Leveraging mHealth and Virtual Reality to Improve Cognition for Alzheimer’s Patients: A Systematic Review

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Abstract: Background: Alzheimer’s Disease (AD) is a global problem affecting 58 million people, expected to reach a prevalence of 88 million people by 2050. The disease affects the brain, memory, cognition, language, and motor movement. Many interventions have sought to improve memory and cognition. mHealth and virtual reality (VR) are two such interventions. Objectives: To analyze studies from the last 10 years with older adults with AD to ascertain the effectiveness of telehealth techniques such as mHealth and VR for memory care. Methods: In accordance with the Kruse Protocol and reported in accordance with PRISMA 2020, five reviewers searched four research databases (PubMed, CINAHL, Web of Science, and ScienceDirect) on 3 August 2022 for studies with strong methodologies that fit the objective statement. Results: Twenty-two studies from 13 countries were analyzed for trends. Four interventions (mHealth/eHealth, VR, mHealth + VR, game console, and telephone) used RCT, quasi-experimental, pre-post, observational, and mixed methods. These interventions improved cognition, memory, brain activity, language, depression, attention, vitality, quality of life, cortical atrophy, cerebral blood flow, neuroplasticity, and mental health. Only three interventions reported either no improvements or no statistically significant improvements. Cost, time, training, and low reimbursement were barriers to the adoption of these interventions. Conclusion: mHealth and VR offer interventions with positive effectiveness for memory care for AD. The long-term effect of this improvement is unclear. Additional research is needed in this area to establish clinical practice guidelines.

Keywords: mHealth; Alzheimer’s Disease; memory care

1. Introduction
1.1. Rationale

Alzheimer’s Disease (AD) is a growing condition around the world. As we approached the COVID-19 pandemic, AD was the largest killer of older adults: it kills more people than breast cancer and prostate cancer [1]. The prevalence of the disease was calculated in 2021 to be 58 million people, but it is predicted to exceed 88 million by 2050 [1]. Of the dementia population, AD accounts for about 2/3s [1]. There is currently no cure for AD, and there are only about 10 pharmaceuticals approved to manage the condition. The disease creates plaque on the brain (tau) that eventually affects the communication of 100 billion neurons in the brain, degrading and ultimately destroying these neurons [2]. Early stages of AD is seen as simple forgetfulness of recently learned facts, but late stages of AD affects speech, motor skills, and long-term memory [1]. Researchers and practitioners do not fully understand the etiology and pathogenesis of AD: we can treat the symptoms, but we cannot prevent or cure the disease [3–5]. Researchers have searched for decades for interventions to improve symptoms of cognitive decline, and one of these is cognitive training through telemedicine.

Many tests are used to assess impairment and symptoms associated with AD. AD affects cognition, which is a complex process in the brain that involves memory, abstraction and iconic concepts, mental operations, consciousness, search strategies, problem solving,
and social context [6]. One common method to measure cognition is the mini-mental state examination (MMSE), which estimates a severity of cognitive impairment through a series of questions organized into seven categories: orientation to time, orientation to place, registration of three words, attention to calculation, recall of three words, language, and visual construction [7]. Given over time, the MMSE can identify rate of decline or document improvement.

Telemedicine is defined as healing from a distance using information communication technology to overcome geographical boundaries and increase health outcomes [8]. mHealth is a subset of telemedicine that leverages mobile technology to deliver some sort of intervention or interaction with a provider. mHealth interventions with patients who have AD suffer from barriers such as cognition, perception, physical ability, frame of mind, speech and language [9]. mHealth design must break steps into very simple, easy to understand modules, must often repeat instructions to keep the attention of the users, and use simple memory tests to avoid overwhelming the user [10]. mHealth has been coupled with other interventions such as transcranial alternating current during cognitive training, but results are not conclusive [11]. Virtual reality (VR) has also entered the area of AD research, specifically in the area of cognitive training. The reason is that VR exercises multiple perception components of psychophysics (visual, tactile, and kinesthetic perceptual sensations) [12]. The proponents of VR like its immersive and adaptable environment. It has been used in the areas of brain damage, poststroke intervention, musculoskeletal recovery, and in cognitive training for AD. This review will focus on the telemedicine-related interventions (mHealth, VR, and serious games) in the area of memory for AD patients. Multiple systematic literature reviews have examined this interaction. Many conclude that telemedicine can assess cognition, monitor activity, and improve communication with provider teams [13]. Telemedicine can positively affect mood, function, and quality of life, but its effect on cognition is unclear [14].

A systematic literature review and meta-analysis was published in 2022 that analyzed 16 Randomized Controlled Trials (RCTs) [15]. The meta-analysis focused on a smaller set of studies. It found that serious games are as effective as no intervention or passive interventions at improving executive functions. It concluded that conventional exercises were just as effective. The reviewers felt their group for analysis was too small for final conclusions.

A systematic literature review was published in 2022 that analyzed 28 studies over 10 years [9]. It evaluated several aspects of mHealth. It found positive perceptions of the users of mHealth (both AD patients and their caregivers). The caregivers attributed positive effect of mHealth interventions on their physical and mental health; however, effectiveness was not evaluated.

1.2. Objectives

The purpose of this review is to analyze the effectiveness of telemedicine-related interventions (mHealth, VR, and serious games) to improve cognition for older adults suffering from Alzheimer’s Disease or mild cognitive impairment (MCI) using published literature from the last 10 years. Secondary outcomes will be memory, language, mood, vitality, attention, brain waves, and other conditions measured and reported in the literature. Our review will be different from previous reviews. We will use a larger group of articles for analysis than the former review [15], and it will analyze effectiveness, different from the latter review [9].

2. Methods

2.1. Eligibility Criteria

Articles eligible for this review required older adults (>50) with early-stage Alzheimer’s Disease or MCI as participants, published in the last ten years, published in peer-reviewed journals, and used strong methods such as RCT or true experiments. Other methods were accepted such as quasi-experimental, mixed method, quantitative, and qualitative.
2.2. Information Sources

We searched in four well-known databases: PubMed (MEDLINE), Complete Index of Nursing and Allied Health Literature (CINAHL), Web of Science, and Embase’s ScienceDirect. We conducted the search on 3 August 2022. We also performed a journal-specific search of Healthcare. MEDLINE was excluded from all but PubMed. We eliminated reviews from our search to not confound the results. We used only published literature to ensure it was peer reviewed.

2.3. Search Strategy

We visited the U.S. Library of Medicine’s website to use the Medical Subject Heading’s (MeSH) indexing database. Using MeSH, we created a Boolean search string to combine key terms. We used the same search string in all databases: (mhealth OR telemedicine OR “virtual reality” OR “serious games”) AND (“Alzheimer disease” OR dementia) AND memory. Due to differences in filter options in each database, we could not use the exact same filters, but we used similar filter strategies. In CINAHL, we filtered by date, full-text, humans, English language, academic journals, excluded MEDLINE, and excluded reviews. In ScienceDirect, we filtered by date, excluded MEDLINE, and excluded reviews and conference proceedings. In Web of Science, we filtered by date, excluded reviews, and excluded MEDLINE. This practice eliminated most duplicates.

2.4. Selection Process

In accordance with the Kruse Protocol, we searched key terms in all databases, filtered results, and screened abstracts for applicability [16]. At least two reviewers screened each abstract, and at least two reviewers analyzed each article for data extraction and thematic analysis.

2.5. Data Collection Process

The Kruse Protocol standardized an Excel spreadsheet for data extraction and analysis. We used a series of three consensus meetings to finalize the group of articles for analysis, identify themes in the literature, and perform additional analysis on the data extracted.

2.6. Data Items

In accordance with the Kruse Protocol, we collected the following fields of data: database source, date of publication, authors, title of study, participant population, experimental intervention, results (compared to a control), medical outcomes, sample size, bias within study, effect size (Cohen’s $d$), sensitivity, specificity, F1, country of origin, statistics used, patient satisfaction, effectiveness, barriers to adoption, strength of evidence, and quality of evidence. Results were reported in comparison to a control group. Outcomes and effectiveness are highly similar fields, but they are designed for different audiences (providers and administrators). A provider might not be as concerned as length of stay or cost savings as much as direct medical outcomes (e.g., improvement in cognition), but the administrator is.

The primary outcome for this study is cognition, as measured by the MMSE or similar tool such as Addenbrooke’s Cognitive Examination-Revised (ACE-R), Cognitive Failures Questionnaire (CFQ), Wechsler Adult Intelligence Scale (WAIS), or Alzheimer’s Disease Assessment Scale-cognitive subscale (ADAS-Cog). Secondary outcomes are reported by studies through a range of measurement tools such as story recall, Hamilton Depression Rating Scale (HAMD), Wechsler Memory Scale 3rd edition (WMS-III), Rey-Osterrieth Complex Figure (ROCF), Controlled Oral Words Association Test (COWAT), Symbol Digit Modalities Test (SDMT), Bayer Activities of Daily Living, etc.

2.7. Study Risk of Bias Assessment and Reporting Bias Assessment

Not only did reviewers note observations of bias in each study, but we also assessed the strength and quality of each study using the Johns Hopkins Nursing Evidence Based
Practice tool (JHNEBP) [17]. The overall ratings of quality from the JHNEDP provided us with an assessment of the applicability of the cumulative evidence. We considered the instances of bias in how to interpret the results because bias can limit external validity [18].

2.8. Effect Measures

Because we accepted mixed methods and qualitative studies, we were unable to standardize summary measures, as would be performed in a meta-analysis. Measures of effect are summarized in tables for those studies in which it was reported. Measures of effect can be reported as Cohen’s d, Wald’s W, $\eta^2$, sensitivity, or specificity. Effects vary based on the statistic used, but they usually follow small (0.0–0.2), medium (0.21–0.79), large (0.8 or higher). An average effect size (ES) can be calculated through a weighted average by using the sample size.

2.9. Synthesis Methods

We performed a thematic analysis of the data combining observations (observed multiple times) into themes [19]. We calculated the frequency of occurrences and reported the findings in a series of affinity matrices. This frequency reporting states the probability of finding that theme in the group for analysis, and it provides confidence in the data analyzed. Although thematic analyses are usually reserved for qualitative studies, there is a pattern in the literature for systematic literature reviews to utilize this technique to help synthesize data extracted [20–22].

2.10. Additional Analyses and Certainty Assessment

Using the standardized spreadsheet, we sorted by intervention and theme to identify interactions. Some interventions appear more effective than others. Sensitivity and specificity were tabulated where reported.

3. Results

3.1. Study Selection

Figure 1 illustrates our study selection process. Four databases and one focused journal search were conducted with a standardized Boolean search string. The initial 1096 results were filtered to remove duplicates. At the end of the filtering exercise, 869 records were screened using filters on each database. This exercise removed 812 articles. The resulting 57 were retrieved for a full analysis for eligibility. Several more were filtered out (protocols, conference papers, and those that were not germane to our research objective). The remaining group for analysis was 22.

![Figure 1. Study selection process.](image-url)
3.2. Study Characteristics

Following the PRISMA 2020 checklist, characteristics for each study were systematically extracted and tabulated to include the following data fields: participants, intervention, comparison (to control or other group), observation, study design (PICOS). The standard PICOS table summarizes study characteristics in a manner commensurate with the literature (See Table 1). Of the 22 studies analyzed over the 10-year period, 0 were from 2012, 1 was from 2013 [23], 3 were from 2014 [24–26], 2 were from 2015 [27,28], 4 were from 2016 [29–32], 2 were from 2017 [33,34], 2 were from 2018 [35,36], 3 were from 2019 [37–39], 3 were from 2020 [40–42], 2 were from 2021 [43,44], and 0 were from 2022. All studies involved older adults mostly above 50 years except one study where participants with MCI were above 42 years. The interventions were heavily loaded with mHealth and eHealth (13/22, 59%), while 6/22 (27%) were VR, and 3 were a combination of telephone, mHealth + VR, and a game console. About 73% (16/22) of the studies were RCTs, 2 were either quasi-experimental or pre-post (using a control), and one each for observational and mixed-methods. Of the 16 RCTs, only 5 provided effect sizes (ES). The weighted average ES was 1.48. Studies originated in 13 different countries, but half were from Korea, the United States, and Italy.

3.3. Risk of Bias in and across Studies

Reviewers exercised the JHNEBP quality assessment tool to identify strength and quality of evidence. Reviewers also made notes of other observations of bias throughout the data extraction. The JHNEBP tool identified 16/22 (73%) of Strength I due to the use of strong methodologies such as RCT and true experiment. Four others (18%) were identified as Strength II due to either quasi-experimental or a pre-post with a control group. Only 2/22 (9%) were identified as Strength III because of the use of observational or mixed methods methodologies. The JHNEBP tool also identified 16/22 (73%) as Quality A due to the use of adequate control groups and sample sizes, and for reporting consistent results. Only 6/22 (27%) were identified as Quality B. No studies were identified as less than Strength III or Quality B.

Reviewers also identified other incidents of bias. [18] There were 22 observations of selection bias, which threatens the internal validity of the studies. These observations stemmed from limiting the population to one region or one country. Reviewers also noted four observations of sample bias, which threatens the external validity of the studies. These observations were noted where the population was a majority of one race or gender. There were two observations of design bias, which threatens the internal validity of the study. These were noted when there seemed to be a significant flaw in the methodology (e.g., short intervention time).

3.4. Results of Individual Studies

Table 2 summarized the results of individual studies. This table shows the themes identified in the literature. In multiple occasions, there were multiple observations of the same theme identified in the same study. This was an artifact of collapsing observations of a similar nature into one theme. An observation-to-theme match can be found in Appendix A. Other observations incident to the data extraction can be found in Appendix B (sample size, bias, effect size, country of origin, statistics used, patient satisfaction, and the JHNEBP strength and quality of evidence).
| Authors          | Participants                                | Experimental Intervention                  | Results (Compared to Control Group)                                                                 | Medical Outcomes Reported                  | Study Design |
|------------------|---------------------------------------------|--------------------------------------------|-----------------------------------------------------------------------------------------------------|--------------------------------------------|--------------|
| Zhuang et al.    | Older Adult (≥70), average age 83, 24% male, 76% female, all Asian (Chinese) | mHealth, eHealth cognitive training program | Intervention group with global cortical atrophy (GCA) showed improvement ($p < 0.05$). No change with baseline cognitive exam. The mean Mini Mental State Examination (MMSE) scores improved significantly in telecommunication technology (LSS-tele) and LSS-direct treatments | Improvement in memory, language, and visuospatial abilities | RCT          |
| Jelic et al.     | Older Adult (≥80), average age 83, 22% male, 77% female, 100% Caucasian | Telephone-based                            | Improvement in working memory and semantic fluency                                                 |                                             | Quasi-experimental |
| Singh et al.     | Older Adult (>55), average age 68.5, 68% female | mHealth, eHealth multidomain cognitive training | Resistance training was 74% higher for executive domain compared with combined training, cognition, and verbal memory | Improvement in global cognition, executive function and verbal/constructional memory | RCT          |
| Tarnanas et al.  | Older Adult (>65), average age 70.5, 73% male, 77% Caucasian | Virtual Reality (VR), and Augmented Reality (AR) | Improvements of specific cognitive functions and working memory ($p < 0.05$) Improvement in decision making, with trend improvements in depression. Non-statistically significant results found in processing speed and auditory attention. | improves untrained cognitive functions in MCI | RCT          |
| Burdea et al.    | Adults (>50 years) with MCI, 70% male | mHealth (BrightBrainer) app                | Repetition-lag training (RLT), a form of recognition memory training reported                        | Improvements in decision making and depression | Pre-post     |
| Finn et al.      | Older Adult (>65), average age 75, 71% male, 29% female, 100% Caucasian | mHealth, VR, Telemedicine                 | (p < 0.05)- Improved task performance over the course of training.                                  |                                             | RCT          |
| Callan et al.    | Older Adult (>64), average age 75, 100% Caucasian, non Latino | mHealth cognitive training task (APVSAT)   | Improved task performance, in terms of speed, by nearly 50%                                        | Reported as useful approach for incorporating device usage into daily routines. | RCT          |
| Cavallo et al.   | Older Adult (>75), average age 76, 100% Caucasian | Structured rehabilitative software         | (p < 0.05)-improvement in the intervention group greater than the control.                          | Improvement in memory                      | RCT          |
| Hagovska et al.  | Older Adult (≥65 years of age), average age 67.07, female 51.02%, male 49%, male, 100% Caucasian | Training battery prog-Cogni-Plus, SCHUHFRIED GmbH Austria, Dynamic balance training | (p < 0.05) improvement in postural reactions, attention, memory and language ability in the intervention group | Improvement in postural reactions, attention, memory and language | RCT          |
| Authors          | Participants                      | Experimental Intervention                                                                 | Results (Compared to Control Group)                                                                 | Medical Outcomes Reported                                                                                      | Study Design |
|------------------|-----------------------------------|--------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------|--------------|
| Hyer et al. [32] | Older Adult (≥65 years)           | Cogmed or a Sham computer program. For Repeatable Battery for Neuropsychological Status and the Clinical Dementia Rating | Cogmed group demonstrated better performance on the Functional Activities Questionnaire (FAQ), a measure of adjustment and far transfer, at follow-up. | Both groups, especially Cogmed, enjoyed the intervention. Cognitive stimulation activities improved mental skills | Pre-post     |
| Boyd et al. [33] | Older Adult (≥74 years)           | Trials to use Apps-evaluation of EnCare diagnostics (ECD) and the brain fit plan (BFP) in healthy older adults | No control group. Improved brain waves                                                                   | ECD is highly acceptable in both healthy older adults and those with early-stage dementia when given the shorter versions to accommodate their diagnosis. | Observational |
| Yang et al. [34] | Older Adult (≥68 years)           | 24 sessions of computer-based cognitive training, over a 12 week period.                     | Computer-based cognitive treatment resulting in self-training and self-learning of a patient            | Improvement in language, attention, calculation, verbal memory, and frontal function for the experimental group | RCT          |
| Lee et al. [35]  | Older Adult (≥70 years)           | 12 sessions of a computerized cognitive rehabilitation program for three weeks              | “No control group”. Two treatment groups only                                                             | Improved attention in subjects who underwent computerized cognitive rehabilitation using Bettercog.         | RCT          |
| Park et al. [36] | Older Adult (≥60 years)           | NCT group showed improvement in vitality, role-emotional, and mental health compared with the CCT group | Cognitive function (attention, memory, and visual spatial ability) showed a significant increase in both groups $p < 0.05$, as did the mental components of health-related quality of life ($p < 0.05$). | Regarding health-related quality of life, the NCT group showed more improvement in vitality, role-emotional, and mental health compared with the CCT group | RCT          |
| Flak et al. [37] | Adults (≥42 years) with MCI       | mHealth memory training app                                                                   | Adaptive training group did not show significantly greater improvement on the main outcome of working memory performance at 1 and 4 months after training | no improvement                                                                                               | RCT          |
| Kahn [38]        | Adults (>50 years) with MCI       | game console with cognitive games                                                              | Theta, delta waves and complexity of EEG significantly improved                                           | Xbox 360 Kinect cognitive games improved EEG indicators and cognitive functions, and, 15–17 increasing cerebral blood flow,59 neural plasticity,60 activation of arousal system,61 neurotransmitters modulation | RCT          |
Table 1. Cont.

| Authors               | Participants                                  | Experimental Intervention | Results (Compared to Control Group)                                                                 | Medical Outcomes Reported | Study Design |
|-----------------------|-----------------------------------------------|---------------------------|----------------------------------------------------------------------------------------------------|---------------------------|--------------|
| Park [39]             | Adults (>50 years) with MCI                   | culture based virtual reality | VR-based training group exhibited no significant differences following the three-month VR program | no improvement            | RCT          |
| Park et al. [40]      | Adults (>59 years, avg age 70.4), with MCI    | VR                        | Improvement in physical, memory and brain stimulation, but the participants have a low focus on decision making | Improvement in physical outcomes, memory and brain stimulation | Mixed Methods |
| Robert et al. [41]    | Adults (>50 years, avg age 79.4), with MCI    | mHealth app (MeMo)        | Significant differences in two attention tests                                                   | Significant differences in two attention tests | RCT          |
| Thapa et al. [42]     | Adults (>50 years) with MCI                   | VR                        | Intervention group exhibited a significantly improved executive function and brain function at the resting state | Improvement in overall cognitive function | RCT          |
| Oliveria et al. [43]  | Adults (>50 years) with MCI                   | VR                        | Improvement in overall cognitive function                                                       | Improvement in overall cognitive function in the experimental group | RCT          |
| Seredakis et al. [44] | Adults (>50 years) with MCI                   | VR                        | No group interaction                                                                               | No group interaction      | Quasi-experimental |

Table 2. Summary of analysis, sorted chronologically.

| Authors               | Intervention Themes | Results Themes | Outcome Themes | Effectiveness Themes | Barrier Themes |
|-----------------------|---------------------|----------------|----------------|----------------------|----------------|
| Zhuang et al. [23]    | mHealth, eHealth    | Improvement in cortical atrophy | Improvement in cortical atrophy | Improvement in overall cognitive function in the experimental group | Cost |
|                       |                     | Improved memory | Improved language | Improved memory | Training |
|                       |                     | Improved language | Improved MMSE scores (cognition) | Improved language | Low reimbursement |
| Jelcic et al. [24]    | Telephone           | Improved resistance training | Improved resistance training | Improved resistance training | Time of providers |
|                       |                     | Improved ADAS-Cog scores (cognition) | Improved ADAS-Cog scores (cognition) | Improved ADAS-Cog scores (cognition) | Training |
| Singh et al. [25]     | mHealth, eHealth    | Improved language | Improved language | Improved language | Cost |
|                       |                     | Improved language | Improved MMSE scores (cognition) | Improved language | Training |
|                       |                     | Improved language | Improved language | Improved language | Low reimbursement |
|                       |                     | Improved language | Improved language | Improved language | Time of providers |
Table 2. Cont.

| Authors           | Intervention Themes | Results Themes                          | Outcome Themes                          | Effectiveness Themes | Barrier Themes                     |
|-------------------|---------------------|-----------------------------------------|-----------------------------------------|----------------------|------------------------------------|
| Tarnanas et al.   | Virtual Reality (VR)| Improved MMSE scores (cognition)        | Improved MMSE scores (cognition)        | Improved MMSE scores (cognition) |
| Burdea et al.     | mHealth, eHealth    | Improved depression                     | Improved depression                     | Improved depression  |
| Finn et al.       | mHealth + VR        | Improved memory                         | Improved memory                         | Improved memory      |
| Callan et al.     | mHealth, eHealth    | Improved MMSE scores (cognition)        | Improved MMSE scores (cognition)        | Improved MMSE scores (cognition) |
| Cavallo et al.    | mHealth, eHealth    | Improved memory                         | Improved memory                         | Improved memory      |
| Hagovska et al.   | mHealth, eHealth    | Improved attention, Improved language   | Improved attention, Improved language   | Improved attention   |
| Hyer et al.       | mHealth, eHealth    | Improved CFQ scores (cognition)         | Improved CFQ scores (cognition)         | Improved CFQ scores (cognition) |
| Boyd et al.       | mHealth, eHealth    | Improved EEG scores (brain waves)       | Improved EEG scores (brain waves)       | Improved EEG scores (brain waves) |

Cost
Training
Low reimbursement
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Dexterity limitations of older adults
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Time of providers
| Authors          | Intervention Themes | Results Themes                     | Outcome Themes                               | Effectiveness Themes                                | Barrier Themes                      |
|------------------|---------------------|------------------------------------|---------------------------------------------|-----------------------------------------------------|-------------------------------------|
| Yang et al. [34] | mHealth, eHealth    | Improved K-MMSE scores (cognition) | Improved K-MMSE scores (cognition)          | Improved K-MMSE scores (cognition)                   | Cost                                |
|                  |                     | Improved memory                    | Improved memory                             | Improved memory                                      | Training                            |
|                  |                     | Improved language                  | Improved language                           | Improved language                                     | Low reimbursement                    |
|                  |                     | Improved attention                 | Improved attention                          | Improved attention                                     | Time of providers                   |
|                  |                     |                                    |                                             |                                                     |                                     |
| Lee et al. [35]  | mHealth, eHealth    | Improved MMSE scores (cognition)   | Improved MMSE scores (cognition)            | Improved MMSE scores (cognition)                      | Cost                                |
|                  |                     | Improved memory                    | Improved memory                             | Improved memory                                      | Training                            |
|                  |                     | Improved attention                 | Improved attention                          | Improved attention                                     | Low reimbursement                    |
|                  |                     |                                    |                                             |                                                     | Time of providers                   |
|                  |                     |                                    |                                             |                                                     |                                     |
| Park et al. [36] | mHealth, eHealth    | Improved memory                    | Improved memory                             | Improved MMSE scores (memory)                        | Cost                                |
|                  |                     | Improved vitality                  | Improved vitality                           | Improved vitality                                     | Training                            |
|                  |                     | Improved mental health             | Improved mental health                      | Improved mental health                                 | Low reimbursement                    |
|                  |                     | Improved quality of life           | Improved quality of life                    | Improved quality of life                              | Time of providers                   |
|                  |                     |                                    |                                             |                                                     |                                     |
| Flak et al. [37] | mHealth, eHealth    | No improvement                     | None reported                               | None reported                                        | Cost                                |
|                  |                     |                                    |                                             |                                                     | Training                            |
| Kah [38]         | Game console        | Improved EEG scores (brain waves)  | Improved EEG scores (brain waves)           | Improved EEG scores (brain waves)                     | Low reimbursement                    |
|                  |                     | Improved MMSE scores (cognition)   | Improved MMSE scores (cognition)            | Improved MMSE scores (cognition)                      | Time of providers                   |
|                  |                     | Improved cerebral blood flow       | Improved cerebral blood flow                | Improved cerebral blood flow                          |                                     |
|                  |                     | Improved neuro plasticity          | Improved neuro plasticity                   | Improved neuro plasticity                             |                                     |
| Park [39]        | Virtual Reality (VR) | No significant differences         | None reported                               | None reported                                        | Low reimbursement                    |
|                  |                     |                                    |                                             |                                                     | Cost                                |
| Kahn [38]        | Game console        | Improved EEG scores (brain waves)  | Improved EEG scores (brain waves)           | Improved EEG scores (brain waves)                     | Time of providers                   |
|                  |                     | Improved MMSE scores (cognition)   | Improved MMSE scores (cognition)            | Improved MMSE scores (cognition)                      |                                     |
|                  |                     | Improved cerebral blood flow       | Improved cerebral blood flow                | Improved cerebral blood flow                          |                                     |
|                  |                     | Improved neuro plasticity          | Improved neuro plasticity                   | Improved neuro plasticity                             |                                     |
| Park et al. [40] | Virtual Reality (VR) | Improved vitality                  | Improved vitality                           | Improved vitality                                     | Low reimbursement                    |
|                  |                     | Improved memory                    | Improved memory                             | Improved memory                                       | Cost                                |
|                  |                     | Improved EEG scores (brain waves)  | Improved EEG scores (brain waves)           | Improved EEG scores (brain waves)                     | Training                            |
|                  |                     |                                    |                                             |                                                     | Low reimbursement                    |
|                  |                     |                                    |                                             |                                                     | Time of providers                   |

Table 2. Cont.
### Table 2. Cont.

| Authors          | Intervention Themes | Results Themes                      | Outcome Themes                      | Effectiveness Themes       | Barrier Themes                                                                 |
|------------------|---------------------|-------------------------------------|-------------------------------------|---------------------------|-------------------------------------------------------------------------------|
| Robert et al. [41] | mHealth, eHealth    | Improved attention                  | Improved attention                  | Improved attention        | Cost Training Low reimbursement Time of providers Cost Training Low reimbursement Time of providers Cost Training Low reimbursement Time of providers |
| Thapa et al. [42]  | Virtual Reality (VR) | Improved EEG scores (brain waves)   | Improved EEG scores (brain waves)   | Improved EEG scores (brain waves) | Cost Training Low reimbursement Time of providers Cost Training Low reimbursement Time of providers Cost Training Low reimbursement Time of providers |
| Oliveria et al. [43] | Virtual Reality (VR) | Improved MMSE scores (cognition)    | Improved MMSE scores (cognition)    | Improved MMSE scores (cognition) | Cost Training Low reimbursement Time of providers Cost Training Low reimbursement Time of providers Cost Training Low reimbursement Time of providers |
| Seredakis et al. [44] | Virtual Reality (VR) | No improvement                       | None reported                       | None reported             | Cost Training Low reimbursement Time of providers Cost Training Low reimbursement Time of providers |
3.5. Results of Syntheses, Additional Analysis, and Certainty of Evidence

We conducted a thematic analysis of the literature to make sense of the data extracted. Through this process, observations noted multiple times became themes. Not all observations were fit into themes: Some remained as individual observations. These themes and observations are reported by category in affinity matrices with frequency distributions. Frequencies do not imply importance—instead they identify the probability the theme was identified in the group of articles analyzed.

3.5.1. Patient Satisfaction

Observations of patient satisfaction can be found in Appendix C. This appendix tabulates these. Only two themes and two individual observations were made. Patients commented their appreciation and how they valued the technology inherent to the interventions. This theme appeared in 11/32 (34%) of the observations [23,26,28–36]. The interventions had a positive effect on the patient experience. This appeared in 10/30 (32%) of the observations [23,24,26–31,33,34]. The intervention improved cognitive function in one study [25], and the technology frustrated patients in another study [37].

3.5.2. Results to the Adoption of mHealth and VR for Memory Care for AD Patients

Table 3 summarizes the results incident to the intervention of mHealth and VR for memory care. Six themes and seven individual observations were identified by the reviewers for a total of 41 occurrences in the literature. Nine interventions improved cognition, as measured by the MMSE, ADAS-Cog, or WAIS tests [24–26,29,32,34,35,38,43]. Seven interventions improved memory [23,28,30,31,34,36,40]. Five interventions improved language [23–25,31,34]. Four interventions improved brain activity, as measured by EEG [33,38,40,42]. Four interventions improved attention [31,34,36,41], and three improved vitality [31,36,40]. One intervention improved cortical atrophy [23]. One intervention improved resistance training through a combination of resistance and cognitive training protocol [25]. One intervention improved both quality of life and mental health [36]. One intervention improved both cerebral blood flow and neuroplasticity [38]. One intervention improved depression [27]. Only three interventions showed either no improvements or no significant improvements [37,39,44].

Table 3. Results to the adoption of mHealth and VR for memory care.

| Results and Observations                                      | Frequency |
|---------------------------------------------------------------|-----------|
| Improved cognition (MMSE, ADAS-Cog, WAIS) [24–26,29,32,34,35,38,43] | 9         |
| Improved memory [23,28,30,31,34,36,40]                        | 7         |
| Improved language [23–25,31,34]                               | 5         |
| Improved EEG scores (brain waves) [33,38,40,42]               | 4         |
| Improved attention [31,34,36,41]                              | 4         |
| Improved vitality [31,36,40]                                  | 3         |
| No improvement [37,44]                                       | 2         |
| Improvement in cortical atrophy [23]                          | 1         |
| Improved resistance training [25]                             | 1         |
| Improved quality of life [36]                                 | 1         |
| Improved mental health [36]                                   | 1         |
| Improved cerebral blood flow [38]                             | 1         |
| Improved depression [27]                                     | 1         |
| No significant differences [39]                               | 1         |
| Improved neuroplasticity [38]                                 | 1         |

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3.5.3. Medical Outcome Commensurate with the Adoption of mHealth and VR for Memory Care

Table 4 summarizes the medical outcomes observed. Six themes and seven individual observations were recorded commensurate with the adoption of mHealth and VR for
memory care for patients with AD, for a total of 41 occurrences. The results and medical outcomes are highly similar.

Table 4. Medical outcomes commensurate with the adoption of mHealth and VR.

| Outcomes Themes and Observations | Frequency |
|----------------------------------|-----------|
| Improved cognition (MMSE, ADAS-Cog, WAIS) [24-26,29,32,34,35,38,43] | 9         |
| Improved memory [23,28,30,31,34,36,40] | 7         |
| Improved language [23-25,31,34] | 5         |
| Improved EEG scores (brain waves) [33,38,40,42] | 4         |
| Improved attention [31,34,36,41] | 4         |
| Improved vitality [31,36,40] | 3         |
| None reported [37,39,44] | 3         |
| Improvement in cortical atrophy [23] | 1         |
| Improved resistance training [25] | 1         |
| Improved quality of life [36] | 1         |
| Improved mental health [36] | 1         |
| Improved cerebral blood flow [38] | 1         |
| Improved neuro plasticity [38] | 1         |
| Improved depression [27] | 1         |

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3.5.4. Effectiveness Themes and Observations

Table 5 summarizes the medical outcomes observed. Six themes and seven individual observations were recorded commensurate with the adoption of mHealth and VR for memory care for patients with AD, for a total of 41 occurrences. The medical outcomes and Effectiveness themes are highly similar. The only difference was that two interventions noted a time savings by using the intervention [34,35].

Table 5. Effectiveness of mHealth and VR for memory care for patients with AD.

| Effectiveness Themes and Observations | Frequency |
|--------------------------------------|-----------|
| Improved MMSE scores (cognition) [24-26,29,32,34,35,38,43] | 9         |
| Improved MMSE scores (memory) [23,28,30,31,34,36,40] | 7         |
| Improved language [23-25,31,34] | 5         |
| Improved attention [31,34,36,41] | 4         |
| Improved EEG scores (brain waves) [33,38,40,42] | 4         |
| Improved vitality [31,36,40] | 3         |
| None reported [37,39,44] | 3         |
| Savings in time [34,35] | 2         |
| Improvement in cortical atrophy [23] | 1         |
| Improved resistance training [25] | 1         |
| Improved quality of life [36] | 1         |
| Improved mental health [36] | 1         |
| Improved cerebral blood flow [38] | 1         |
| Improved neuro plasticity [38] | 1         |
| Improved depression [27] | 1         |

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3.5.5. Barriers to the Adoption of mHealth and VR for Memory Care for Patients with AD

Table 6 summarizes the barriers to the adoption of mHealth and VR for memory care for patients with AD. Four themes and one individual observation was recorded commensurate with the adoption of the interventions, for a total of 88 occurrences. The most common barriers, which occurred together in many of the studies, was time of providers (to manage the intervention and administer tests) [23-44], training (providers, staff, and patients) [23-44], cost (of technology and tests) [23,25-44], low reimbursement (which is highly correlated with cost) [23,25-44], and dexterity limitations of older adults [33].
Table 6. Barriers to the adoption of mHealth and VR for memory care.

| Barrier Themes and Observation | Frequency |
|--------------------------------|-----------|
| Time of providers [23–44] *    | 23        |
| Training [23–44]              | 22        |
| Cost [23,25–44]               | 21        |
| Low reimbursement [23,25–44]   | 21        |
| Dexterity limitations of older adults [33] | 1   |

* Multiple occurrences in one study.

3.5.6. Interactions between Observations

About 60% of the interventions were mHealth, eHealth. This intervention was associated with improvements in cognition [25,29,32,34,35], memory [23,30,31,34,36], language [23,25,31,34], attention [31,34,36,41], brain activity [33], cortical atrophy [23], resistance training [25], and depression [27]. Only one study that used this intervention reported no improvement [37]. The VR interventions reported improved cognition [26,43], brain activity [40,42], memory [40], and vitality [40]. Two VR studies reported either no improvement or no statistically significant improvements [39,44]. The mHealth + VR intervention reported improved memory [28]. The game console intervention reported improved cognition, brain activity, cerebral blood flow, and neuro plasticity [38]. The telephone intervention reported an increase in cognition and language [24].

4. Discussion

4.1. Summary of Evidence

This systematic literature review analyzed 22 studies from 13 countries published over 10 years to analyze the effectiveness of mHealth and VR for memory care for patients with AD. Five interventions were identified; however, the dominant intervention was mHealth, eHealth. The lines between mHealth and eHealth are significantly blurred due to the capabilities of mobile devices. This intervention comprised 13/22 (59%) of the studies. Virtual Reality was the most often cited intervention, appearing in 6/22 (27%) studies. Methodologies were very strong in the studies analyzed. About 73% of the studies used RCT as the study design [23,25,26,28–31,34–39,41–43]. The strong study designs resulted in a low rate of bias within and among studies because the studies used adequate sample sizes and controls, and they reported consistent results. Very small observations of internal and external bias were observed in all studies. There were 9 instances of an improvement of cognition [24–26,29,32,34,35,43], 7 instances of an improvement in memory [23,28,30,31,34,36,40], 5 instances of an improvement in language [23–25,31,34], four improvements in EEG scores [33,38,40,42], four improvements in attention [31,34,36,41] three improvements in vitality [31,36,40], and several individual improvements in cortical atrophy, resistance training, quality of life, mental health, cerebral blood flow, depression, and neuro plasticity [25,27,36,38].

This review highlights are large diversity of results from these five interventions. The mHealth and eHealth interventions consistently showed the largest improvements in cognition [25,29,32,34,35], memory [23,30,31,34,36], language [23,25,31,34], attention [31,34,36,41], brain activity [33], cortical atrophy [23], resistance training [25], and depression [27]. The game console intervention reported improvements in several areas: cognition, brain activity, cerebral blood flow, and neuro plasticity [38]. The VR interventions did not report as many improvements: cognition [26,43], brain activity [40,42], memory [40], and vitality [40]. The telephone intervention reported improvements in two areas: cognition and language [24]. The mHealth + VR intervention only improved memory [28].

Future research should focus on the improvements in cognition, memory, and brain waves to identify the duration of the improvements. The studies analyzed did not imply the results would be long term. Both mHealth and VR offer some good interventions to provide temporal relief and improvement of AD symptoms. Only three studies identified
no improvement or no statically significant improvement \cite{37,39,44}. The rest identified improvements in at least one area. Future considerations should focus on the interventions with the largest reported improvements. In this review, those would be mHealth, eHealth.

The results of this review should provide options for providers and care givers who want to see an improvement in one area or another. The results of these studies are positive. However, providers do face several barriers to the adoption of these interventions. The cost to acquire the equipment would not currently be reimbursed with current treatment codes. It would help to codify some of these interventions into critical practice guidelines. An existing CPG would have a better chance of being reimbursed. After acquiring the equipment, the provider would need to train the staff and the users of the equipment for each intervention. The provider and staff would need additional time to operate the equipment, administer and analyze the measurement tests like the MMSE, and EEG. These barriers are not compelling, but they present significant stumbling blocks to universal adoption.

4.2. Limitations

To control for sample bias, we queried four well-known databases, and we used every article that emerged from the abstract screening step. We chose only four databases, but others may have identified additional studies with additional interventions. We also limited the search to published articles that had been peer reviewed. This publication bias may have prevented us from identifying other interventions with various margins of success. To control for confirmation bias, we had multiple reviewers participate in every step: screening, data extraction, and analysis. To control for design bias, we stuck with a published protocol aligned with more than 40 published systematic literature reviews.

4.3. Conclusions

mHealth and VR offer promising interventions to help memory and cognition for those who suffer from AD. Several interventions show temporary improvement in cognition, memory, and brain activity. The mHealth and eHealth interventions seem to affect a larger scope of measurable criteria, and they may be easier to implement without complicated VR apparatus. Several barriers stand in the way of universal adoption. Additional reimbursement mechanisms would enable providers to adopt these interventions or test them under different circumstances. The AD patients and their caregivers look for answers and an improvement in the AD symptoms. With additional development, mHealth and VR might provide some viable solutions.

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Institutional Review Board Statement: Not Applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Data from this study can be obtained by asking the lead author.

Conflicts of Interest: The authors declare no conflict of interest.
## Appendix A

### Table A1. Observation-to-theme conversion (Intervention, Results, and Medical Outcomes).

| Authors          | Experimental Intervention | Intervention Themes | Results (Compared to Control Group) | Results Themes | Medical Outcomes Reported | Outcome Themes                        |
|------------------|---------------------------|---------------------|-------------------------------------|----------------|---------------------------|---------------------------------------|
| Zhuang et al.    | mHealth, eHealth cognitive training program | mHealth, eHealth | Intervention group with global cortical atrophy (GCA) showed improvement ($p < 0.05$). No change with baseline cognitive exam. | Improvement in cortical atrophy | Improvement in memory, language, and visuospatial abilities | Improvement in cortical atrophy |
| Jelcic et al.    | Telephone-based           | Telephone           | The mean Mini Mental State Examination (MMSE) score improved significantly in Telecommunication technology (LSS-tele) and LSS-direct treatments | Improved MMSE scores (cognition) | Improvement in working memory and semantic fluency | Improvement in working memory and semantic fluency |
| Singh et al.     | mHealth, eHealth multiddomain cognitive training | mHealth, eHealth | Resistance training was 74% higher for Executive Domain compared with combined training, cognition, and verbal memory | Improved resistance training | Improved MMSE scores (cognition) | Improvement in global cognition, executive function and verbal/constructional memory |
| Tamanas et al.   | Virtual Reality (VR), and Augmented Reality (AR) | Virtual Reality (VR) | Improvements of specific cognitive functions and working memory | Improved MMSE scores (cognition) | Improved MMSE scores (cognition) | Improved MMSE scores (cognition) |
| Burdea et al.    | mHealth (BrightBrainer) app | mHealth, eHealth | Statistically significant improvement in decision making, with trend improvements in depression. Non-statistically significant results found in processing speed and auditory attention. | Improved depression | Improved depression | Improved depression |
| Finn et al.      | mHealth, VR, Telemedicine | mHealth + VR | ($p < 0.05$). Improved on the task itself over the course of training. | Improved memory | Improved memory | Improved memory |
| Callan et al.    | mHealth cognitive training task (APVSAT) | mHealth, eHealth | Improved task performance, in terms of speed, by nearly 50% | Improved MMSE scores (cognition) | Improved MMSE scores (cognition) | Improved MMSE scores (cognition) |
| Cavallo et al.   | structured rehabilitative software | mHealth, eHealth | ($p < 0.05$). Improvement in the intervention group greater than the control. | Improved memory | Improvement in memory | Improvement in memory |
| Hagovska et al.  | Cogni-Plus, SCHUHFRIED GmbH Austria, Dynamic balance training | mHealth, eHealth | ($p < 0.05$). Improvement in postural reactions, attention, memory and language ability in the intervention group | Improved attention | Improved memory | Improved memory |
| Hyer et al.      | Repeatable Battery for Neuropsychological Status and the Clinical Dementia Rating | mHealth, eHealth | The Cogned group demonstrated better performance on the Functional Activities Questionnaire (FAQ), a measure of adjustment and far transfer, at follow-up. | Improved MMSE scores (cognition) | Improved MMSE scores (cognition) | Improved MMSE scores (cognition) |
| Authors      | Experimental Intervention                                                                 | Intervention Themes | Results (Compared to Control Group)                       | Results Themes                          | Medical Outcomes Reported                                                                 | Outcome Themes          |
|-------------|-------------------------------------------------------------------------------------------|---------------------|-----------------------------------------------------------|-----------------------------------------|------------------------------------------------------------------------------------------|-------------------------|
| Boyd et al. | Trials to use Apps-evaluation of EnCare diagnostics (ECD) and the brain fit plan (BFP) in healthy older adults | mHealth, eHealth    | No control group. Improved brain waves                     | Improved EEG scores (brain waves)       | ECD is highly acceptable in both healthy older adults and those with early stage dementia when given the shorter versions to accommodate their diagnosis. | Improved EEG scores (brain waves) |
| Yang et al. | 24 sessions of computer-based cognitive training, over a 12 week period.                  | mHealth, eHealth    | Computer-based cognitive treatment resulting in self-training and self-learning of a patient | Improved MMSE scores (cognition)        | Improvement in language, attention, calculation, verbal memory, and frontal function for the experimental group | Improved memory Improved language |
| Lee et al.  | 12 sessions of a computerized cognitive rehabilitation program for three weeks            | mHealth, eHealth    | “No control group”. Two treatment groups only               | Improved MMSE scores (cognition)        | Improvement in subjects who underwent computerized cognitive rehabilitation using Bettercog. | Improved MMSE scores (cognition) |
| Park et al. | NCT group showed improvement in vitality, role-emotional, and mental health compared with the CCT group | mHealth, eHealth    | Cognitive function (attention, memory, and visual spatial ability) showed a significant increase in both groups ($p < 0.05$), as did the mental components of health-related quality of life ($p < 0.05$) | Improved attention Improved memory Improved vitality Improved mental health Improved quality of life | Regarding health-related quality of life, the NCT group showed more improvement in vitality, role-emotional, and mental health compared with the CCT group | Improved attention Improved memory Improved vitality Improved mental health Improved quality of life |
| Flak et al. | mHealth memory training app                                                                | mHealth, eHealth    | Adaptive training group did not show significantly greater improvement on the main outcome of working memory performance at 1 and 4 months after training | No improvement                         | No improvement                                                                           | None reported            |
| Authors          | Experimental Intervention                                      | Intervention Themes | Results (Compared to Control Group)                                                                 | Results Themes                                                                 | Medical Outcomes Reported                                                                 | Outcome Themes               |
|-----------------|---------------------------------------------------------------|---------------------|-----------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------|-------------------------------|
| Kahn            | Game console with cognitive games                            | Game console        | Theta, delta waves and complexity of EEG significantly improved                                    | Improved EEG scores (brain waves)                                               | Improved EEG scores, improved MMSE scores (cognition)                                      | Improved EEG scores (brain waves)                                      |
|                 |                                                                |                     |                                                                                                     | Improved MMSE scores (cognition)                                                | Improved EEG indicators and cognitive functions probably through multiple mechanisms, such as, cognition improvement, 15–17 increasing cerebral blood flow, 59 neural plasticity, 60 activation of arousal system, 61 neurotransmitters modulation | Improved MMSE scores (cognition)                                      |
|                 |                                                                |                     |                                                                                                     | Improved cerebral blood flow                                                     | Improved cerebral blood flow                                                        | Improved cerebral blood flow                                      |
|                 |                                                                |                     |                                                                                                     | Improved neuro plasticity                                                        | Improved neuro plasticity                                                             | Improved neuro plasticity                                      |
| Park            | culture based virtual reality                                | Virtual Reality (VR) | VR-based training group exhibited no significant differences following the three-month VR program No control group. No improvement in physical, memory and brain stimulation, but the participants have a low focus on decision making | No significant differences                                                        | No significant improvements noted in the decision making                                | None reported                 |
| Park et al.     | VR                                                             | Virtual Reality (VR) | Improvement in physical, memory and brain stimulation, but the participants have a low focus on decision making | Improved vitality                                                               | Improvement in physical outcomes, memory and brain stimulation                      | Improved vitality                                    |
|                 |                                                                |                     |                                                                                                     | Improved memory                                                                 | Improved EEG scores (brain waves)                                                    | Improved memory                                    |
|                 |                                                                |                     |                                                                                                     | Improved EEG scores (brain waves)                                               | Improved EEG scores (brain waves)                                                    | Improved EEG scores (brain waves)                                      |
| Robert et al.   | mHealth app (MeMo)                                            | mHealth, eHealth     | Significant differences in two attention tests                                                      | Improved attention                                                              | Improvement in attention tests                                                         | Improved attention                    |
| Oliveria et al. | VR                                                             | Virtual Reality (VR) | Intervention group exhibited a significantly improved executive function and brain function at the resting state | Improved EEG scores (brain waves)                                               | Intervention group exhibited a significantly improved executive function and brain function at the resting state | Improved EEG scores (brain waves)                                      |
| Oliveria et al. | VR                                                             | Virtual Reality (VR) | An improvement in overall cognitive function in the experimental group                              | Improved MMSE scores (cognition)                                                | Improved MMSE scores in the experimental group                                        | Improved MMSE scores (cognition)                                      |
| Oliveria et al. | VR                                                             | Virtual Reality (VR) | No group interaction                                                                                   | No improvement                                                                  | No group interaction                                                                  | None reported                 |

Table A1. Cont.
## Appendix B

Table A2. Observation-to-theme conversion (Effectiveness and Barriers to adoption).

| Authors       | Effectiveness                                                                 | Effectiveness Themes                                      | Barriers to Adoption                                                                 | Barrier Themes                  |
|---------------|-------------------------------------------------------------------------------|-----------------------------------------------------------|-------------------------------------------------------------------------------------|--------------------------------|
| Zhuang et al. | pts value technology, improvement in memory, language, and visuospatial abilities | Improvement in cortical atrophy                           | Cost to acquire equipment, staff training, low reimbursement, time to administer tests | Cost Training                  |
|               |                                                                               | Improved memory                                           |                                                                                     | Low reimbursement              |
|               |                                                                               | Improved language                                         |                                                                                     | Time of providers              |
|               |                                                                               |                                                           |                                                                                     | Training                       |
| Jelcic et al. | Improvement in memory, phonemic fluency, semantic fluency, stabilizing delayed/working memory | Improved MMSE scores (cognition)                          | Time of providers/staff on phone, training of staff, time to administer tests       | Time of providers Training     |
|               |                                                                               | Improved language                                         |                                                                                     | Time of providers              |
|               |                                                                               | Improved resistance training                               |                                                                                     | Training                       |
| Singh et al.  | trials of isolated moderate-high intensity resistance training had significant effects on memory, cognition, and language | Improved MMSE scores (cognition)                          | Cost to acquire equipment, staff training, low reimbursement, time to administer tests | Cost                           |
|               |                                                                               | Improved language                                         |                                                                                     | Training                       |
|               |                                                                               |                                                           |                                                                                     | Low reimbursement              |
|               |                                                                               |                                                           |                                                                                     | Time of providers              |
| Tarnanas et al.| improves untrained cognitive functions in MCI                                 | Improved MMSE scores (cognition)                          | Cost to acquire equipment, staff training, low reimbursement, time to administer tests | Cost                           |
|               |                                                                               |                                                           |                                                                                     | Training                       |
|               |                                                                               |                                                           |                                                                                     | Low reimbursement              |
|               |                                                                               |                                                           |                                                                                     | Time of providers              |
|               |                                                                               |                                                           |                                                                                     | Training                       |
| Burdea et al. | Improvements in decision making and depression                               | Improved depression                                        | Cost to acquire equipment, staff training, low reimbursement                        | Cost                           |
|               |                                                                               |                                                           |                                                                                     | Training                       |
|               |                                                                               |                                                           |                                                                                     | Low reimbursement              |
|               |                                                                               |                                                           |                                                                                     | Time of providers              |
| Finn et al.   | repetition-lag training (RLT), a form of recognition memory training reported | Improved memory                                           | Cost to acquire equipment, staff training, low reimbursement, time to administer tests | Cost                           |
|               |                                                                               |                                                           |                                                                                     | Training                       |
|               |                                                                               |                                                           |                                                                                     | Low reimbursement              |
|               |                                                                               |                                                           |                                                                                     | Time of providers              |
| Callan et al. | Improved task performance, in terms of speed, by nearly 50%                  | Improved MMSE scores (cognition)                          | Cost to acquire equipment, staff training, low reimbursement, time to administer tests | Cost                           |
|               |                                                                               |                                                           |                                                                                     | Training                       |
|               |                                                                               |                                                           |                                                                                     | Low reimbursement              |
|               |                                                                               |                                                           |                                                                                     | Time of providers              |
| Cavallo et al.| Improvement in memory                                                          | Improved memory                                           | Cost to acquire equipment, staff training, low reimbursement, time to administer tests | Cost                           |
|               |                                                                               |                                                           |                                                                                     | Training                       |
|               |                                                                               |                                                           |                                                                                     | Low reimbursement              |
|               |                                                                               |                                                           |                                                                                     | Time of providers              |
Table A2. Cont.

| Authors          | Effectiveness                                                                 | Effectiveness Themes                                                                 | Barriers to Adoption                                                                 | Barrier Themes                                      |
|------------------|-------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|---------------------------------------------------|
| Hagovska et al.  | improvement in postural reactions, attention, memory and language             | Improved attention                                                                  | Cost to acquire equipment, staff training, low reimbursement, time to administer tests | Low reimbursement, Time of providers               |
|                  |                                                                                | Improved memory                                                                     |                                                                                      |                                                   |
|                  |                                                                                | Improved attention                                                                  | Cost to acquire equipment, staff training, low reimbursement, time to administer tests | Low reimbursement, Time of providers               |
|                  |                                                                                | Improved language                                                                   | dexterity limitations, use of touch screen and accidental screen presses,             | Dexterity limitations of older adults              |
|                  |                                                                                | Improved language                                                                   | cost to acquire equipment, staff training, low reimbursement, time to administer tests |                                                   |
|                  |                                                                                | Improved language                                                                   |                                                                                      |                                                   |
| Hyer et al.      | improvement in mental sharpness                                                | Improved MMSE scores (cognition)                                                    |                                                                                      |                                                   |
|                  |                                                                                | Improved attention                                                                  | Cost to acquire equipment, staff training, low reimbursement, time to administer tests | low reimbursement, Time of providers               |
|                  |                                                                                | Improved memory                                                                     |                                                                                      |                                                   |
| Boyd et al.      | Improved brain waves                                                            | Improved EEG scores (brain waves)                                                   |                                                                                      |                                                   |
|                  | Improvement in language, attention, calculation, verbal memory, and frontal     | Improved MMSE scores (cognition)                                                    |                                                                                      |                                                   |
| Yang et al.      | function for the experimental group, convenience, savings in time              | Improved memory                                                                     |                                                                                      |                                                   |
|                  |                                                                                | Improved language                                                                   |                                                                                      |                                                   |
|                  |                                                                                | Improved language                                                                   |                                                                                      |                                                   |
|                  | convenience, savings in time, improved cognition                               | Improved MMSE scores (cognition)                                                    |                                                                                      |                                                   |
| Lee et al.       |                                               |                                                                                |                                                                                      |                                                   |
|                  | Regarding health-related quality of life, the NCT group showed more improvement | Improved attention                                                                  |                                                                                      |                                                   |
|                  | in vitality, role-emotional, and mental health compared with the CCT group     | Improved memory                                                                     |                                                                                      |                                                   |
|                  | none                                                                           | Improved vitality                                                                   |                                                                                      |                                                   |
|                  |                                                                                | Improved mental health                                                               |                                                                                      |                                                   |
|                  |                                                                                | Improved quality of life                                                             |                                                                                      |                                                   |
| Park et al.      |                                               |                                                                                |                                                                                      |                                                   |
| Flak et al.      |                                               |                                                                                |                                                                                      |                                                   |
| Kahn             | Increase in brain waves, increase in cognition, increase in cerebral blood      | Improved EEG scores (brain waves)                                                   |                                                                                      |                                                   |
|                  | flow, improved neuro plasticity                                                 | Improved MMSE scores (cognition)                                                    |                                                                                      |                                                   |
|                  |                                                                                | Improved cerebral blood flow                                                        |                                                                                      |                                                   |
|                  |                                                                                | Improved neuro plasticity                                                           |                                                                                      |                                                   |
|                  |                                                                                |                                                                                      |                                                                                      |                                                   |
| Authors        | Effectiveness                                                                 | Effectiveness Themes                        | Barriers to Adoption                                                                 | Barrier Themes                   |
|---------------|-------------------------------------------------------------------------------|---------------------------------------------|---------------------------------------------------------------------------------------|---------------------------------|
| Park          | none                                                                          | None reported                               | Cost to acquire equipment, staff training, low reimbursement                          | Cost                            |
| Park et al.   | Improvement in physical outcomes, memory and brain stimulation                | Improved vitality                           | Cost to acquire equipment, staff training, low reimbursement                          | Training                        |
|               |                                                                               | Improved memory                             |                                                                                        | Low reimbursement               |
|               |                                                                               | Improved EEG scores (brain waves)           |                                                                                        | Time of providers               |
| Robert et al. | significant differences in two attention tests                               | Improved attention                          | Cost to acquire equipment, staff training, low reimbursement                          | Cost                            |
| Thapa et al.  | Intervention group exhibited a significantly improved executive function and brain function at the resting state | Improved EEG scores (brain waves)           | Cost to acquire equipment, staff training, low reimbursement                          | Training                        |
| Oliveria et al.| an improvement in overall cognitive function in the experimental group       | Improved MMSE scores (cognition)            | Cost to acquire equipment, staff training, low reimbursement                          | Low reimbursement               |
| Seredakis et al.| No group interaction                                                          | None reported                               | Cost to acquire equipment, staff training, low reimbursement                          | Time of providers               |
## Appendix C

**Table A3.** Other observations incident to review.

| Authors          | Sample Size (#s only) | Bias within Study Selection Bias, Sample Bias, etc. | Effect Size | Country of Origin (Where the Study Was Conducted) | Statistics Used                                                                 | Patient Satisfaction                                                                 | Strength of Evidence | Quality of Evidence |
|------------------|-----------------------|-----------------------------------------------------|-------------|---------------------------------------------------|---------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|----------------------|---------------------|
| Zhuang et al.    | 33                    | China only (selection bias), Mostly female (sample bias) Short intervention period (design bias) | Not reported | China                                              | Measures of central tendency, MANOVA, ANOVA, Wilk’s lambda                     | Positive effect on patient experience                                                  | I                     | A                   |
| Jelcic et al.    | 27                    | Venice only (selection bias), Mostly female and Caucasian (sample bias) Australia and New Zealand only (selection bias) | not reported | Venice                                             | Measures of central tendency, Kruskal–Wallis ANOVA, Mann–Whitney U-test        | Positive effect on patient experience                                                  | II                    | B                   |
| Singh et al.     | 100                   | small (0.2)                                         | Small Effect (0.2) | Australia and New Zealand                          | Measures of central tendency, Odds ratio                                        | Improved global cognitive function                                                    | I                     | A                   |
| Tamanas et al.   | 114                   | Greece only (selection bias) one country (selection bias), majority male (sample bias) | Sensitivity 80.4%, specificity 94.3%, Large effect (3.91) | Greece                                           | Measures of central tendency, ANOVA                                           | Positive effect on patient experience, pts value technology                          | I                     | A                   |
| Burdea et al.    | 10                    | Sydney, Australia only (selection bias)              | not reported | USA                                               | Measures of central tendency, ANOVA, t-test                                      | Positive effect on patient experience, pts value technology                          | II                    | B                   |
| Finn et al.      | 31                    | Pittsburg, USA only (selection bias)                | Small Effect (0.17) | Australia                                        | Measures of central tendency, paired t-test, Fisher’s exact test                | Positive effect on patient experience, pts value technology                          | I                     | A                   |
| Callan et al.    | 27                    | Moncalieri, Italy (selection bias)                  | not reported | Italy                                            | Measures of central tendency, repeated measures GLM, t-tests                  | Positive effect on patient experience, pts value technology                          | I                     | A                   |
| Cavallero et al. | 80                    | Kosice, Slovak Republic only (selection bias)       | Medium Effect (0.64) | Slovakia                                        | Measures of central tendency, ANOVA, t-tests, Shapiro–Wilk test, D’Agostino-Pearson test | Positive effect on patient experience, pts value technology                          | I                     | A                   |
| Hyer et al.      | 68                    | US only (selection bias)                            | Medium       | USA                                               | Measures of central tendency, ANOVA                                             | Positive effect on patient experience, pts value technology                          | II                    | A                   |
| Boyd et al.      | 19                    | Northern Ireland only (selection bias)              | not reported | Ireland                                          | Measures of central tendency, t-tests                                          | Positive effect on patient experience, pts value technology                          | III                   | B                   |
| Yang et al.      | 20                    | Namyangju, south Korea only (selection bias)        | not reported | Korea                                            | Measures of central tendency, Mann–Whitney U-test, t-tests                    | Positive effect on motivation and mood pts value technology                          | I                     | B                   |
## Table A3. Cont.

| Authors          | Sample Size (#s only) | Bias within Study (Selection Bias, Sample Bias, etc.) | Effect Size | Country of Origin (Where the Study Was Conducted) | Statistics Used                                                                 | Patient Satisfaction | Strength of Evidence | Quality of Evidence |
|------------------|-----------------------|------------------------------------------------------|-------------|---------------------------------------------------|---------------------------------------------------------------------------------|----------------------|----------------------|---------------------|
| Lee et al.       | 20                    | Chungbuk National University Hospital, Korea only (selection bias) limited number of treatment sessions (design bias) | not reported | Korea                                             | Measures of central tendency, independent t-test, Mann-Whitney U-test           | not reported         | I                    | B                   |
| Park et al.      | 78                    | one country (selection bias)                         | not reported | Korea                                             | Measures of central tendency                                                   | pts value technology | I                    | A                   |
| Flak et al.      | 68                    | Norway only (selection bias), majority male (sample bias) | Not reported | Norway                                           | Linear mixed models                                                            | pts value technology | I                    | A                   |
| Kahn             | 38                    | Pakistan only (selection bias)                       | not reported | Pakistan                                         | ANOVA with Scheffe post hoc analysis, paired t-test                           | not reported         | I                    | A                   |
| Park             | 21                    | Korea only (selection bias)                          | not reported | Korea                                            | ANOVA with Shapiro–Wilks test, student’s t-test                                | not reported         | I                    | A                   |
| Park et al.      | 45                    | One country (selection bias)                         | not reported | Korea                                            | GLM                                                                             | not reported         | III                  | A                   |
| Robert et al.    | 46                    | One country (selection bias)                         | not reported | France                                           | Student t-test, Wilcoxon-Mann–Whitney, Chi-square, Fisher’s exact, and Wilcoxon | not reported         | I                    | A                   |
| Thapa et al.     | 66                    | One country (selection bias)                         | not reported | Korea                                            | ANOVA, Shapiro–Wilk                                                            | not reported         | I                    | A                   |
| Oliveria et al.  | 34                    | One country (selection bias)                         | large       | Portugal                                         | ANOVA with Bonferroni correction                                                | not reported         | I                    | A                   |
| Seredakis et al. | 43                    | One country (selection bias)                         | medium       | Australia                                        | Chi-square, Shapiro–Wilk, Wilcoxon signed rank test, Mann–Whitney U test       | not reported         | II                   | A                   |
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