | ADRDA ⁸ | | | 3/8 | 73.8 ± 7.5 | - | medication |
| Noonan et al. (2012) [40] | 8 AD ² | Probable AD ² | NINCDS- ADRDA ⁸ | - | - | - | - | - | - |
| Spironelli et al. (2013) [41] | 11 AD ² | Mild-to- moderate AD ² | NINCDS- ADRDA ⁸ | - | - | 2/11 | 78.18 (±4.99) Range = 70–88 | 7.54 (±3.59) | Anticolinesterasic drugs |
| Cavallo et al. | 40 AD ² (TG ⁹) | Early stage | NINCDS- | - | - | 13/40 | 76.50 ± 2.88 | 8.53 ± 3.00 | Acetylcholinesterase inhibitors (36/40) |
| (2016) [37] | 40 AD ² (CG ¹⁰) | - probable AD ² | ADRDA ⁸ | | | 16/40 | 76.33 ± 3.83 | 8.12 ± 2.79 | Acetylcholinesterase inhibitors (38/40) |
| Martínez- Morenoetal. (2016) [42] | 60 AD ² | Probable AD ² (mild stage) | NINCDS- ADRDA ⁸ | - | Mild stage | 25/60 | 75 ± 6.35 Range = 58–92 | $\begin{array}{c} Type \ 1 \ ^{11} = 37 \ (62\%) \\ Type \ 2 \ ^{12} = 13 \ (21\%) \\ Type \ 3 \ ^{13} = 7 \ (12\%) \\ Type \ 4 \ ^{14} = 1 \ (2\%) \\ Type \ 5 \ ^{15} = 0 \ (0\%) \\ Type \ 6 \ ^{16} = 2 \ (3\%) \end{array}$ | No ChEIs ¹⁷ = 27 (45%) ChEIs ¹⁷ = 33 (55%) |
| Nousia et al. | 25AD ² (TG ⁹) | Mild (early | NINCDS- | 1 | 2.40 (±1.61) | 9/25 | 76.24 (±5.14) | 8.08 (±3.01) | - |
| (2018) [38] | 25 AD ² (CG ¹⁰) | stage) AD ² | ADRDA ⁸ | 1 | 3.28 (±2.30) | 5/25 | 76.32 (±5.38) | 8.92 (±2.83) | - |
| Bajpai et al. (2020) [43] | 15 AD ² | Early AD ² | NINCDS ⁸ | 1 | ≤8 | 9/15 | 60–69: 4/15 (26.7%) 70–79: 7/15 (46.7%) 80–89: 4/15 (26.7%) | $\begin{array}{c} 0-5:\ 0/15\ (0.0\%)\\ 6-9:\ 1/15\ (6.7\%)\\ 10-12:\ 5/15\ (33.3\%)\\ \geq 13:\ 9/15\ (60.0\%) \end{array}$ | - |
| Parlak et al. | 16 AD ² (TG ⁹) | (TG ⁹) ^{6 moderate} , | _ | | 7/16 | 75.00 ± 6.38 | 3.19 ± 2.90 | Acetylcholinesterase | |
| (2023) [39] | 16 AD ² (CG ¹⁰) | 6 mild, 6 moderate, 4 severe | DSM-5 ¹⁸ & NIA-AA ¹⁹ | - | - | 6/16 | 74.63 ± 6.60 | 3.19 ± 2.31 | inhibitors for at least 3 months |

¹ N = Number; ² AD = Alzheimer's disease; ³ CDR = Clinical Dementia Rating; ⁴ GDS = Geriatric Depression Scale; ⁵ SD = Standard Deviation; ⁶ LT = Lexical Therapy; ⁷ OT = Occupational Therapy; ⁸ NINCDS-ADRDA = National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association; ⁹ TG = training group; ¹⁰ CG = control group; ¹¹ Type 1 = incomplete primary education; ¹² Type 2 = complete primary education; ¹³ Type 3 = secondary education; ¹⁴ Type 4 = vocational education and training; ¹⁵ Type 5 = undergraduate degree; ¹⁶ Type 6 = university degree (bachelor's degree); ¹⁷ ChEIs = cholinesterase inhibitors; ¹⁸ DSM-5 = Diagnostic and Statistical Manual for Mental Disorders, fifth edition; ¹⁹ NIA-AA = National Institute on Aging and Alzheimer's Association.

The age of the participants ranged from 58 to 92 years old. There were no significant differences in age and gender between the groups [36–41,43], except for the study conducted by Martinez-Moreno et al. [42]. Moreover, the formal education of the participants varied from 2 to \geq 13 years.

Six studies used the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS/ADRDA) criteria [36,38,40–43]. Cavallo et al. [37] provided no further information about the diagnostic process; in the study of Parlak et al. [39], the Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-5) and the Nationals' Institute on Aging and Alzheimer's Association (NIA-AA) criteria were fulfilled. The AD stage of the participants varied from mild to severe.

3.3. Intervention Characteristics

In all studies, participants underwent training programs that lasted for periods ranging from 5 to 48 weeks, with a frequency of sessions varying from 1 to 5 times per week (Table 3). The duration of each session ranged from 30 min to 2 h. Specifically, in the study of Bajpai et al. [43], participants had daily sessions (5 days/week) lasting 30–45 min, with a total intervention period of 8 weeks. In the study of Spironelli et al. [41], there were 4 sessions/week, lasting a total of 2 h, along with additional practice activities of daily living at home for a total of 5 weeks. Nousia et al. [38] included 2 sessions per week, with a total duration of 15 weeks, consisting of 60 min of multidomain intervention. Cavallo et al.'s [37] intervention consisted of 3 weekly 30 min sessions over a period of 12 weeks. Parlak et al. [39] conducted five 60-min sessions/week for 7 weeks. Martinez-Moreno et al.'s [42] study implemented a 1-year group program, with 2–3 weekly two-to-three-hour sessions. Lastly, Ousset et al. [36] provided 16 sessions, once a week, over a period of 5 months, lasting 45 min each, with a 2-week break in intervention between the 8th and 12th week.

Table 3. Summary of the procedural characteristics and quality of life findings of the retrieved studies.

| Study | Other Cognitive Domains | Language Domains | Duration of Sessions | Quality of Life |
|---------------------------------------|--|--|--|--|
| Ousset et al. (2002) [36] | - | Lexical Therapy (naming sessions) | 5 months—45 min/session (i) 8 sessions (one session per week) (ii) 2 weeks off (iii) 8 sessions (one session per week) | - |
| Noonan et al. (2012) [40] | - | Name relearning | 10 sessions (participants were seen twice a week over a period of 5 weeks), each lasting between 40 and 60 min | - |
| Spironelli et al. (2013) [41] | Spatial and temporal orientation, attention, memory, logic reasoning, praxis and arithmetic skill | Language | 2 h/day and 4 days/week for 5 weeks + daily living activities (answering a phone call and remembering the message, or reading the newspaper and commenting the news of the day) | The experience of working together encouraged the sens of responsibility of patients with higher cognitive functioning for supporting those with more severe deficits when all participants carried out different everyda activities and tasks |
| Cavallo et al. (2016) [37] | Memory, attention, executive function | Language | Three 30 min sessions per week, for 12 weeks | The comparison of patients' scores on the HADS ¹ did no show any statistically significant difference (anxiety patients' score = 7.65 ± 2.41 controls' score = 7.57 ± 1.33 depression: patients' score = 6.42 ± 2.21 , controls score = 6.35 ± 2.21) |
| Martínez-Moreno et al. (2016) [42] | Reality orientation, memory, executive functions, activities of daily living training | Language (1. discussing actual information of interest, 2. tasks involving reading, oral, and written comprehension and writting, 3. communication between participants) | 1 year group program (10–12 patients per group) of two to three weekly sessions (mean 115 sessions/year) of cognitive stimulation and occupational therapy of 2 or 3 h each | Functional capacity in the follow-up after the treatmen showed that Responders hav a better performance of IADL ² |
| Nousia et al. (2018) [38] | Episodic and delayed memory, attention, processing speed, and executive function | Morphology, syntax, semantics, naming, verbal fluency, and word recall | 15 weeks 2 days/week 60 min/session +extra cognitive and language tasks for practice at home, in a weekly basis | The training group had verbal positive feedbacl on daily activities and functional communication |
| Bajpai et al. (2020) [43] | Memory (picture recognition task) Attention (spot the differences task) | Verbal learning task | 3 tasks per day (30–45 min) for 8 weeks | - |
| Parlak et al. (2023) [39] | Orientation, reminiscence, executive functions, short-term memory, attention and visual spatial functions, communication board | Language (functional expressions, naming and and showing what is said) | 1 h each day for 3 days a week (app sections) and 30 min. each day for 2 days (reminiscence section) Total 5 days/week for 7 weeks | Statements from patients' caregivers regarding better functioning in everyday life |

¹ HADS = Hospital Anxiety and Depression Scale; ² IADL = Instrumental Activities of Daily Living.

The participants performed the sessions either individually [36–39,41,43], within groups [42], or both [38]. In 4 out of 8 studies, tasks were developed and performed with computer aid [36,37,39,41]. Two studies used paper-pencil training [42,43]. In the study of Nousia et al. [38], the intervention was performed using both computer aid and paper-pencil means, while Noonan et al. [40] did not provide further information about the means of training. In the study of Bajpai et al. [43], caregivers were trained to perform the training using paper and pencil.

3.4. Language and Cognitive Domains Targeted

Most of the studies focus on the training of more than one cognitive domain [37–39,41–43]. Specifically, apart from language, the main functions these studies tried to enhance were memory, attention, and executive functions. There are two studies, however, that solely targeted language [36,40]. In particular, Noonan et al. [40] aimed to improve patients' name relearning, and Ousset et al. [36] conducted a lexical therapy with naming sessions.

Regarding outcome assessment, participants in five studies [37,38,40–42] completed screening cognitive tests (Mini-Mental State Examination, Trail-making test A and B, digit forward and backward span, etc.). The language domain was assessed through naming tasks (such as the Boston Naming Test) and semantic or phonological fluency tasks. Only one study [39] included a more detailed language evaluation; the Language Assessment Test for Aphasia (LATA) investigated speech fluency, auditory comprehension, repetition, naming, reading, grammar, word actions, and writing. Although most studies based the reported improvement in patients' performance on specific neuropsychological tests, Bajpai et al. [43] measured the difference in reaction time before and after intervention in order to infer the positive effect of training on memory, attention, and language domains. Similarly, Ousset et al. [36] measured participants' naming hits and errors. Detailed outcomes are provided in Table 4.

Four out of eight studies [36–39] can be characterized as randomized controlled trials (RCT). In the study of Ousset et al. [36], seven out of eight patients in the study group demonstrated improved performance on naming post-therapy. The second RCT [37] revealed that the training group performed significantly better on the digit span-forward, digit span-backward, two-syllable words repetition test, Rivermead Behavioral Memory Test (RBMT)-story immediate, RBMT-story delayed, Token test and Brixton test compared to the control group. These improvements were sustained for at least 6 months after training. The third RCT [38] demonstrated better results for the patients who underwent the intervention in all cognitive domains. Specifically, improvements were noted in delayed memory, visuospatial abilities, executive functions, working memory, naming, semantic fluency, and attention/processing speed, whereas milder improvements in recall and recognition was also noticed. Finally, Parlak et al. [39] observed that their intervention was effective in improving speech fluency and auditory comprehension for mild and moderate AD, grammar for all stages, and repetition and speech act skills for moderate AD. In addition, the mean Language Assessment Test for Aphasia (LATA) and Mini Mental State Examination (MMSE) scores of the study group were increased.

The four observational studies [40–43] provide supporting evidence regarding the effectiveness of language and cognitive training, as well. More specifically, Bajpai et al. [43] demonstrated improvement in practiced tasks, especially in the domains of episodic and semantic memory. In the study by Martínez-Moreno et al. [42], 51.7% of patients classified as responders exhibited better performance on global cognitive performance, orientation, and executive function compared to non-responders, whereas all participants showed improvement in spatial orientation abilities. Noonan et al. [40] showed that both errorless and errorful learning can benefit the naming ability of pwAD. On the contrary, participants in Spironelli et al.'s [41] study did not show significant changes in neuropsychological tests after cognitive training.

| Table 4. Detailed results. |
|----------------------------|
|----------------------------|

| Study | Outcome Measures | | | p Value | | | | <i>p</i> Value |
|----------------------------------|--|--------------------------------|--------------------------------|---------|-----------------------|-----------------------|--------------|----------------|
| | | LT group (n | nean \pm SD) | | OT | group (mean \pm SD) | | |
| | Naming Hits | Pre | Post | | | Pre | Post | |
| | Narrative LT items | 31.6 ± 3.7 | 33.6 ± 3.1 | | Narrative LT items | 32.5 ± 2.8 | 31.4 ± 2.9 | |
| | LT items | 30.1 ± 3.2 | 31.7 ± 4 | | LT i tems | 28.1 ± 4 | 28.9 ± 3.5 | |
| Ousset et al. (2002) [36] | External items | 22.9 ± 6.1 | 24.6 ± 8 | | External items | 23.7 ± 3.5 | 21.9 ± 4.9 | |
| | Naming Errors | Pre | Post | | | Pre | Post | |
| | Absence of production | 14.7 ± 8.1 | 13.6 ± 8.3 | | Absence of production | 16.7 ± 7 | 20.5 ± 7.3 | |
| | Semantic errors | 14.6 ± 5.1 | 9.9 ± 4.8 | | Semantic errors | 11.7 ± 5.1 | 12.4 ± 4.6 | |
| | Perceptual errors | 6 ± 4.3 | 6.5 ± 7.3 | | Perceptual errors | 6.6 ± 4.1 | 5.1 ± 3.8 | |
| | | Week 1 post-therapy | | | Week 5 post-therapy | | | |
| | Picture version of the Pyramids and Palm Trees Test | r = 0.81, p = 0.01 | | | | | | |
| | Boston Naming Test | r = 0.67, p = 0.071 | | | | | | |
| | 100-item naming test | r = 0.67, p = 0.066 | | | r = 0.68, p = 0.062 | | | |
| Noonan et al. (2012) [40] | 64-item word-picture matching task | | | | r = 0.65, p = 0.076 | | | |
| | Forward digit span | r = 0.69, p = 0.057 | | | | | | |
| | Camden Recognition Memory for Faces Test | r = 0.62, p = 0.09 | | | | | | |
| | Elevator Counting with Distraction | | | | r = -0.7, p = 0.077 | | | |
| | | Pre-treatment | Post-treatment | | | | | |
| | MMSE | 22.09 ± 0.58 | 21.73 ± 0.69 | | | | | |
| | MODA | 76.26 ± 1.85 | 77.62 ± 1.98 | | | | | |
| | ENB-2: M. I10 s | 2.45 | 2.82 | | | | | |
| | ENB-2: S.RI. | 4.64 | 5.09 | | | | | |
| Spironelli et al. (2013) [41] | ENB-2: Abs. | 3.45 | 4.18 | 0.05 | | | | |
| (2013) [41] | ENB-2: Flu. | 7.64 | 8.40 | | | | | |
| | ENB-2: Over. Figure | 17.09 | 17.36 | | | | | |
| | RTs for LF words | $921.02\pm56.94~\mathrm{ms}$ | $1062.85 \pm 67.34 \ {\rm ms}$ | | | | | |
| | RTs for HF words | $845.69\pm48.54~\mathrm{ms}$ | $973.00\pm59.80~\mathrm{ms}$ | | | | | |
| | RTs | $1008.83 \pm 73.17 \text{ ms}$ | $757.88 \pm 48.78 \text{ ms}$ | <0.1 | | | | |

| Table 4. | Cont |
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| Study | Outcome Measures | | | p Value | | | <i>p</i> Value |
|------------------------|-----------------------------------|----------------------------|--------------------------------------|---------|---|--------------------------------------|----------------|
| | | TG Pre (mean \pm SD) | TG 6-month follow up (mean \pm SD) | | CG Pre (mean \pm SD) | CG 6-month follow up (mean \pm SD) | |
| | MMSE | 22.65 ± 1.74 | 22.32 ± 0.97 | | 23.05 ± 2.44 | 22.64 ± 0.96 | |
| | DSF | 4.85 ± 1.60 | 5.95 ± 1.80 | | 5.20 ± 1.85 | 5.18 ± 1.82 | |
| | DSB | 3.20 ± 1.26 | 5.78 ± 1.44 | | 4.10 ± 0.63 | 4.02 ± 0.88 | |
| | Two-syllables word test | 4.80 ± 1.72 | 6.14 ± 1.42 | | 6.00 ± 2.15 | 5.05 ± 2.15 | |
| | RBMT (standardized profile score) | 8.60 ± 1.12 | 8.60 ± 1.12 | | 8.80 ± 1.36 | 8.80 ± 1.36 | |
| | RBMT (story immediate) | 6.72 ± 1.09 | 8.72 ± 1.24 | | 7.04 ± 1.66 | 6.00 ± 1.41 | |
| Cavallo et al. | RBMT (story delayed) | 5.35 ± 1.73 | 6.35 ± 1.73 | | 6.52 ± 1.66 | 4.52 ± 1.44 | |
| (2016) [37] | GNT | 21.95 ± 2.57 | 22.04 ± 2.53 | | 22.15 ± 2.17 | 22.18 ± 2.27 | |
| | Token test | 30.30 ± 2.42 | 32.30 ± 2.42 | | 30.69 ± 2.10 | 27.69 ± 2.10 | |
| | VOSP (object decision) | 18.20 ± 0.72 | 18.25 ± 0.93 | | 18.42 ± 0.81 | 18.45 ± 0.81 | |
| | VOSP (position discrimination) | 19.22 ± 0.70 | 19.15 ± 0.74 | | 19.29 ± 0.72 | 19.22 ± 0.70 | |
| | VOSP (number location) | 8.87 ± 0.69 | 8.85 ± 0.58 | | 9.00 ± 0.68 | 9.02 ± 0.62 | |
| | Verbal fluency (letters) | 35.88 ± 2.66 | 36.57 ± 2.46 | | 36.52 ± 2.45 | 37.35 ± 2.26 | |
| | Verbal fluency (category) | 17.10 ± 1.88 | 16.27 ± 1.71 | | 17.27 ± 1.76 | 15.95 ± 1.60 | |
| | Hayling test (overall score) | 5.82 ± 1.24 | 5.42 ± 0.98 | | 5.95 ± 1.15 | 5.37 ± 0.86 | |
| | Brixton test | 4.95 ± 0.85 | 5.95 ± 1.34 | | 5.22 ± 1.32 | 3.82 ± 1.65 | |
| | | $ m R-Pre$ (mean \pm SD) | NR-Pre (mean \pm SD) | | $\begin{array}{c} \text{R-Post} \\ (\text{mean} \pm \text{SD}) \end{array}$ | NR-Post (mean ± SD) | |
| | Person orientation | 55.76 ± 15.31 | 49.04 ± 18.92 | 0.16 | 54.55 ± 16.71 | 46.66 ± 18.18 | 0.086 |
| | Space orientation | 46.52 ± 17.02 | 41.76 ± 18.16 | 0.33 | 58.29 ± 13.99 | 52.28 ± 19.67 | 0.18 |
| | Time orientation | 32.03 ± 16.25 | 36 ± 19.04 | 0.41 | 40.52 ± 20.26 | 28.31 ± 18.40 | 0.018 |
| lartínez-Moreno et al. | DSF | 49.87 ± 10.12 | 43.64 ± 8.7 | 0.015 | 47.06 ± 9.38 | 43.81 ± 8.06 | 0.17 |
| (2016) [42] | DSB | 46.97 ± 8.99 | 40.52 ± 10.99 | 0.018 | 46.17 ± 8.89 | 43.73 ± 9.9 | 0.34 |
| | List learning | 27.65 ± 10.86 | 24.48 ± 9.9 | 0.28 | 29.24 ± 11.38 | 26.72 ± 11.86 | 0.45 |
| | Story memory | 24.44 ± 10.47 | 19.04 ± 8.23 | 0.048 | 23.16 ± 12.13 | 19.72 ± 9.37 | 0.27 |
| | List learning free recall | 19.64 ± 13.31 | 19.08 ± 13.68 | 0.88 | 16.32 ± 13.23 | 17.26 ± 14.33 | 0.81 |
| | List learning recognition | 19.04 ± 9.45 | 15.88 ± 8.92 | 0.23 | 21.16 ± 14.63 | 19.44 ± 11.93 | 0.65 |

| | Table 4. Cont. | | | | | | | |
|---------------------------|-------------------------|--------------------------|---------------------------|----------------|--------------------|-------------------|----------------|--------------------------------------|
| Study | Outcome Measures | | | p Value | | | | <i>p</i> Value |
| | Story free recall | 14.96 ± 7.58 | 16.20 ± 8.82 | 0.60 | 17 ± 9.48 | 16.04 ± 8.89 | | 0.72 |
| _ | Figure free recall | 27.96 ± 13.68 | 22.20 ± 12.92 | 0.13 | 25.76 ± 15.65 | 22.04 ± 14.88 | | 0.40 |
| | Visuoverbal naming | 41.76 ± 16.71 | 31.81 ± 15.95 | 0.027 | 39.48 ± 14.82 | 31.13 ± 15.07 | | 0.056 |
| Martínez-Moreno et al. | Constructional praxis | 47 ± 16.31 | 40.75 ± 17.45 | 0.20 | 47.96 ± 14.64 | 40.42 ± 17.45 | | 0.11 |
| (2016) [42] | Category evocation | 37.59 ± 9.99 | 32.12 ± 9.78 | 0.1 | 36.79 ± 10.65 | 30.81 ± 10.96 | | 0.045 |
| | MMSE | 22.84 ± 3.37 | 22.79 ± 4.4 | 0.96 | 25.23 ± 3.22 | 20 ± 4.38 | | 0.001 |
| | BI | 95.97 ± 3.96 | 93.97 ± 7.24 | 0.19 | 92.58 ± 7.29 | 89.66 ± 9.06 | | 0.17 |
| | IADL | 5.13 ± 1.67 | 4.52 ± 1.92 | 0.19 | 4.68 ± 1.49 | 3.72 ± 1.96 | | 0.038 |
| | | TG—pre | TG—post | <i>p</i> value | CG—pre | CG—post | <i>p</i> value | <i>p</i> value (TG post- CG post) |
| | Recall | 17.44 ± 3.66 | 18.16 ± 3.48 | 0.151 | 16.60 ± 3.26 | 16.20 ± 2.45 | 0.33 | 0.887 |
| | Delayed memory | 0.16 ± 0.37 | 1.20 ± 1.08 | ≤0.001 | 0.40 ± 0.50 | 0.12 ± 0.33 | 0.08 | ≤0.001 |
| | Word recognition | 18.08 ± 1.32 | 18.68 ± 1.28 | 0.028 | 18.40 ± 1.25 | 17.96 ± 1.48 | 0.20 | 0.008 |
| Nousia et al. | BNT | 11.84 ± 1.57 | 13.40 ± 1.04 | ≤ 0.001 | 11.64 ± 1.32 | 11.40 ± 1.30 | 0.22 | ≤ 0.001 |
| (2018) [38] | SF | 22.12 ± 6.05 | 28.16 ± 6.08 | ≤ 0.001 | 23.36 ± 7.44 | 22.16 ± 6.31 | 0.13 | ≤0.001 |
| _ | CDT | 8.96 ± 2.22 | 10.28 ± 2.59 | 0.01 | 9.72 ± 1.93 | 9.52 ± 1.36 | 0.24 | ≤ 0.001 |
| | DSF | 5.48 ± 0.71 | 6.60 ± 1.35 | ≤ 0.001 | 5.04 ± 0.93 | 4.88 ± 1.13 | 0.35 | ≤ 0.001 |
| | DSB | 3.68 ± 0.75 | 4.32 ± 0.75 | 0.001 | 3.36 ± 0.81 | 3.32 ± 0.98 | 0.80 | 0.004 |
| | TMT A | 177.24 ± 45.88 | 151.80 ± 39.48 | ≤ 0.001 | 177.56 ± 56.02 | 210.16 ± 66.58 | 0.01 | ≤0.001 |
| _ | TMT B | 300 ± 00.00 | 290.60 ± 24.67 | 0.017 | 297.84 ± 10.80 | 299.00 ± 5.00 | 0.32 | 0.003 |
| | | Week 1 | Week 8 | | | | | |
| | Memory | $48.5\pm22.9~\mathrm{s}$ | $60.5\pm21.8~\mathrm{s}$ | | | | | |
| Bajpai et al. (2020) [43] | Attention | $216.6\pm78.2~\text{s}$ | $286.8\pm87.0~\mathrm{s}$ | | | | | |
| | Language | $211.8\pm68.4s$ | $270.4\pm104.9\mathrm{s}$ | | | | | |

Table 4. Cont.

| | - | - |
|-------|----|-------|
| Table | 4. | Cont. |

| Study | Outcome Measures | | | p Value | | | | p Value |
|------------------------------|---------------------------|------------------------|-------------------------|---------------------------------|------------------------|-------------------------|---------------------------------|--------------------------------|
| | | TG pre (mean \pm SD) | TG post (mean \pm SD) | <i>p</i> value (TG pre-TG post) | CG pre (mean \pm SD) | CG post (mean \pm SD) | <i>p</i> value (GG pre-CG post) | <i>p</i> value (TG -CG post |
| | MMSE | | | | | | | |
| | Orientation | 5.19 ± 1.97 | 6.81 ± 2.48 | < 0.001 | 4.56 ± 2.15 | 4.25 ± 2.11 | 0.096 | 0.004 |
| | Registration | 2.50 ± 0.89 | 2.81 ± 0.54 | 0.136 | 2.38 ± 1.08 | 2.69 ± 0.60 | 0.173 | 0.542 |
| | Attention and Calculation | 1.81 ± 1.90 | 2.50 ± 2.36 | 0.007 | 2.75 ± 1.98 | 2.25 ± 1.94 | 0.015 | 0.747 |
| | Recall | 0.20 ± 0.41 | 0.20 ± 0.41 | 1.000 | 0.25 ± 0.57 | 0.13 ± 0.50 | 0.164 | 0.654 |
| | Language | 5.69 ± 2.024 | 7.25 ± 1.06 | 0.001 | 6.19 ± 1.37 | 6.00 ± 1.50 | 0.383 | 0.011 |
| | Total | 15.38 ± 5.80 | 19.56 ± 5.76 | < 0.001 | 16.13 ± 5.65 | 15.19 ± 5.46 | 0.055 | 0.035 |
| Parlak et al. (2023) [39] | LATA | | | | | | | |
| (2023) [39] | Speech fluency | 23.69 ± 5.33 | 26.06 ± 4.69 | < 0.001 | 24.38 ± 7.38 | 22.81 ± 7.54 | 0.001 | 0.154 |
| | Auditory comprehension | 43.81 ± 17.10 | 52.81 ± 14.88 | < 0.001 | 44.88 ± 13.58 | 44.31 ± 11.97 | 0.771 | 0.085 |
| | Repetition | 13.38 ± 4.74 | 16.00 ± 4.14 | 0.001 | 14.81 ± 4.94 | 13.56 ± 3.03 | 0.083 | 0.067 |
| | Naming | 34.44 ± 11.62 | 37.38 ± 9.59 | 0.009 | 33.25 ± 8.50 | 32.63 ± 7.88 | 0.574 | 0.136 |
| | Reading | 31.36 ± 13.60 | 34.73 ± 13.52 | 0.007 | 32.91 ± 14.50 | 30.82 ± 15.05 | 0.006 | 0.529 |
| | Grammar | 12.25 ± 4.83 | 15.06 ± 5.06 | < 0.001 | 11.56 ± 5.27 | 10.31 ± 3.96 | 0.091 | 0.006 |
| | Word actions | 15.50 ± 5.06 | 17.69 ± 4.42 | < 0.001 | 16.00 ± 4.39 | 15.13 ± 3.96 | 0.084 | 0.095 |
| | Writing | 22.73 ± 16.52 | 25.73 ± 15.08 | 0.081 | 25.00 ± 14.58 | 24.73 ± 14.67 | 0.341 | 0.876 |
| | Total | 198.63 ± 76.11 | 223.18 ± 70.43 | 0.001 | 211.72 ± 68.83 | 203.54 ± 58.59 | 0.210 | 0.485 |
| | | | | | | | | |

LT = Lexical Therapy; SD = Standard Deviation; OT = Occupational Therapy; EL = Errorless Learning; EF = Errorful Learning; AD = Alzheimer's Disease; MMSE = Mini Mental State Examination; MODA = Milan Overall Dementia Assessment; ENB-2 = EsameNeuropsicologico Breve-2; M.I.-10 s = memory with interference-10 s; S.R.-I. = story recall-immediate; Abs. = abstract verbal reasoning; Flu. = phonemic verbal fluency; Over. Figure = overlapping figure test; RTs = response times; LF = low frequency; HF = high frequency; ms = milliseconds; TG = Training Group; CG = Control Group; DSF = digit span forward; DSB = digit span backward; RBMT = Rivermead Behavioral Memory Test; GNT = Graded Naming Test; VOSP = Visual Object and Space Perception battery; R = Responders after treatment; NR = Non Responders after treatment; BI = Barthel Index; IADL = Instrumental Activities of Daily Living; BNT = Boston Naming Test; SF = Semantic Fluency; CDT = Clock-drawing test; TMT A = trail-making test A; TMT B = trail-making test B; s = seconds; LATA = Language Assessment Test for Aphasia.

Only two studies [37,40] investigated the duration of the training outcome by exploring its effects five weeks and six months after the completion of the intervention, respectively. Noonan et al. (2012) [40] found only borderline significant correlations between overall relearning scores and the 100-item naming test, the 64-item word–picture matching task and Elevator Counting with Distraction from the Test of Everyday Attention. On the contrary, Cavallo et al. (2016) [37] concluded that patients in TG showed a better performance in comparison to CG on digit span-forward, digit span-backward, two-syllable words repetition test, RBMT-story immediate, RBMT-story delayed, Token test and Brixton test, exactly as observed at the post-treatment assessment.

3.5. Noncognitive Outcomes: Quality of Life Outcome Measures

More than half of the aforementioned studies, in addition to assessing language and cognitive domains, also evaluated the potential impact of training on patients' quality of life and psychological status. Two studies [37,42] used specialized tests, such as the Instrumental Activities of Daily Living (IADL) and the Hospital Anxiety and Depression Scale (HADS), whereas the other three [38,39,41] relied on subjective statements from caregivers (Table 3).

Among these studies, three were RCT [37–39]. The latter two [38,39] revealed promising outcomes based on patients' verbal feedback after the completion of the intervention. On the contrary, Cavallo et al. [37] compared patients' scores on the HADS before and after treatment and did not find any statistically significant difference. In the other two studies, participants described as responders in Martínez-Moreno et al.'s study [42] showed a better performance in IADL after treatment, whereas in Spironelli et al.'s study [41] treatment helped participants to develop a sense of support towards those with more severe deficits.

4. Discussion

The enhancement of patients' language skills is vital, given that the loss or impairment of communication ability affects not only patients but also their caregivers and relatives [26,44], leading to a profound deterioration in patients' quality of life [45]. Apart from the psychological burden, families and caregivers have to contend with enormous healthcare expenses [46]. The yearly worldwide cost of dementia is estimated at \$1.3 trillion [47]. Thus, accurate and prompt intervention is of utmost importance [48,49].

The examination of the retrieved studies revealed considerable benefits from language rehabilitation alone, as well as in combination with other cognitive tasks. The studies that showed greater improvements were those that implemented holistic language-cognitive intervention programs. In particular, training groups in the studies conducted by Cavallo et al. [37], Martínez-Moreno et al. [42], Nousia et al. [38], and Parlak et al. [39] demonstrated better outcomes on various assessment tools evaluating both language and cognitive domains. The other two surveys [41,43] showed fewer substantial results; the first one concluded that pwAD demonstrated improved mean time in the tasks, and the second one found that patients' performance improved significantly only in abstraction and phonemic fluency subtests. In addition, an interaction effect appears to be present in the study by Bajpai et al. [43]. On the other hand, two of the studies that applied pure language intervention [36,40] examined the performance solely on naming tasks. Of note, only four studies were RCTs [36–39]. Of these, only one [36] consisted of pure language treatment, whereas the others included both language and cognitive interventions. As a result, it is risky to draw conclusions based only on the RCTs.

To the best of our knowledge, the present review is the first to focus on the impact of specific language and communication interventions on the overall language profile, cognitive status, and quality of life of pwAD. Our findings are in agreement with those of Morello et al.'s study [50], which examined the effects of non-pharmacological interventions in pwAD and found that lexical-semantic approaches and treatments targeting various cognitive domains (including language) appear effective. This study, however, does not exclusively focus on language restoration but it also includes interventions that combine language with physical activities, various conversational techniques, and communicative training of caregivers. Other systematic reviews have investigated the effect of cognitive rehabilitation, which also includes language interventions in some cases, but they do not exclusively involve pwAD. Instead, the population in these studies consisted of pwAD and other types of dementia or mild cognitive impairment (MCI) [30,33,51–53].

The limited evidence regarding exclusive language rehabilitation may result from the fact that most studies do not focus on language interventions and do not compare language with global cognitive intervention. Future studies should be conducted with a focus on exclusive language rehabilitation and the comparison between language and cognitive treatment techniques.

Additional limitations need to be acknowledged. These limitations stem, mainly, from the heterogeneity among studies. A methodological limitation is the fact that the participants in all the included surveys, except for one, were patients with mild AD. Future studies should organize the presentation of their findings based on dementia type (i.e., Alzheimer's disease, vascular dementia, etc.) and the severity of the disease (i.e., mild, moderate, or severe) to reflect the clinical importance of potential benefits at each stage of severity. In addition, future surveys should give prominence to language interventions with longer durations and follow-up evaluations. Finally, some selected articles included only a few patients, and none of them adhered to an optimum methodological quality with blinding procedures.

Moreover, significant inconsistencies are apparent regarding the evaluation tools used in the analyzed articles. Language evaluation should be conducted with batteries that have good psychometric properties and can investigate various aspects of language and communication difficulties that pwAD experience frequently. According to recent data [54] such tools are the Arizona Battery for Cognitive-Communication Disorders (ABCD) [55], the Sydney Language Battery (SydBat) [56], and the Addenbrooke's Cognitive Examination (ACE-III) [57]. Nevertheless, this review includes studies that evaluate language outcomes with other tools that assess various cognitive domains, including language in general. Moreover, as discussed above, language evaluation cannot completely exclude other cognitive domains, such as memory, due to the strong connection between language and cognitive brain networks [23].

5. Conclusions

In conclusion, the present systematic review revealed a significant positive effect of the combination of language and cognitive intervention in both language and cognitive domains. On the other hand, pure language interventions showed improvement only in language tasks. In respect to the possible improvement of the quality of patients' life, the evidence are weak or subjective, often relying on statements from patients' caregivers.

Considering these findings, the inclusion of language and communication training (either alone or in combination with cognitive training) is recommended for healthcare practitioners to enhance their patients' neuropsychological function, thereby improving their quality of life.

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Conflicts of Interest: The authors declare no conflicts of interest.

| Section and Topic | Item # | Checklis Titem | Location WHere, Item Is Reported |
|-------------------------------|--------|--|----------------------------------|
| Title | | | , sepone |
| Title | 1 | Identify the report as a systematic review. | 1 |
| Abstract | | | |
| Abstract | 2 | See the PRISMA 2020 for Abstracts checklist. | 1 |
| Introduction | | | |
| Rationale | 3 | Describe the rationale for the review in the context of existing knowledge. | 2, 3 |
| Objectives | 4 | Provide an explicit statement of the objective(s) or question(s) the review addresses. | 3, 4 |
| Methods | | | |
| Eligibility criteria | 5 | Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses. | 4, 5 |
| Information sources | 6 | Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted. | 4,5 |
| Search strategy | 7 | Present the full search strategies for all databases, registers and websites, including any filters and limits used. | 5 |
| Selection process | 8 | Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process. | 4, 5 |
| Data collection process | 9 | Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process. | 4 |
| Data items | 10a | List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g., for all measures, time points, analyses), and if not, the methods used to decide which results to collect. | NA |
| | 10b | List and define all other variables for which data were sought (e.g., participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information. | NA |
| Study risk of bias assessment | 11 | Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process. | 6 |
| Effect measures | 12 | Specify for each outcome the effect measure(s) (e.g., risk ratio, mean difference) used in the synthesis or presentation of results. | NA |
| | 13a | Describe the processes used to decide which studies were eligible for each synthesis (e.g., tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)). | 2 |
| | 13b | Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions. | NA |
| Synthesis methods | 13c | Describe any methods used to tabulate or visually display results of individual studies and syntheses. | NA |
| | 13d | Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used. | NA |
| | 13e | Describe any methods used to explore possible causes of heterogeneity among study results (e.g., subgroup analysis, meta-regression). | NA |
| | 13f | Describe any sensitivity analyses conducted to assess robustness of the synthesized results. | NA |
| Reporting bias assessment | 14 | Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases). | NA |
| Certainty assessment | 15 | Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome. | 6 |

Appendix A. PRISMA Guidelines

| Results | | | |
|--|-----|---|-------|
| Study selection | 16a | Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram. | 4, 5 |
| | 16b | Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded. | NA |
| Study characteristics | 17 | Cite each included study and present its characteristics. | 6, 7 |
| Risk of bias in studies | 18 | Present assessments of risk of bias for each included study. | 6 |
| Results of individual studies | 19 | For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g., confidence/credible interval), ideally using structured tables or plots. | 10–19 |
| Results of syntheses | 20a | For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies. | NA |
| | 20b | Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g., confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect. | NA |
| | 20c | Present results of all investigations of possible causes of heterogeneity among study results. | NA |
| | 20d | Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results. | NA |
| Reporting biases | 21 | Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed. | NA |
| Certainty of evidence | 22 | Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed. | 15–19 |
| Discussion | | | |
| Discussion | 23a | Provide a general interpretation of the results in the context of other evidence. | 16 |
| | 23b | Discuss any limitations of the evidence included in the review. | 16 |
| | 23c | Discuss any limitations of the review processes used. | 16 |
| | 23d | Discuss implications of the results for practice, policy, and future research. | 16 |
| Other Information | | | |
| Registration and protocol | 24a | Provide registration information for the review, including register name and registration number, or state that the review was not registered. | NA |
| | 24b | Indicate where the review protocol can be accessed, or state that a protocol was not prepared. | NA |
| | 24c | Describe and explain any amendments to information provided at registration or in the protocol. | NA |
| Support | 25 | Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review. | 22 |
| Competing interests | 26 | Declare any competing interests of review authors. | 22 |
| Availability of data, code and other materials | 27 | Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review. | NA |

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