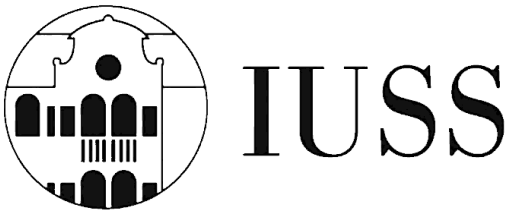
UNIVERSITY OF PAVIA – IUSS SCHOOL FOR ADVANCED STUDIES PAVIA

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HomeCoRe App: prelude of a usability and user experience study, a qualitative approach

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INDEX

Abstract 1

Introduction 3

Chapter 1: Cognitive decline: definitions, risk factors, neurobiological markers and cognition-oriented treatments 7

1.1 Physiological and pathological ageing 7

1.2 Neurobiological mechanisms underlying cognitive decline 9

1.3 Risk factors associated with cognitive decline 11

1.3.1 Non-modifiable risk factors 11

1.3.2 Modifiable risk factors 12

1.4.1 Cognition-Oriented Treatments 19

1.4.2 Cognitive Stimulation, Cognitive Training and Cognitive Rehabilitation 19

1.4.3 Restorative and Compensatory methods 22

1.4.4 Delivery modalities 23

1.4.5 Efficacy of interventions and new rehabilitative methods 24

1.5 Synopsis 25

Chapter 2. Computerised cognitive interventions: history, efficacy and tools 27

2.1 Terminology and conceptual distinctions 27

2.1.1 Computerised Cognitive Rehabilitation 27

2.1.2 Computerised Cognitive Training 29

2.1.3 Computerised Cognitive Stimulation 31

2.2 Historical becoming of computerised interventions 33

2.3 Theoretical mechanisms of Computerised Cognitive Interventions 34

2.4 Comparative evidence 36

2.5 Technological platforms and delivery tools 36

2.5.1 Desktop and Laptop computers 37

2.5.1.1 CoRe: a Computerised Cognitive Rehabilitation System 39

2.5.2 Tablets and Touchscreen devices 41

2.5.3 Virtual Reality-based interventions 42

2.5.4 Serious Games 43

2.5.5 Platform specific considerations in neurodegenerative disease 43

2.6 Emerging technological trends and future pathways 43

2.6.1 Functional outcomes, QoL, and participation 44

2.6.2 Adherence, user experience and motivation 45

2.6.3 Implementation and health-systems perspectives 45

2.7 Synopsis and next directions: towards telerehabilitation 46

Chapter 3. Telerehabilitation within contemporary telehealth ecosystems: foundations, evidence, and usability 49
3.1 Telemedicine – clinical care in digitally supported environments 51
3.2 TR as a continuum of care 52
3.2.1 Clinical and technological requirements for TR 53
3.2.2 Design principles for computerised cognitive intervention systems 54
3.3 Evidence base for TR in cognitive and neurodegenerative conditions: scope, benefits, and limits 56
3.4 TR studies: trial designs, workflows, and outcome architecture 57
3.4.1 Usability, feasibility, and adherence as determinants of TR effectiveness 62
3.4.2 Evidence from cognitive TR applications 63
3.5 Synopsis 66
Chapter 4. HomeCoRe: qualitative study of a clinician-guided application for computerised cognitive TR 69
4.1 Transitioning from CoRe to HomeCoRe – from in hospital settings to patients' homes 69
4.2 Conceptual foundations of the HomeCoRe system 71
4.2.1 Ontology-based model and semantic continuity between CoRe and HomeCore 72
4.2.2 Usability and clinical effectiveness evidence 73
4.3 Rationale for HomeCoRe as an app-based TR system 75
4.4 Functional design and operational workflow of the HomeCoRe app 77
4.4.1 Patient interface and home-based workflow 77
4.4.2 Therapist interface and remote clinical management 80
4.4.3 Exercises modules and cognitive domains targeted 82
4.5 Methodology: a qualitative approach 85
4.5.1 Participants 86
4.5.2 Images selection for the Puzzle exercise 87
4.5.4 Creation of visual sequences for Scene ordering 89
4.6 Levels testing 91
Chapter 5. Results 95
5.1 Legacy tasks 95
5.2 Newly added tasks 96
5.3 Recurring categories of bugs and usability-related difficulties in the patient interface 97
5.4 Therapist interface technical bugs and usability related difficulties 100
Chapter 6. Discussion 103
6.1 Outcomes overview 103
6.2 Technical reliability and migration challenges 103
6.3 Task design and interface-level problems 104

6.4 Development implications and refinements implemented 105
6.5 Role in the HomeCoRe validation pathway and context of deployment 107
6.6 Strengths and limitations 108
6.7 Future directions and conclusion 109
Chapter 7. Conclusion 111
Bibliography 113

Abstract

Ageing is associated with an increasing prevalence of cognitive deterioration and neurodegenerative conditions, making a rising amount of people in need for rehabilitative interventions that are effective and sustainably delivered at the same time. Cognition Oriented Treatments (COTs) can support functional autonomy, while telerehabilitation (TR) approaches enable structured interventions to be delivered beyond clinical settings and into patients' homes. Within this framework, HomeCoRe is a clinician guided cognitive TR system derived from the validated CoRe platform and it is designed to provide adaptive, remotely supervised training through an application-based environment. The present study aimed at contributing to the technological validation pathway of the HomeCore app by the evaluation of its technical functionality and usability prior to formal user-based testing. A structured qualitative internal testing process was conducted over a three-month period by a multidisciplinary team. Both already existing exercises in the system and newly added tasks were systematically executed, while adaptive progression mechanisms, interface elements, feedback computation, and therapist-side workflow features were examined. Technical bugs and usability-related observations were logged, coded, and clustered in order to identify recurrent issues and inform targeted adjustments. Results showed a predominance of system-level technical bugs, particularly affecting migrated legacy exercises, while usability refinements were more frequent in newly added tasks. The testing process enabled corrections to adaptive progression logic, response features, stimulus presentation, and data export functions, improving the technological robustness and interaction clarity of the platform. Overall, this work represents an intermediate yet essential step in the HomeCoRe validation pathway. By embedding structured qualitative testing within the development process, the study strengthens the software readiness for future usability studies with healthy participants and clinical populations, in addition to supporting the development of accessible, scalable, and clinician-guided digital solutions for home-based cognitive TR.

Keywords: Cognition Oriented Treatments (COTs); Telerehabilitation (TR); HomeCoRe; Usability testing

Introduction

Over the past decade, the global population has undergone a profound and unprecedented demographic transformation, characterised by a steady increase in life expectancy that is leading to both challenges and opportunities for healthcare systems around the world. Indeed, a combination of factors, such as improved living conditions, changing societal dynamics and advances in healthcare, facilitated the ongoing increase in life expectancy (Islam, 2021). This resulted in a substantial change in the demographics, where a growing proportion of the population consists of elderly individuals (Ogugua et al., 2024). As a consequence, an increased prevalence of chronic diseases were reported in the ageing population, such as cardiovascular conditions, diabetes, neurodegenerative disorders (World Health Organization, 2015) and an augmented risk of mental health problems (Ogugua et al., 2024). In particular, cognitive decline represents one of the most concerning aspects associated with ageing, with Mild Cognitive Impairment (MCI) – a term used to describe a transitional status between physiological aging and the possible development of early dementia, characterised by a cognitive decline that does not interfere with activities of the daily life (Bernini et al., 2023) – affecting a notable proportion of older individuals. Although determining an exact percentage of people affected has proven rather complicated (Casagrande et al., 2022), estimates suggest that the prevalence of MCI in adults aged 60 years and above ranges from 6.7 to 25.2%, increasing with age and lower educational attainment (Salari et al., 2025). More importantly, even though the risk of developing dementia may be affected by other comorbidities (Livingston et al., 2020), a significant proportion of individuals who received an MCI diagnosis will ultimately convert to dementia over 2-5 years; thus emphasising the critical need for early intervention and continuous cognitive stimulation (Menegon et al., 2024).

Healthy ageing encompasses more than the mere absence of disease: The World Health Organization (WHO) adopts a functional perspective that accounts for the entire duration of the lifespan. It defines healthy ageing as the process of developing and maintaining the functional ability that enables well-being in older adults, referring to all the health-related factors that allow individuals to act according to their preferences and beliefs, to learn, grow, make decisions, be mobile, to form and maintain relationships, to meet their basic needs and contribute to society (W. Zhang & Wang, 2025). Within this perspective, preserving cognitive functioning is central, since it directly influences emotional health, autonomy and the overall quality of life (Jeon et al., 2025). In light of this goal, and considering the limited effectiveness of pharmaceutical solutions in stabilizing cognitive decline or attenuating its rate (Bernini et

al., 2019), cognition-oriented treatments aim at maintaining or, if possible, improving people's cognitive functions and functional abilities. Furthermore, cognitive rehabilitation appeared to be the most effective method in diminishing caregivers burden, thus suggesting a more comprehensive approach (Paggetti et al., 2024). To serve the purpose of enhancing quality of life in the ageing population, a recent innovation has been successfully introduced across several rehabilitation fields. Telerehabilitation, or the delivery of rehabilitation services via communication technologies, has become increasingly popular thanks to its ability to overcome the known barriers of traditional paper-and-pencil, face-to-face cognitive rehabilitation (Shnitzer et al., 2025). With this knowledge in mind, developing tools that are accessible, engaging and effective to support cognitive health in older adults is not only an urgent societal priority, but also a research one; especially considered the constraints of different nature – accessibility, mobility and transportation, dependence on caregivers, financial ones – that characterize more traditional methods (Jeon et al., 2025).

In fact, the present research aims to contribute to this goal through the design and evaluation of a specifically developed computerized tool, particularly investigating its usability and user experience. CoRe is a software first designed and tested in the early 2000s which is administered in hospital settings, using a computer-supported cognitive rehabilitation program with face-to-face sessions between patients and therapists. CoRe has been successfully tested in participants affected by early cognitive decline in terms of usability, as well as immediate and long term effectiveness. From the positive results obtained, the patients' and their caregivers feedback, stemmed another system: HomeCoRe, a new version of the software that allows for continuity of care for discharged patients (Quaglini et al., 2019). Compared to its previous versions, it is innovative in that it is implemented directly in patients' homes via a tablet and does not require the constant presence of a healthcare professional, thereby promoting both autonomy and accessibility, two factors that have proven to be essential in elderlies' quality of life (QoL) and care (Quaglini et al., 2019; Jeon et al., 2025). The broader objective of HomeCoRe is to facilitate the maintenance of a high QoL through continuous and adaptive cognitive engagement. Specifically, this system automates the generation of personalised cognitive exercises by leveraging a vast repository of stimuli, therefore enabling the creation of diverse, tailored training sessions. In addition to that, other pillars of this system are the simplification and streamline data collection processes, known to optimise the monitoring of users' progress and reduce the workload for both clinicians and researchers (Bottiroli et al., 2024).

The present research is situated within the developmental phase of the HomeCoRe app-based implementation and adopts a qualitative, iterative design aimed at supporting the transition from a computer-based home delivery to an Android-operated mobile application. Instead of evaluating clinical outcomes, this study focuses on the operational refinement of the system, which includes the creation and validation of new stimuli, the systematic testing of adaptive progression and regression mechanisms, the verification of feedback and scoring coherence, characterised by structured documentation of technical and usability-related difficulties. Conducted over a three-month period by a multidisciplinary team, this phase constitutes a pre-validation step, intended to ensure that the newly redesigned and adapted interface, the exercise contents, and remote supervision architecture remained consistent with the underlying ontological rehabilitation model while being suitable for independent use in home environments. The qualitative study took place through spreadsheet-base logging, cross-verification with the therapist interface, and iterative bug clustering, thus being able to identify technical inconsistencies and usability vulnerabilities prior to deployment in clinical or healthy populations. In this sense, the present study contributes to the methodological consolidation of the HomeCoRe app as a clinically grounded, technologically reliable, and scalable telerehabilitation system.

Chapter 1: Cognitive decline: definitions, risk factors, neurobiological markers and cognition-oriented treatments

In the past decade, global demographics have undergone a marked shift driven by continuous increases in life expectancy, a trend that simultaneously present complex challenges and strategic opportunities for modern healthcare systems. Advances in medical science, sustained improvements in living conditions, and broader socioeconomic developments have collectively contributed to this longevity expansion (Islam, 2021). As a result, older adults now constitute an increasingly substantial proportion of the population (Ogugua et al., 2024). This demographic transition is accompanied by a corresponding rise in age-associated chronic conditions – including cardiovascular and metabolic diseases, as well as neurodegenerative disorders (World Health Organization, 2015) – and by heightened susceptibility to mental health difficulties within ageing cohorts (Ogugua et al., 2024).

1.1 Physiological and pathological ageing

Ageing represents the most influential risk factor for neurodegeneration, and it profoundly shapes the biological landscape in which it occurs. Even in healthy individuals, ageing is accompanied by progressive deterioration in cognitive abilities, which are the result of structural and molecular modifications in the brain (Gonzales et al., 2022). When mentioning cognitive abilities, we are referring to measurable mental capacities reflected in performance on tasks that require processing information, and that range from simple perceptual operations to complex reasoning and problem solving. According to Otero and colleagues, these abilities encompass general cognitive functioning as well as specific domain such as verbal, numerical, spatial, and working-memory skills, and they are known to explain individual differences in how people learn, reason, and adapt to different environments and situations (Otero et al., 2022).

While mild changes in cognition are expected within age, thus highlighting a physiological process, pathological decline develops beyond normative ageing and often ultimately leads to a significant functional impairment (Jessen et al., 2020). This similarity between physiological and pathological ageing suggest that many of the mechanisms historically known for leading to dementia may actually arise from a broader biological process, which puts ageing not merely as a background factor, but as a central driver of cognitive vulnerability. Indeed, cognitive decline begins subtly in early adulthood and it particularly impacts processing speed, reasoning, episodic memory and visuospatial abilities; whereas other, more crystallised skills remain

comparatively steady. In this pattern, different cognitive domains are differentially vulnerable, depending also on the specific type of pathology developed (Gonzales et al., 2022).

For instance, episodic memory, supported by hippocampal and medial-temporal regions, is – among all and especially in Alzheimer's disease – the first cognitive function to be affected. Likewise, working memory, reliant on fronto-parietal circuits, also tends to decline with age as a consequence of a reduced efficiency in processing abilities (Reuter-Lorenz & Park, 2014). On the other hand, procedural memory – a type of implicit memory that relies on the striatum, the cerebellum and other subcortical areas and that is expressed through performance – is often less affected even in neurodegenerative conditions (De Wit et al., 2021). Regarding executive functioning, evidence shows a deterioration with age affecting panning, inhibitions, and multitasking, as those are domains particularly susceptible to frontal and cerebrovascular pathology (McDonald et al., 2018). In addition to this, declines in attention and processing speed seem to be ubiquitous as meta-analytic work on aging consistently highlights a reduction in information-processing capacity as one of the most robust changes detected in this stage of life (Wu et al., 2022). Evidence suggests that in healthy ageing many language abilities such as vocabulary and semantic knowledge, remain relatively intact or show only subtle declines (for instance a slowed lexical retrieval); whereas in pathological ageing, like MCI and Alzheimer's disease, language impairments tend to be more pronounced and clinically detectable, impacting naming, semantic processing, and fluency (Alexander et al., 2012; Taler & Phillips, 2008). In fact, in neurodegenerative diseases such as Primary Progressive Aphasia (PPA), language becomes profoundly impaired (Spinelli et al., 2017). Finally, neurodegeneration can also affect the posterior parietal lobe, therefore causing a decline in visuospatial abilities. Importantly, as researchers have shown, visuospatial impairment was the earliest sign of MCI, resulting from both attention and memory impairment (Derbie et al., 2022). Therefore, a more focused prevention approach is encouraged (Berente et al., 2022).

Rather than emerging abruptly in later life, these changes accumulate gradually overtime, and are accompanied by measurable shifts in brain structure and function (Gonzales et al., 2022). Consequently, cognitive decline needs to be conceptualised not as a monolithic process, but as a multifaceted phenomenon shaped by neurobiological, environmental, and psychological factors (Prince et al., 2024). A growing body of literature describes cognitive decline as a continuum where dementia represents the most advanced stage of cognitive impairment and is characterised by deficits severe enough to interfere with activities of daily living that compromise personal independence; while MCI involves measurable cognitive decline without

the functional impairment. Also, at an earlier stage, some individuals may report subjective cognitive difficulties (Subjective Cognitive Decline, abbreviated with SCD) despite exhibiting normal performances on standard neuropsychological assessments and retaining intact everyday functioning (Jessen et al., 2020). Even at the earliest stages of SCD, people might be already accumulating underlying neuropathology (Hanseeuw et al., 2019). For this exact reason, subjective cognitive decline must not be underestimated: it has been associated with a higher risk of progression to MCI and dementia, therefore making it a critical window for early identification and intervention (Jessen et al., 2020).

1.2 Neurobiological mechanisms underlying cognitive decline

Understanding why cognitive decline occurs requires an investigation of the underlying neurobiological mechanisms. In neuroimaging studies, people with a diagnosis of a neurodegenerative disease showed a steady reduction in grey matter volume, especially within frontal and parietal regions, alongside degradation in white matter integrity (Habes et al., 2016; Ziegler et al., 2012). These microstructural changes, which reflect demyelination, oligodendrocyte decline, and small vessel pathology contribute to a slower neural transmission, which in turn diminishes executive and procedural-speed performance. In addition to this, ageing neurons have been proven to show disrupted pattern of excitability, with some population exhibiting a reduced firing capacity, and others displaying maladaptive hyperexcitability (Dunn & Kaczorowski, 2019), which not only increase the probability of seizures, but also the acceleration of cognitive decline (Beagle et al., 2017).

These structural and functional alterations unfold in parallel with the gradual accumulation of neuropathological proteins. For instance, β-amyloid plaques and tau neurofibrillary tangles (NFTs) emerge decades before the onset of cognitive symptoms, with evidence of the presence of pathological processes detectable even in midlife. These proteins, known to play a central role in Alzheimer's disease, both have prion-like properties that enable their spreading along neural networks. Yet, neuropathological burden alone seems to be unable to explain the entirety of cognitive outcomes: many older adults with significant proteinopathies remain cognitively intact, suggesting the presence of some resilience mechanisms centred possibly on synaptic function and cellular homeostasis (Gonzales et al., 2022).

Within this network, several hallmarks of ageing are worth mentioning. Among these, disruptions in autophagy that cause the inability of the neurons to dilute cellular waste emerge as a central factor. In fact, normally neurons rely on efficient autophagy to clear toxic proteins

and damaged organelles. Ageing, unfortunately, is associated with impaired autophagic flux, reduced expression of key regulators, and diminished activation of lysosomal pathways. These deficits hinder the clearance of misfolded proteins, facilitating their aggregation and spreading (Gonzales et al., 2022). Highly related with the autophagic impairment is the mitochondrial dysfunction. Mitochondria, with their high metabolic demand, regulate cellular energy production, calcium homeostasis, redox balance, and apoptosis. Across the lifespan, mitochondrial DNA mutations, reduction in their biogenesis and increases in oxidative stress accumulate, thus contributing to the alteration detectable in neurodegenerative diseases. Importantly, proteins such as tau and β-amyloid exacerbate the mitochondrial injury, creating a self-reinforcing cycle that contribute to synaptic failure and neuronal loss (Gonzales et al., 2022).

Another relevant aspect to mention is chronic neuroinflammation: paired with oxidative stress, it accelerates the onset of neuronal dysfunction. As a result of this, neurogenesis may be impaired by the presence of activated microglia, pro-inflammatory cytokines, and reactive oxygen species (ROS), degrading synaptic integrity. In fact, microglia serve as the primary component of the brain's immune system and has the ability of detecting exogenous pathogens. Upon activation, microglia elicit a neuroinflammatory cascades, characterised by the release of pro-inflammatory cytokines, chemokines and ROS in the attempt of preserving homeostasis. Unfortunately, a persistent microglial activation or dysregulation can result in an inflammatory state, known to initiate the onset of the neurodegenerative disease and sustain its progression (Ahmad et al., 2022). Although mild inflammation may initially exert protective effects, sustained neuroinflammatory signalling – driven by microglial activation, maladaptive T-cell responses, and cytokine dysregulation – plays a decisive role in the acceleration of neurodegenerative diseases (Gonzales et al., 2022).

However, these are only some of the possible pathways an ageing brain encounters. Increasing evidence has been reported on the contribution of vascular dysfunctions on cognitive decline in ageing and dementia. Cerebrovascular events – such as microinfarcts, microbleeds and white-matter hyperintensities (WMH) – are highly prevalent in older adults and significantly contribute to cognitive decline via a reduction of cerebral blood flow, a loss of blood-brain barrier function or a combination of these two factors (Anderle et al., 2025).

Finally, it is necessary to briefly report the role played by epigenetic alterations and lipid dysregulation: the former have gained increasing relevance with the emergence of epigenetic

clocks that offer promising evidence for estimating biological brain age and predicting vulnerability to cognitive decline (Gonzales et al., 2022); the latter has been systematically linked with ageing and often arises early in the course of Alzheimer's disease, thus making lipid disturbances promising biomarkers for preclinical detection (Yin, 2023). Collectively, cognitive decline cannot be ascribed to a single pathological pathway. Instead, it arises from the convergence of multiple age-related processes that interact in nonlinear and mutually reinforcing ways (Mattson & Arumugam, 2018). Understanding these interconnected mechanisms highlights the importance of approaches aimed at modifying fundamental ageing pathways, which may hold promise not only for delaying neurodegenerative diseases but also for preserving cognitive function across the lifespan (Fillit et al., 2023).

1.3 Risk factors associated with cognitive decline

As individuals age, cognitive capacities increasingly reflect the influence of a constellation of factors that may exert either beneficial or detrimental effects on brain functioning. The literature identifies a broad array of risk and protective factors – spanning lifestyle, behavioural, social, medical, genetic, and environmental domains – that have been associated with both declines and enhancements in cognitive performance. Consequently, an individual's cognitive trajectory can be shaped in diverse ways over the long term (Wajman et al., 2019). Research aimed at preventing preclinical forms of dementia, including MCI, has therefore increasingly focused on the proactive identification and management of these determinants given their potential contribution to cognitive deterioration (Chowdhary et al., 2022).

1.3.1 Non-modifiable risk factors

First of all, it is essential to recognise that the risk of cognitive decline is modulated by a constellation of modifiable and non-modifiable factors. Cognitive trajectories can be influenced by a variety of factors that cannot be easily altered – hence the term non-modifying. They include age, genetic predisposition, sex differences, and early life development. These factors set a baseline level of vulnerability, however, stating that they are able to determine cognitive outcomes in isolation would be incorrect (Livingston et al., 2024). Among non-modifiable determinants, age remains the strongest predictor of cognitive deterioration, reflecting cumulative neurobiological changes such as synaptic loss, reduced neuroplasticity, oxidative stress, and microvascular degeneration (Committee on the Public Health Dimensions of Cognitive Aging et al., 2015). Moreover, genetic predispositions, particularly the presence of risk alleles such as the APOE- ε4, further contribute to vulnerability through mechanisms involving lipid dysregulation, neuroinflammation, and altered amyloid processing. Additional

inherent factors – such as sex differences and early-life neurodevelopmental conditions – contribute to baseline risk, although not independently determining an individual's cognitive trajectory (Committee on the Public Health Dimensions of Cognitive Aging et al., 2015). Similarly, the literature highlights the contribution of several other specific genetic variants to increased risk. For instance, mutations in the Amyloid Precursor Protein (APP) – which encodes a membrane-bound protein – have been implicated in altered amyloid processing (Espinosa et al., 2018). Variants in Complement Receptor 1 (CR1), a key regulator that down-modulates the complement cascade, have also been associated with heightened susceptibility. Additional genes linked to cognitive decline include EPHA1, which encodes a tyrosine-kinase receptor, and CHRNA7, the gene for the α7 nicotinic acetylcholinesterase inhibitors (Felix et al., 2019).

1.3.2 Modifiable risk factors

Beyond these fixed characteristics, a substantial body of evidence highlights the central role of modifiable risk factors, which exert significant influence over the rhythm and pattern of cognitive decline. It is essential to consider them as behavioural components to build the prevention on: specifically, dementia prevention should take a tailored approach depending on the different groups of determinants, with the ultimate goal of reducing both structural and sociocultural barriers (Livingston et al., 2024). In the figure below, a graphical representation of all the determinants reported by Livingston and colleagues that aims to serve this purpose.

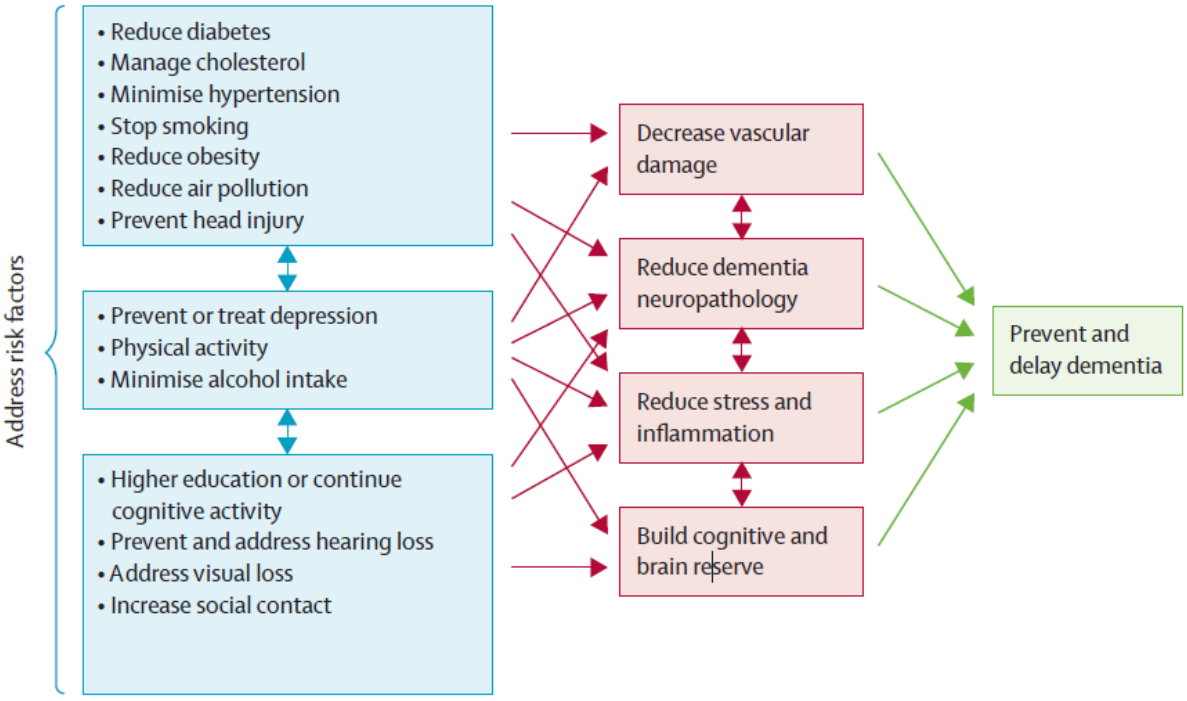


Figure 1: Risk factors to acknowledge in dementia prevention (Livingston et al., 2024)

1.3.2.1 Educational attainment

Research consistently shows that educational attainment is a major protective factor against cognitive decline and dementia. Not only does higher childhood and adult education correlate with reduced dementia risk, but the quality of education also must be taken into account (Livingston et al., 2020). Evidence consistently suggests that it is educational attainment, rather than simply years of schooling, that confers the strongest long-term cognitive protection. International studies further underscore this pattern (Seblova et al., 2020; Seblova et al., 2021). In China, for instance, rising dementia rates have been concentrated among individuals with very low schooling, likely because improvements in overall health have allowed more low-educated individuals to reach older ages, where dementia becomes inevitably more common (Ding et al., 2020). In contrast, dementia prevalence in the United States has declined alongside parallel to increased educational access, with the most pronounced improvements observed in Black older adults. Furthermore, similar protective associations with higher education have been reported among various Asian American groups (Livingston et al., 2024).

1.3.2.2 Occupational stimulation

In the pursuit of investigating the many protective factors, researchers have identified the following as having a solid role in preventing cognitive decline: exposure to craiognitive stimulation in the workplace. Over the course of decades, large longitudinal studies showed that individuals in cognitively demanding occupations experience a substantially lower dementia risk compared with others in less stimulating roles, even controlling for educational attainment (Hyun et al., 2022). As a matter of fact, occupational complexity appears to partially mediate the cognitive benefit of education, although evidence suggests that associations may vary across racial and socioeconomic groups (Livingston et al., 2024).

1.3.2.3 Cognitive reserve and intelligence related traits

Considered the relevant variability of rate, severity and speed of decline in people, underscoring the existence of many different trajectories of cognitive and functional decline, it is essentially impossible not to factor in the role of cognitive reserve (Boyle et al., 2019). The findings mentioned align with the broader concept of cognitive reserve, a latent property of the brain that enables individuals to maintain higher-than-expected cognitive performance in spite of age-related changes, disease or injury. It reflects the brain's ability to adaptively and flexibly recruit and re-configure functional networks and cognitive strategies in response to damage or pathology (Kremen et al., 2022; Stern, 2002). This ability could be mediated by a number of mechanisms, including, increased occupational attainment – paired with improved financial

situation, leading to more choices about housing, better access to health-care facilities, physical health, and health awareness altogether – greater efficiency of and less decline in functional brain networks, and higher concentrations of circulating proteins to enable the brain's reparative processes thorough axonogenesis and synaptogenesis. Moreover, genetic studies also indicate that the cognitive benefits associated with education are partly mediated by underlying intelligence related traits (Livingston et al., 2024).

1.3.2.4 Hearing loss

Another modifiable risk factor that has been extensively studied is hearing loss. In itself, hearing loss is considered a significant, independent risk factor for cognitive decline and dementia. Globally, approximatively one in five individuals experiences some degree of hearing impairment, and prevalence is known to rise sharply with age: more than 60% of adults with hearing loss are over 50, and the condition often remain untreated (Haile et al., 2021). Based on the results obtained by epidemiological high-quality cohort studies, it is possible to affirm that individuals with objectively measured peripheral hearing loss are at a higher risk of developing dementia at some point in life. Also, multiple meta-analysis corroborate this association, and even more recent research demonstrates the presence of a clear dose-response relationship, whereby each 10-dB worsening in hearing sensitivity increases dementia risk by approximately 10-20% (Livingston et al., 2024). To strengthen the evidence base, updated systematic searches identified six longitudinal studies meeting strict methodological criteria, such as including hearing assessments, adequate control for confounding variables, and sufficient follow-up duration. A random-effects-meta-analysis of these studies confirmed that hearing loss increases the risk of dementia by approximately 37%: importantly this estimate is considered conservative as it includes individuals who use hearing aids, even though a possible mitigation effect might be happening. In support of this interpretation, supplementary analyses suggest that cohorts with higher hearing-aid use show lower dementia incidence, although the precision of these estimates remains limited (Livingston et al., 2024). For the sake of thoroughness, it is crucial to weigh the severity and type of hearing impairment, as they both could influence the discussed association. Studies repeatedly report that greater hearing loss correspond to progressively higher dementia risk. Beyond pure-tone thresholds, impairment in speech-in-noise perception – the ability to understand speech in complex auditory environments – also predicts increased dementia incidence. Large scale data from the UK Biobank demonstrate that even moderate speech-in-noise deficits meaningfully elevate risk (Stevenson et al., 2022).

Several mechanisms have been proposed to explain these associations. First of all, hearing loss may lead to reduced cognitive stimulation, thereby diminishing cognitive reserve and promoting neural vulnerability. It can also enhance the effects of social isolation, depression and loneliness, all of which are established risk factors for cognitive decline. In addition to this, compensatory listening effort may divert cognitive resources away from other processes, thereby accelerating decline overtime (Griffiths et al., 2020). A further hypothesis is a shared underlying pathology affecting both the auditory system and brain regions implicated in dementia, such as common cardiovascular involvement: unfortunately, the insufficient evidence available impedes researchers to prove this possible association for the time being (Griffiths et al., 2020). Given these pathways, the potential role of hearing aids in conceptualising dementia prevention has become a question of increasing interest. Findings from the ACHIEVE randomised controlled trial (RCT) prove that while hearing aids did not improve cognitive performance across all participants, they provided substantial cognitive benefits among individuals at higher dementia risk, reducing cognitive decline by nearly 50% over three years in the subgroup with greater baseline vulnerability (Livingston et al., 2024).

1.3.2.5 Visual impairment

Similarly, visual impairment has also been associated with a higher risk of cognitive decline and an eventual dementia diagnosis (Shang et al., 2021), with meta-analysis indicating roughly a 35-50% increase in risk among older adults (Livingston et al., 2024); an association that in some studies seem to weaken following cataract surgery, thus highlighting the promising preventative aspect of accounting for this factor (Ma et al., 2023).

1.3.2.6 Depression

One key determinant that has been thoroughly studied and successfully linked with dementia is receiving a diagnosis of depression. Evidence accumulated over the past decades indicates that the relationship between the two is complex and likely bidirectional. Depressive symptoms may precede dementia as an early manifestation of neurodegeneration, emerge as a psychological reaction to subtle cognitive deficits, or independently contribute to cognitive decline through biological and behavioural pathways. In fact, researchers also noted a major gap in the literature concerning whether treatment of depression alters long-term dementia risk (Livingston et al., 2020). Recent work has further strengthened the association between depressing and subsequent dementia. For instance, focusing specifically on high-quality prospective studies with extended follow up (10-14 years), a new analysis conducted for the Lancet Commission confirmed a robust association, with individuals with depression having a 2.25-fold higher risk

of developing dementia compared with those without depression. These findings were consistent across cohorts differing in age, sex, socioeconomic status (SES), and comorbid health conditions (Livingston et al., 2024). Interestingly, a Danish case-control study involving over a million participants found that depression was associated with substantially higher dementia risk across the entire adult lifespan – even when depression occurred decades before dementia diagnosis. This increased risk was evident for early-life, midlife and late-life depression, which suggested that vulnerability is not restricted to any particular age group (Elser et al., 2023); however, the Lancet Commission has classified depression as an elevated risk factor when it occurs in midlife (Livingston et al., 2024).

Although the precise biological pathways remain uncertain, several explanations have been proposed. Depression may contribute to dementia through reduced social engagement, diminished self-care, and lifestyle factors that negatively affect the health of the brain. On this note, neurobiological pathways have also been suggested, including chronic cortisol elevation, hippocampal atrophy, and increased inflammatory responses, all of which may compromise neural integrity and resilience (Ouanes & Popp, 2019). Specifically, treating depression, whether with psychotherapy, pharmacotherapy, or a combined approach, was proven to have a notably lower risk of developing dementia, with combined therapy showing the strongest protective association (L. Yang et al., 2023).

Recent studies also indicate that treating depression may reduce the risk of receiving a dementia diagnosis: it is the consistency of the evidence that supports the notion that managing depression is crucial not only to improve quality of life (QoL), but also as a potential strategy to reduce the risk of developing the pathology altogether. All in all, current data identifies depression as a major, modifiable risk factor whose early identification and treatment might contribute meaningfully to dementia prevention efforts (Livingston et al., 2024).

1.3.2.7 Traumatic Brain Injury

Moving to the next modifiable risk factor, considering Traumatic Brain Injury (TBI) as a variable to be accounted for with the aim of designing preventative measures, has been demonstrated purposeful. A substantial body of evidence now indicates that TBI increases the risk of developing dementia, with analyses consistently reporting risk estimates between 1.6 and 1.9 times higher among individuals who suffered a TBI (Livingston et al., 2024). Surprisingly, these associations are strongest when injury occurs earlier in life – before 65 years of age – and tend to be more pronounced in men (Gardner et al., 2023). However, the evidence for mild TBI (mTBI) seems to be more mixed, partly due to mismatching definitions. Despite

this, meta-analytic data using WHO criteria indicate a modest but significant elevation in Alzheimer's disease risk following a mTBI, with the possibility that earlier injuries confer greater vulnerability (Graham et al., 2022). Furthermore, several mechanisms may explain how TBI contributes to eventual neurodegeneration: axonal injury, accelerated accumulation of amyloid-β and hyperphosphorylated tau, microglial activation, cortical thinning and reduced cognitive reserve. Overall, current evidence identifies TBI as associated not only with increased dementia risk, but also with an earlier onset – typically two or three years earlier than in individuals without a TBI history (Livingston et al., 2024).

1.3.2.8 Smoking

Another modifiable risk factor that should not be ignored is smoking. Midlife smoking, in particular has been underscored as an important and preventable contributor to dementia risk. While earlier research linked smoking in later life to higher dementia incidence, more recent, large scale studies suggest that smoking earlier in adulthood poses an even greater risk, likely because improved treatment of smoking-related diseases now allows more smokers to survive the age at which dementia becomes clinically evident (Livingston et al., 2024). Some evidence also indicates sex-specific patterns, with particularly high risks reported for men (Juul Rasmussen et al., 2020). It is also important to underline how former smokers do not show this elevated risk: several studies report that people who quit smoking have a reduced likelihood of developing dementia compared to those don't, and the effect appears strongest when cessation happens before the age of 65 (Livingston et al., 2024).

1.3.2.9 Cardiovascular and lifestyle risk factors

Although individual cardiovascular and lifestyle risks are often examined separately, research increasingly highlights the importance of their combined influence on cognitive ageing (Livingston et al., 2024). Behaviours such as smoking, hypertension, diabetes, low educational attainment, physical inactivity, and social isolation, are also associated with heightened dementia risk (R. Wang et al., 2021). However, not all individuals with these conditions develop a neurodegenerative disorder, partly because some may die earlier from other causes before cognitive symptoms emerge (Song et al., 2022). For instance, a Chinese study involving more than 29,000 older adults demonstrated that people meeting at least four out of six healthy lifestyle criteria – a balanced diet, regular physical activity, frequent social engagement, participation in cognitive activities, non-smoking, and minimal alcohol consumption were observed in both APOε4 carriers and non-carriers, suggesting that healthy behaviour clusters may help counteract even genetic predispositions and vulnerabilities (Jia et al., 2023).

1.3.2.10 Air pollution

In addition to the risk factors presented until this point, air pollution might be the one of the newest considered. Growing evidence indicated that long-term exposure to fine particulate air pollution – particularly PM2.5 and PM10 – is associated with an increased risk of developing dementia, despite some degree of variability in study methods and pollutant measurements. Multiple recent meta-analyses confirm this relationship, showing that even small increases in PM2.5 are linked to a higher incidence of dementia (Livingston et al., 2024). Specifically, both outdoor and indoor pollution contribute to risk, with household sources such as solid fuel use and wood or coal stoves also associated with faster cognitive decline, especially in low and middle-income countries (Pu et al., 2023; Saenz et al., 2021). Air pollution appears to exert stronger effects in individuals with pre-existing cardiovascular conditions, suggesting to an overlap of cardiovascular and neurodegenerative pathways. Fortunately, improvements in overall air quality are associated with lower dementia rates and slower cognitive decline, underscoring pollution as a potentially modifiable environmental risk factor (Livingston et al., 2024).

1.3.2.11 Other worth mentioning risk factors

Finally, with the intent of describing the modifiable risk factors of developing dementia in the most comprehensive manner possible, others must be acknowledged: sleep deprivation, an unhealthy diet, mental health conditions, and infections. Even though these weren't associated with consistent enough evidence, it is still important to explore these variables as they have a degree of influence in the development of the disease (Livingston et al., 2024). In sum, it is possible to deduct the existence of protective factors such as cognitive reserve (built through education, occupational complexity, and mentally stimulating activities), social engagement, and heathy lifestyle behaviours. These, as reported, have a strong evidence base (Livingston et al., 2024).

1.3.2.12 The lifelong protective role of cognitive reserve

The concept of cognitive reserve helps explain why individuals with similar neuropathology may exhibit very different clinical symptoms, and why certain cognitive abilities or daily functioning are differently exposed to brain ageing, injury or pathology (Y. Liu et al., 2024). In fact, according to previous research on dementia prevention (Livingston et al., 2020), cognitive reserve is able to offer protection against the onset of dementia. The concept of cognitive reserve was initially proposed in the early 2000s by Stern and colleagues (Stern, 2002b), and it

referred to the adaptability of cognitive processes. Also, cognitive reserve has to be conceptualised as a dynamic construct, that is influenced by both lifelong exposure and more intrinsic factors, like the intelligence quotient (IQ) (Stern et al., 2020). Overall, taking into considerations different life stages – early-life, mid-life, and late-life – the protective role of cognitive reserve appears to be similar as increasing it is always beneficial; even though it might confer a higher protective effect in early and late life stages (Y. Liu et al., 2024).

Importantly, risk and protective factors do not act in isolation: they dynamically interact across the lifespan. Mid-life seems especially critical, as vascular risk, educational attainment, social engagement and lifestyle behaviours during this period of time exert profound influence on late-life cognitive trajectories. At last, the resilience of neural networks – either attributed to compensatory reorganisation or functional redundancy – may be bolstered by lifelong cognitive and social engagement, protecting against or delaying clinical decline (Livingston et al., 2024).

1.4.1 Cognition-Oriented Treatments

Given this rich and complex background, it became inevitable and nonetheless necessary to design therapeutic approaches. First of all, considering the limited effectiveness of pharmacological treatments, researchers have sought to identify additional factors in patient care that might delay the onset or slow the progression of cognitive decline (Yao et al., 2020).

1.4.2 Cognitive Stimulation, Cognitive Training and Cognitive Rehabilitation

In recent years, Cognition-oriented treatments (COTs), a group of non-pharmacological interventions designed to maintain or improve cognitive functioning (Paggetti et al., 2024), have drawn increasing attention. They are employed across multiple populations, including healthy older adults, individuals with SCD, MCI, and mild-to-moderate dementia, and can be delivered in a variety of settings ranging from outpatient clinics and day-care centres to long-term residential facilities. COTs are inherently non-invasive and generally carry fewer adverse effects compared to pharmacological treatments, making them appealing adjunct or alternative in multi-domain prevention and rehabilitation frameworks (Castellano-Tejedor, 2022). COTs have gained prominence also because they are aligned with public-health models of dementia prevention: large-scale epidemiological evidence shows that modifiable lifestyle, health, environmental factors across the life span – such as education, physical activity, cardiovascular risk control, and social engagement – influence cognitive resilience and dementia risk (Y. Liu et al., 2024; Livingston et al., 2024).

Differently from other treatments that are mainly oriented towards behavioural, emotional and physical outcomes, COTs are designed to improve or maintain cognitive functions, and even to address the impact the impairment can have on patients' daily lives (Gavelin et al., 2020). COTs specifically target cognitive functioning and typically include Cognitive Stimulation (CS), Cognitive Training (CT), and Cognitive Rehabilitation (CR). While these interventions share certain features (structured sessions, therapeutic engagement, and emphasis on repetition or compensatory learning), the literature distinguishes them based on differing aims and methods, and mechanisms of action. Notably, the NICE Guideline 97 (NG97) on dementia assessment, management, and support provides clear operational definitions for each (Paggetti et al., 2024).

CS involves engaging individuals in a variety of activities and discussions intended to enhance general cognitive and social functioning. It may be delivered individually or, as it happens more frequently, in group sessions. Two widely implemented protocols are available, such as Reality Orientation Therapy (ROT), and Cognitive Stimulation Therapy (CST). ROT can be implemented in non-clinical environments and delivered by caregivers directly in patients' homes (Chiu et al., 2018), whereas CST follows a standardised, evidence-based, 14-session group protocol – delivered twice a week over 7 weeks, with optional maintenance cycles – that integrates multiple techniques, including reality orientation, multisensory stimulation, reminiscence, and implicit learning (Desai et al., 2024; Paggetti et al., 2024). Recent neuroimaging findings have shown that CS may influence large-scale functional networks associated with cognitive reserve, such as the default-mode-network, possibly by enhancing compensatory communication between regions involved in attention, executive functioning, and semantic processing (T. Liu et al., 2021). Furthermore, CS benefits may be partially mediated by social engagement, a well-established protective factor across the dementia trajectory (Livingston et al., 2024). Recent meta-analyses indicate small-to-moderate improvements in global cognition for people with mild-to-moderate dementia, and some evidence also points to gains in memory, language, and working memory, alongside improvements in reported QoL and a reduction in neuropsychiatric symptoms (Desai et al., 2024).

Moreover, CR constitutes another personalised, goal-oriented intervention that focus on helping individuals, together with their caregivers, achieve objectives that are meaningful to their daily lives. Its primary objective is not to improve cognition directly, but to support functional performance and independence in patients with reduced cognitive abilities. The evidence for CR in dementia remains mixed and variable, and interventions often require caregiver

involvement: who help with goal selection, strategy rehearsal and environmental structuring. This dyadic framework enhances adherence and functional transfer. The goals of cognitive rehabilitation are multifaceted and therefore need to be customised to the individual (Paggetti et al., 2024). CR uses a combination of restorative and compensatory strategies, including structured practice, environmental modifications, external memory aids, metacognitive techniques – which include self-monitoring and error awareness – as well as goal-oriented, task specific training focused on improving functional performance in everyday activities (Cicerone et al., 2011; Clare et al., 2019; Clare & Woods, 2004). Furthermore, it recruits both preserved and impaired neural networks and supports behavioural adaptation to cognitive decline (Bahar-Fuchs et al., 2013; Huntley et al., 2015). Moreover, CR interventions are highly individualised and variable. For example, in the GREAT trial, CR consisted of 10 weekly sessions over three months, followed by four maintenance sessions over six months, delivered directly in the participant's home. Therefore, participants and their caregivers collaboratively set personal goals and tailored strategies, with ongoing reassessments and adaptations taken in order to adaptively reflect their changing needs (Clare et al., 2019). In clinical practice and research reviews, CR programmes frequently use goal setting tools such as Goal Attainment Scaling or the Canadian Occupational Performance Measure to define and monitor meaningful person-centred goals, thus highlighting the flexible, adaptive nature of CR (Jogie et al., 2021).

CT, on the other hand, consists of guided practice on standardised tasks designed to target specific cognitive functions, such as attention, working memory, processing speed, or executive function. Programs may focus on a single cognitive domain or train multiple domains simultaneously. CT can also be delivered individually or in groups, though individualised – and computerised – formats often allow for better personalisation (Paggetti et al., 2024). In terms of principles of action, CT is thought to have a neuroprotective effect that is able to delay or counteract both age and disease related degeneration, following the "use it or lose it" principle. Additionally, its aim is to improve cognition thorough repeated engagement of cognitive processes by using adaptive and challenging tasks, thus reflecting a process-based training or drill training approach (Van Balkom et al., 2020). Notably, it is able of doing so via stimulation of neuroplasticity – the brain's ability to undergo functional and structural modifications by altering neurogenesis, neurotransmission and synaptogenesis – and consequent enhancement of the existing cognitive reserve (Van Balkom et al., 2020). When it comes to dosage, it can vary considerably across studies, though many CT programmes use 1-3 sessions per week, each lasting approximately 45-60 minutes, over a period of several weeks –often 6-12 (Bahar-Fuchs

et al., 2013). Interestingly, evidence from therapist led CT suggests that moderate train intensity tends to be more effective than high-frequency schedules, since excessive cognitive load may reduce benefits in older adults, thus becoming counterproductive (Bahar-Fuchs et al., 2013). Overall, CT produces small-to-moderate improvements in trained cognitive domains such as attention, executive functions, and memory strategies; however, far transfer to untrained abilities or everyday functioning still remains limited (Simons et al., 2016).

Interestingly, a meta-analysis observed changes in brain activation during task performance and resting state functional connectivity in people who underwent CT: in particular CT induced increases and decreases in task-related activity in fronto-parietal brain regions. Also, multi-domain CT has been shown to counteract dysfunctional connectivity patterns in brain networks typically affected by ageing or pathological neurodegeneration, notably increasing intra-network connectivity within the Default Mode Network (DMN) and improving network segregation between DMN and Fronto Parietal Network (Van Balkom et al., 2020). Digital and remote CT delivery has further expanded accessibility, with recent systematic reviews highlighting the capability of achieving comparable outcomes to face-to-face interventions, supporting continuous, adaptive monitoring of patients' cognitive performance (Jeon et al., 2025)

1.4.3 Restorative and Compensatory methods

Restorative goals aim to improve impaired cognitive functions through repetitive, structured tasks that harness neuroplasticity (Berlucchi, 2011; Gopi et al., 2022). Conversely, compensatory goals rely on internal strategies – memory mnemonics, chunking, visualisation – or external aids, such as (notebooks, smartphone reminders, environmental restructuring) to bypass or mitigate deficits (Paggetti et al., 2024). Perhaps most importantly, CR emphasises functional, patient-centred outcomes: rather than focusing solely on test scores, CR practitioners work with patients and caregivers to define goals for meaningful daily activities, as can be managing medications, maintaining social engagement, or preserving independence in instrumental activities of daily living (IADLs) (Livingston et al., 2024; Paggetti et al., 2024). In this scenario, interdisciplinary integration is critical to deliver effective and contextually grounded intervention (Livingston et al., 2024).

A foundational aspect of successful COTs is assessment-guided planning. In fact, high quality neuropsychological assessments are of utmost importance in order to identify what cognitive functions are impaired, which ones are intact, and how these deficits map to real-life challenges

(Paggetti et al., 2024). Nonetheless, functional or ecological assessments should not be excluded, as they are essential to ensure that the intervention goals align with daily life demands. In order to structure patient-tailored sessions, clinicians often use structured goal-setting frameworks, such as SMART goals or Goal Attainment Scaling. Regarding the former, "SMART" is an acronym that stands for Specific, Measurable, Achievable, Relevant, time-bound that describes the qualities a rehabilitation plan must have; whereas the latter refers to a method that provide clear benchmarks for success in a tailored rehabilitation plan (Paggetti et al., 2024).

Cognitive rehabilitating interventions can be categorised into several broad approaches, each with empirical support. Restorative Methods include repetitive practice, computerised cognitive training, and memory rehabilitation techniques like spaced retrieval and errorless learning. Meta-analyses and reviews do support these intervention: for instance, a network meta-analysis comparing cognitive interventions in Alzheimer's disease found that all of the approaches mentioned earlier (CS, CR, CT), significantly improved global cognition: effect size g=0.43, with combined interventions ranking highest in benefit (Paggetti et al., 2024). Compensatory Approaches – such as external aids, internal cognitive strategies, and environmental modifications – are especially valuable thanks to their ability to translate rehabilitation into daily life (Paggetti et al., 2024). Moreover, Metacognitive Interventions, which cultivate self-monitoring, error awareness, and strategic problem solving, have shown to improve real-world functioning across clinical populations hinging on their ability to foster self-regulation and adaptability (Bampa et al., 2021). At last, another method worth mentioning consists of ecologically valid approaches (Clare & Woods, 2004). Specifically, these leverage task specific training and are focused in both ADL and IADL, expanding even onto virtual reality (VR) environments in order to better generalise gains to everyday contexts (Optale et al., 2010).

1.4.4 Delivery modalities

When considering delivery modalities, COTs have the merit of being increasingly flexible. In fact, even though traditional face-to-face individual or group sessions remain relatively standard, tele-rehabilitation not only has grown rapidly in recent years, especially in light of the COVID-19 pandemic, but also shows promising feasibility and efficacy (Jeon et al., 2025). Digital platforms, gamified training, and serious games provide scalable, engaging options: their effectiveness, however, depends on design, supervision, and personalisation (Jeon et al., 2025). To reach the optimal state, interdisciplinary collaborations is needed to ensure that

cognitive interventions are embedded in broader care plans, enhancing adherence and sustainability (Livingston et al., 2024).

1.4.5 Efficacy of interventions and new rehabilitative methods

When it comes to examine the intrinsic effect of cognitive rehabilitation, it is fundamental to lean on evidence based studies. Meta-analysis focusing on people living with dementia reported that cognitive stimulation (both delivered individually and in group) and training (particularly when delivered in group) produced small-to-moderate improvements in global cognition. Interestingly, cognitive rehabilitation specifically showed more consistent effects on functional abilities rather than pure cognitive test performance (Paggetti et al., 2024). Another noteworthy meta-analysis of clinical trials in Alzheimer's disease demonstrated that cognitive rehabilitation significantly improved QoL and occupational performance, thought effects on specific cognitive domains were more variable. These findings underscore that CR's greatest strength may lie in real-world functional gains rather than in narrow cognitive metrics (Paggetti et al., 2024).

Beyond conventional rehabilitation methods, novel interventions are progressively emerging. Among them, some recent studies combining non-invasive brain stimulation – for instance, transcranial direct current stimulation (tDCS) or transcranial magnetic stimulation (TMS) – with cognitive training suggest that multimodal approaches may produce synergistic effects on neuroplasticity and cognitive performance in MCI and AD patients, possibly by enhancing brain excitability or through the facilitation of functional network reorganisation (T. Yang et al., 2024).

Despite these positive finding, the field still faces significant challenges: heterogeneity in study designs, patient populations, intervention dose, delivery format, and outcome measures complicates drawing definitive conclusions or recommend standard protocols (Paggetti et al., 2024; Xiang & Zhang, 2024). Many studies lack long-term follow-up, limiting the understanding available on the maintenance of gains (Harrison et al., 2016; Paggetti et al., 2024). Therefore, there is the underlying need for more rigorous, adequately powered randomised controlled trials using ecologically valid outcome measures (Harrison et al., 2016; Reilly & Harding, 2025). As a consequence, prediction remain under-explored, although emerging evidence suggests that early intervention, active engagement, caregiver involvement and preserved metacognitive abilities increase the probability to benefit from such interventions (Forte et al., 2025; Rotenberg et al., 2024). Looking forward, COTs stand at an exciting

crossroads, with advances in biomarkers offering an additional potential tool aiming to tailor intervention to individuals' biological profiles and to monitor treatment response in real time (Z. Zhang et al., 2024).

1.5 Synopsis

In summary, this chapter has outlined cognitive decline as a multidimensional and lifespan-dependent phenomenon, stemming from the dynamic interplay between neurobiological ageing processes, neuropathological mechanisms, and a wide constellation of modifiable risk factors (Gonzales et al., 2022; Livingston et al., 2024). By integrating evidence from molecular and systems neuroscience, epidemiology, and prevention research, it has highlighted why trajectories diverge markedly across individuals, and how constructs such as cognitive reserve and neural resilience help explain variability in clinical outcomes (Y. Liu et al., 2024; Stern, 2002). Within this framework, COTs emerge as a theoretically grounded and clinically relevant response to the limitations of pharmacological approaches, offering pathways to preserve cognitive functioning, support daily life competence and enhance QoL (Castellano-Tejedor, 2022; Paggetti et al., 2024). However, the heterogeneity of patient profiles, outcome measures, and intervention protocols underscores the need for more flexible, adaptive, and scalable rehabilitation models (Paggetti et al., 2024; Xiang & Zhang, 2024).

In this regard, the increasing convergence between COTs principles and digital technologies represents a critical evolution of the field. Computerised approaches hold particular promise for the individualisation of training parameters, the enablement of continuous performance monitoring, the support of remote delivery, and embedment of rehabilitation within ecologically valid and data-driven environments (Jeon et al., 2025). Building upon the conceptual and empirical foundations established in the present chapter, the following will therefore focus on computerised cognitive rehabilitation methods, examining their historical becoming, the theoretical rationale, the technological characteristics, and evidence base, as well as their potential to address current known methodological and clinical challenges relevant to the field.

Chapter 2. Computerised cognitive interventions: history, efficacy and tools

In light of the cognitive changes that typically accompany the onset of neurodegenerative diseases such as MCI and dementia, pharmacological treatments have demonstrated limited efficacy in altering disease progression, especially in the early and moderate stages of the disease (Cummings et al., 2019; Schneider et al., 2014). As a result, non-pharmacological interventions have assumed an increasingly central role in clinical management and research (Irazoki et al., 2020). Among these approaches, Computerised Cognitive Interventions (CCIs) – including Computerised Cognitive Rehabilitation (CCR), Computerised Cognitive Training (CCT), and Computerised Cognitive Stimulation (CCS) – have gained substantial prominence. Advances in digital technology have enabled the development of scalable, standardised, and adaptable cognitive interventions that can be delivered in both clinical and non-clinical settings. Contemporary reviews emphasise that digital technologies function primarily as delivery modalities that enable the implementation of theoretically grounded cognitive interventions (Irazoki et al., 2020). However, the rapid expansion of this field has been consistently accompanied by heterogeneous methodologies, and mixed findings when it came to efficacy, in particular across populations and cognitive domains (N. T. M. Hill et al., 2017; Irazoki et al., 2020).

2.1 Terminology and conceptual distinctions

The literature on cognitive interventions is characterised by overlapping and inconsistently applied terminology, which consequently complicates the analysis of the findings (Clare & Woods, 2004; Irazoki et al., 2020).

2.1.1 Computerised Cognitive Rehabilitation

Traditionally, CR is defined as a goal-oriented, individualised therapeutic process that aims to improve everyday functioning thorough the restoration of impaired cognitive processes or via the development of new compensatory strategies. In fact, it is inherently contextualised within the individual's daily life and is delivered with clinician guidance (Cicerone et al., 2011; Clare & Woods, 2004). Its computerised counterpart, CCR, represents an extension, rather than a replacement as it integrates digital tools within an established clinical rehabilitation framework. In fact, CCR typically employs computer-based tasks to deliver structured cognitive exercises, while maintaining core CR principles such as individualisation, goal orientation, and clinician supervision (Clare & Woods, 2004; Irazoki et al., 2020). Importantly, implemented within a

clinical framework, its computerised tasks are selected and adapted based on neuropsychological assessment and are explicitly linked to functional goals that are relevant to patients' daily life (Irazoki et al., 2020).

From a therapeutic perspective, CCR can support both restorative exercises, aimed at improving specific cognitive processes through repeated practice and graded difficulty; and compensatory exercises that focus on teaching strategies that bypass or reduce the functional impact of cognitive deficits, such as via the use of external aids or structured routines (Irazoki et al., 2020). In this context, digital platforms may facilitate these approaches by enabling adaptive task difficulty, as well as automated feedback, and systematic monitoring of patients' performance over time, thereby potentially enhancing treatment intensity and consistency compared to exclusively paper-and-pencil methods (Boltaboyeva et al., 2025).

Furthermore, evidence from systematic reviews indicates that CCR may yield modest but meaningful improvements in global cognition in individuals with MCI, in particular when interventions are intensive, structured, and clinician-guided (García-Casal et al., 2017).

Specifically, meta analytic evidence suggests that CCR programs that integrate adaptive difficulty, structured task progression, and therapist supervision are associated with small-to-moderate gains in global cognition and memory, with more consistent effects observed in earlier disease stages. These findings indicate that CCR efficacy is not merely dependent on task delivery modality, but is suggests that it is critically influenced by the structure of the intervention and the therapeutic context in which is carried out (García-Casal et al., 2017).

Further supporting this view, descriptive reviews of CCR technologies highlighted that CCR interventions embedded within a broader clinical rehabilitation framework with exercises tailored to patients' profiles, paired with professional supervision, tend to yield more consistent cognitive benefits than unguided or self-administered programmes, although robust comparative efficacy data remain limited (Irazoki et al., 2020). As such, improvements are most reliably observed in trained domains, whereas evidence for far transfer to untrained domains remains less robust (García-Casal et al., 2017; Irazoki et al., 2020)

In contrast, evidence for CCR efficacy in dementia population is more heterogeneous. For instance, while some studies report a stabilisation or modest improvements in cognitive performance, the effect sizes are overall smaller and less consistent than observed in MCI patients, likely reflecting disease-related constraints on learning capacity and neuroplasticity (Clare & Woods, 2004; García-Casal et al., 2017). In fact, as cognitive decline progresses,

compensatory approaches may play a more prominent role than restorative training within CCR paradigms (García-Casal et al., 2017).

A central and ongoing challenge in both CR and CCR research concerns the generalisation of training effects to everyday functioning. Although CCR places a strong emphasis on ecological validity and functional relevance, empirical support for far transferability from computerised tasks to real-world activities remains limited. In fact, many studies continue to rely primarily on neuropsychological test outcomes, which may insufficiently capture meaningful changes in daily functioning. This limitation underscores the need for outcome measures that more directly assess functional performance, participation, and QoL, particularly in the context of digital and home-based interventions (Irazoki et al., 2020).

2.1.2 Computerised Cognitive Training

Differently from CR, CT refers to structured and repetitive practice on tasks on standardised tasks specifically designed improve targeted cognitive abilities through drill-based exercises with a progressive difficulty (Clare & Woods, 2004; Reijnders et al., 2013). The computerised version, CCT, represents the most extensively studied category of CCI. CCT programs use digital platforms to deliver COTs, and differ from traditional CT in their mode of delivery, automation, and scalability, while often reducing reliance on face-to-face clinician involvement, which characterise paper-and-pencil approaches (Irazoki et al., 2020). CCT programs are generally characterised by standardised, task-based protocols that prioritise performance improvement on specific cognitive domains rather than explicit functional goal attainment (Irazoki et al., 2020; Reijnders et al., 2013). For instance, training targets multiple domains implicated in age-related cognitive decline – attention, memory, processing speed, and executive functions – and incorporates adaptive algorithms that adjust task difficulty in response to user performance to maintain an optimal challenge level. This adaptive structure is widely implemented to support engagement and learning, particularly in MCI patients (Lampit et al., 2014) and is a common design feature of contemporary CCT platforms (Irazoki et al., 2020).

From a feasibility perspective, studies consistently indicate that CCT is well tolerated by older adults and individuals with MCI, with adherence rates that are comparable to – or exceeding – those reported for traditional, non-digital approaches (N. T. M. Hill et al., 2017), and the digital delivery is generally feasible and acceptable across diverse settings and platforms (Irazoki et al., 2020). Additionally, the home-based and self-paced nature of many CCT programmes has

been repeatedly cited as a factor that facilitates a sustained participation, in particular when interventions are brief, user-friendly, and supported by minimal supervision (Lampit et al., 2014; Li et al., 2022).

With respect to efficacy, meta-analytic evidence suggests that CCT produces a small-to-moderate but statistically relevant improvement in global cognitive performance in individuals with MCI (N. T. M. Hill et al., 2017; Li et al., 2022): effects that appear to be most robust in early stages of cognitive decline, whereas outcomes in individuals with established dementia are more heterogeneous and overall weaker, likely reflecting a reduced learning capacity, paired with a greater neuropathological burden (Irazoki et al., 2020; Reijnders et al., 2013). This factor has fuelled ongoing debate on the clinical significance of CCT-related cognitive gains.

Specifically, it has been argued that many outcome measures used to detect changes in performance rely heavily on neuropsychological tests, therefore not being able to capture meaningful functional change or real-world benefit (Irazoki et al., 2020; Simons et al., 2016). Also, a recent comprehensive meta-analysis by Li and colleagues, which synthesized results from 18 randomised controlled trials involving MCI patients, aiming to quantify the impact of CCT on cognitive function, showed a statistically significant and moderate effect of CCT on global cognitive function, favouring CCT over control conditions (Li et al., 2022). Beyond global cognition, Li and colleagues reported a marginal, but consistent improvements in domain-specific cognitive outcomes, including executive function, working memory, and episodic memory. These domain specific cognitive gains suggest that CCT may support cognitive processes closely aligned with trained tasks, albeit with variability in magnitude (Li et al., 2022). Diving deeper, subgroup analyses within the same review further illuminated factors that may moderate CCT efficacy. Notably, improvements in global cognition were observed when performed within patients' groups, ones that used interactions and feedback between patients and providers, training frequency and training duration. Although the effects did not significantly differ between subgroups, the emerging patterns indicated a slightly larger gain for multidomain programs and those with longer duration, thus suggesting that broader cognitive engagement and sustained practice may ameliorate outcomes (Li et al., 2022).

These meta-analytic findings, although aligning with other systematic reviews (N. T. M. Hill et al., 2017; Reijnders et al., 2013), the clinical significance of these effects remains debated as questions persists about the magnitude of real-world impact. In fact, concerns raised in the literature include the limited individualisation of highly standardised CCT protocols, the

questionable ecological validity of abstract training tasks, and the uncertain durability of effects over time, as follow-up assessments are often absent or conducted after a short period of time (Irazoki et al., 2020; Reijnders et al., 2013). As a consequence, these limitations have prompted calls for hybrid approaches that integrate CCT within a broader, functionally oriented rehabilitation frameworks (Li et al., 2022).

Nevertheless, despite these criticisms, CCT remains a compelling option for large-scale cognitive intervention for cognitive decline in MCI. Its relatively low-cost, scalability, ease of dissemination, and capacity to dynamically tailor task difficulty make it relevantly suitable for population-level prevention strategies and early intervention in cognitive ageing (Irazoki et al., 2020; Lampit et al., 2014. With careful considerations – pursuing larger, methodologically rigorous trials with robust, ecologically valid outcomes measures and extended follow up durations – and when embedded within supervised or multimodal care models, such as ones that combine it with VR, CCT may consequently contribute meaningfully to cognitive maintenance, even if its standalone impact on everyday functioning remains constrained (Li et al., 2022).

2.1.3 Computerised Cognitive Stimulation

CS, instead, is conceptualised as a broad, engagement-oriented approach that aims to enhance general cognitive and social functioning: it is therefore commonly used in dementia care and it incorporates social interaction, discussions, and recreational activities rather than targeted cognitive exercises (Clare & Woods, 2004; Woods et al., 2023).When delivered via digital platforms, CCS attempts to retain its traditional characteristics, with technology serving primarily as a means of delivery rather than modifying the theoretical intent of the intervention (Perkins et al., 2022). In contrast to CCT, where digitisation often enables the adaptive algorithms and task personalisation, CCS interventions typically replicate existing CST principles by using digital media to facilitate conversation, reminiscence, and shared activities. As such, the underlying mechanisms of action, that are social engagement, multimodal stimulation, and enjoyment, remain essentially unchanged, while digital delivery may enhance accessibility and flexibility (Irazoki et al., 2020; Woods et al., 2023).

In dementia care, for instance, traditional CST has proven to have a positive effect on general cognition, working memory, depression, language, neuropsychiatric symptoms, communication, severity of symptoms, and self-reported QoL (Desai et al., 2024). Digital adaptations of CS, such as the Computer Interactive Reminiscence and Conversation Aid

(CIRCA) system, and Individual Cognitive Stimulation Therapy (iCST) app aim to preserve these benefits while enhancing accessibility and flexibility of delivery, aiding the dissemination across multiple care settings, including residential facilities and private homes (Astell et al., 2018; Rai et al., 2020, 2021). Among the most frequently cited digital CCS application, the CIRCA system delivers CS by prompting reminiscence through an array of multimedia stimuli, as can be photographs, music, and videos, that are displayed on touchscreen devices. The app is typically used in dyadic or group contexts, with the technology serving as a shared focus that supports conversation between people with dementia and their caregivers. Empirical findings seem to suggest that, when it is implemented in group sessions, the CIRCA system can have positive impacts on quality of life, general cognition, and – importantly – on the perceived quality of caregiver-patient relationship. Considering its non-demanding and intuitive design makes it particularly suitable for individuals whose disease is more advanced, for whom structured task-based interventions may be excessively draining (Rai et al., 2021).

Another notable example is in the iCST app, which represents a digital adaptation of the individual CST protocol. Unlike CIRCA, iCST is designed for home use, and relies on the active involvement of informal carers. Also, the app provides structured conversation prompts and activities across a range of topics that include reminiscence, but that expands further onto the stimulation of specific cognitive functions such as language and memory. In this sense, the iCST app position itself between CCS and more targeted approaches, capable of blending engagement-oriented interactions with elements that resemble cognitive exercises. While early studies indicate that iCST may support communication and relational quality between patients and their caretakers, evidence for robust cognitive benefits remains mixed (Rai et al., 2021). Compared with CCR and CCT, CCS has received a limited and less rigorous evaluation in computerised formats. This disparity reflects a broader scarcity of randomised controlled trials and standardised outcome measures within CCS literature (Rai et al., 2021). For instance, methodological challenges – such as small sample sizes, heterogeneity in intervention formats, and variability in outcome measures – currently limits the strength of conclusion that can be drawn regarding efficacy. Nevertheless, the emphasis of CCS on engagement, enjoyment, and social interaction may make it particularly suitable for individuals with moderate dementia, for whom more demanding, performance-based interventions may be less feasible and acceptable (Rai et al., 2021).

Although CCR, CCT, and CCS differ in their theoretical intent, mechanisms of action, and clinical applications, they can be situated along a continuum of cognitive engagement. In

practice, these approaches frequently overlap, particularly in digital contexts where hybrid interventions may incorporate elements of training, rehabilitation, and stimulation. Despite this overlap, maintaining clear conceptual distinctions remains essential for both research and clinical evaluation. Such distinctions allow for more precise interpretation of empirical outcomes and facilitate a clearer understanding of which components of an intervention are responsible for the observed effects (Irazoki et al., 2020).

2.2 Historical becoming of computerised interventions

The evolution of computerised interventions reflects a trajectory that spans more than four decades of work and research, all of which began with early explorations of electronic adjuncts to cognitive rehabilitation (Lynch, 2002) and that culminates in today's sophisticated, evidence-based digital interventions. For example, contemporary CCT systems, now psychometrically validated, rely on algorithms to ensure adaptability as well as to support remote deployment (Ge et al., 2018). Interestingly, the foundational theoretical bases and initial implementations emerged through the gradual integration of microcomputing technology with clinical neurorehabilitation theory (Lynch, 2002).

In the late 1970s, therapists first began to experiment with alternative approaches to rehabilitation. In fact, videogames and electronic aids with the ultimate aim of supporting cognitive functions in clinical populations, serving as recreational add-ins with a potential cognitive benefit, were tested. Although these early attempts were not officially formalised as proper rehabilitation systems, they certainly constitute the first conceptual stage for harnessing interactive computational tools in clinical settings. This historical precursor phase has been documented in historical reviews that trace the origin of Computer Assisted Cognitive Retraining (CACR) to this period (Lynch, 2002).

The first explicit proposal to leverage microcomputers for structured cognitive rehabilitation appeared in the early 1980s, when affordable personal computers began entering clinical practice. Historical reviews note that Rosamond Gianutsos was among the first researchers to demonstrate the therapeutic potential of microcomputer-based tasks, presenting her work on cognitive rehabilitation applications at professional meeting in 1981. Around the same time, a software with structured exercises for domains such as perception and memory was developed. These initiatives are deemed the first examples of computer-assisted cognitive rehabilitation systems (Lynch, 2002). Through the mid-1980s, clinicians and rehabilitation specialists developed and distributed an increasing number of therapeutic software and manuals, often on

IBM PC and Apple Macintosh hardware. During these years, clinicians without formal programming backgrounds began creating and sharing tailored software: a trend that significantly expanded the practical use of computerised tools in cognitive retraining. Historical surveys chart this expansion and observe clinicians' use of simplified programming codes to create such programs (Lynch, 2002).

By the late 1980s, the theoretical underpinnings of cognitive rehabilitation became increasingly more structured, thus influencing computerised applications. In this phase, a known seminal contribution was the Attention Process Training (APT) program, developed by Sohlberg and Mateer. In their study, they applied a hierarchical, process-specific remediation protocol for people who suffered a brain injury, that was useful in defining clinical objectives for attention training specifically, which would later inform computerised implementations (Sohlberg & Mateer, 1987).

As CACR evolved into the 1990s, empirical studies evaluated the effectiveness of computer-based tasks across broader cohorts, moving beyond case reports to systematic group evaluations with standardised outcome measures. Even though early results were mixed as a result of methodological limitations, this research laid the groundwork for the integration of computerised training into more structured cognitive rehabilitation protocols (Lynch, 2002). The transition from CACR to CCT in contemporary research reflects both a deeper integration of cognitive neuroscience principles and technological advances like cloud computing, big data analytics, high-performance computing, and edge computing. In particular, modern CCT platforms incorporate adaptive difficulty algorithms, remote access capabilities, and large normative databases, in addition to being systematically reviewed across different patients' populations, such as with people affected by TBI, older adults, and clinical disorders. Also, systematic reviews demonstrate that computerised interventions are capable of producing measurable improvements domains such as attention, executive functions, and memory; although outcomes may vary depending on population, training parameters and task design (Bogdanova et al., 2016; Kueider et al., 2012).

2.3 Theoretical mechanisms of Computerised Cognitive Interventions

Several theoretical frameworks have been proposed in the attempt to explain the potential effects of CCIs in neurodegenerative diseases. Similarly to traditional methods, a central concept upon which they are based is experience-dependent neuroplasticity, which posits that repeated cognitive engagement can induce functional and structural changes in neural networks

(Kolb & Whishaw, 1998; Lövdén et al., 2010). Although neuroplastic potential is reduced in neurodegenerative conditions, evidence suggests that residual plasticity remains present, especially in earlier stages of the disease, allowing for improvements in cognition when possible (Cespón et al., 2018; Chou et al., 2022; N. L. Hill et al., 2011).

In addition, from a learning-theoretical perspective, CCIs are further informed by principles derived from learning and skill acquisition framework, particularly those associated with reinforcement learning and practice optimisation. In fact, repeated engagement with structured tasks combined with immediate performance feedbacks reflects mechanisms through which behaviour and performance are shaped via feedback-driven learning processes and experience-dependant neural plasticity (Kleim & Jones, 2008; Shams & Seitz, 2008). Importantly, despite progressive neuropathology, core learning mechanisms remain at least partially preserved in several neurodegenerative conditions, thus suggesting a theoretical basis for structured cognitive training (Belleville et al., 2011; Reijnders et al., 2013). Moreover, computerised platforms enable the systematic implementation of spaced practice and adaptive difficulty adjustment, both of which are known for their ability to enhance learning efficiency and long term retention (Cepeda et al., 2006, 2008). These features are extremely relevant in neurodegenerative populations, since the adaptive difficulty adjustment implementable allows tasks to remain within an individual's zone of achievable performance, thereby mitigating overload while maintaining sufficient challenge. This calibration has been consistently highlighted as a critical feature for aiding engagement, motivation, and adherence in older adults and individuals with cognitive impairment (Lampit et al., 2014; Reijnders et al., 2013; Tortora et al., 2024) . Also, other characteristics that support the ideal amount of stimulation are the use of engaging motivational cues and real time feedback, followed by response time demands that may vary frequently both during and across sessions, thus additionally providing an increased training time in areas of measured weakness (Bernini et al., 2019).

Finally, cognitive reserve provides a complementary framework for understanding how sustained cognitive activity may mitigate the functional impairment brought on by neuropathology. From this perspective, even computerised interventions are unlikely to halt disease progression, but they may stimulate compensatory mechanisms that preserve cognitive performance along with everyday functioning for longer periods (Stern, 2002b; Stern et al., 2020). Accordingly, in the context of neurodegenerative diseases, CCIs are generally seen as supportive or mitigating, rather than restorative in a curative sense (Irazoki et al., 2020).

2.4 Comparative evidence

Given the vast availability of interventions that can be administered in patients affected by neurodegenerations, comparative reviews – as well as a thorough assessment – can be useful in the choice of the right program to deliver. In particular, they suggest that the effectiveness of CCIs varies as a function of disease stage. For instance, individuals with MCI consistently demonstrate greater benefit than those with dementia, supporting the idea that residual learning capacity is an essential moderator (Chan et al., 2024; N. T. M. Hill et al., 2017). However, across intervention types, the effects on cognition tend to be generally modest, with heterogeneity in study designs posing as an additional obstacle. Nevertheless, converging evidence supports the use of computerised interventions, considering them as adjunctive strategies in the management of early cognitive decline (Irazoki et al., 2020). In fact, technology-based interventions offer several potential advantages, including improved accessibility and cost effectiveness, immersive and comprehensive user experiences, and the ability to adapt dynamically to individual performance (Ge et al., 2018). CCI programmes are commonly delivered via computer or tablets and can objectively record performance data to provide real time feedbacks to users and therapists. Some studies indicate that technology-mediated interventions may produce greater gains in cognitive function and QoL than traditional cognitive training and rehabilitation methods. Although the mechanisms underlying these findings of superiority are not fully understood, they may be related to increased usability and motivation associated with the real time interaction and feedback available (Ge et al., 2018).

2.5 Technological platforms and delivery tools

A wide range of technological platforms have been employed to deliver CCIs, including traditional desktop and laptop computers, more portable tools such as tablets and mobile devices, serious game-based environments, non-immersive virtual reality systems, and virtual reality (VR) systems (Canapa et al., 2025; Tortora et al., 2024). The review by Irazoki and colleagues underscores that no platform is inherently superior of the others; rather, the effectiveness depends on how well the platform characteristics align with the participant capabilities as well as his intervention goals (Irazoki et al., 2020). For instance, traditional computer-based platforms offer high levels of standardisation and a robust experimental control, thus making them well suited for CCT paradigms. Notably, tablets and mobile devices are known to enhance accessibility and usability, in particular for older adults with limited technological literacy (Irazoki et al., 2020). Moving to a more recent advancement, VR systems offer increased ecological validity by the simulation of real-world environments, although with

some limitations such as a heightened cost, the potential for motion sickness or nausea, as well as hardware limitation (Tortora et al., 2024). Importantly, the use of a specific technological tool does not define the nature of the intervention itself: in fact, the available platforms function as delivery mechanisms through which CR, CS, or CT paradigms are implemented (Irazoki et al., 2020).

Consistently with earlier meta-analyses (N. T. M. Hill et al., 2017), more recent work reports that individuals with MCI derive greater benefit from CCIs than those with a diagnosis of dementia. This pattern most likely reflects the preserved learning capacity and grater neuroplastic potential available in earlier disease stages (Chan et al., 2024). Across intervention types, the effects reported on global cognition tend to be modest but reliable, especially when the interventions are designed to be adaptive, theory driven, and of sufficient intensity (Chan et al., 2024; N. T. M. Hill et al., 2017; Li et al., 2022), while descriptive reviews highlight the heterogeneity of program designs and delivery formats across platforms (Irazoki et al., 2020).

2.5.1 Desktop and Laptop computers

Traditional computer-based platforms are the most established and widely used tools in both CCR and CCT research, owing to their ability to provide a precise control over stimulus presentation, timing, response recording, and an automated performance feedback, thus making them particularly suitable for structured cognitive training paradigms (Jiao et al., 2025; Maggio et al., 2023). From a methodological perspective, computer-based platforms are able to offer a high standardisation, which in turns facilitates replication across experimental designs (Jiao et al., 2025). Beyond their relevance for research purposes, conventional computers and laptops remain the most established and widely used delivery tools for CCIs. Implemented in both clinical and home-based contexts, they are delivered via personal computers and they typically rely on keyboard and mouse interaction (Maggio et al., 2023). In addition to this, a meta-analysis reports that computer-delivered CT produces moderate improvements in global cognition and domain-specific functions in individuals with MCI, offering a valuable alternative to traditional methods when applicable (Jiao et al., 2025). Similarly, computer-assisted CR highlights the predominance of personal computers in both research-grade and purely clinical rehabilitation software (Maggio et al., 2023).

In particular, besides the mere tailoring of task difficulty – which still remains a crucial component in effective interventions – the true innovative aspects that computer-based interventions carry are the abilities to accurately track performance overtime and to remotely

access training data. As such, computers and laptops function not only as delivery tools but also as clinician management interfaces that support data storage and monitoring, data-driven decision making, and continuity of care accessible anytime it is needed (Bernini et al., 2019; Maggio et al., 2023).

However, the literature has underscored some limitations associated with conventional computer interfaces. First, keyboard and mouse-based interaction may constitute a barrier for individuals suffering from motor impairments, sensory decline, or limited digital literacy, causing patients to potentially have a lower adherence to treatments and dimming the effectiveness of the program (Li et al., 2022; Maggio et al., 2023). Moreover, their relatively abstract task environments could limit ecological validity, a concern that is particularly in the salient in neurodegenerative populations, where transferability to everyday functioning is a primary clinical goal (Irazoki et al., 2020).

In the attempt to catch the vastity of new programs that have been created and implemented in recent years, a thorough review conducted by Irazoki and colleagues has identified eleven distinct computerised programs developed overtime, used for CCIs in older adults with MCI and dementia (Irazoki et al., 2020). Underscoring the diversity of software available rather than considering all program as equivalent, the review classified these technologies into CS, CT, and CR categories, with programs such as Brainer, GRADIOR, NeuronUp, and ComCog serving rehabilitation purposes and others like Captain's Log, CogMed, CogniFit, CogniPlus, COGPACK, SOCIABLE, and FesKits supporting various form of training and stimulation (Irazoki et al., 2020). These tools are designed to target multiple cognitive domains – with a focus on memory and attention – and enable therapists to create tailored treatment plans, define session parameters (duration and frequency), and adjust difficulty levels. Some programs operate with standardised training sessions that deliver the same tasks to all users, while others adapt exercise selection automatically according to individuals' performance (Irazoki et al., 2020). Technological variations include native applications (Captain's Log, CogniPlus), and web-based platforms (Brainer, Cogmed, CogniFit), many of which are remotely accessible, enhancing the possibility of application across settings. Moreover, these programs differ in device support: some are optimised for touchscreens, others extend to tablets or smartphones, but most work on personal computers (Irazoki et al., 2020).

In addition to this, all the software identified by Irazoki and colleagues generate progress reports to facilitate monitoring and longitudinal tracking of cognitive performance, besides some of

them including additional features such as assessment tools or serious games to enhance engagement. Notably, in the review is clearly highlighted that these additional tools are flexible and can therefore be used for people with neurodegenerative conditions, even though their usability may be limited in users with sensory-motor or digital literacy limitations. Also, it is important to acknowledge that while no single program is optimal for all users, the variety of available software allows clinicians to select the tool that best match individuals' therapeutic goals and users' capabilities (Irazoki et al., 2020). Finally, of essential relevance is understanding that many other programs have been brought to life and many more are following. In the image below, a representation of the clinical use of different devices and software is pictured.

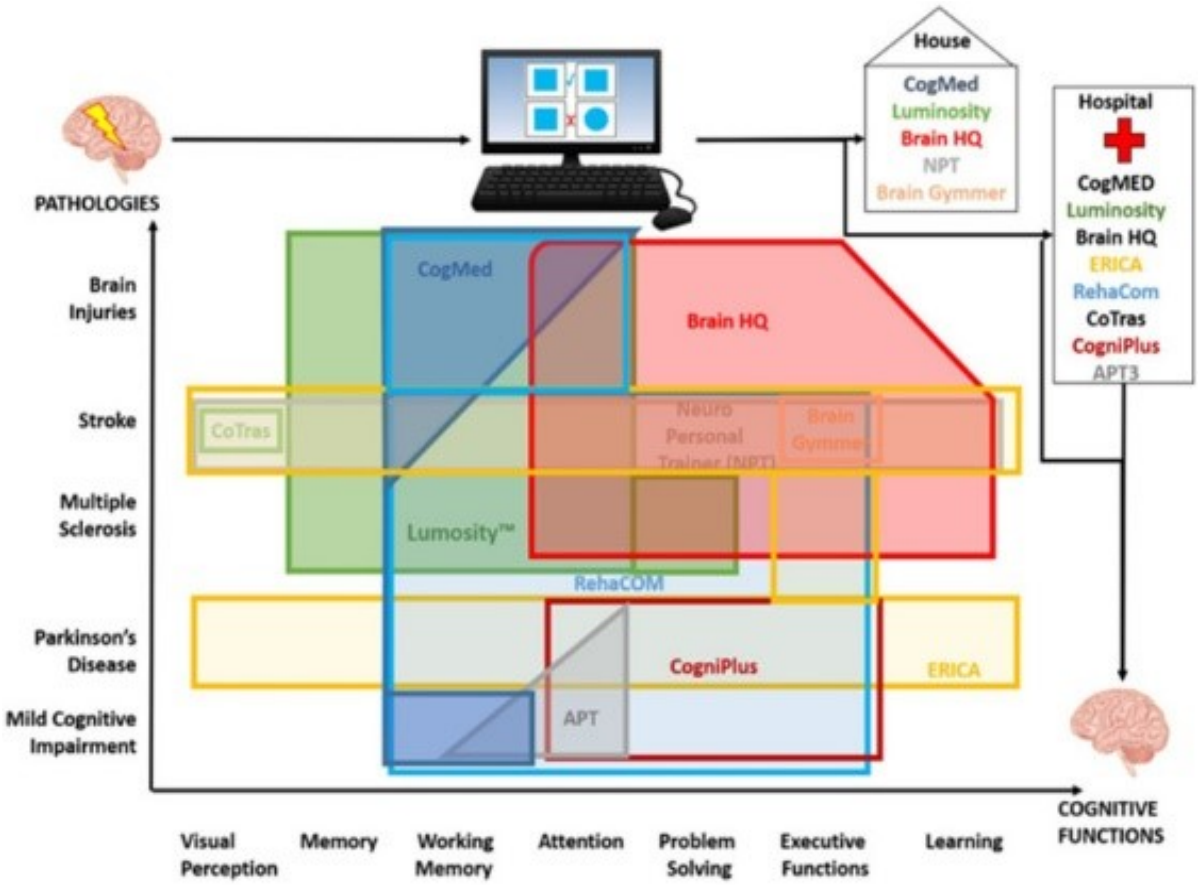


Figure 2.1: the different devices and cognitive functions trained in the different conditions and their settings –home or hospital (Maggio et al., 2023)

2.5.1.1 CoRe: a Computerised Cognitive Rehabilitation System

In the wide landscape of CCIs available at the moment, the CoRe system (an acronym for Cognitive Rehabilitation) is a software that was developed to address limitations of traditional, therapist-led, pen-and-paper cognitive training. As such, it was designed to support clinicians in delivering adaptive cognitive exercises by making task generation and performance tracking

automated. In fact, instead of relying on static exercise sets, CoRe hinges on a large body of stimuli – including sounds, images, and words – into a structured ontology. The latter enables a dynamic generation of tasks based on the user's performance profile, adjusting the difficulty in real time as a result of the user's accuracy and response metrics (Alloni et al., 2017).

A central aim of the system was to improve both usability and engagement for populations with a scarce digital literacy, as older adults often are, by providing a varied set of exercises and automated difficulty modulation. With the integration of performance indicators such as response time, task complexity, and accuracy, CoRe facilitates an individualised training while monitoring objective progress every step of the way (Alloni et al., 2017). At the heart of the CoRe system is an ontology-based engine that generates cognitive exercises. In this context, an ontology refers to a formal framework that represents relationships among stimuli and task demands, supporting the generation of a diverse set of exercise formats and difficulty levels without a manual configuration is needed by therapists (Alloni et al., 2018). This exact design was made to address a key challenge in cognitive rehabilitation: the need to balance novelty and engagement, to maintain user motivation, with task repetition, necessary for neuroplasticity and overall training. Since the ontology defines structured relationships between task elements, the system can systematically vary the content presented while preserving cognitive targets (Alloni et al., 2018).

In terms of efficacy, CoRe has been evaluated empirically in clinical populations, including individuals with Parkinson's Disease (PD) and MCI. In a randomised controlled study involving PD-MCI patients, those assigned to the CoRe CT group demonstrated significant improvements in global cognition and executive functions compared with control conditions at multiple time points. Said intervention integrated computerised cognitive exercises tailored by the CoRe system, and benefits were observed in standardised cognitive outcomes such as the Montreal Cognitive Assessment (MoCA) – a primary outcome measure – and several executive and non-executive tests, considered as secondary outcome measures (Bernini et al., 2019). In particular, investigating if the post-training improvement measured immediately after receiving the treatment was maintained, no post-training improvement was detected at the first follow up, probably due to the shortness of the intervention itself. This effect was thought to be attributable to the fact that executive functions, as a domain, need to be continuously stimulated in order to maintain an efficient functioning in the long term, suggesting that increasing the number of weekly sittings while patients are receiving the treatment and encouraging them to continue the treatment at home may be a solution to overcome this limitation (Bernini et al., 2019).

Additionally, concerning how the CT affects the evolution of the patients' cognitive decline, results showed that the CoRe group had a better evolution of cognitive decline, probably as a consequence of the targeted intervention they received: for instance, comparing the baseline results with the post training assessment, within the group, the global cognitive functioning scores improved, contrarily to the decline detected in the control group. As a matter of fact, most patients in this group improved their global cognitive level, whereas in the control group showed stability or worsening of their profile. Overall, it is possible to conclude that efficacy-wise, CoRe seems to a valid solution for PD-MCI, in the attempt of stabilising their decline or delaying the downward disease trajectory (Bernini et al., 2019).

About the system features, CoRe's adaptive mechanisms allow clinicians to set baseline parameters while the system automatically adjust task demands within sessions. For instance, given the case of a user that automatically performs well on a given type of task, the algorithm increases difficulty to maintain an adequate stimulation; conversely, the complexity of tasks is reduced if the user's performance suggests a persistent difficulty. The present adaptability supports a sustained engagement and may stimulate neuroplastic changes through appropriately scaled cognitive demands. Moreover, CoRe computes a Weighted Score (WS), designed to integrate performance metrics across sessions. As such, the WS serves as a composite indicator of rehabilitation progress as it balances the accuracy of response, the response speed, and task complexity. This comprehensive metric, implemented also in its telerehabilitative counterpart, provides clinicians with a quantitative summary of cognitive change over time, in addition to allowing for longitudinal performance monitoring and comparisons within and across individuals (Bernini et al., 2025).

2.5.2 Tablets and Touchscreen devices

Tablet-based delivery tools represent a significant advancement in the use of CCIs for older adults with cognitive decline. Systematic reviews and meta-analyses indicate that tablet-based cognitive decline programs produce cognitive outcomes comparable to those achieved via traditional computer-based platforms, particularly in individuals with MCI (Jiao et al., 2025). In fact, tablets are frequently identified as a more accessible alternative to desktop or laptop computers due to their touchscreen interfaces, portability, and reduced interaction complexity, which may lower technological barriers brought on by a scarce digital literacy in some users (Wilson et al., 2022). In this sense, touchscreen-based applications minimise the need for fine motor precision and abstract input devices –as those needed for the use of keyboards and mice

– characteristics that seems to be especially advantageous for MCI or dementia patients (Wilson et al., 2022).

For instance, tablet-delivered cognitive interventions commonly target memory, attention, visuospatial processing, and executive functions, as well as incorporating gamified elements to enhance user engagement and adherence (Jiao et al., 2025). In this context, evidence suggests that both adherence and motivation have been reported to be higher in some tablet-based interventions compared to conventional computer-based approaches, although cognitive effect sizes are generally comparable across platforms (Jiao et al., 2025). Also, systematic reviews that focus on community-dwelling older adults further emphasises the suitability of tablets for home-based cognitive interventions. In fact, tablet-based platforms support both minimally supervised or fully unsupervised training models, facilitating a scalable delivery that aligns with telehealth and digital care strategies. Furthermore, their relatively low cost, ease of deployment, and flexibility are identified as practical facilitators for a broader implementation in community and home settings (Chae & Lee, 2023). Despite these advantages, it must be acknowledged that some limitations are frequently reported in literature reviews, such as heterogeneity in intervention design, outcome measures, and application quality across tablet-based cognitive programs (Jiao et al., 2025; Wilson et al., 2022). In particular, many commercially available applications lack a rigorous clinical validation, limiting firm conclusions regarding their therapeutic efficacy and underscoring the need for additional research (Wilson et al., 2022).

2.5.3 Virtual Reality-based interventions

Virtual reality (VR) has emerged as a promising alternative to traditional COTs by offering immersive, multisensory environments that allow for a controlled manipulation of cognitive demands. These features are hypothesised to enhance engagement and neuroplasticity relative to conventional CR approaches, although direct evidence for superiority remains limited (Tortora et al., 2024). In fact, evidence suggests that VR-based interventions are at least comparable to traditional CR, and, in some cases, associated with larger gains on trained cognitive outcomes – with reported benefits in attention, executive functions, and memory on trained or near-transfer measures. Additionally, hinging on its higher level of immersion achievable, particularly via the use of head-mounted displays, VR may further support transfer to functional outcomes by increasing ecological validity, although empirical support for said far transfer effects is still preliminary. However, current conclusions are limited as a result of methodological heterogeneity, small samples, and scarce longitudinal data, thus highlighting the need for more rigorous trials (Tortora et al., 2024).

2.5.4 Serious Games

In the attempt of designing scalable, engaging, and effective COTs, interactive serious games have emerged as a distinctive class of digital interventions that combine goal-oriented cognitive interventions with game-based mechanics, designed to enhance motivation and engagement. As such, serious games represent a class of CCIs that, integrating structured training within game-based interfaces, have been reported to support both motivation and adherence in some intervention contexts. Grounded in models of cognitive plasticity, these interventions emphasise active engagement, adaptive challenge, and feedback as hypothesised mechanisms supporting cognitive change (Canapa et al., 2025). In terms of efficacy, evidence indicates that serious games can improve the trained cognitive domains, such as attention, working memory, and visuospatial abilities, particularly when progressive difficulty and feedback are provided. Nevertheless, substantial methodological variability and limited evidence for transfer to untrained domains poses a constrain to firm conclusions, therefore positioning serious games as a promising, but still developing, approach to cognitive intervention (Canapa et al., 2025).

2.5.5 Platform specific considerations in neurodegenerative disease

It is essential to consider that, in neurodegenerative populations, platform selection must consider many factors, including disease severity, the presence of sensory and motor limitations, and user familiarity with technology. Therefore, while immersive platforms such as VR may offer increased ecological validity, simpler interfaces may be more appropriate for individuals with moderate dementia – or generally with a higher level of cognitive deterioration. Overall, current evidence suggests that the content of intervention and its theoretical groundings are to be considered as more critical determinants of efficacy rather than the specific technological platform employed. Yet, platform characteristics may moderate engagement, adherence, and functional transfer, underscoring the importance of calibrating tools with individual capabilities and intervention goals (Canapa et al., 2025; Tortora et al., 2024).

2.6 Emerging technological trends and future pathways

Recent technological developments are reshaping the design and implementation of CCIs. In fact, adaptive algorithms and artificial intelligence (AI) – especially in CCT – are increasingly being employed to better personalise task difficulty and progression based on the individual's performance (Rossi & Rehman, 2025). Also, immersive technologies, including virtual and augmented reality, are gaining attention for their potential to enhance ecological validity particularly in rehabilitative contexts. As such, early studies suggest that virtual environments

may facilitate transfer to real-world functioning by embedding cognitive demands within everyday scenarios (Buele et al., 2023; Manera et al., 2017).

Additionally, the integration of wearable sensors and passive data collection is enabling a continuous monitoring of both behaviour and cognitive functioning, supporting emerging models of digital phenotyping (Kourtis et al., 2019). Another aspect of relevance in this context is the existence of social computing features, particularly important for CCS, where shared digital experiences can facilitate interaction, motivation, and emotional engagement (Rai et al., 2021). Overall, these developments align with the broader, substantial shift towards person-centred and relationship-oriented care models that are increasingly being explored and implemented in dementia research (Woods et al., 2023).

Mindful of its current state, future research on CCIs should prioritise several key pathways of expansion. First, a greater standardisation of outcome measures and intervention frameworks is required to enable meaningful comparisons across studies and intervention types, given the heterogeneity in program design and intervention types (Irazoki et al., 2020). To do so, consensus-driven core outcome sets that can integrate cognitive, QoL, and functional measures – successfully developed for non-pharmacological dementia intervention – would represent a significant advance if extended to CCIs (Harding et al., 2021). Second, large-scale, pragmatic trials in real-world settings are essential in order to establish the effectiveness, the long term sustainability, and the cost-effectiveness of such interventions. To obtain a large body of solid evidence, these trials should explicitly address adherence, implementation barriers when present, and user diversity, including individuals with limited digital literacy. Finally, ethical and regulatory considerations will become increasingly salient as CCIs incorporate AI-driven decision making and, more importantly, large-scale data collection, as issues related to data privacy, algorithmic transparency, and clinical oversight must be addressed through interdisciplinary collaboration and appropriate governance frameworks (Perez et al., 2025; Qu, 2025).

2.6.1 Functional outcomes, QoL, and participation

A growing body of literature critiques the narrow focus on neuropsychological test outcomes, as aforementioned, and calls for higher attention to functional, psychosocial, and participation-level endpoints. On this note, reviews in this field emphasise that even modest cognitive stabilisation may be clinically meaningful if accompanied by improvements in daily task management, self-efficacy, or caregiver burden (Zuschnegg et al., 2023). As a matter of fact,

interventions aligned with personally relevant goals, as are those operated in CCR, have shown promise in supporting activities of daily living and perceived competence, even in the absence of large cognitive gains (Clare et al., 2019; Zuschnegg et al., 2023).

2.6.2 Adherence, user experience and motivation

Another expanding line of inquiry concerns engagement and adherence, which are now recognised as central determinants of intervention effectiveness in neurodegenerative populations, and are therefore core pillars of CCIs. In fact, studies consistently report that sustained participation and adherence are strongly influenced by usability, perceived task relevance, clarity of feedback, and the emotional experience elicited by the technology (Contreras-Somoza et al., 2021). In neurodegenerative conditions – where apathy, reduced motivation, and fatigue are prevalent – poor engagement is a major contributor to diminished intervention effects. In fact, reviews of computerised and technology-based cognitive interventions further highlight the central role of adherence, with higher engagement levels associated with greater exposure to training dose, more consistent practice, and ultimately larger cognitive and psychosocial effects (Kueider et al., 2012; Lampit et al., 2014).

From this perspective, effectiveness no longer should be conceptualised solely in terms of cognitive gain, but as a by-product of a dynamic interaction between technology design, disease characteristics, and psychosocial context, including user motivation support systems (Manera et al., 2017).

2.6.3 Implementation and health-systems perspectives

More recent literature also situates CCIs within implementation science and health-service innovation frameworks, thus indicating a shift from efficacy-driven trials towards evaluations centred on real-world applicability, feasibility, scalability, and integration into routine care pathways (Irazoki et al., 2020; Reilly et al., 2020; Rosenberg et al., 2020). For instance, tele-delivered and home-based CCT and CCR programs are increasingly evaluated for feasibility, scalability, and integration into routine care pathways: such approaches are particularly relevant for dementia care, where access barriers, caregiver burden, and service fragmentation are pervasive (Irazoki et al., 2020). From a public health standpoint, CCT has been proposed as a secondary prevention strategy for individuals at elevated risk for dementia, complementing multidomain lifestyle interventions. While cognitive training alone is insufficient to alter disease trajectory, its integration within multimodal, digitally supported care models represents a key direction for future intervention development (Livingston et al., 2024; Rosenberg et al.,

2020). As a result of this acknowledgement, current trends are suggesting a transition from isolated digital tools towards integrated cognitive care frameworks that combine computerised interventions with monitoring, clinician feedback, and caregiver involvement (Irazoki et al., 2020). Notably, advances in AI and data-analytics approaches have been proposed as potential enablers of early detection of cognitive change, adaptive intervention delivery, and personalised progression pathways within digital cognitive interventions, although these applications remain largely prospective and require further validation in clinical dementia populations (Ranson et al., 2023; Rossi & Rehman, 2025).

2.7 Synopsis and next directions: towards telerehabilitation

Taken together, the literature reviewed in this chapter indicates that CCIs represent a heterogeneous – yet theoretically coherent – class of non-pharmacological approaches, whose effectiveness is shaped primarily by the cognitive principles, delivery conditions, and task characteristics underlying their design rather than by technological platform per se (Irazoki et al., 2020). Across CCIs, digital technologies operate mainly as delivery modalities that enable standardisation, scalability, and adaptive difficulty, while the active mechanisms of change remain grounded in experience-dependent neuroplasticity, learning principles, and compensatory processes associated with cognitive reserve (Kolb & Whishaw, 1998; Lövdén et al., 2010; Stern et al., 2020). Moreover, empirical evidence consistently suggests that cognitive benefits, when present, tend to be modest and moderated by disease stage, the intervention intensity, and residual learning capacity, with individuals with MCI deriving greater benefit than those with established dementia (Chan et al., 2024; N. T. M. Hill et al., 2017; Lampit et al., 2014; Li et al., 2022). At the same time, platform-specific feature such as usability, ecological validity, and overall interface complexity appear to influence adherence, engagement, and the likelihood of a functional transfer, especially in populations with sensory, cognitive, or motor limitations (Irazoki et al., 2020; Tortora et al., 2024).

Within this framework, the increasing integration of CCIs into telerehabilitation models represents a logical extension of the field rather than a conceptual distancing. In fact, the same technological features that characterise effective computerised interventions also underpin their suitability for remote delivery, therefore allowing interventions to be administered beyond traditional clinical settings while maintaining a structured therapeutic oversight (Ge et al., 2018; Irazoki et al., 2020). As such, telerehabilitation may further enhance accessibility and continuity of care, as a potentially cost-efficient delivery modality – although formal economic evaluations are still limited – particularly for individuals with mobility constraints or limited access to

specialised services, while aiming to preserve the core cognitive mechanisms targeted by CCIs (Ge et al., 2018; Lampit et al., 2014). However, as with in-presence CCIs, the effectiveness of remotely delivered interventions is likely to be modulated by disease stage, user engagement, and interface usability, and the extent to which remote platform can support factors such as motivation, feedback presence, and individualisation (Irazoki et al., 2020; Tortora et al., 2024). As a consequence, telerehabilitation should be thought of not as a universally superior alternative to traditional delivery, but as a complementary modality whose clinical value depends on the alignment between intervention content, technological affordances, and patients' characteristics (Ge et al., 2018; Irazoki et al., 2020).

Chapter 3. Telerehabilitation within contemporary telehealth ecosystems: foundations, evidence, and usability

In recent years, rising life expectancy has driven a significant demographic shift, resulting in a growing proportion of older adults worldwide. This transition has been paired by an increasing prevalence of age-related chronic and neurodegenerative conditions placing substantial demands on healthcare systems and highlighting the need for scalable rehabilitation (Islam, 2021; Ogugua et al., 2024; World Health Organization, 2015). In the attempt of adapting to these changes, and in response to epidemiological, demographic, and organisational pressures, continuous adjustments have been made, thus leading to a transformation that characterises how healthcare is seen nowadays. Among them, the development and subsequent implementation of telehealth has gained increasing attention. Precisely, telehealth is a multifaceted concept described as the distribution of health-related services which rely on the use of electronic technologies (De Marchi et al., 2021; Schwedler et al., 2026).

Domain	**Definition**
Telehealth	General term referring to technological information services, healthcare services and education.
Telemedicine	It refers to education conducted over a distance of healthcare via telecommunications. Conceptualised as the use of information technologies and electronic communication, it is used to provide clinical patients remotely to patients.
Telecoaching	Telecoaching is coaching delivered using an electronic medium. In this context, it is referred to as the process of mentoring the use of devices, as well as patient's management.
Telecare	It is a specific method to monitor fragile patients via the use of alarms, sensors anf other tools to help people maintain their independece as long as possible. It comprises patients-tailored assistive technologies and

	services and can monitor activity and change over time, as well as the possibility to call for help if needed.

Rather than constituting a discrete set of tools, telehealth now represents an integrated framework – as presented in the table above (De Marchi et al., 2021) – that includes remote clinical service, health monitoring, patient education, and care coordination mediated through digital technologies (De Marchi et al., 2021; Schwedler et al., 2026).

From a systems perspective, telehealth rewrites the spatial and temporal boundaries of care delivery, making it no longer confined to institutional settings, but increasingly distributed and available across patients' homes and community environments. This shift is particularly relevant for home-care contexts, where digital health applications act as mediators between patients, infromal caregivers, and gealthcare practitioners, mitigating the logistical burdens associated with in-person service delivery, and consequently aiding continuity of care, and supporting long-term management of chronic conditions (De Marchi et al., 2021; Schwedler et al., 2026).

However, telehealth adoption is neither automatic, nor uniform. As such, patient-level determinants such as digital literacy, perceived usefulness, trust, and prior experience with technology are known to play a critical role in shaping utilisation pattern. In this regard, empirical evidence indicates that patients' engagement with telehealth services is strongly influenced by how relevant they perceive the intervention to their needs, the ease of use, as well as their confidence in the reliability of digital platforms: suggesting that telehealth effectiveness depends as much on human factors as it does on technological capability (Qu, 2025).

At the organisational level, nonetheless healthcare professionals have reported precious insights derived from their work experience on substantial implementation challenges. Wang and colleagues report that practitioners tend to perceive barriers related to interoperability, workflow disruption, regulatory uncertainty, and inadequate institutional support (K.-C. Wang et al., 2025).

Mindful of its own limitation regarding access to idle devices, data privacy and security, heterogeneity in regulatory frameworks and reimbursement regulations (Toosi et al., 2025), telehealth prompts consumer stakeholders to emphasise the importance of user-centred designs and of improving engagement, creating a dialogue to align its services with patients' and

caregivers' priorities. In order to do so, it becomes essential the need for research protocols that incorporate end-user perspectives into the development and evaluation of telemedicine (Jenkinson et al., 2025).

3.1 Telemedicine – clinical care in digitally supported environments

Telemedicine, a key component of modern telehealth, refers to the remote delivery of clinical health services, including diagnosis, treatment, monitoring, and follow ups through digital technologies, therefore allowing access to healthcare even beyond traditional in-person settings (De Marchi et al., 2021; Gherman et al., 2025). Overtime telemedicine – which spans from synchronous to asynchronous interactions (Gherman et al., 2025) – has expanded well beyond its initial role in providing specialist consultations to underserved areas, and it now comprises routine clinical management of chronic diseases, and long-term monitoring: in neurodegenerative conditions, telemedicine addresses critical challenges associated with disease chronicity and progression. In this specific scenario, frequent clinical monitoring, symptom management, and medications adjustment are fundamental, placing telemedicine as a valuable alternative in situations where traditional models of in-person care impose burdens on both patients and caregivers; thus enabling more continuous clinician-patient interaction, potentially improving responsiveness to clinical changes while reducing travel-related strain (De Marchi et al., 2021). Additionally, it has successfully demonstrated its particular utility in easing multidisciplinary interventions, hosting collaboration among healthcare providers, which in turn proved effective in enhancing patient participation in their care plans, and extending specialised care to underserve or remote populations (Gherman et al., 2025).

Recent literature places increasing emphasis on the role of AI in telemedicine. For instance, Toosi and colleagues argue that AI may represent a turning point in telemedicine's evolution thanks to its capability of exploiting data-driven support in decisional processes, pattern recognition, and predictive analytics (Toosi et al., 2025). Similarly, Rossi and Rehman describe AI as a mechanism for diagnostic accuracy, triage efficiency, and personalisation of care enhancement (Rossi & Rehman, 2025). Still, both contributions underscore unresolved challenges: first, the tangentially aforementioned integration into already existing care pathways; as well as algorithmic transparency, and clinical accountability. As such contemporary telemedicine largely reflects hybrid models in which AI augments rather than replaces clinician judgement (Rossi & Rehman, 2025; Toosi et al., 2025). Crucially, health care providers' perspectives state that successful telemedicine implementation depends on various factors, such as trust in technology, clarifications of clinical responsibility, and institutional

readiness, as reported by Wang and colleagues, who emphasise that without clear strategies for integration into routine practice, telemedicine runs the risk of remaining fragmented or even underutilised, in spite of its demonstrated technical feasibility (K.-C. Wang et al., 2025).

As healthcare systems adapt to demographic trends and rising chronic disease burden, the integration of telemedicine and cognitive telerehabilitation (TR) offers a strategic method not only to extend rehabilitative care, but also to enhance service accessibility, and accommodate patients' needs (De Marchi et al., 2021; Jenkinson et al., 2025).

3.2 TR as a continuum of care

As anticipated, telehealth is used as an umbrella term that encompasses multiple concepts. Among them, TR – a specialised application of telemedicine – is referred to as the delivery of rehabilitation services at a distance via the use of Information and Communication Technologies (ICTs). Unlike acute medical care, rehabilitation is inherently longitudinal, goal-oriented, and participatory, making it particularly compatible with telehealth-enabled delivery models (Maresca et al., 2020). TR can comprise multiple phases: assessment, therapeutic intervention, monitoring of progress, as well as patient education, all delivered via digital platforms. By enabling home-based rehabilitation, TR addresses key barriers to a sustained engagement, namely transportation difficulties, schedule-bound constraints, and uneven service availability. Within the context of neurodegenerative diseases and age-related cognitive decline, TR has gained increasing relevance as a tool capable of addressing the needs of patients, caregivers and healthcare systems; while aiming at maintaining functionality and at promoting adaptation over an extended disease trajectory (Maresca et al., 2020; Schwedler et al., 2026).

After the catalyst reaction induced by the COVID-19 pandemic, TR continued to grow not merely as a contingency solution, but as a structurally meaningful extension of traditional rehabilitation paradigms (De Marchi et al., 2021; Maresca et al., 2020). In the cognitive rehabilitation domain specifically, TR has been conceptualised as an extension of established intervention frameworks thorough the relocation of delivery from hospital-based environments to home or community settings, while preserving assessment-driven prescription, structured task design, and clinician supervision (Quaglini et al., 2019; Bottiroli et al., 2024). This shift is frequently supported by the hub-and-spoke mechanism, which redistributes specialised expertise while maintaining clinical oversight: with a main supplier centre, the hub, whose work is integrated by secondary centres, the spokes, who generally have more limited services

available (Maresca et al., 2020). This advancement preserves traditional methods' core therapeutic principles – as are structured practice, adaptive difficulty, feedback, and clinician supervision – while rethinking how, where, and by whom interventions are accessed (Maresca et al., 2020; Bottiroli et al., 2024). In doing so, TR raises not only technical questions of feasibility and efficacy, but also conceptual, ethical and social considerations concerning accessibility, equity, data governance, and the redefinition of care how the public knows it (Qu, 2025; Rossi & Rehman, 2025; K.-C. Wang et al., 2025).

The Italian experience with TR, specifically, provides valuable insights into both opportunities and challenges. As such, Maresca and colleagues describe TR as a feasible and overall promising approach, yet one that requires not only significant infrastructural investment, but systematic professional training, and regulatory adaptations as well. In fact, their analysis highlights that TR success depends on its integration into existing healthcare structures, rather than merely an isolated technological deployment (Maresca et al., 2020).

3.2.1 Clinical and technological requirements for TR

Neurodegenerative diseases do represent a priority area for TR due to their progressive nature, long disease duration, and their profound impact on patients' functional independence. In this field, telehealth applications are intended to support patients across cognitive, motor, and psychosocial domains, while also factoring in the caregiver and avoidance of his/her burden when possible (De Marchi et al., 2021). As a consequence, TR allows for flexible and adaptive interventions that can evolve and adapt alongside disease progression. Neurodegenerative conditions are therefore known to pose unique challenges which include, within cognitive decline, a fluctuation of symptoms paired with what seems to be a reduced tolerance for complex interfaces (De Marchi et al., 2021). A crucial aspect to mention is that TR also plays a systemic role in supporting informal caregivers: it has been highlighted how telehealth applications are able to alleviate caregiver burden by providing a structured guidance, along with professional oversight, and shared responsibility of care. Thus, TR should be understood as a family-centred intervention, integrated within a broader care ecosystem (Schwedler et al., 2026).

Intrinsic to this context, computerised cognitive TR represents a convergence of cognitive rehabilitation principles with digital delivery (Di Lorito et al., 2022; Maresca et al., 2020). Computerised cognitive TR differs from generic CT applications in its clinical orientation: rather than prioritising self-directed use or performance optimisation, clinical systems are

designed around assessment-driven intervention, therapeutic goals, and ongoing professional monitoring (Di Lorito et al., 2022; Reijnders et al., 2013). This distinction is particularly salient in populations with neurocognitive disorders, where unsupervised intervention may be insufficient or even inappropriate (De Marchi et al., 2021). Moreover, the use of computerised platforms enables repeated practice, adaptive difficulty, and objective performance tracking, all factors fundamental in CR (Bernini et al., 2021; Bottiroli et al., 2024). When delivered remotely, these systems are able to extend care while preserving key therapeutic elements: individualisation and goal orientation (Maresca et al., 2020; Bottiroli et al., 2024).

3.2.2 Design principles for computerised cognitive intervention systems

Translating cognitive rehabilitation into TR contexts requires more than the mere digitisation of already existing exercises. In fact, to conceive an effective computerised cognitive TR system it is necessary to reconcile therapeutic fidelity with technological feasibility, while accommodating the clinical, cognitive, and psychosocial characteristics of neurodegenerative populations (De Marchi et al., 2021; Maresca et al., 2020).

First of all, guarantying continuity with established cognitive rehabilitation is fundamental. As outlined in Chapter 2, core elements remain foundational, regardless of the modality in which the intervention is delivered (Cicerone et al., 2011; Clare & Woods, 2004). As such, preliminary work on computerised cognitive TR suggests that core principles can be retained thorough remote platforms when therapists oversight and task personalisation are both preserved (Bottiroli et al., 2024).

Moreover, both usability and accessibility constitute primary design constraints in neurodegenerative populations, as the known reduced digital literacy, the sensory-motor impairments, the instability in attention, and the fluctuating cognitive capacity justifies the need for simplified interfaces, with a low interaction complexity, and characterised by tolerance for performance variability (De Marchi et al., 2021). From this perspective, even the functions of the interface design serve as therapeutic variables instead of being neutral technical feature (De Marchi et al., 2021).

Also, systems must support individualisation and clinical oversight: as such, unlike generic cognitive training applications, computerised cognitive TR requires the implementation of mechanisms for remote monitoring, performance tracking, as well as a therapist-controlled parameter adjustment, and a bidirectional communication between patients and clinicians (Maresca et al., 2020; Quaglini et al., 2019). In fact, TR frameworks emphasise that the

adoption of adaptive task difficulty and structured feedback are necessary, but insufficient, unless embedded within a clinician-supervised workflow that permits a treatment calibration and goal revision along the treatment plan (Bernini et al., 2021; Maresca et al., 2020). Notably, this requirement is particularly salient in neurodegenerative populations, where unsupervised interventions may be poorly tolerated – if not clinically inappropriate – due to the progressive nature of cognitive decline (De Marchi et al., 2021).

In this scenario, scalability and interoperability are being considered as crucial when designing interventions. As TR systems are part of broader telehealth ecosystems, they must be able of integration with electronic health records, as well as coordinating with remote monitoring tools and institutional workflows, while maintaining compliance with data protection and governance frameworks (Toosi et al., 2025; K.-C. Wang et al., 2025). Indeed, implementation research consistently indicates that factors as interoperability barriers, regulatory uncertainty, and workflow disruption represent primary obstacles to reaching a sustainable health deployment, even in conditions when technical feasibility has been conquered (K.-C. Wang et al., 2025). At the same time, emerging analyses of AI-augmented telemedicine highlight the importance of guaranteeing transparency when it comes to the algorithms supporting the tools, clinical accountability, and governance readiness as inescapable prerequisites for a safe and scalable deployment (Rossi & Rehman, 2025; Toosi et al., 2025).

Taken together, these design principles delineate a conceptual template for the righteous development and evaluation of computerised cognitive TR systems. Hence, they specify not only technical requirements, but also clinical, ethical, and organisational constraints that shape real-world viability (Maresca et al., 2020; K.-C. Wang et al., 2025). The HomeCoRe app, which will be formally introduced in the following chapter, was developed precisely in this framework, with the aim of operationalising these principles in a clinically deployable system for MCI patients and early neurodegenerative conditions.

Crucially, before examining empirical findings, it is necessary to clarify how usability and user experience (UX) are conceptualised within TR research. First, usability is defined as the extent to which a system can be used by specified users in order to achieve specified goals with effectiveness, efficiency, and satisfaction in a given context of use (International Organization for Standardisation, 2018). In applied health research, usability is commonly operationalised through standardised instruments such as the System Usability Scale (SUS), whose validity and interpretability have been extensively demonstrated (Bangor et al., 2008). UX, by contrast,

refers to users' subjective perceptions and emotional responses arising from interaction with a system, encompassing perceived usefulness, engagement, confidence, and affective reactions (Hassenzahl & Tractinsky, 2006). In cognitive TR, usability and UX are tightly interrelated and jointly influence adherence and therapeutic exposure, thereby moderating clinical effectiveness (Di Lorito et al., 2022).

3.3 Evidence base for TR in cognitive and neurodegenerative conditions: scope, benefits, and limits

The clinical rationale for TR in neurodegenerative and cognitive populations is pragmatic rather than disruptive: instead of aspiring to outperform traditional in-person rehabilitation, TR is primarily designed to extend access, preserve continuity of care, and increase intervention dose in contexts where conventional delivery is constrained by geography, mobility, or service capacity (De Marchi et al., 2021; Maresca et al., 2020). Consequently, a consistent part of the empirical literature frames TR effectiveness in terms of non-inferiority to in-person care or equivalence to in-person care, rather than outright superiority (Cotelli et al., 2019; Jeon et al., 2025). Across cognitive TR studies in individuals with MCI and early dementia, clinical efficacy is primarily evaluated through changes in cognitive functioning, typically assessed using standardised neuropsychological instruments targeting global cognition, memory, attention, and executive functioning (Di Lorito et al., 2022). In addition to these primary endpoints, the outcomes evaluated often comprise functional or participation measures and psychosocial indicators, considered as secondary domains. Hence, systematic reviews indicate that when intervention content and clinical supervision are preserved, cognitive outcomes obtained through TR are frequently comparable to those achieved via in-person CR (Cotelli et al., 2019; Jeon et al., 2025). At the same time, the reported effect sizes in cognitive TR studies are generally modest and highly heterogeneous, reflecting variability in many factors such as patient characteristics, intervention intensity, task specificity, and supervision models (Cotelli et al., 2019; Di Lorito et al., 2022).

Alongside these cognitive endpoints, many TR studies also report functional and psychosocial and experience-related outcomes including QoL, perceived benefit, and caregiver burden. These outcomes – as non-representing direct indicators of cognitive change – are therefore considered secondary endpoints and are interpreted as indicators of a broader clinical relevance rather than of direct measures of cognitive efficacy (Di Lorito et al., 2022; Schwedler et al., 2026). In this context, several studies report subjective benefit and high levels of acceptability even in cases where objective cognitive change is limited, underscoring the relevance of

outcomes reported by patients and their caregivers in progressive neurodegenerative conditions (Cotelli et al., 2019; Di Lorito et al., 2022). Crucially, in such populations, even modest cognitive stabilisation combined with improved wellbeing or reduced caregiver burden may still represent a meaningful therapeutic outcome to consider (Schwedler et al., 2026). Evidence further suggests that the cognitive benefits of TR do not seem to be distributed uniformly across patient groups. In this sense, the literature indicates that individuals with MCI or affected by an early stage neurodegenerative disease tend to derive grater benefit than those with more advanced pathology, likely reflecting a residual learning capacity, better sustained attention, and a greater ability to engage with structured digital tasks (Cotelli et al., 2019; Jeon et al., 2025). Analogously, TR appears particularly advantageous for patients with mobility limitations, those living in rural or underserved areas, and those whose access to specialised rehabilitation is otherwise sporadic or logistically burdensome (De Marchi et al., 2021; Maresca et al., 2020).

Indeed, TR should not be conceptualised as a universal replacement for traditional models of care, but as a complementary modality instead, whose value depends on disease stage, intervention design, and implementation quality. Crucially, while outcomes concerning cognitive functioning remain the primary indicators of therapeutic efficacy, other aspects as usability, acceptability, and broader psychosocial outcomes play a distinct but essential role in determining whether sufficient therapeutic exposure can be achieved in real world conditions (Di Lorito et al., 2022; Schwedler et al., 2026).

3.4 TR studies: trial designs, workflows, and outcome architecture

In order to interpret TR findings appropriately, it is crucial to understand how studies in this field are typically designed and operationalised, as different trials prioritise distinct categories of outcomes. Methodologically, the TR literature is dominated by three principal trial archetypes: feasibility trials (Burton & O'Connell, 2018), non-inferiority randomised controlled trials (Bernini et al., 2021), and pragmatic effectiveness trials (Di Lorito et al., 2022).

Early stage feasibility trials are typically designed to determine whether a TR intervention can be implemented under real-world household conditions. As such, their primary outcomes focus on implementation-related indicators, which include recruitment capability, adherence to prescribed sessions, session completion rates, technological reliability, and user tolerance rather than on definitive cognitive efficacy endpoints (Burton & O'Connell, 2018). A paradigmatic example of this approach is provided by Burton and colleagues, who conducted a randomised

controlled feasibility trial of telehealth-based cognitive rehabilitation in individuals with cognitive impairment (Burton & O'Connell, 2018). Their study demonstrated that the participants who actually participated in the study were able to adhere to prescribed home-based training schedules, that technological failures were manageable, and that user acceptability tended to be high. In terms of efficacy, modest pre-post cognitive improvements were observed so that the authors explicitly refrained from making strong claims, emphasising that their study was not powered nor designed to establish therapeutic effectiveness. Instead, feasibility was conceptualised as a multidimentional construct encompassing technical functionality, participant engagement, and caregiver support, thereby illustrating how TR viability must be empirically demonstrated rather than assumed, independently of cognitive outcome evaluation (Burton & O'Connell, 2018).

Moreover, as TR interventions matured conceptually as well as technologically, non-inferiority randomised controlled trials were increasingly adopted with remote delivery framed as an alternative modality to already validated face-to-face rehabilitation protocols (Di Lorito et al., 2022). In contrast to feasibility studies, these trials explicitly target cognitive functioning as primary endpoints, testing whether TR-based interventions fall within a predefined margin of inferiority relative to conventional in-person care, instead of seeking superiority. For example, Jeon and colleagues' meta-analysis of digital cognitive interventions for dementia and MCI reports that, in terms of efficacy, clinician-guided TR programmes produce cognitive outcomes that are frequently not statistically inferior to those of face-to-face rehabilitation, given that intervention content, dosage, and supervision intensity are matched. However, the author stress that this equivalence should not be intended as generalising to unsupervised digital programmes, which in turn show smaller and less reliable effects (Jeon et al., 2025).

Across the TR literature, a broadly convergent intervention logic can be identified, although it is not formalised as a single standardised workflow. In the Italian context, Maresca and colleagues describe TR as a modality that enables the delivery of individualised rehabilitation in the home environment, which also increases the frequency and intensity of treatment sessions, and that supports the remote evaluation of patient progress as a means of maintaining continuity of care across settings (Maresca et al., 2020). While their work does not specifically point out discrete procedural phases, it establishes the conceptual foundations for home-based rehabilitation models that preserve professional oversight and structured intervention delivery without directly addressing cognitive efficacy outcomes (Maresca et al., 2020). Instead, more granular descriptions of how cognitive TR interventions are operationalised emerge from

empirical trial reports and systematic reviews, where intervention workflows and outcomes domains are more explicitly distinguished. For instance, Burton and colleagues describe a telehealth rehabilitation programme for individuals with cognitive impairment that begins with baseline cognitive screening to determine eligibility and guide intervention tailoring, followed by home-based task delivery through a digital platform and ongoing monitoring of adherence and performance via remotely logged session data. Interestingly, although modest changes in cognitive performance were observed, the study was explicitly framed as a feasibility trial rather than an efficacy-centred one. As such, the primary contribution of this workflow lies in demonstrating the practical viability, usability, and adherence of a clinically supervised TR workflow, thus underscoring how remote cognitive rehabilitation can be cautiously embedded within a clinically supervised workflow, instead of being implemented as self-directed digital activity (Burton & O'Connell, 2018).

Similarly, Cotelli and colleagues, in their systematic review of cognitive TR in MCI and dementia, report that the majority of effective programmes associated with cognitive stabilisation or modest improvements share common structural features, thus incorporating selected task content, structured session schedules, and periodic professional review of patient progress (Cotelli et al., 2019). Additionally, they also stated that therapist supervision and theory-driven task design are methodological prerequisites for achieving an increase or stabilisation in cognitive performance – rather than as outcomes themselves – reinforcing the view that remote delivery must preserve core rehabilitation principles for clinically meaningful cognitive effects to emerge (Cotelli et al., 2019). At a broader level, Di Lorito and colleagues synthesise evidence from digital cognitive intervention trials, underscoring the demonstrated positive cognitive outcomes, which typically include individualised intervention planning, structured task progression, and monitoring of engagement and adherence (Di Lorito et al., 2022). Furthermore, their meta-analysis shows that studies reporting higher adherence rates and sustained user engagement are associated with larger effect sizes concerning cognitive performance, not since usability or engagement outcomes are to be thought of as cognitive outcomes per se, but because they determine the extent to which therapeutic exposure is achieved in home-based interventions. In this sense, usability and adherence function as moderating and enabling conditions, necessary for cognitive outcomes to be reached, rather than interchangeable indicators of therapeutic effectiveness (Di Lorito et al., 2022).

Specifically, when referring to home-based delivery, studies typically describes interventions implemented through web-based or tablet-based platforms, with patients completing the

prescribed cognitive tasks under asynchronous clinician oversight (Bernini et al., 2023; Burton & O'Connell, 2018). This delivery model concerns how rehabilitation is operationalised, rather than what cognitive effects are achieved. For instance, Burton and colleagues report that participants completed structured training sessions at home using a telehealth interface with predefined task schedules and minimal real-time supervision (Burton & O'Connell, 2018). Within this framework, remote monitoring refers to the automated logging of performance usage and metrics, such as accuracy, response times, and task completion rates, which are to be reviewed subsequently by clinicians when assessing engagement patterns and progression trends (Bernini et al., 2023). These monitoring indicators do not constitute cognitive outcomes per se, but rather inform the clinician about contextual information that can support the clinical interpretation of the behaviour and adherence of the patients during home-based sessions. Furthermore, studies distinguish different modalities of support provided to patients, including passive assistance – activated upon patient's request – proactive input, or dyadic support mediated by caregivers, depending on the individual's needs and performance patterns (Burton & O'Connell, 2018). On this note, iterative adaptations within TR refer to the clinician-mediated adjustment of task difficulty or exercise selection in response to observed trends over time (Maresca et al., 2020; Quaglini et al., 2019). This process preserves a central element of traditional CR – namely ongoing professional calibration of intervention parameters – while operating within a remote delivery context (Cicerone et al., 2011; Quaglini et al., 2019; Bottiroli et al., 2024). Importantly, these adaptations must be considered purely as mechanisms of personalisation and supervision, rather than outcome measures themselves (Di Lorito et al., 2022; Maresca et al., 2020).

In light of these considerations, these sources support a conservative – yet coherent – depiction of cognitive TR as a process that generally involves an initial cognitive assessment to establish patient profiles and the cognitive domains to be targeted (Burton & O'Connell, 2018; Cotelli et al., 2019), followed by a clinician-driven prescription of task content, with tailored difficulty level and session frequency (Cotelli et al., 2019; Di Lorito et al., 2022), which will be delivered at home in a structured manner (Burton & O'Connell, 2018; Maresca et al., 2020). Then, the data regarding performance and adherence recorded will be remotely monitored through logged usage and outcome data (Burton & O'Connell, 2018; Di Lorito et al., 2022), and a periodic professional review along with intervention adjustment parameters in response to observed patient needs and engagement levels are performed in response to observed patient needs and engagement levels (Cotelli et al., 2019; Di Lorito et al., 2022). Crucially, this architecture

should not be interpreted as a rigid procedural template, but rather conceptualised as a set of recurring design and implementation features, distinguishing clinically oriented TR from generic self-administered cognitive training. As highlighted in the Italian experience, reviewed by Maresca and colleagues, the real-world viability of these approaches depends on their integration into existing healthcare infrastructures, the availability of trained professionals, and the presence of regulatory and organisational support mechanisms, instead of the merely technical functionality (Maresca et al., 2020).

In addition to intervention design, the outcome architecture of TR trials is similarly structured around a limited number of recurring domains: cognitive outcomes remain the most frequently reported primary endpoints, and are assessed using standardised neuropsychological instruments targeting global cognition or specific domains (Di Lorito et al., 2022). For example, Burton and colleagues measured changes in memory and executive function using validated cognitive tests, reporting small but statistically detectable pre-post improvements following telehealth-based interventions. Again, these cognitive measure in this specific case were interpreted within the constraints of a feasibility-oriented design and were not presented as evidence of absolute therapeutic efficacy (Burton & O'Connell, 2018).

Adding to cognitive-oriented endpoints, some studies include functional outcomes intended to capture real-world impact of intervention on ADLs. However, such outcomes are less consistently assessed across trials, and systematic reviews note that the evidence for functional transfer remains limited (Di Lorito et al., 2022). Psychosocial outcomes, which usually include QoL, mood, and caregiver burden, are occasionally reported. These outcomes are tipically framed as secondary endpoints and are highlighted as clinically meaningful even in cases where objective cognitive gains are modest, particularly in progressive neurodegenerative conditions (De Marchi et al., 2021). In this regard, distinct from efficacy-related domains, contemporary rehabilitation research explicitly treats usability and feasibility not as secondary issues, but as core scientific implementation outcomes. As such, usability is commonly operationalised using structured instruments, as the SUS, complemented by qualitative interviews, error rates, and task completion metrics, which together assess how effectively and comfortably users can interact with the system in real-world conditions (Di Lorito et al., 2022). Similarly, several studies reviewed by Di Lorito and colleagues report that the perceived ease of use and task clarity are among the strongest predictors of sustained engagement in older adults with cognitive impairment, posing usability as a determinant of intervention uptake (Di Lorito et al., 2022). In parallel, feasibility is typically assessed through indicators as recruitment success,

session adherence, technological stability, and attrition rates (Burton & O'Connell, 2018; Maresca et al., 2020). For instance, in their randomised controlled trial protocol, Burton and colleagues explicitly identify adherence to prescribed sessions, dropout rates, and the occurrence of technical problems as primary feasibility outcomes for evaluating telehealth-based cognitive rehabilitation, clearly separating them from cognitive efficacy endpoints (Burton & O'Connell, 2018).

Importantly, systematic reviews emphasise that both usability and feasibility – while not constituting cognitive outcomes – moderate cognitive efficacy by shaping the effective dose of intervention the patients receive and their sustained engagement. As such, Di Lorito and colleagues show that studies reporting a higher adherence rates in participants, paired with structured supervision, also tend to report larger cognitive effect sizes, consequently reinforcing the interdependence of technological design, UX, and therapeutic effectiveness (Di Lorito et al., 2022).

3.4.1 Usability, feasibility, and adherence as determinants of TR effectiveness

In cognitive TR, usability cannot be regarded as a secondary or merely aesthetic concern: instead, it constitutes a core determinant of therapeutic exposure and, by extension, of clinical effectiveness (Di Lorito et al., 2022; Maresca et al., 2020). Unlike in-clinic rehabilitation settings, where attendance, technical setup, and troubleshooting are largely managed by institutional staff, home-based delivery shifts a substantial portion of execution responsibility onto the patient and, consequently, onto informal caregivers (Maresca et al., 2020; Schwedler et al., 2026). Within this framework, usability evaluations in cognitive TR tend to adopt a multi-layered methodological approach that integrates qualitative components with objective and subjective ones (Bernini et al., 2023; Di Lorito et al., 2022).

First, objective usability indicators are commonly employed. They include session completion rates, dropout frequency, task completion time, interaction error rates, as well as the number of technical assistance requests, which together provide an operational measure concerning whether a system can be used independently and consistently over time in real-world conditions (Bernini et al., 2023; Burton & O'Connell, 2018). Second, subjective usability and UX are assessed through standardised questionnaires and structured rating scales that capture perceived ease of use, clarity of instructions, navigation burden, and overall satisfaction, which are dimensions that often predict sustained engagement and that may not be evident from performance logs alone (Bernini et al., 2023; Di Lorito et al., 2022). Third, qualitative

evaluative methods, such as diaries, semi-structured interviews, and open-ended feedback, are increasingly incorporated to document difficulties arising in any moment, fatigue, emotional responses to task failure, as well as the perceived relevance of the intervention. These methods are particularly informative in cognitively vulnerable populations where engagement is fragile and highly context-dependent (Di Lorito et al., 2022; Schwedler et al., 2026).

Evidence from feasibility trials and systematic reviews suggests that this layered evaluation strategy seems to be particularly appropriate for cognitive TR, as it enables usability to be thought of not solely as users' subjective appreciation of an interface, but as their capacity to complete the prescribed rehabilitation schedules autonomously and consistently in their everyday lives (Burton & O'Connell, 2018; Maresca et al., 2020). In this sense, usability functions as a prerequisite for therapeutic exposure (Burton & O'Connell, 2018; Di Lorito et al., 2022; Maresca et al., 2020).

Crucially, contemporary TR trials increasingly conceptualise usability and adherence variables as mediating variables, rather than as ancillary feasibility indicators or surrogate efficacy outcomes (Di Lorito et al., 2022; Kang et al., 2026). From this perspective, interpreting efficacy requires demonstrating not only that cognitive change occurred, but also how the intervention was actually used and prescribed, whether a sufficient therapeutic exposure was achieved, and what forms of support – human or technical – were required to sustain engagement over time (Burton & O'Connell, 2018; Maresca et al., 2020). This interpretative stance reflects a broader shift towards considering TR as a socio-technical intervention, where clinical effectiveness emerges from the interaction between therapeutic content, technological affordances, and human support systems, rather than from any of these component isolated (Maresca et al., 2020; K.-C. Wang et al., 2025)

3.4.2 Evidence from cognitive TR applications

The studies reviewed in this subsection report both cognitive efficacy outcomes and implementation-related indicators, which are discussed separately in line with the conceptual distinctions outlined above. In the current literature, the empirical evaluation of cognitive TR applications has predominantly relied on small-scale randomised controlled trials, feasibility studies, and systematic reviews, which tend to prioritise methodological conservatisms over technological novelty. One of the clearest empirical demonstrations of feasibility and adherence in cognitive TR is provided by Mosca and colleagues (Mosca et al., 2020), who evaluated a newly developed home-based TR programme for individuals with MCI and Vascular Cognitive

Impairment (VCI). The study adopted a controlled longitudinal design, in which participants receiving the TR intervention were compared against a usual-care control condition, which consisted of standard clinical follow-ups without structured remote rehabilitation. Crucially, the primary outcomes of the study were implementation-related. Feasibility was operationalised through recruitment success, attrition rates across study phases, technological stability, and completion of scheduled intervention sessions. Adherence, on the other hand, was quantified as the proportion of prescribed rehabilitation activities effectively carried out by participants over the intervention period (Mosca et al., 2020). Additionally, user appreciation and usability were assessed through structured questionnaires addressing ease of use, clarity of instructions, and perceived burden. The obtained results indicated a high feasibility, with limited attrition and no-systematic drop outs attributable to technological difficulties, alongside a high adherence, with participants completing approximately 84% of prescribed activities. In fact, usability ratings were overall positive, suggesting that the system examined could be managed independently by cognitively impaired users in a home setting (Mosca et al., 2020). By contrast, cognitive and functional outcomes were rather exploratory and secondary. Although, preliminary analyses suggested stabilisation or modest improvements in selected cognitive and functional measures. Accordingly, the authors emphasise that, in order to obtain comprehensive results, future research should move beyond feasibility studies towards adequately powered randomised controlled trials that include longer follow-up periods, and that integrate standardised cognitive, functional, and caregiver-related outcomes to clarify the clinical significance and durability of TR effects (Mosca et al., 2020).

Within the same research landscape, but with a primary focus on cognitive efficacy outcomes, a key empirical demonstration of structured cognitive TR is provided by Manenti and colleagues, who conducted a controlled study comparing therapist-guided remotely delivered CR with the same intervention delivered in person in individuals with MCI and mild Alzheimer's disease (Manenti et al., 2020). In this study, participants in the experimental group completed structured cognitive exercises under remote professional supervision; whereas the control group received an identical rehabilitation protocol in a conventional face-to-face format. The primary outcome measures consisted of standardised neuropsychological assessments targeting memory, attention, and executive functioning, as well as indices of affect. The results indicated comparable improvements across cognitive domains in both groups, with no systemic disadvantage associated with remote delivery (Manenti et al., 2020). The findings were interpreted within a non-inferiority framework, suggesting that TR can preserve the

effectiveness of CR when therapeutic structure and clinician supervision are kept when it comes to cognitive performances. Importantly, while the study provides evidence regarding cognitive performance outcomes, the authors explicitly acknowledge limitations regarding sample size and follow up duration. In their discussion, in fact, the authors underscore the need for future research involving larger samples, longer follow-up periods, and enhanced technological solutions that support engagement and long-term adherence in home-based cognitive rehabilitation (Manenti et al., 2020).

Furthermore, Di Lorito and colleagues provide a systematic review and meta-analysis of digital health interventions created purposefully for people living with dementia and MCI, which includes multiple apps for cognitive TR (Di Lorito et al., 2022). Across the randomised controlled trials included in the study, the intervention protocols typically involved home-based digital task delivery combined with periodic contact with the clinician; whereas control conditions consisted of usual care, waitlist assignment, or non-specific cognitive stimulation. It is to be noted that the primary outcomes synthesised in the meta-analysis were cognitive efficacy measures, most commonly global cognition and domain-specific neuropsychological outcomes. The pooled results revealed a small but statistically significant effect of digital cognitive interventions on global cognition, with larger effects observed in studies incorporating therapist supervision and structured intervention schedules (Di Lorito et al., 2022). At the same time, the authors remain cautious against over-interpreting these cognitive effects, as in spite of these positive findings, substantial heterogeneity was noted across intervention formats, outcome measures, and study durations, limiting the generalisability of efficacy estimates. On the other hand, the authors underscore how the current evidence available seems to support feasibility and modest cognitive efficacy, rather than robust or clinically transformative effects. Crucially, the review also identifies important implementation-level gaps that are analytically distinct from cognitive outcomes. these include the overall scarcity of long-term follow up data and the limited evaluation of usability and engagement variables. Together, these limitations highlight that while TR shows a promise at the level of short term cognitive performance, further research is required to clarify its durability, its functional relevance, and overall real world applicability(Di Lorito et al., 2022).

Another example of recent app-based TR trials reinforcing these conclusions consists of the work conducted by Kang and colleagues (Kang et al., 2026), with a multicentre randomised clinical trial evaluating the efficacy and safety of a mobile app-based metamemory CT programme in older adults with MCI. In their study, participants were randomly assigned to

either the digital intervention group, which completed structured cognitive exercises using a mobile application over a 12-week period of time, or to a sham-device control group, designed to control for expectancy and contact effects. The intervention was delivered in a home-accessible format, with adherence and safety monitored remotely. With respect to the cognitive efficacy outcomes, the primary endpoints included the Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-COG-14), and other secondary measures of daily functioning and QoL were used. Importantly, the results demonstrated statistically significant improvements in global cognitive performances in individuals pertaining to the intervention group relative to controls at both 12- and 24-week follow-ups, with no major adverse effect detected (Kang et al., 2026). Therefore, the authors interpret these findings as evidence of modest but clinically meaningful cognitive benefit, yet emphasising that the observed effects were limited in magnitude and that longer-term durability remains uncertain. Accordingly, and in line with others, they identified the need for extended follow-up periods, as well as for the integration of ecologically valid functional outcomes, and replication in more diverse clinical populations as critical future research directions (Kang et al., 2026).

With these studies in mind, it is possible to spot a convergent methodological pattern in cognitive TR research: interventions are typically structured around baseline cognitive assessment, clinician guided prescription of digital exercises, and remote monitoring of adherence and performance; control conditions, on the other hand, most often involve usual care, as well as wait-list allocation, or low-intensity cognitive activities (Di Lorito et al., 2022; Kang et al., 2026; Manenti et al., 2020; Mosca et al., 2020). Across trials, the results consistently demonstrate feasibility, high user acceptability, and small-to-moderate improvements in trained cognitive domains, but only limited evidence for durable or functionally meaningful transfer effects (Di Lorito et al., 2022; Manenti et al., 2020; Mosca et al., 2020). As a result of this, and with the final aim of developing tools that are truly person-centred, future directions reported across this literature include the need for adequately powered multi-centre randomised controlled trials, standardisation of outcome measures, integration of functional and caregiver-related endpoints, and the development of hybrid models, balancing technological automation with sustained professional oversight (Di Lorito et al., 2022; Kang et al., 2026).

3.5 Synopsis

All in all, the evidence reviewed in this chapter suggests that cognitive TR is most likely to be clinically meaningful when it preserves the defining characteristics of CR, while exploiting digital delivery to extend care into the home environment (Di Lorito et al., 2022; Manenti et

al., 2020; Maresca et al., 2020). Across feasibility studies and controlled trials, cognitive efficacy outcomes, assessed through standardised neuropsychological measures, indicate that remotely delivered, clinician-guided interventions can achieve cognitive results that are comparable to those obtained thorough in-person protocols, particularly in MCI ot early neurodegenerative conditions patients (Di Lorito et al., 2022; Manenti et al., 2020). At the same time, the literature consistently shows that effectiveness in real-world settings is strongly contingent on factors related to implementations: for instance, interventions that that rely predominantly on self-directed or minimally supervised digital training tend to show limited therapeutic exposure and high variability in adherence, particularly in patients with cognitive vulnerability, thereby limiting their practical effectiveness despite technically adequate task content (Di Lorito et al., 2022). In contrast, clinician-guided models demonstrate a more stable engagement pattern and more implementable links between intervention delivery and the observed cognitive outcomes, not because usability constitutes a therapeutic outcome per se, but because it enables a sustained participation during sessions and an adequate intervention dosage (Di Lorito et al., 2022).

Implementation and telehealth research further highlights that such clinician-guided approaches are viable only when supported by technological infrastructures that are capable of enabling remote prescription, monitoring, and adjustments of rehabilitation plans without increasing user burden or compromising usability (Maresca et al., 2020; Schwedler et al., 2026; K.-C. Wang et al., 2025). In this sense, usability and feasibility should be understood as enabling conditions for effectiveness, rather than as substitutes for cognitive efficacy outcomes. Their role is to ensure that evidence-based rehabilitation protocols can be executed consistently and autonomously in home environments, allowing the efficacy already demonstrated under controlled conditions to translate into the household (Burton & O'Connell, 2018; Di Lorito et al., 2022; Maresca et al., 2020).

In sum, the convergence of these findings suggests that effective cognitive TR systems must be conceived as extensions of clinical rehabilitation workflows – not as generic digital tools – that are capable of integrating therapeutic logic and technological affordances within a coherent system-level design (Di Lorito et al., 2022; Manenti et al., 2020). Therefore, it is within this empirically grounded and methodologically constrained framework that the following chapter introduces the HomeCoRe app, a specific computerised cognitive TR system, developed to operationalised clinician-guided rehabilitation principles in a home-based format for individuals with MCI and early neurodegenerative conditions.

Chapter 4. HomeCoRe: qualitative study of a clinician-guided application for computerised cognitive TR

The HomeCoRe system, (an acronym for Home Cognitive Rehabilitation), is the outcome of a long-standing research and clinical development trajectory, which exists with the aim of translating structured, computer-based cognitive rehabilitation into a home-delivered format without compromising its therapeutic integrity (Alloni et al., 2018; Bottiroli et al., 2024). The original system was designed as a clinician-guided rehabilitation environment stemming from three integrated components: a library of parameterisable cognitive exercises organised by cognitive domain; an ontological model encoding relationships among cognitive functions, task characteristics, patient profiles, and rehabilitation goals; a clinician-facing control interface that supports assessment-driven prescription, monitoring, and iterative adaptation of intervention plans (Alloni et al., 2018). Within CoRe, the rehabilitation plan was generated on the basis of a formal neuropsychological assessment and mapped ontologically to specific task classes and difficulty parameters, where clinicians retained full control over task selection, the sequencing, and progression; thereby ensuring that the computer-mediated exercises remained embedded within the broader therapeutic logic, characterised by goal orientation, individualisation, and – logically – professional oversight (Alloni et al., 2018; Bottiroli et al., 2024).

Despite its demonstrated feasibility and clinical utility in outpatient rehabilitation settings, CoRe exhibited some structural limitations inherent to in-person delivery, which included a restricted scalability, a reduced training intensity due to logistical constraints, discontinuity of care between clinic visits, and a limited accessibility for individuals with mobility impairments, or those living far from specialised centres (Bottiroli et al., 2024). When considering these limitations, it is fundamental to convey that they were organisational and infrastructural in nature, and did not reflect weaknesses in the rehabilitation model itself, but rather in their delivery modality (Quaglini et al., 2019; Bottiroli et al., 2024). HomeCoRe was conceived explicitly to address these delivery-level limitations while preserving the core therapeutic architecture of CoRe (Quaglini et al., 2019; Bottiroli et al., 2024).

4.1 Transitioning from CoRe to HomeCoRe – from in hospital settings to patients' homes

The first CoRe implementations focused on three principal goals. First, it was centred around an automated generation of exercises, which used a large repository of stimuli to produce exercises that varied across sessions and that therefore reduced the event of repetition. Then, of

a fundamental role was the standardised performance recording, enabling the systematic collection of data concerning response accuracy and execution times, via the use of the WS, which also factored in task complexity. At last, of a high motivational impact was the attempt of reducing the therapist workload, thanks to which it was possible to focus on the therapeutic interaction instead of on the manual preparation of tasks (Bottiroli et al., 2024). Although this model improved session efficacy and data reliability, the rehabilitative intervention remained constrained by the availability of the clinic and by patients' limitations (Bottiroli et al., 2024).

Over the years, CoRe underwent multiple development iterations driven by user feedback and technological advances. For instance, five key milestones can be identified: the progressive redesign of graphical interfaces, meant to improve accessibility for the elderly and neurologically impaired patients; the integration of ontology-based organisation of stimuli, allowing automatic generation of exercises with a graded complexity; the introduction of quantitative performances indexed enabling the systematic tracking of each patient's progress; the development of adaptive difficulty mechanisms tailored to the performance of the patient; and finally, the experimental integration with physiological sensors in order to monitor fatigue and emotional responses during training (Bottiroli et al., 2024).

In addition to this, it is possible to identify two major clinical and organisational challenges that prompted the transition towards a remote rehabilitation delivery. First, it was noticed how healthcare services frequently lack the sufficient personnel dedicated to cognitive rehabilitation, thus limiting the accessibility and intensity of treatment deployable. Second, the evidence accumulated during clinical studies pointed towards a decrease of rehabilitation benefits after the treatment was discontinued, therefore hinting the need for more prolonged or maintenance interventions that could reach patients beyond hospital discharge (Bottiroli et al., 2024). Consequently, these factors highlighted the necessity of extending rehabilitation into patient's homes while maintaining clinician supervision and treatment personalisation (Bottiroli et al., 2024).

In fact, the transition from the two did not involve new rehabilitation principles, but it required the re-engineering of the delivery infrastructure, yet preserving the known therapeutic logic, already validated in clinical settings (Bottiroli et al., 2024). Specifically, the transformation involved several core changes, beginning with the separation of execution and control environments: while CoRe required the patient and clinician to operate within the same physical environment, HomeCoRe introduced a dual-interface architecture that separates the clinician

interface – used for the configuration of treatment plans, the monitoring of performance, and the adaptation of interventions when needed – and a patient interface, enabling the exercises to be executed independently at home (Bottiroli et al., 2024). Furthermore, as exercise performance, response times, adherence, and session outcomes are automatically logged and transmitted to clinicians, making room for longitudinal supervision, it is deducible how the remote monitoring and data transmission resulted in a significant core change (Bottiroli et al., 2024). Naturally, the interface needed to be redesigned for an independent use: since patients were performing exercises outside the clinical environments, the system required substantial usability adaptations, which included a simplified navigation, the integration of guidance aids – at the pre-exercise level, at exercise-level, and at session-level; as well as tolerance for execution variability (Bottiroli et al., 2024). Also, the exercises and difficulty levels had to be adjusted in order to compensate for the absence of immediate therapist assistance. These modifications allowed the rehabilitation plans to be prescribed and executed remotely, still maintaining professional oversight and preserving continuity of care from the hospital to patients' homes (Bottiroli et al., 2024).

4.2 Conceptual foundations of the HomeCoRe system

The HomeCoRe system was grounded in a set of conceptual principles that define its rehabilitation model independently of specific technological implementations (Bottiroli et al., 2024). At the core of HomeCoRe lies a clinician-guided model of cognitive rehabilitation, in which digital technologies function as instruments supporting every step of the rehabilitative process (Alloni et al., 2017, Alloni et al., 2018). In the original CoRe system, the rehabilitation plans were generated on the basis of formal neuropsychological evaluation and later implemented under direct clinician oversight, ensuring alignment between task selection, difficulty progression, and individual therapeutic goals (Alloni et al., 2018). This clinician-driven logic was explicitly retained in the transition from his predecessor (Quaglini et al., 2019; Bottiroli et al., 2024). A second foundational principle is the preservation of therapeutic structure across different contexts of care, originated in CoRe and maintained for the HomeCoRe system (Alloni et al., 2018; Quaglini et al., 2019). HomeCoRe also recognises that variability in performance and interaction is an inherent feature of computerised rehabilitation, particularly in populations with neurocognitive disorders. In fact, empirical evidence from home-based deployments indicates that users exhibit fluctuating engagement, task completion rates, and subjective ease of use across sessions, which should be interpreted within the context of a real-world execution instead of as an isolated feature (Bernini et al., 2023). As a result, the

system conceptualises execution variability as clinically informative data, supporting trend-based evaluations across sessions and tolerance for interrupted or assisted task execution, as discussed in analyses of HomeCore usability and user experience (Bernini et al., 2023; Bottiroli et al., 2024).

Together, these conceptual foundations position HomeCoRe as a clinically grounded and methodologically conservative system for computerised cognitive TR. In fact, they provide the theoretical basis upon which the ontology-based model and the functional design of the system are described in the following sections (Alloni et al., 2018; Quaglini et al., 2019; Bottiroli et al., 2024).

4.2.1 Ontology-based model and semantic continuity between CoRe and HomeCore

A defining and distinguishing feature of both the CoRe system and its home-based evolution is the adoption of a formal ontology as the semantic backbone of the rehabilitation framework. The ontology was originally developed within the CoRe system with the explicit aim of encoding clinical reasoning in a transparent, structured, and reproducible manner, therefore supporting the desired assessment-driven prescription and personalised CR (Alloni et al., 2018). The ontological model, as anticipated in Chapter 2, formally represents the relationships among four core components of the rehabilitation process: cognitive domains, task characteristics and their difficulty parameters, the patients' profiles derived from neuropsychological assessment, and their rehabilitation goals. Through these relationships, the ontology allows for a systematic mapping of the individual patient's needs to appropriate task classes and training parameters.

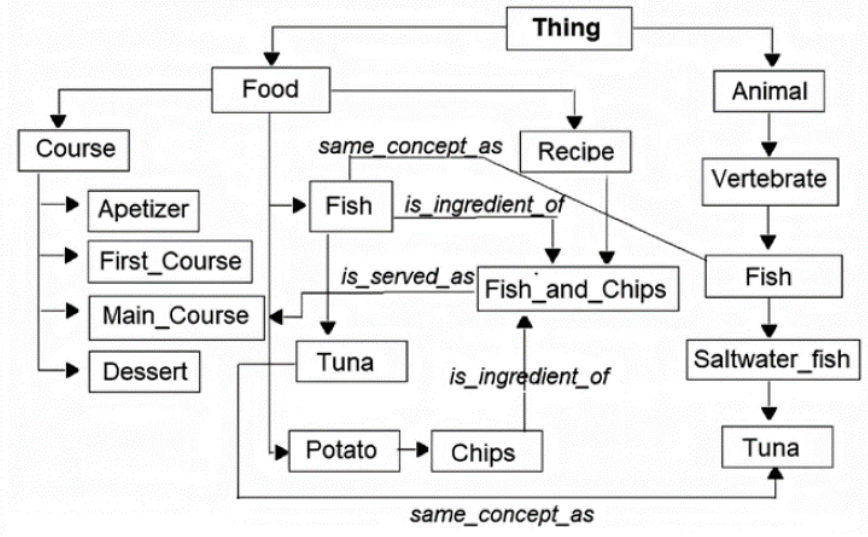


Figure 4.1: the ontology in the CoRe system, depicted as a scratch, with some examples of classes and relationships (Bottiroli et al., 2024).

Notably, in the transition from the versions of this long project, the conceptual model – the ontology – was not reformulated. As explicitly described in the development of HomeCoRe, the ontological knowledge base was retained and continues to govern how rehabilitation plans are generated, structured, and adapted overtime (Quaglini et al., 2019; Bottiroli et al., 2024). Within HomeCoRe, the ontology supports several key methodological functions. First, it enables consistency in task selection by explicitly associating each exercise with specific cognitive domains and predefined difficulty levels, thus constraining rehabilitation planning to clinically meaningful task-goal mappings. Second, it allows rehabilitation plans to be generated and modified in a principled manner, as well as on the basis of patient profiles – via the matching of ontology classes with patents' interests and skills, which are stored in the patient's profiles. Thirds, it facilitates reproducibility across sessions and across system evolutions, while simultaneously allowing for the automatic generation of a vast amount of stimuli; so that, even with continuity possible from session to session, the stimuli encountered are never the identical, increasing patient's interest and avoiding learning effects (Alloni et al., 2018; Bottiroli et al., 2024). Also, given its hierarchical structure – comprising classes, subclasses, and relationships – the exercises can be generated with many levels of complexity. For instance, an exercise generated hinging on the inner taxonomy levels will have a higher difficulty level, whereas the ones hinging on the upper levels result to be of a lower difficulty level. Moreover, semantic relationships such as "is-a" links connect a noun to its belonging conceptual class, which can be declined both as an upper level and an inner level link (Bottiroli et al., 2024). From a methodological perspective, this ontology-driven approach is particularly relevant in cognitive TR, where the physical separation between the clinician and patient increases the risk that digital interventions devolve into unsupervised or poorly structured training. However, by maintaining a formal semantic layer that encodes therapeutic intent, HomeCoRe preserves clinician control, individualisation, and goal orientation (Quaglini et al., 2019).

In the current app-based implementation of HomeCoRe, the ontology continues to operate as a stable conceptual layer underlying system functionality, remaining unchanged. In this scenario, additional systems components related to adherence monitoring, session scheduling, and usability management are implemented at the infrastructural level and therefore of not alter the core ontological model.

4.2.2 Usability and clinical effectiveness evidence

The conceptual foundations of the HomeCoRe system are supported not only by its ontology-based rehabilitation framework, but also by a progressive body of empirical evidence evaluating

usability, feasibility, and clinical effectiveness of earlier HomeCoRe implementations (Bernini et al., 2021; Bernini et al., 2023; Bernini at al., 2025). The available evidence refers to HomeCoRe deployments implemented in institution-managed devices – a touch-screen laptop – provided within research protocols, thereby informing the validity of the rehabilitation framework and delivery model (Bernini et al., 2023; Bernini et al., 2025), rather than the app-based deployment currently under development.

The initial empirical support for HomeCoRe usability and user experience derives from the pilot study conducted by Bernini and colleagues, which investigated the home-based use of the system in individuals with SCD or Mild Neurocognitive Disorder (mNCD) (Bernini et al., 2023). In this study, participants completed an adaptive, patient-tailored CR programme consisting of 18 home-based sessions delivered through the HomeCoRe platform (Bernini et al., 2023). The intervention was executed using touch-screen devices (touch screen laptops) configured for study participation, which allowed a controlled observation of usability under real home conditions (Bernini et al., 2023). In the study, usability was operationalised via adherence metrics and data deriving from task execution, whereas user experience was assessed using self-report questionnaires – the SUS, the User Experience Questionnaire (UEQ), the HomeCoRe User Experience questionnaire (HUXQ), and the Patient Global Impression of Change (PGIC) – and qualitative diary entries, therefore enabling a multidimensional evaluation of interaction burden, motivation, and perceived ease of use (Bernini et al., 2023). Overall, the results indicated a satisfactory usability and positive user experience, with high levels of motivation and engagement reported across sessions (Bernini et al., 2023). Additionally, technological skills were found to be associated primarily with perceived autonomy in initiating exercises, rather than with global usability with the tool or with engagement, suggesting that the system was found to be accessible even to users with limited prior digital experience (Bernini et al., 2023). Although with some limitations concerning sample size and the exploratory nature of the pilot design, these findings provide foundational support for the feasibility of HomeCoRe in cognitively vulnerable populations (Bernini et al., 2023).

In terms of efficacy, the intended clinical evaluation strategy for HomeCoRe was formalised in a single-blind non-inferiority randomised controlled trial protocol involving 40 participants with mild or major neurocognitive disorders, published by Bernini and colleagues, which explicitly aimed at comparing the same cognitive rehabilitation intervention delivered in the hospital – using CoRe – and remotely, via HomeCoRe (Bernini et al., 2021). This specific study

design was chosen in order to isolate the effect of delivery modality while holding therapeutic content constant, thus aligning with the conceptual goal of HomeCoRe as an alternative delivery system rather than a novel intervention (Bernini et al., 2021).

The completed non-inferiority randomised controlled trial subsequently was able to provide empirical confirmation of this conceptual premise (Bernini et al., 2025). In this study, 77 older adults with mild or major neurocognitive disorders were randomised to receive six weeks of intervention using either CoRe or HomeCoRe, with the outcomes assessed at baseline and post-intervention through a combination of standardised neuropsychological tests, and system-derived performance indices (Bernini et al., 2025). Specifically, global cognitive functioning was evaluated using validated neuropsychological instruments, while domain-specific outcomes focused in particular on working-memory and logical-executive functions (Bernini et al., 2025).

The results demonstrated that HomeCoRe was indeed non-inferior to CoRe in terms of cognitive outcomes, supporting then the conclusion that the home-based delivery did not, in fact, compromise therapeutic effectiveness when clinician-guided structure and task content were maintained (Bernini et al., 2025). In addition to this, it is possible to confirm that both delivery modalities yielded improvements in working memory and logical-executive functions, indicating comparable domain-specific benefits detected across conditions (Bernini et al., 2025). On this note, it was also found an increase in composite performance indices, the WSs, which were observed in both groups, reflecting a structured progression overtime within the rehabilitation programmes (Bernini et al., 2025). Altogether, these findings reinforce the conceptual position that HomeCoRe can function as a delivery modality preserving the effectiveness of a validated framework (Bernini et al., 2025).

Taken together, the available usability and clinical effectiveness evidence substantiates the conceptual validity of the system (Bernini et al., 2021, Bernini et al., 2025). While this evidence does not directly evaluate the app-based implementation described in the present work, it provides a robust empirical foundation for the underlying rehabilitation model, delivery logic, and supervision structure that the app-based evolution seeks to preserve whilst improving accessibility and scalability (Bottiroli et al., 2024).

4.3 Rationale for HomeCoRe as an app-based TR system

HomeCoRe is a research software tool developed through a long-standing collaboration between clinicians and bioengineers with the objective of translating structured cognitive

rehabilitation into a format deployable within patients' home environments. The system supports patient-tailored rehabilitation programmes targeting multiple cognitive domains including executive functioning, attention, processing speed, working memory, and episodic memory, hinging on the use of repeated sessions of computer-based exercises (Bernini et al., 2023). Importantly, once clinicians remotely configure treatment plans according to the individuals' cognitive profiles, the exercises are executed automatically in adaptive mode across sessions, reducing the need for continuous manual configuration. This automation contributes to lowering therapist workload while ensuring that rehabilitation remains structured and personalised, thereby facilitating scalable delivery of clinician-guided cognitive rehabilitation beyond in-person clinical settings (Bernini et al., 2023).

Although the CoRe platform demonstrated feasibility and clinical usefulness in outpatient cognitive rehabilitation, its deployment remained intrinsically confined to in-person clinical settings (Alloni et al., 2018; Quaglini et al., 2019; Bottiroli et al., 2024). In CoRe, rehabilitation sessions were conducted within specialised centres under direct professional supervision, requiring patients to attend schedules visits to access computer-based training in order to receive care. While this configuration ensured high levels of clinician control and therapeutic fidelity, it also implicated both organisational and logistical constraints that limited treatment scalability and continuity. In fact, the frequency of sessions to which patient could attend was constrained by service availability, patient mobility, and travel requirements, whereas rehabilitation intensity frequently decline after discharge due to absence of structured home-based continuation programmes (Alloni et al., 2018; Quaglini et al., 2019; Bottiroli et al., 2024). Consequently, despite the sound therapeutic architecture of CoRe, having access to sustained rehabilitation remained uneven, in particular for patients with limitations of different nature (Quaglini et al., 2019; Bottiroli et al., 2024).

Additionally, in order to achieve this goal, more than a simple relocation of exercises from the clinic to patients' homes was required. For these reasons exactly, HomeCoRe was implemented as a digital, web based application capable of functioning both online and offline, enabling clinicians to record performance metrics automatically, as well as securely transmit data derived from usage, and access to patients' progress remotely. As such, this technological infrastructure make exercises schedulable and monitorable at a distance while preserving the structured, assessment-guided prescription logic that was originally implemented in CoRe (Alloni et al., 2018; Bernini et al., 2021; Quaglini et al., 2019; Bottiroli et al., 2024). At the same time, an interface redesign was necessary to ensure usability for older adults and individuals with

neurocognitive disorders, so that fundamental aspects were prioritised: simplicity of interaction, consistency of navigation patterns, and a minimisation of unnecessary interface complexity, always maintaining the task demands consistent with rehabilitation goals (Bernini et al., 2023).

However, early implementations of HomeCoRe relied on the use of institution managed devices that were provided, configured, and managed by the healthcare institution, as exhibited in the initial home-based deployments of the system (Bernini et al., 2021; Quaglini et al., 2019; Bottiroli et al., 2024). While this solution enabled the extension of structured cognitive rehabilitation beyond in-clinic settings, it introduced new organisational constraints, as access to treatment remained dependent on the hospital's capacity to supply and maintain dedicated devices. These logistical requirements may limit scalability and delay access for some patients, despite the demonstrated feasibility and usability of the HomeCoRe framework (Bernini et al., 2023; Bottiroli et al., 2024). Consequently, in order to overcome these limitations, the current development of HomeCoRe is oriented towards an application-based deployment. This transition is intended to remove the logistical bottleneck associated with device provision, thereby improving accessibility, continuity of care after discharge, and scalability of clinician-guided cognitive rehabilitation. The present work contributes to this development phase by focusing on the design and verification of the application-based implementation.

4.4 Functional design and operational workflow of the HomeCoRe app

This sections describes the functional design and operational workflows of the HomeCore app, focusing on how TR plans are executed, supervised, and adapted in practice, rather than on underlying architectural principles already introduced in previous sections, which still apply to this project. The technical characteristics of the app were described on the internal user manual provided by the developers, in an unpublished document.

4.4.1 Patient interface and home-based workflow

The HomeCoRe app patient interface was designed to enable independent home use in the context of CR in older adults and individuals with neurocognitive conditions. During the interface development, usability was prioritised, along with predictable navigation patterns and minimisation of interaction complexity in order to accommodate populations characterised by reduced digital familiarity, attentional fluctuations, and overall cognitive vulnerability. Concretely, the application is accessed via individual credentials that are assigned to each participant, therefore guaranteeing that the therapeutic plan configured remotely by clinicians

is automatically loaded upon login. Once authentication is completed, the main interface displays the patient's identity and the information concerning the progression within the rehabilitation program, as well as a set of action buttons which can be used by the patient not only to initiate exercises, but also to visualise therapist communications when present, or even exit the application. In order to allow asynchronous interaction between clinicians and patients, a messaging function is enabled. In this sense, a notification signals the presence of unread messages, thus allowing therapists to provide guidance, encouragement, or procedural clarifications without necessarily requiring a synchronous contact. In fact, the communication channel is designed to support remote supervision while preserving patient autonomy during home-based execution.

Subsequently, upon the selection of the exercise, the system initiates the session workflow, which begins with a short affect self-report (Figure 4.2) and a brief time orientation phase (4.3). This step allows the system to capture contextual information regarding the patient's emotional and subjective state at the beginning of the sessions, which could influence task engagement and performance. As such, although affect ratings do not modify directly task difficulty, they are nonetheless logged and made available to clinicians as supplementary interpretative information during remote monitoring.



Figure 3.2: in the screenshot, the affect self-report, using five valenced faces



Figure 4.3: in the screenshot, the first orientation phase (in years), which is then followed by others on month, day (number), and weekday

After this phase, an explicit auditory confirmation step may be presented (e.g., "Have you heard the sound"), allowing the patient to either replay the audio input or proceed. This mechanism ensures that critical auditory instructions are correctly perceived before task execution, reducing the risk of errors attributable to either perceptual or attentional lapses, rather than cognitive difficulty. Following this initial routine, the system displays the list of exercises

scheduled for the current session, which appear in the order defined within the therapeutic plan. Once completed, they are automatically moved to the bottom of the list and disabled. Specifically, this structure guides patients through the prescribed sequence without requiring an independent task selection or planning. Importantly, when the exercises foreseen for previous sessions have not been completed, a dedicated recovery section becomes available, allowing patients to perform them within a limited temporal window, corresponding to two days, thereby supporting adherence while accommodating the possibility of occasional missed sessions or interruptions.

Each exercise begins with a standard introductory screen, which presents the exercise name and the task instructions – delivered both visually and acoustically. The auditory instructions are delivered through a computer-generated voice, ensuring consistency and clarity across sessions. Also, a guided demonstration is provided before the task is initiated. Both the verbal instruction and the demonstration can be replayed multiple times upon patient request, permitting users to familiarise themselves with task demands without their score being affected.

Moreover, during task execution, patients are provided with optional support mechanisms. For instance, the exercises include a limited number of aids that can be activated through a dedicated help button, which is positioned within the interface for easy access. The aids, depending on the exercise type, may include the repetition of instructions, replaying the stimuli, or even task specific hints. Also, the interface displays a visual countdown of remaining aids, which will influence the scoring of the performance if used. Similarly, some additional controls allow the patient to pause the exercise or temporarily interrupt the session without an automatic loss of the progress made, or without the task being invalidated.

Finally, at the end of each exercise, both visual and auditory feedback is provided in order to indicate correctness of performances, reinforcing patients' engagement and supporting their learning processes. In some exercises, feedback is presented through a colour-coded summary in which the elements completed correctly are highlighted in green and errors in red. This visual differentiation is explicitly designed to sustain motivation even in cases of suboptimal performance, by clearly differentiating partial success from failure. Importantly, incorrect responses do not interrupt task execution nor trigger immediate corrective feedback, but are logged as clinically informative events, allowing performance errors to contribute to a longitudinal assessment instead of functioning as punitive signals. At the conclusion of each session, notably, additional mood or engagement-related screens may be presented, along with

a brief motivational message. In HomeCoRe, feedback then operates on two complementary levels: task-level feedback for immediate information on correctness and supporting of learning within the exercise, and session-level feedback, motivational in nature and designed to sustain engagement across repeated home-based sessions.

Overall, these elements contribute to a longitudinal monitoring of patients' engagement and adherence support. In terms of performance evaluation, instead, it is based on trends across sessions computed via the WS rather than isolated outcomes, so that fluctuations in executions can be tolerated without compromising the global therapeutic structure.

4.4.2 Therapist interface and remote clinical management

Concretely, therapist access the system through their individual professional credentials, ensuring traceability of all actions performed within the platform. Crucially, within the HomeCoRe architecture, the therapist interface should not be entirely equated with the system backend, which instead corresponds to the infrastructural component that manages data storage, authentication, performance logging, the algorithms dictating progression and regression, as well as the ontological knowledge base governing exercise-domain relationships. In fact, the backend implements the computational logic and services that enable remote supervision, traceability, and continuity of care across sessions.

Upon login, they are presented with a dashboard that provides an overview of all active rehabilitation plans, highlighting operational alerts as those present for a program near its completion, for missed sessions, or even indicator of reduced adherence – non-compliant patients who haven't accessed the app for some time. Additionally, from this dashboard, clinicians can navigate dedicated modules for patient management (Figure 4.4), rehabilitation plan configuration, and performance monitoring. In the therapist interface, rehabilitation plans can be created either by adapting the predefined templates (Figure 4.5) or thorough manual configuration. Concretely, creating a plan involves selecting the cognitive exercises to be included, defining the weekly or biweekly frequency and number of sessions to be completed, assigning initial difficulty levels and specifying the overall duration of the program.

Then, once a plan is activated, the system governs exercise progression and regression in autonomy on the basis of predefined performance thresholds embedded in the system logic. This adaptive management reduces the need for continuous manual intervention while preserving clinician control over the selection of tasks, the training intensity, and overall therapeutic.

Furthermore, the therapist interface provides comprehensive monitoring tools that allow clinicians to inspect both adherence-related indicators and performance-related metrics. These include session completion rates, frequency of missed or recovered exercises, response accuracy, response times, and aggregated performance indices computed across the sessions. Crucially, data deriving from execution also capture contextual parameters such as pauses, interruptions, use of help aids, and delayed task completion. All this data then enables clinicians to interpret cognitive performance of patients within the ecological context of home-based delivery, instead of treating performance scores as isolated or decontextualized outcomes. Moreover, performance data can be visualised at multiple levels of granularity, namely individual exercises, entire sessions or longitudinal time windows spanning the full rehabilitation program; as well as being extracted onto an Excel file.

This supports both routine clinical follow-up and secondary research analyses, enabling clinicians to identify trends, irregular engagement patterns that may warrant intervention adjustments, and plateaus. Furthermore, among previously mentioned features, a tutorial one has been inserted, enabling storage of all exercises tutorial, in case a therapist who is not familiar with the exercises needs to revise them before inserting them into a rehabilitation plan. Through this architecture, HomeCoRe preserves clinician authority over rehabilitation planning while allowing a scalable delivery of CR in home environments.

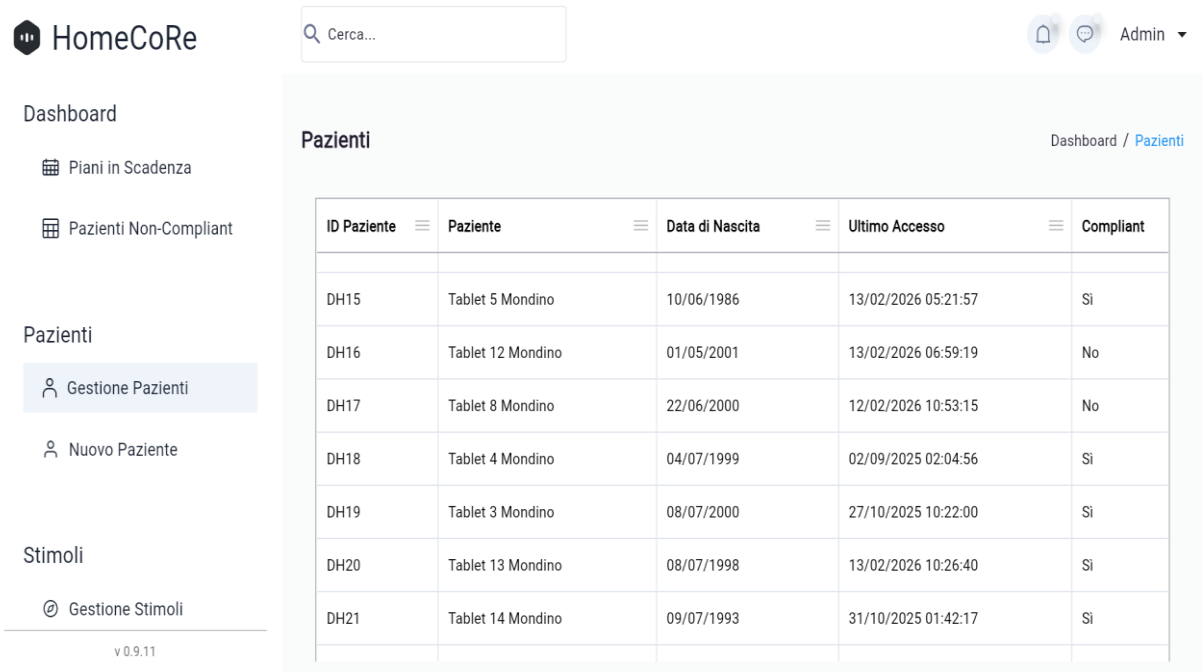


Figure 4.4: HomeCoRe dashboard, the patients' management section, where all patients with a plan are presented, along with their ID, their date of birth, the last time they accessed HomeCoRe and whether they are compliant.

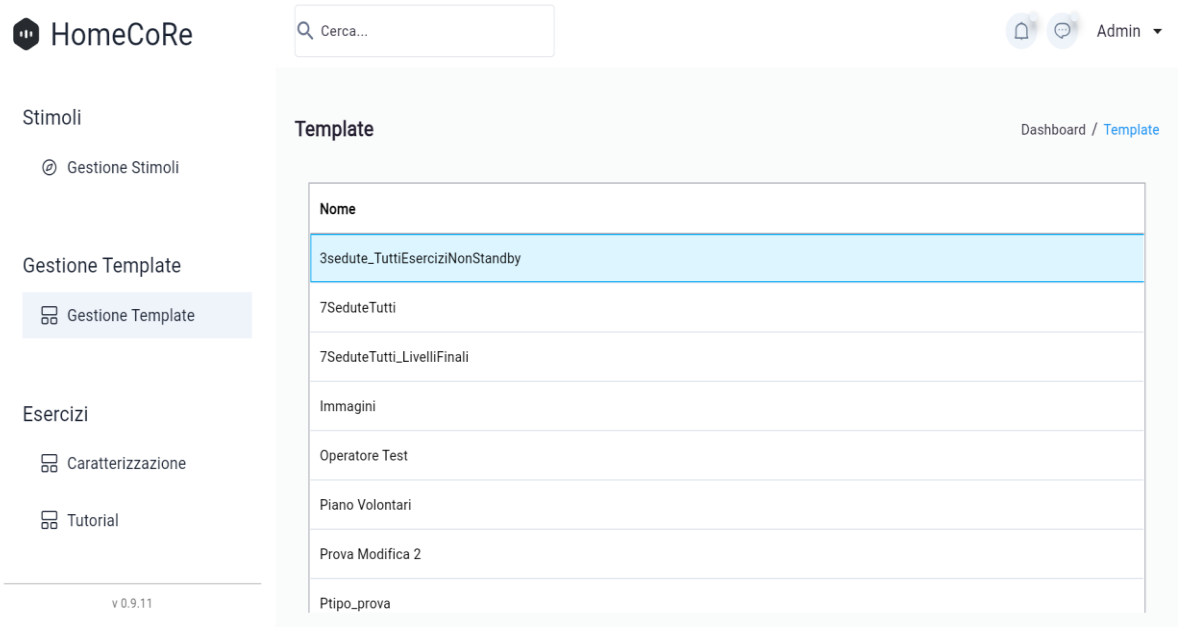


Figure 4.5: HomeCoRe dashboard, the templates management, which allow selection from already created templates.

4.4.3 Exercises modules and cognitive domains targeted

The HomeCoRe app incorporates a structured and heterogeneous library of computerised exercises, which have been designed to engage multiple cognitive domains that are typically compromised in pathological ageing. It is to be noted that the exercise set implemented in the current app-based version includes both tasks inherited from the original CoRe system and additional modules specifically introduced to support home-based delivery, adherence monitoring, and session structuring. The complete inventory of exercises, including their scoring status, the primary cognitive domains involved, and their adaptive parameters, is presented in the table below.

Table 4.1: HomeCoRe exercises

Exercise name	**Cognitive domains targeted**	**Core task description**	**Adaptation mechanism**
Backward digit span	Verbal working memory	Recall digit sequences in reverse order	Length if sequence (2-9 digits)
Backword letter span	Verbal working memory	Recall letter sequences in reverse order	Length of sequence (2-9 letters)

Exercise name	**Cognitive domains targeted**	**Core task description**	**Adaptation mechanism**
Number ordering	Working memory, sequencing	Order numbers ascending or descending	Length of sequence (2-9 items)
Letter ordering	Working memory, sequencing	Order letters alphabetically	Length of sequence (2-9 items)
Visuospatial matrices	Visuospatial working memory, attention	Reproduce spatial patterns on grids	Grid size (3x3/5x5), number of items
Corsi sequences	Visuospatial working memory	Recall spatial sequences of cubes	Sequence length and grid size (3x3/5x5)
Image-sound association	Inhibition, attention	Judge congruency between image size and sound tone	Number of trials, removals of replay option
Word-pair learning	Episodic memory	Learn and recall paired words	Number and semantic relatedness of pairs
Word categorisation	Semantic memory, executive control	Group words into categories	Number of words/categories, cue removal
Sentence ordering	Language, executive function	Reorder scrambled sentences	Sentence length, cue visibility
Procedure ordering	Planning, executive functions	Order steps of everyday activities	Number of steps, cue visibility
Scene ordering	Temporal reasoning	Arrange images into the correct sequence	Time limits, scene complexity
Puzzle	Visuospatial reasoning	Reconstruct fragmented images	Pieces (4-12), colour, cue removal
Logical sequences	Reasoning	Complete visual/logical sequences	Number of options (2-6), complexity

Exercise name	**Cognitive domains targeted**	**Core task description**	**Adaptation mechanism**
Memory	Visuospatial memory	Match hidden image pairs	Number of cards (4-26), category similarity
Visual search (numbers/letters)	Selective attention	Locate targets among distractors	Number of targets, time limits
Visual search (images)	Selective attention	Locate shapes among distractions	Number of target shapes, time limits
Position memory	Visuospatial memory	Recall position of markers	Grid size, number of markers
Visual memory	Visual memory	Recall sets of images	Number of images, motion
Directional decisions (arrows)	Processing speed, attention	Identify direction under interference	Number of stimuli, size variation

The present section therefore focuses on the functional organisation and clinical role of the exercise library. The HomeCoRe app preserves the full set of legacy CoRe exercises, whose clinical relevance and feasibility have been documented in earlier in-clinic and home implementations (Alloni et al., 2018; Bottiroli et al., 2024). These task include, among others, backward span paradigms, visuospatial matrices, logical sequences, paired associative learning, and categorisation tasks. Their inclusion in the app ensures semantic and therapeutic continuity with previously validated rehabilitation protocols. While the added elements do not alter the underlying rehabilitation logic, they may enhance ecological validity and usability in unsupervised environments. This coexistence of legacy and new components reflects a conservative design strategy in which innovation is directed towards delivery conditions and usability.

Additionally, all the scored exercises within HomeCoRe app are governed by adaptive mechanisms that are responsible to regulate progression and regression across difficulty level through predefined, exercise-specific performance thresholds. Although the difficulty parameters vary by task, they typically involve changes in sequence length, stimulus complexity, number of distractors, cues reduction, temporal constraints, or combinatorial demands. Specifically, for the system to activate progression to a higher difficulty level, the

performance must exceed the criterion thresholds, such as maintaining accuracy above a predefined level – generally 0.75-0.85, depending on the exercise – with response times remaining within task-specific acceptable ranges and with limited or no use of aids. On the other hand, regression mechanisms are activated when performance falls below threshold – for example when repeated errors occur across trials – sustained response latencies are present, exceeding the predefined temporal limits, or when excessive reliance on support tools is detected, thereby indicating that the current task demands exceed the patient's capacity at that time. These thresholds are tightly bound to the exercise levels and are applied automatically across sessions, ensuring consistency in modulating difficulty while substantially reducing the need for continuous manual adjustment by clinicians. Alongside scored exercises, HomeCoRe includes non-scored quizzes and session routines, as the orientation checks and the affective self-report previously covered, and engagement prompts (Visual Memory), which are intentionally excluded from the adaptive logic that governs the app and from the performance indices, serving a supportive and contextual functions without influencing progression rules. Overall, the exercise set should thus be interpreted not solely as a collection of tasks, but as an operational layer through which the ontological model, clinician supervision, and patient engagement converge.

4.5 Methodology: a qualitative approach

The present study adopted a qualitative approach in order to carefully examine and support the transition of the HomeCoRe system from a computer-based home delivery model to an application-based implementation. This transition required a substantial adaptation of both the interface and the exercise stimuli. On the one hand, previously used materials had to be replaced or redesigned to ensure compliance with copyright constraints. On the other hand, and more importantly from a clinical and usability perspective, the interaction structure and visual content required further optimisation for independent use in domestic environments by older adults and individuals with neurocognitive vulnerability. As such, because the primary objective of the app-based version is to enable autonomous, home-based execution while still preserving a form of clinician supervision, a qualitative evaluation became necessary to verify that the redesigned interface, instructions, and stimuli remained coherent with the therapeutic framework and accessible to target population. This need was further reinforced by the technological transition from a Java-based system operating on institution-managed devices to an Android-based mobile application, which naturally required a renewed verification of usability, visual clarity within a touchscreen, and interaction patterns. Additionally, the transition was partly motivated

by the intention of aligning the software with the requirements for CE marking under the European regulatory framework for medical devices (European Parliament & Council of the European Union, 2017), which in order to be reached, it proved necessary the presence of documented evidence of usability, safety, and consistency of use in real-world conditions.

Furthermore, within the multidisciplinary development project, new cognitive stimuli were created and selected in accordance with predefined task instructions and with the constraints imposed by the underlying ontological structure, ensuring coherence with cognitive domains and difficulty parameters. Alongside stimulus preparation, systematic testing was then conducted across multiple exercise levels to verify the correct functioning of adaptive mechanisms governing progression and regression, as well as scoring accuracy, feedback behaviour, and overall session flow. These activities involved both the patient and therapist interface, aiming to ensure that rehabilitation plans were executed as intended within the remote delivery architecture. As such, the testing was primarily performed on iterative development versions of the software, allowing both identification and reporting of technical issues related to task behaviour, performance logging, and interface consistency, supporting a progressive refinement by the engineering team. As such, operational support tools included a structured tracking through spreadsheets-based logs and the use of AI resources for stimulus search and generation. In this context, the specific procedure adopted varied based on the exercise type and interaction modality, reflecting the known heterogeneous cognitive demands present across modules. Finally, considering that the software implementation was carried out with the aid of a technical development team, this phase involved also the verification that the functional specifications provided by the research group had been translated accurately into the final application. All things considered, this qualitative study was refined with the ulterior motive of spotting technical difficulties of the systems – bugs – or usability traits that have room for improvement.

4.5.1 Participants

The qualitative study was conducted over a three-months period and it involved a multidisciplinary group of nine collaborators, which included six psychologists with experience in cognitive rehabilitation and neuropsychological practice, one biomedical engineer, and two Master's degree students. Precisely, participation in this phase was not oriented towards clinical outcome evaluation but towards the iterative verification and refinement of the HomeCoRe app during this transition to an application-based delivery format. In fact, within this timeframe, activities were organised according to two complementary areas of focus: the interface structure

and the exercise modules. As such, the focus was distributed among assessing the application usability, clarity of navigation, and interaction flow within the patient interface, as well as within the review of cognitive exercises, the appropriateness of newly implemented stimuli previously formulated, and the coherence of difficulty progression across levels. Consequently, this differentiated organisation allowed parallel evaluation of both interaction design and therapeutic content.

4.5.2 Images selection for the Puzzle exercise

First of all, the *Puzzle* exercise is a visuospatial and planning task in which the patient is required to reconstruct completely and correctly an image. To do so, they have to arrange the fragmented visual sections within a predefined grid. The task, designed to stimulate visuospatial processing, visuo-perceptual organisation, sustained attention, and planning abilities, is organised so that the patient must identify the global configuration from partial cues and organise the fragments accordingly. Specifically, at the beginning of such exercise, an introductory screen illustrates the exercise name, along with the instruction, which are delivered both visually and through a computer-generated voice. The user can then listen to these instructions – and demonstration – more than once before starting the task, therefore reducing the need of relying on memory and supporting patients with attentional fluctuations. Subsequently, the target image is presented and kept on screen for a maximum of thirty seconds. Nonetheless, users can shorten their observation time by touching anywhere on the screen, as explained by the instructions. Once the observation time is over, they are presented with the fragments of the image on the lower part of the screen, which have to be positioned correctly on the grid in order to reconstruct the full image. The interaction occurs through simple touch selection and placement. Also, a limited number of aids can be activated through the help button: when used, these allow the user to see the full image one more time. Additionally, as the difficulty level increases, the image may be composed by a higher number of sections, may lose colour (black and white images), may be present as irregularly cut (puzzle-like) during the action phase or presented with a different spatial orientation.

In the current HomeCoRe implementation, the stimuli used for earlier versions could not be selected for copyright reasons, so new images used in the *Puzzle* exercise were specifically selected to meet predefined criteria. For instance, all new images had to be in landscape orientation – with width greater than height, (e.g., 1920x1080) – and, once selected, saved in a uniform .jpg format onto a spreadsheet divided by participant. A crucial aspect considered was for the images to remain understandable even after being segmented into puzzle components,

as well as ensuring that, once fragmented, the image did not present identical segments or empty ones. Moreover, in order to guarantee free and reusable visual material, candidate images were sourced from open repositories (Iconfinder, n.d.; Pixabay, n.d.), and then uploaded onto a shared spreadsheet, where they were additionally checked so that all requirements were met and moved to the backend. Importantly, the images were analysed actively during the testing phase, ensuring that once implemented and segmented by the software, the requirements remained present.



Figure 4.6: example of selected image



Figure 4.7: example of selected image

4.5.3 Creation of sentences for Procedure ordering

The *Procedure ordering* exercise is designed to train temporal organisation, planning, and executive functioning by requiring a patient to arrange a set of images representing the steps of an everyday activity into the correct chronological order. Each item depicts a familiar scenario, as can be preparing food or call a relative, so that the task primarily challenges sequencing and reasoning instead of semantic recognition. As such, at the beginning of the exercise, instructions are presented both visually and aurally, with the customary possibility of replaying the example more than once before starting. Additionally, during execution, the steps forming the sequence are displayed in a scrambled configuration and must therefore be ordered via touch interaction until the correct sequence is properly reconstructed. In the event of a correct response, the steps touched becomes yellow and the corresponding positive auditory feedback is heard. Conversely, the steps touched do not become yellow and the corresponding negative feedback is reproduced. In this exercise, the difficulty is primarily manipulated through the number of steps included in the sequence. For instance, lower levels typically involve short sequences – starting with three steps – that represent highly familiar routines. Intermediate levels, instead, increase the sequence length – with five or six steps – thereby requiring greater maintenance of temporal relations. Finally, higher levels introduce even longer and more structurally similar

sequences – seven to nine steps. Also, the difficulty level was modulated by the possibility of seeing the steps already identified on the lower part of the screen, which aids in better remembering the sequence, as well as the time available to complete the exercise.

As there was no database containing the sequences, the participants had to create them with these exercise instructions in mind. As such, several sequences – ideally at least twenty-five per number of steps – were identified, with the correct possible answers to complete the exercise noted, as many sequences were possible to be completed in more than one way. Once identified, they were uploaded onto a shared spreadsheet, where they were divided by number of steps contained. In addition to uploading the sequence itself, which was pre-set to be shown in steps numbered alphabetically, participants had to add their name for internal traceability, as well as the alphabetic order corresponding to the answer. In cases where more than one way of composing the sequence was identified, all possible combinations were paired to their sequence. One example of sequence selected and inserted into the backend was the following, already translated from Italian: "reading a book". Such sequence was identified as a three step procedure, divided into these actions: "taking a book off the shelf", "open the book to the desired page", "start reading". In the shared spreadsheet, this sequence was then inserted among the three-steps proposals, along with its composing actions and the right order to be made by the user in order to perform accurately. Once reported in the file, the accepted ones – characterised by clarity and reduced ambiguity and interpretability – were inserted in the back end.

4.5.4 Creation of visual sequences for Scene ordering

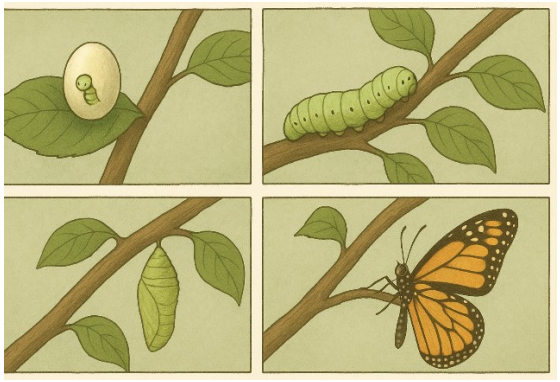
In the *Scene ordering* exercise, the patient is required to reconstruct the correct chronological order of a sequence of events, illustrated through images, conceptualised to stimulate planning, temporal sequencing, and executive control processes. The instruction, which recites – once translated to English – "Arrange the images on the screen in chronological order", is presented visually and aurally. At the beginning of each trial, several scenes depicting a sequence are displayed on the screen in a random fashion. The patients then select the images one at a time in order to identify the correct sequence: when a correct scene is chosen, the system provides a positively valenced auditory feedback, as well as highlighting the image with a green outline, and automatically positioning it in the lower part of the screen, within the reconstructed sequence. On the other hand, incorrect selections trigger negatively valenced auditory feedbacks. In this case, the image remains in its initial position, thereby allowing the patient to correct their response and proceed. This exercise, which has to be executed within a time range,

and similarly to all exercises present in the HomeCoRe App, is equipped with an initial guided demonstration with step-by-step audio instructions. Moreover, level difficulty is modulated by the number of scenes, as well as being categorised into three intrinsic levels: easy, intermediate, and difficult. These difficulty levels were originally determined hinging on scenes from neuropsychology manuals. Additionally, the *Scene ordering* exercise relies on randomly selected scene sets stored in the system database, which for the purpose of the app development, had to be replaced with appropriately licensed images without altering the task structure.

With the aim of controlling and recreating old scenes free from copyright novel stimuli were conceptualised following the instructions and the logic intrinsic of this exercise. Such process required several steps. First of all, 138 scenes pertaining to previous versions of the software were used as starting points: precisely, they were stored in two shared file, accessible to all participants. One named "Tabella sequenze" – sequences table – which contained the number of all old vignettes, informing participants of which sequences had already been completed and which had still to be created; and another named "SEQUENZE_TEMPORALI", or temporal sequences, where the vignettes could be found in a .jpg format, both integrally and divided scene by scene. Then, the underlying story they were illustrating was kept as identical as possible, extracting a prompt based on the participant's description of the old image. This prompt followed a scheme, which asked the AI software to create a sequence of images that together could tell a story on a certain topic, explaining each scene. Alternatively, the old image was uploaded onto the AI software chat, with the demand of reproducing the scenes in a temporal sequence in a rectangular shape, while maintaining the scenes clearly separated in squares. Sometimes, a black and white image was uploaded in order to receive a coloured output.

Subsequently, AI was exploited for the generation of novel images. Precisely, a prompt was given to either ChatGPT or Microsoft Copilot, describing in detail how each scene had to be depicted. Such prompt had to be clear and simple, and had to ask the software to generate a sequence that was internally coherent to avoid misinterpretation, guided by the scheme introduced. Importantly, once an image was generated successfully, the relative prompt, along with the whole conversation with the AI software chat that led to the creation of the image was pasted in a section of a spreadsheet named "Tabella_stimoli scene". In this spreadsheet, other important information was noted: the number of the old vignette, the new temporary number, the name assigned to the new vignette, the status – which could correspond to "ongoing" or "done" depending on completion, the software used – weather ChatGPT or Microsoft Copilot

if not both, the participant who created the image, an evaluation section allowing to determine the viability of the image and the need of potentially needed changes, the difficulty level, a section establishing whether it had been inserted in the backend, and the new definitive number assigned to the vignette. Additionally, the vignettes obtained were uploaded in .jpg format onto a shared folder named "Stimoli scene_HomeCoRe App", both integrally and divided scene by scene. Ultimately, discarded and accepted vignettes were moved to two separate folders, with the discarded ones typically being judged excessively interpretable or unclear in their temporal sequencing. Finally, a total of 93 vignettes were inserted in the back end, respectively 36 pertaining to the easy difficulty level, 28 to the intermediate one, and 29 to the difficult one.



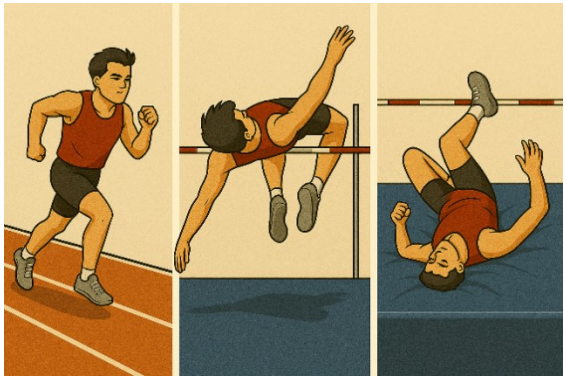


Figure 4.8: example of a discarded vignette due to logical inconsistencies.

Figure 4.9: example of an accepted vignette – easy level. Logical temporal parameters and graphical coherence in between scenes are maintained.

In the figures above an accepted vignette and a discarded one are exemplified. In the first, (Figure 4.2), the logical coherence that must govern the barrage of scenes is violated, as in the first frame, a caterpillar seems to be exiting an egg, which is unnatural and conceptually wrong. In the second, instead – Figure 4.3 – a clear temporal sequence is identifiable between scenes: the same graphical style and colour patterns are maintained, and the person illustrated has the same features in every scene, allowing an immediate understanding, avoiding confusion.

4.6 Levels testing

At the same time, while new stimuli were created, the exercises whose stimuli were – initially – already inserted in the back end were available for the testing phase. First and foremost, in order to test the exercises and the overall functioning of the application, participants were given tablets (Samsung Galaxy Tab A9+, 11") with the pre-installed HomeCoRe app. Importantly, the first version tested over these three-month timespan was the 0.9.15 one, and it was followed by three more versions, respectively 0.9.16, 0.9.17, and 0.9.18 – the currently available one. Concretely, a version was tested, the data derived from the testing of available exercises was

registered onto a spreadsheet named “Piani test HomeCoRe App”, where considerations and future fixes were suggested and then implemented by the engineers, who could consequently release another version, ready to be tested again. To begin with, the app was downloadable via an invite link, which was sent to the Gmail account accessed on the tablet each time a new version was released. Opening the app, the rehabilitation plan assigned to the specific account was accessible in form of an exercise list. These rehabilitation plans were elaborated for every participants and, for research purposes, they had to be accessed once a day, every day – until the version 0.9.17, as starting from the version 0.9.18, it was possible to test the same exercise more than once a day. The plans were mainly assigned to participants using predefined templates already existing in the software, as they could be created in the therapist interface in order to ease the therapist’s workflow. The rehabilitation plans were accessible on the app prior authentication via dedicated credentials.

Additionally, to ensure technical reliability, internal coherence, and adherence to the predefined rehabilitation logic, the HomeCoRe app underwent a structured testing phase, conducted by the participants across iterative development versions. As such, the testing sessions were systematically documented using a dedicated spreadsheet designed to capture both expected system parameters and observed behaviour during the execution of sessions. Consequently, for each exercise tested, the following variables were logged: testing date, the application version, the exercise identifier – the number associated to the exercise name, the proposed difficulty level, the expected number of instances and stimuli per level, the expected amount of aids, the proposed feedback expressed as performance percentages, the expected subsequent level, and qualitative notes documenting discrepancies, anomalies, or behavioural inconsistencies.

Furthermore, each tested configuration was cross-verified through the therapist interface, using the dedicated web access link reported on the spreadsheet, to confirm that performance data, progression and regression outcomes, stimuli presented, and the execution logs were successfully and correctly transmitted and visualised within the remote supervision environment. This was possible thanks to the therapist interface features, which were purposefully created in order to keep track of such aspects. Specifically, the possibility to export data from terminated and ongoing plans in form of tables, graphs, or – more relevant to this qualitative study – the downloadable Excel file enabled the comparison of the data displayed in the patient interface with the one registered by the therapist interface. Said dual-level verification allowed the assessment not only of front-end exercise execution within the patient interface, but also of the back end coherence in terms of data logging, clinician-facing reporting,

adaptive threshold functioning, and scoring accuracy. This spreadsheet-based monitoring approach therefore functioned as a quality control instrument, ensuring that adaptive mechanisms, the scoring algorithms, and the interface behaviour operated consistently with the ontological framework and with the therapeutic constraints foreseen in the HomeCoRe rehabilitation model.

Crucially, the testing phase did not merely function as a technical verification of the software – although this was one of its purposes – but became progressively the methodological driver of the qualitative study. In particular, the "Note" section of the "Piani test HomeCoRe App" structured spreadsheet assumed a central analytic role for the evaluation of both technical and usability-related aspects. As such, while the predefined columns allowed the verification of the expected parameters, the open-ended note column was used to document discrepancies between the expected and observed behaviour of the app, as well as recurrent technical bugs, interface inconsistencies, ambiguity in the clarity of instructions, and usability-related difficulties observed during the simulated execution of the exercises. Over time, the systematic documentation of these observations enabled the research team to identify problems both at the exercise-level and recurring patterns of issues across exercises. Consequently, these observations were then organised through a structured coding procedure: each recorded issue was in fact classified into two primary categories – technical bugs, which referred to problems that interfered with overall task execution, stimuli presentation, scoring, or general system behaviour; and usability-related difficulties, which referred to aspects that did not directly prevent the completion of tasks, but that could nonetheless affect their clarity, perceptual discriminability of stimuli, the efficiency of interactions or the overall workflow coherence. Within this macro-categories, issues were further clustered into thematic groups, which mainly concerned technical mechanisms, as could be feedback mismatches, logging errors, incorrect progression or regression between tasks, or stimuli being presented incorrectly; as well as interface-related usability aspects, as ambiguity in the activation of aids, insufficient clarity of instructions or examples, and unclear navigation flow; along with stimulus-level characteristics, including an excessive cognitive load at some specific levels or ambiguity in its interpretation.

Subsequently, all data collected up to version 0.9.17 were then integrated in a dedicated spreadsheet, named "Problematiche test interni_HomeCoRe App", where issues were organised by interface, namely patient versus therapist, by task, and by task novelty – legacy tasks versus newly added ones. For instance, the distinction between interfaces was methodologically necessary as the patient and therapist interfaces serve different functional purposes and operate

responding to different demands. As such, analysing them separately captured the identification of usability-related and technical issues specific to each user role, therefore preventing task-execution related problems on the patient side to be confused with those pertaining to workflow on the therapist side. Also, the distinction between legacy and newly implemented tasks was methodologically relevant as legacy exercises had been migrated from previous system versions into the updated operational architecture, whereas newly added ones were developed directly within it. In fact, analysing these two groups separately allowed the participants to distinguish issues potentially arising from the translation and adaptation of already existing tasks into the new app-based software from those inherent to newly developed tasks. Additionally, said structured organisation enabled participants to quantify the recurrence and frequency of presentation of problems, as well as to identify criticalities shared across multiple exercises, and create the frequency-based qualitative summaries that will be reported in the next chapter. The cluster analysis derived from the present process directly informed the implementation of bug fixes and usability-related improvements, leading to the development of version 0.9.18, which is the one currently being tested following the same systematic procedure used for earlier versions.

As such, this iterative process made of logging, comparing, clustering, and resulting eventually in re-evaluations transformed the spreadsheet from a mere monitoring tool into a structured qualitative source of data. This qualitative approach allowed for systematic analysis of the global functioning of the app and of how end-users might experience its use in their home environment. Therefore, the qualitative dimension of the present study emerged in an inductive manner, from the documented evidence of execution, instead of from a subjective impression alone, thus grounding the usability consideration and development decision to be made in this systematically recorded testing-derived data.

Chapter 5. Results

The analysis of the legacy HomeCoRe tasks, the ones already implemented in previous version of the system, led to the identification of several issues affecting task administration and user interaction with the app. For reporting purposes, as anticipated these issues were classified into technical bugs, which interfered with task execution per se affecting stimulus presentation and scoring of the responses; and pre-usability issues, or those aspects that did not directly prevent completion but could potentially affect clarity, perceptual discriminability, or ease of interaction with the app. Moreover, such analysis was carried out with the same methodology for the newly added exercises, and then moved to analysing all exercises with the aim of identifying frequently arising issues categories. Finally, an additional inquiry was conducted for the therapist interface.

5.1 Legacy tasks

Table 5.1: summary of problems detected in legacy exercises

Task	**Technical bugs**	**Usability-related issues**
Backward Digit Span	Missing feedback; incorrect difficulty; scoring errors; audio failure	Need visual dashes; more aids; keypad too small
Visuospatial Matrices	Example failure/noise; wrong difficulty; single trial shown	None
Image–sound	Wrong level; missing audio; faulty/noisy examples	High vs low sounds hard to distinguish
Word-pair Learning	Incorrect stimulus display; unsupported accented/foreign letters	Poor phase distinction (learning vs testing); small keyboard
Word Categorisation	Wrong accuracy/feedback; faulty examples; wrong level; mis-scored answers; bad stimuli; foreign characters	Small keyboard
Sentence Ordering	Wrong level; unexpected highlighting; valid orders rejected; repeated stimuli	None
Scene Ordering	Stimuli repetition; wrong level; single trial; inaccurate	None

Task	Technical bugs	Usability-related issues
	scoring; database stimuli revision needed	
Puzzle	Reversed images; wrong scoring; single trial; wrong level; blank tiles; repetition; faulty examples	Difficulty levels organisation; tile distribution/size
Logical Sequences	Stimuli repetition; cut responses; missing targets; wrong level; single trial	Stimulus size; revise difficulty structure
Memory	Incorrect stimuli/category rule; wrong level	Increase stimulus size
Visual Search (numbers/letters)	Example restarts; excessive prompts; incorrect stimuli	Revise difficulty tables

5.2 Newly added tasks

Table 5.2: summary of problems detected in newly added exercises

Task	Technical bugs	Usability issues
Backward Letter Span	Letter repetition in recent trials; missing feedback; wrong level administered; wrong stimulus count; faulty examples	Visual dashes; phonetic confusion (e.g. V/B); more time needed; small keypad
Number Ordering	No feedback; task fails to start	Larger keypad; more time needed
Letter Ordering	Correct response marked incorrect; faulty/noisy examples	Small keyboard; more time needed; show order rule; phonetic confusion
Corsi Sequences	Excessive incomplete-response warning; wrong level	Revise difficulty tables; add sounds for enlightening cubes
Procedure Ordering	Multiple valid orders feature not supported; wrong level	Stimuli too difficult/ambiguous
Visual Search (images)	Wrong stimuli; wrong level	Revise difficulty tables; limited token variety
Position Memory	Wrong stimuli; single trial only	Remove yellow tokens for low visibility on the screen;

Task	Technical bugs	Usability issues
		revise tables; colour rules must be applied; fixed external tokens in an equally distributed and tidy manner on screen; allow adjustment
Visual Memory	Scrolling failures (images don't scroll when expected to or, when fixated, some of them remain blank); improperly cropped images; phase failures (learning vs. testing); scoring/audio issues; repetitions; fast-quizzes with few targets;	None
Directional Decision	Single trial; wrong level; excessive reminders	Revise tables; increase inter-trial interval

5.3 Recurring categories of bugs and usability-related difficulties in the patient interface

The analysis conducted had a total of 75 technical bugs affecting the HomeCoRe app functionality, along with 36 usability-related improvements needed across all tasks (Table 5.1). As such, technical bugs were more frequently observed in legacy tasks (61%, n=46), than in newly added ones (39%, n=29), meanwhile usability-related difficulties were more often associated with newly added tasks (64%, n=23) than legacy ones (36%, n=13).

Table 5.3: distribution of technical bugs and usability-related improvements

Issue category	Total Issues	% in legacy tasks	% in newly added tasks
Technical bugs	75	61%	39%
Usability-related improvements	36	36%	64%

Table 5.4: frequency categories of technical bugs and usability-related difficulties

Category	Type	Tasks Involved	% of total tasks
Difficulty levels not updating within the same session	Technical bug	20 (all tasks)	100%
Incorrect level presented in the following session	Technical bug	15 (9 legacy and 6 new)	75%
Incorrect stimulus presentation	Technical bug	12 (8 legacy and 4 new)	60%
Accuracy/feedback incorrect or missing at exercise end	Technical bug	7 (4 legacy and 3 new)	35%
Example malfunction	Technical bug	7 (5 legacy and 2 new)	35%
Incorrect instance presentation	Technical bug	6 (4 legacy and 2 new)	30%
Correct response marked as incorrect	Technical bug	4 (2 legacy and 2 new)	20%
Audio malfunction	Technical bug	3 (2 legacy and 1 new)	15%
Response reminders mistimed or excessively frequent	Technical bug	3 (1 legacy and 2 new)	15%
Revision of difficulty level tables and parameters	Usability-related modification needed	11 (4 legacy and 7 new)	55%
Response keypad and stimulus layout/size to be improved	Usability-related modification needed	6 (3 legacy and 3 new)	30%

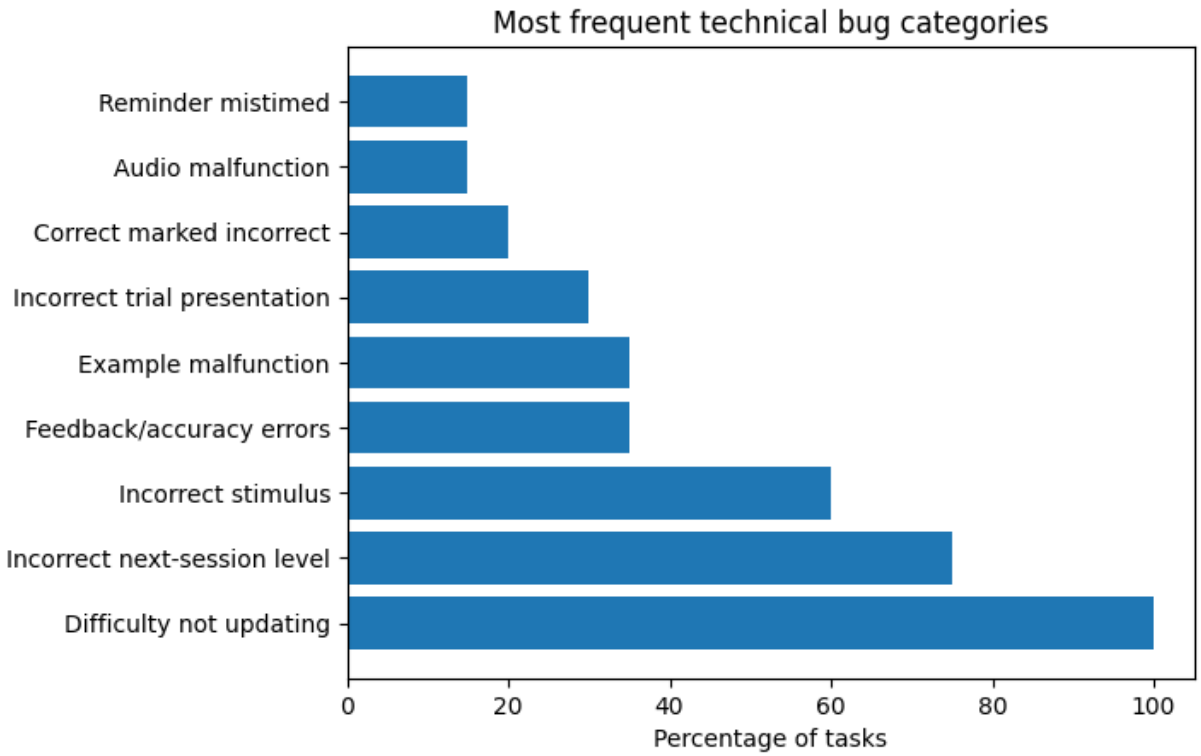


Figure 5.1: frequently detected technical bugs categories among all tasks

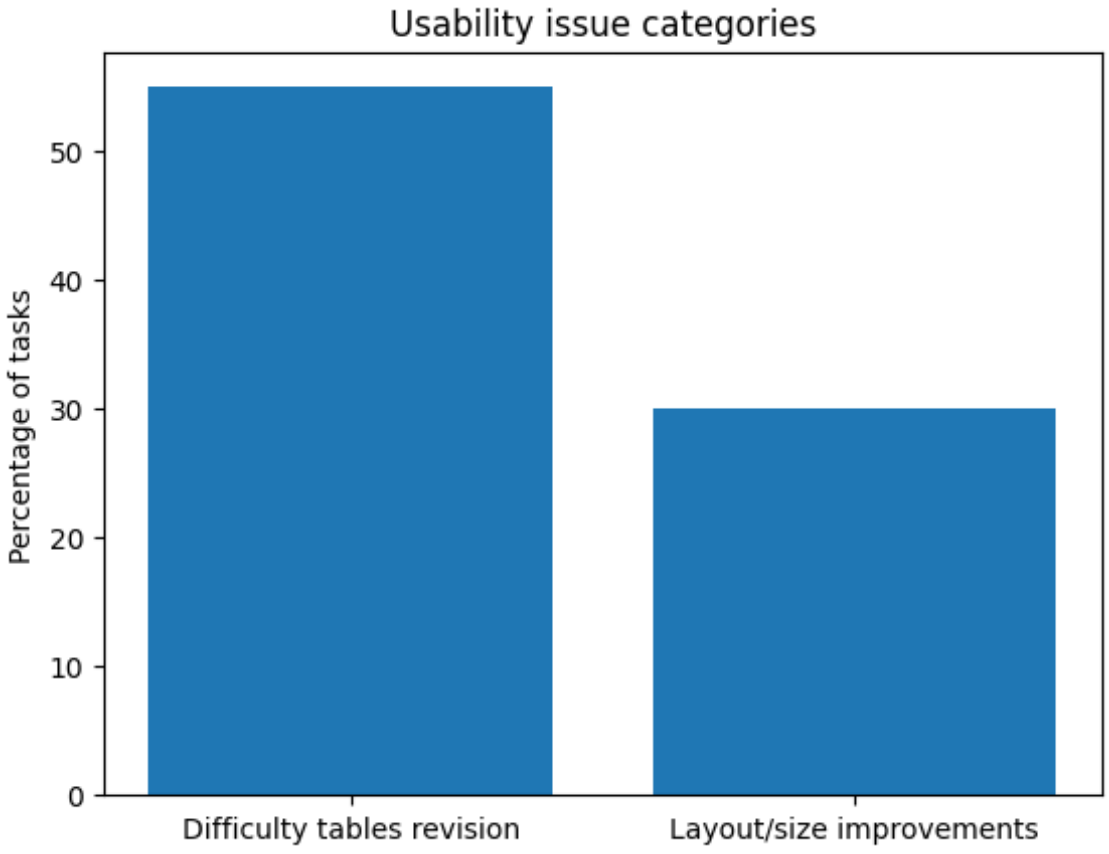


Figure 5.2: recurring categories of usability-related difficulties detected among all tasks

5.4 Therapist interface technical bugs and usability related difficulties

The analysis of the HomeCoRe therapist interface, in the other hand, identified 12 issues in total: 83% of them were technical bugs and 17% of them concerned usability-related difficulties. Overall, these affected several areas of HomeCoRe app, including stimulus management, therapeutic plans, patients' profiles, templates, tutorials, statistics report, and exercise configuration.

Table 5. 5: technical bugs detected in the therapist interface

Area	**Issue**
Stimulus management	System does not enable multiple valid action orders in procedural tasks.
Therapeutic plans	System displays two therapeutic plans as active simultaneously despite one being terminated.
Therapeutic plans	Missing warning of last difficulty level when creating a new plan.
Plan interruption	Active plan can only be deleted; interrupt function required to preserve data.
Backend accessibility	Patient list not displayed, preventing access to functions.
Statistics export	Exported Excel incorrectly formatted; mood data missing.
Exercise configuration	Characterisation tables cannot be directly modified.
Templates	Edit button does not work for existing templates.
Tutorials	Examples for individual exercises are missing.

Table 5.6: usability-related difficulties detected in the therapist interface

Area	**Issue**
Session assignment workflow	Allow same exercise to be assigned more than once in the same session.

Patient profile/password	Therapist cannot view or reset patient password; reset workflow required.

Overall, the results on the therapist interface showed that concerns were centred on core system functionality and data management, specifically in therapeutic plan management, backend accessibility, and configuration tools, whereas only a small proportion was related to workflow usability (Table 5.7).

Table 5.7: distribution of therapist interface issues by type

Issue type	**Number of issues**	**Percentage**
Technical bugs	10	83%
Usability-related difficulties	2	17%

Chapter 6. Discussion

6.1 Outcomes overview

The present study evaluated the functionality and usability of the HomeCoRe platform through a structured internal testing process aimed at identifying technical inconsistencies and limitations related to interaction before the implementation of a formal usability study involving healthy individuals. In fact, as described in Chapter 4, the testing phase was conceived not only as a technical verification step, but as a systematic qualitative process, in which discrepancies were logged, coded, and clustered into functional bugs and usability-related difficulties. The result reported in Chapter 5 therefore reflected both the operational workflow and functional behaviour of the HomeCoRe app, as well as the methodological framework through which the testing process was transformed into analysable data. Overall, these findings indicated that technical bugs constituted the majority of the issues detected, with 75 functional problems identified across tasks compared to 36 usability-related improvements to be made. Concretely, technical bugs were more frequently associated with legacy tasks, whereas usability refinements were more often detected in newly added exercises. This distribution suggests that the stability of the system was primarily affected by factors concerning implementation and migration of pre-existing tasks, while refinements related to interaction design were more typical of tasks that were more recently developed.

6.2 Technical reliability and migration challenges

Importantly, these findings are consistent with research showing that usability and technical reliability represent essential preconditions for an effective home-based cognitive intervention, as they factually determine whether structured interventions can be consistently carried out outside in-hospitals settings (Di Lorito et al., 2022; Maresca et al., 2020). Concerning the migration of legacy exercises into the new HomeCoRe app, such implementation represented a critical step that introduced technical and usability challenges, even though the original task design remained logically and visually unchanged. In fact, migrating exercises from earlier system implementations required ensuring compatibility between the progression logic of the system, the parameter tables, stimulus databases, and interaction models with those of the updated platform. In this scenario, any discrepancy may lead to bugs such as incorrect update of difficulty levels, presentation of the wrong level in subsequent sessions, or mismatches in feedback and scoring. These issues were, in fact, observed in every legacy exercise. Moreover, although HomeCoRe preserves the same ontology and conceptual task structure as the original

CoRe system and its computer based TR version, differences in technical implementation, such as how data are stored, accessed or loaded, may still lead to problems such as incorrect stimulus retrieval, repetition of recently already used items, or improper level administration. Similarly, the interface and multimedia adaptations can further generate problems, such as a reduced keypad size, malfunctioning instructional examples, or audio failures. These findings underscore how translating exercises into a new system is not merely a duplication process, but a complex integration process affecting both how the user interacts with the tools and how accurately the software runs an exercise the way it was designed to run. This interpretation is consistent with usability engineering principles indicating that the effectiveness of a system depends not only on its conceptual design, but also on implementation performance in the real context of use (International Organization for Standardisation, 2018). Concretely, the presence of recurring technical problems at the system-level, particularly those related to the adaptive progression and stimulus presentation, implies that several detected issues stemmed from shared infrastructural mechanisms rather than from isolated task design errors. System-level reliability is indeed crucial in clinician-guided TR systems, where both a correct task delivery and rehabilitation monitoring are central aspects in treatment personalisation and effectiveness (Di Lorito et al., 2022; Maresca et al., 2020).

6.3 Task design and interface-level problems

Additionally, the separate analysis of legacy and newly added tasks proved informative in understanding the origin of different issues types. As such, legacy exercises, which were translated from previous versions into the new app-based architecture, showed a higher proportion of technical bugs, suggesting that part of the detected instability derived from adaptation processes such as parameters mismatching or database integration errors. On the other hand, newly developed tasks were more frequently associated with usability-related observations, which included the need for timing adjustments, increased stimulus discriminability, and refinements of the response interface layout. Such findings are coherent with iterative development models in digital health, in which newly implemented modules often require a progressive optimisation after interaction testing and execution feedback (Hassenzahl & Tractinsky, 2006; International Organization for Standardisation, 2018). Consequently, distinguishing between these two groups of tasks enabled participants to differentiate between migration-related technical bugs and design-related usability refinements, facilitating the prioritisation of development actions.

Furthermore, this study also demonstrated the importance of analysing the patient and therapist interfaces separately. For instance, patient side issues mainly affected the correct running of exercises, the clarity and visibility of stimuli, the ease of responding for users, and the reliability of feedback. These aspects are crucial as they directly affect whether users understand the tasks, remain engaged, and produce reliable performance data (Hassenzahl & Tractinsky, 2006; International Organization for Standardisation, 2018). By contrast, the issues identified in the therapist interface were fewer and mostly technical in nature. Rather than affecting user interaction, they predominantly involved system-management functions such as the administration of therapeutic plans, the access to backend data, statistics export, template editing, and configuration settings. Notably, because these features support treatment planning, monitoring, and data documentation, even a limited instability in this interface would have disproportionate operational consequences that would hinder proper administration (International Organization for Standardisation, 2018).

This distinction reflects the conceptual structure of a clinician-guided TR system, where the execution environment and the clinical control environment operate as complementary and equally important components of the intervention (Quaglini et al., 2019; Bottiroli et al., 2024). Moreover, minor interface inconsistencies were also observed, such as device-level elements, including the tablet calendar app icon, visible at all times while using the app, including during the orientation phase. Although not functionally disruptive, this small detail may introduce a visual distraction or reduce the overall interface coherence, thus underscoring the importance of controlling system-level overlays in clinical applications.

6.4 Development implications and refinements implemented

Importantly, the purpose of this qualitative analysis was not solely descriptive, but development-oriented. In fact, the identified bugs and usability-related difficulties directly informed targeted platform refinements, including corrections to adaptive progression logic, improvements in stimulus presentation mechanisms, adjustments to interface layout and workflow functions, and stabilisation of the computation of feedbacks. Some design choices adapted to enhance scalability may also have implications for user experience. In particular, the use of computer generated voice instructions, which was adopted for cost-efficiency and maintainability reasons, may influence user engagement compared to human-recorded audio. Particularly, although this feature might be functionally adequate for comprehension, a synthetic speech may be perceived as unnatural or reduce the motivational appeal (Rodero & Lucas, 2023), therefore suggesting that future iterations could explore alternative audio

solutions or adaptive voice design. However, an empirical comparison between human and synthetic voice in complex agent interactions has shown that overall likeability and trust can be similar between the two voice types, even if synthetic voice is perceived as more eerie, making the exploration of alternative solutions a possibility, not a priority (Abdulrahman & Richards, 2022). Moreover, the iterative cycle of testing, subsequent refinement, and eventual re-evaluation aligns with the recommended user-centred development approaches in digital health technologies, where usability verification and technical stabilisation are progressively being integrated into development cycles in order to ensure a safe and reliable deployment (European Parliament & Council of the European Union, 2017; International Organization for Standardization, 2019; K.-C. Wang et al., 2025). On the basis of the qualitative analysis conducted, several concrete refinements were implemented to the HomeCoRe app software. Specifically, corrections were made to the adaptive progression mechanisms to revise difficulty level characteristics, as well as the proper updating and administration of said levels across and within sessions. Concerning this last aim, the implemented refinements will need further adjustments as preliminary results of the current testing phase suggest difficulties in level update between sessions. Similarly, another example of pending fixes concerns the *Position Memory* task, where yellow tokens are still present despite having been flagged for low visibility on screen. Also, additional modification concerned the stimulus presentation and feedback computation. Regarding patient interface, these included the revision of response layouts and addition of visual dashes in the exercises for whom they were considered necessary (see Figure 6.1), instruction presentation (see Figure 6.2), timing and difficulty parameters, alongside fixes to therapist interface functionalities, as the now functioning Excel export on patient's rehabilitation parameters.

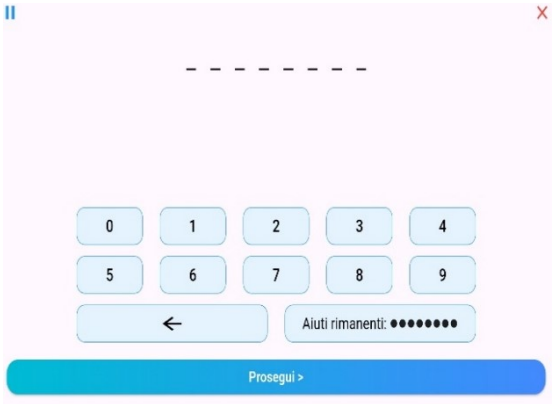


Figure 6.1: example of modified keyboard, with bigger and spaced keys

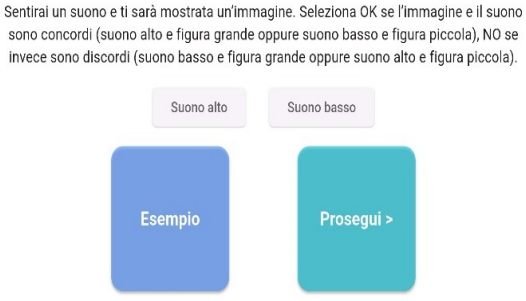


Figure 6.2: usability-related refinement in the Image and Sound task involving the possibility to listen to the sounds presented before the exercise begins

6.5 Role in the HomeCoRe validation pathway and context of deployment

In terms of positioning this study within the HomeCoRe validation pathway, it should be conceived as an intermediate step within a broader validation trajectory, rather than a final usability or even effectiveness evaluation. For instance, if previous research has demonstrated the feasibility and the clinical validity of the HomeCoRe rehabilitation framework and its non-inferiority to in-clinic delivery with therapeutic logic and supervision preserved (Bernini et al., 2023; Bernini et al., 2025), the current work instead focused specifically on ensuring that the app-based technological implementation reliably supports this rehabilitation model. Overall, while application-based deployment enhances accessibility and scalability, it also introduces contextual challenges. As such, tablet-based use in a home environment may expose users to external digital distractions, as are notifications, background updates, or competing applications, as device notifications represent a common source of task interruption that can negatively affect performance and continuity (Ohly & Bastin, 2023). As a consequence, future deployment protocols may benefit from the implementation of notification suppression modes intrinsic to the application itself or activated on the device, and features that guide the user through the session in a full screen environment, thus reducing the risk of interruption during sessions (International Organization for Standardisation, 2018).

From a regulatory perspective, such preparatory verification is also fundamental in light of the European framework governing medical software: telerehabilitation platforms intended for clinical use may fall under the category of Software as a Medical Device and must comply with the Medical Device Regulation (EU 2017/745). Within this framework, the CE marking certifies that the system meets the requirements concerning safety, performance, usability and risk management, ensuring that it can be safely deployed for medical purposes. Importantly, the CE marking does not guarantee clinical effectiveness in itself, but it requires evidence that the software runs reliably and that the risks associated with its use are controlled properly (European Parliament & Council of the European Union, 2017). For this reason, the systematic internal testing conducted and the subsequent refinement processes utilised in this study contribute to the broader body of technical and usability related evidence supporting both compliance to the European regulation system and a safe deployment. Possibly, based on its intended use as a clinician-guided TR platform that monitors performance and supports therapeutic management, HomeCoRe would likely fall under Rule 11 of the EU Medical Device Regulation (2017/745) and be classified as Class IIa Software as a medium risk Medical Device,

requiring demonstration of safety, usability, and performance prior to receiving the CE marking (European Parliament & Council of the European Union, 2017).

Following the corrections resulting from this analysis, the version 0.9.18 of the HomeCoRe app software is currently still undergoing testing using the same structured methodology. Among preliminary observations, some additional adjustments need to be made. For instance, although exercises can technically be repeated within the same day, this repetition is presently enabled only after all other scheduled exercises have been completed. This constraint may limit the intended flexibility of repeated task exposure in patients with specific cognitive difficulties and represents an aspect requiring further refinement. Another practical consideration relates to the fact that, as an application-based system, HomeCoRe can be installed on different tablet models with varying hardware and software characteristics. Therefore, differences in screen size, resolution, operating system version, processing capacity, or audio performance may influence the correct visualisation of stimuli, responsiveness of interactions, or stability of multimedia components. To ensure a reliable functioning and a positive UX, it is consequently essential to clearly specify minimum device requirements and compatibility criteria for patients' devices prior to installation. As such, providing explicit technical guidelines or supported-device lists may then help prevent performance issues related to inadequate hardware or outdated systems and to support a smoother deployment in home environments (European Parliament & Council of the European Union, 2017; International Organization for Standardisation, 2018).

6.6 Strengths and limitations

Beyond the developmental nature of the present work, several strengths of the HomeCoRe app should be noted. The system builds on an already validated framework, preserving its therapeutic logic, clinician-guided supervision model, and adaptive structure while transferring it into an app-based version. Additionally, HomeCoRe integrates features as adaptive progression, remote therapist control, and automated performance monitoring in a single software, supporting a personalised treatment while ensuring a standardised delivery. Finally, the structured and development-oriented testing methodology adopted in this qualitative study represents a further strength, as it allowed for systematic identification and prioritisation of technical and usability-related issues, thus supporting iterative refinement and strengthening the platform's readiness for subsequent user-based validation phases.

Despite its potential, some limitations should be acknowledged. First of all, the analysis conducted relied on a structured internal testing process rather than a direct observation of end-

users. While this step has been necessary for the development and refinement of the overall system, any usability conclusion must be considered with caution, as it is a result of simulated execution – necessary for thorough testing – rather than behavioural or subjective end-users measures. Secondly, the frequency of detected issues does not necessarily equal their functional severity or clinical impact, which was then not formally determined. Furthermore, additional practical limitations concern the current system configuration: the application at present is only available in Italian, which significantly restricts a broader international deployment besides limiting accessibility in multilingual clinical contexts, making it an aspect to be addressed in future implementations of the HomeCoRe app.

6.7 Future directions and conclusion

Also, future versions should include user-based usability studies, beginning with healthy participants and subsequently extending to clinical populations, in order to evaluate not only feasibility, but also adherence and experiential usability alongside technical stability. Moreover, next evaluation phases should progressively incorporate testing in ecologically valid context – as home based unsupervised settings – in order to capture variability in real-world interaction patterns and potential environmental constraints that can hardly be reproduced under controlled conditions. Crucially, in this perspective, the planned usability studies should be conceived as formative evaluations with the aim of identifying interaction issues, cognitive overload risks, and workflow inconsistencies present at early stages of deployment. These investigations would also allow the identification of potential mismatches between system demands and the actual residual cognitive resources of end-users, thus supporting the development of adaptive interaction strategies aimed at reducing task related burden and at promoting engagement over time. In fact, according to the IEC 62366-1 usability engineering standard for medical devices, this type of formative usability testing is typically conducted by a limited number of representative users or domain experts, as even small samples are sufficient to detect the majority of problems in the interface (International Electrotechnical Commission, 2015). Also, previous usability research similarly indicates that in order to reveal most critical user-related issues, groups of approximately three to eight participants can suffice, particularly when testing is iterative and development-oriented (Nielsen, 1994; Virzi, 1992). Within a translational perspective, this staged usability focused approach may serve as a preparatory step towards future evaluations required for regulatory-grade validation, ensuring that any interaction-related risks are mitigated before final deployment.

Specifically, for TR applications, such early stage testing of usability seems to be especially important, since inadequate interface design may generate frustration, misunderstanding of tasks or excessive cognitive demands for end-users, ultimately affecting adherence and therapeutic effectiveness (Di Lorito et al., 2022; International Organization for Standardisation, 2018). Furthermore, usability shortcomings in TR systems may indirectly influence intervention fidelity by altering patterns of task execution, which could in turn compromise the reliability of outcome measures collected during remote administration. Accordingly, next HomeCoRe validation phases should adopt a mixed-method approach combining both qualitative techniques with quantitative indicators: such strategy would allow both the identification of design weaknesses and the objective measurement of user performance, ultimately supporting a systematic optimisation of the application before clinically validation at scale (Hassenzahl & Tractinsky, 2006; Maramba et al., 2019).

All in all, the present findings provide a structured overview of the technical and usability-related refinements required for the HomeCoRe app. From a longer term perspective, these usability-related refinements may contribute to the positioning of HomeCoRe within scalable digital rehabilitation ecosystems, where system stability, user engagement and clinical effectiveness need to coexist as interdependent dimensions of interventions quality. The reported predominance of system-level technical bugs underscored the importance of stabilising shared infrastructural mechanisms, while the usability-related observations derived from the qualitative study highlighted the necessity of a continued optimisation of the clarity of interactions and of workflow coherence. By the embedding within a systematic qualitative process, this study contributed to the progressive refinement of the platform and supported its preparation for subsequent user-based validation phases. Future developments should therefore prioritise not only usability readiness, but also interoperability with existing telehealth infrastructures and the capacity to sustain long-term adherence across heterogeneous user profiles.

Chapter 7. Conclusion

Cognitive deterioration represents an increasing clinical and societal challenge, requiring rehabilitation strategies that are not only theoretically grounded but also practically sustainable over time. As outlined in the introductory chapters, COTs play a key role in supporting patients' autonomy, functional engagement, and QoL (Castellano-Tejedor, 2022; Paggetti et al., 2024), while TR is offered as a means of extending structured interventions beyond the traditional setting and into patients' everyday life and environment (Di Lorito et al., 2022; Maresca et al., 2020). In this scenario, the overarching aim of this work was to contribute to the technological validation pathway of the HomeCoRe app by ensuring that the software reliably supported the clinician-guided rehabilitation model on which it was based.

Hinging on prior evidence, which demonstrated the feasibility and clinical validity of the HomeCoRe framework and its non-inferiority compared to CoRe (Bernini et al., 2023; Bernini et al., 2025; Quaglini et al., 2019; Bottiroli et al., 2024), the present study focused specifically on functionality and usability as prerequisites for safe and effective deployment. Through the structured qualitative internal testing process described in Chapter 4 and analysed in Chapter 5, system-level technical issues and usability-related refinements were identified, categorised, and addressed. This process not only improved the technological robustness and reliability of the software, but also reinforced the principle that digital rehabilitation systems must be evaluated at the level of operational behaviour, in addition to their clinical rationales. Future validation phases should extend this perspective toward sustained real-world use, accounting for variability in domestic environments and long-term patient interaction patterns. Beyond the technical contribution of which is capable, the HomeCoRe app demonstrated concrete practical value for both patients and therapists: for patients, a home-based access to structured cognitive interventions enhances accessibility, reduces logistical and geographical barriers, and facilitates continuity of care within daily habits and routines; for therapists, the system enables remote configurations of plans, automates task administration, and collects performance data, reducing organisational burden and minimising repetitive operational demands, and thereby allocating more time to clinical reasoning, monitoring, and personalisation while maintaining structured supervision.

Importantly, the qualitative development-oriented methodology adopted in this work reflects a patient-centred perspective, as it allowed potential interaction difficulties, cognitive load considerations, and interface inconsistencies to be identified prior to official validation. By embedding these usability verifications within the development process, the study reinforces

that technological stability and interaction clarity are not secondary aspects of digital health systems, but essential factors of their therapeutic viability. Such refinements may support long-term adherence by mitigating interaction fatigue and reducing task-related burden.

Looking ahead, the continued evolution of TR systems such as HomeCoRe will need to consider not only technological stability and clinical validation, but also take into account broader societal and generational changes in digital literacy and technology use. As future patients become increasingly accustomed to touchscreen devices, mobile applications, and other cutting-edge technologies, the expectations regarding usability, responsiveness, and interface intuitiveness are likely to evolve. Consequently, future TR applications should remain adaptable and responsive to these necessary changes. Beyond generational familiarity with technology, future versions will likely need to address heterogeneity in user profiles, including variations in sensory functioning, motor abilities, and attentional resources. This highlights the importance of developing flexible interfaces and multimodal interaction options, capable of accommodating varying functional needs and trajectories. The adjustments implemented within HomeCoRe, such as the modifications to response keyboards, stimulus presentation and workflow elements, show how a targeted design improvement, even when specific, can significantly contribute to accessibility, clarity and overall user comfort.

In conclusion, the present work represents a necessary strategic step within the broader validation trajectory of the HomeCoRe system, strengthening the foundations upon which subsequent user-based validations and implementations can be built. In the longer term, these usability-driven refinements may support the integration of the HomeCoRe app within broader continuous remote care frameworks. Finally, ensuring that TR tools are accessible, reliable, and clinician-guided proves once again to be a fundamental aspect in making TR a valuable and sustainable solution.

Bibliography

Abdulrahman, A., & Richards, D. (2022). Is natural necessary? Human voice versus synthetic voice for intelligent virtual agents. *Multimodal Technologies and Interaction*, *6*(7), 51. https://doi.org/10.3390/mti6070051

Ahmad, M. A., Kareem, O., Khushtar, M., Akbar, M., Haque, M. R., Iqubal, A., Haider, M. F., Pottoo, F. H., Abdulla, F. S., Al-Haidar, M. B., & Alhajri, N. (2022). Neuroinflammation: a potential risk for dementia. *International Journal of Molecular Sciences*, *23*(2), 616. https://doi.org/10.3390/ijms23020616

Alexander, G. E., Ryan, L., Bowers, D., Foster, T. C., Bizon, J. L., Geldmacher, D. S., & Glisky, E. L. (2012). Characterizing cognitive aging in humans with links to animal models. *Frontiers in Aging Neuroscience*, 4, 21. https://doi.org/10.3389/fnagi.2012.00021

Alloni, A., Quaglini, S., Panzarasa, S., Sinforiani, E., & Bernini, S. (2018). Evaluation of an ontology-based system for computerized cognitive rehabilitation. *International Journal of Medical Informatics*, *115*, 64–72. https://doi.org/10.1016/j.ijmedinf.2018.04.005

Alloni, A., Sinforiani, E., Zucchella, C., Sandrini, G., Bernini, S., Cattani, B., Pardell, D. T., Quaglini, S., & Pistarini, C. (2017). Computer-based cognitive rehabilitation: the CoRe system. *Disability and Rehabilitation*, *39*(4), 407–417. https://doi.org/10.3109/09638288.2015.1096969

Anderle, S., Dixon, M., Quintela-Lopez, T., Sideris-Lampretsas, G., & Attwell, D. (2025). The vascular contribution to cognitive decline in ageing and dementia. *Nature Reviews Neuroscience*, *26*(10), 591–606. https://doi.org/10.1038/s41583-025-00950-1

Astell, A. J., Smith, S. K., Potter, S., & Preston-Jones, E. (2018). Computer interactive reminiscence and conversation aid groups—delivering cognitive stimulation with technology. *Alzheimer's & Dementia: Translational Research & Clinical Interventions*, *4*(1), 481–487. https://doi.org/10.1016/j.trci.2018.08.003

Bahar-Fuchs, A., Clare, L., & Woods, B. (2013). Cognitive training and cognitive rehabilitation for mild to moderate Alzheimer's disease and vascular dementia. *Cochrane Database of Systematic Reviews*, *2013*(6), CD003260. https://doi.org/10.1002/14651858.CD003260.pub2

Bampa, G., Moraitou, D., & Metallidou, P. (2021). Metacognition in cognitive rehabilitation in adults: A systematic review. *Trends and Prospects in Metacognition Research across the Life Span: A Tribute to Anastasia Efklides*, 273-295. https://doi.org/10.1007/978-3-030-51673-4_13

Bangor, A., Kortum, P. T., & Miller, J. T. (2008). An empirical evaluation of the system usability scale. *International Journal of Human-Computer Interaction*, *24*(6), 574–594. https://doi.org/10.1080/10447310802205776

Beagle, A. J., Darwish, S. M., Ranasinghe, K. G., La, A. L., Karageorgiou, E., & Vossel, K. A. (2017). Relative incidence of seizures and myoclonus in Alzheimer's disease, dementia with Lewy bodies, and frontotemporal dementia. *Journal of Alzheimer's Disease*, *60*(1), 211-223. https://doi.org/10.3233/JAD-170031

Belleville, S., Clément, F., Mellah, S., Gilbert, B., Fontaine, F., & Gauthier, S. (2011). Training-related brain plasticity in subjects at risk of developing Alzheimer's disease. *Brain*, *134*(6), 1623–1634. https://doi.org/10.1093/brain/awr037

Berente, D. B., Zsuffa, J., Werber, T., Kiss, M., Drotos, A., Kamondi, A., Csukly, G., & Horvath, A. A. (2022). Alteration of visuospatial system as an early marker of cognitive decline: a double-center neuroimaging study. *Frontiers in Aging Neuroscience*, *14*, 854368. https://doi.org/10.3389/fnagi.2022.854368

Berlucchi, G. (2011). Brain plasticity and cognitive neurorehabilitation. *Neuropsychological Rehabilitation*, *21*(5), 560–578. https://doi.org/10.1080/09602011.2011.573255

Bernini, S., Alloni, A., Panzarasa, S., Picascia, M., Quaglini, S., Tassorelli, C., & Sinforiani, E. (2019). A computer-based cognitive training in mild cognitive impairment in Parkinson's disease. *NeuroRehabilitation*, *44*(4), 555–567. https://doi.org/10.3233/NRE-192714

Bernini, S., Panzarasa, S., Quaglini, S., Costa, A., Picascia, M., Cappa, S. F., Cerami, C., Tassorelli, C., Vecchi, T., & Bottiroli, S. (2023). HomeCoRe system for telerehabilitation in individuals at risk of dementia: a usability and user experience study. *Frontiers in Medicine*, *10*, 1129914. https://doi.org/10.3389/fmed.2023.1129914

Bernini, S., Panzarasa, S., Sinforiani, E., Quaglini, S., Cappa, S. F., Cerami, C., Tassorelli, C., Vecchi, T., & Bottiroli, S. (2021). HomeCoRe for telerehabilitation in mild or major neurocognitive disorders: a study protocol for a randomized controlled trial. *Frontiers in Neurology*, *12*, 752830. https://doi.org/10.3389/fneur.2021.752830

Bernini, S., Valcarenghi, A., Panzarasa, S., Quaglini, S., Costa, A., Ramusino, M. C., Picascia, M., Barbieri, M., Tassorelli, C., Vecchi, T., & Bottiroli, S. (2025). HomeCoRe for telerehabilitation in mild or major neurocognitive disorders: a non-inferiority randomized controlled trial. *GeroScience*. https://doi.org/10.1007/s11357-025-02006-9

Bogdanova, Y., Yee, M. K., Ho, V. T., & Cicerone, K. D. (2016). Computerized cognitive rehabilitation of attention and executive function in acquired brain injury: a systematic review. *Journal of Head Trauma Rehabilitation*, *31*(6), 419–433. https://doi.org/10.1097/HTR.0000000000000203

Boltaboyeva, A., Baigarayeva, Z., Imanbek, B., Ozhikenov, K., Getahun, A. J., Aidarova, T., & Karymsakova, N. (2025). A review of innovative medical rehabilitation systems with scalable AI-assisted platforms for sensor-based recovery monitoring. *Applied Sciences*, *15*(12), 6840. https://doi.org/10.3390/app15126840

Bottiroli, S., Bernini, S., Panzarasa, S., Tassorelli, C., & Quaglini, S. (2024). From CoRe to HomeCoRe: a long-term experience on computer-based cognitive rehabilitation. *Rivista di Neurologia, 1*(1), 32–41. https://doi.org/10.1727/4201.41901

Boyle, P. A., Yu, L., Schneider, J. A., Wilson, R. S., & Bennett, D. A. (2019). Scam awareness related to incident Alzheimer dementia and mild cognitive impairment: a prospective cohort study. *Annals of Internal Medicine*, *170*(10), 702–709. https://doi.org/10.7326/M18-2711

Buele, J., Varela-Aldás, J. L., & Palacios-Navarro, G. (2023). Virtual reality applications based on instrumental activities of daily living (iADLs) for cognitive intervention in older adults: a systematic review. *Journal of NeuroEngineering and Rehabilitation*, *20*(1), 168. https://doi.org/10.1186/s12984-023-01292-8

Burton, R. L., & O'Connell, M. E. (2018). Telehealth rehabilitation for cognitive impairment: randomized controlled feasibility trial. *JMIR Research Protocols*, *7*(2), e43. https://doi.org/10.2196/resprot.9420

Canapa, G., Paternò, F., & Santoro, C. (2025). Interactive serious games for cognitive training of older adults: a systematic review. *IEEE Transactions on Computational Social Systems*, *12*(5), 2445–2468. https://doi.org/10.1109/TCSS.2025.3532307

Casagrande, M., Marselli, G., Agostini, F., Forte, G., Favieri, F., & Guarino, A. (2022). The complex burden of determining prevalence rates of mild cognitive impairment: a systematic review. *Frontiers in Psychiatry*, *13*, 960648. https://doi.org/10.3389/fpsyt.2022.960648

Castellano-Tejedor, C. (2022). Non-pharmacological interventions for the management of chronic health conditions and non-communicable diseases. *International Journal of Environmental Research and Public Health*, *19*(14), 8536. https://doi.org/10.3390/ijerph19148536

Cepeda, N. J., Pashler, H., Vul, E., Wixted, J. T., & Rohrer, D. (2006). Distributed practice in verbal recall tasks: a review and quantitative synthesis. *Psychological Bulletin*, *132*(3), 354–380. https://doi.org/10.1037/0033-2909.132.3.354

Cepeda, N. J., Vul, E., Rohrer, D., Wixted, J. T., & Pashler, H. (2008). Spacing effects in learning: a temporal ridgeline of optimal retention. *Psychological Science*, *19*(11), 1095–1102. https://doi.org/10.1111/j.1467-9280.2008.02209.x

Cespón, J., Miniussi, C., & Pellicciari, M. C. (2018). Interventional programmes to improve cognition during healthy and pathological ageing: Cortical modulations and evidence for brain plasticity. *Ageing Research Reviews*, *43*, 81–98. https://doi.org/10.1016/j.arr.2018.03.001

Chae, H. J., & Lee, S. H. (2023). Effectiveness of online-based cognitive intervention in community-dwelling older adults with cognitive dysfunction: a systematic review and meta-analysis. *International Journal of Geriatric Psychiatry*, *38*(1), e5853. https://doi.org/10.1002/gps.5853

Chan, A. T. C., Ip, R. T. F., Tran, J. Y. S., Chan, J. Y. C., & Tsoi, K. K. F. (2024). Computerized cognitive training for memory functions in mild cognitive impairment or dementia: A systematic review and meta-analysis. *Npj Digital Medicine*, *7*(1), 1. https://doi.org/10.1038/s41746-023-00987-5

Chiu, Y.-C., Tsai, H.-H., Hsu, C.-Y., & Wang, J.-J. (2018). Reality orientation therapy benefits cognition in older people with dementia: a meta-analysis. *International Journal of Nursing Studies, 78*, 106–116. https://doi.org/10.1016/j.ijnurstu.2017.10.008

Chou, Y., Sundman, M., Ton That, V., Green, J., & Trapani, C. (2022). Cortical excitability and plasticity in Alzheimer's disease and mild cognitive impairment: A systematic review and meta-analysis of transcranial magnetic stimulation studies. *Ageing Research Reviews*, *79*, 101660. https://doi.org/10.1016/j.arr.2022.101660

Chowdhary, N., Barbui, C., Anstey, K. J., Kivipelto, M., Barbera, M., Peters, R., Zheng, L., Kulmala, J., Stephen, R., Ferri, C. P., Joanette, Y., Wang, H., Comas-Herrera, A., Alessi, C., Suharya (Dy), K., Mwangi, K. J., Petersen, R. C., Motala, A. A., Mendis, S., … Dua, T. (2022). Reducing the risk of cognitive decline and dementia: WHO recommendations. *Frontiers in Neurology*, *12*, 765584. https://doi.org/10.3389/fneur.2021.765584

Cicerone, K. D., Langenbahn, D. M., Braden, C., Malec, J. F., Kalmar, K., Fraas, M., Felicetti, T., Laatsch, L., Harley, J. P., Bergquist, T., Azulay, J., Cantor, J., & Ashman, T. (2011). Evidence-based cognitive

rehabilitation: updated review of the literature from 2003 through 2008. *Archives of Physical Medicine and Rehabilitation*, *92*(4), 519–530. https://doi.org/10.1016/j.apmr.2010.11.015

Clare, L., Kudlicka, A., Oyebode, J. R., Jones, R. W., Bayer, A., Leroi, I., Kopelman, M., James, I. A., Culverwell, A., Pool, J., Brand, A., Henderson, C., Hoare, Z., Knapp, M., Morgan-Trimmer, S., Burns, A., Corbett, A., Whitaker, R., & Woods, B. (2019). Goal-oriented cognitive rehabilitation for early-stage Alzheimer's and related dementias: the GREAT RCT. *Health Technology Assessment*, *23*(10), 1–242. https://doi.org/10.3310/hta23100

Clare, L., & Woods, R. T. (2004). Cognitive training and cognitive rehabilitation for people with early-stage Alzheimer's disease: a review. *Neuropsychological Rehabilitation*, *14*(4), 385–401. https://doi.org/10.1080/09602010443000074

Committee on the Public Health Dimensions of Cognitive Aging, Board on Health Sciences Policy, & Institute of Medicine. (2015). *Cognitive aging: Progress in understanding and opportunities for action* (D. G. Blazer, K. Yaffe, & C. T. Liverman, Eds.). National Academies Press. http://www.ncbi.nlm.nih.gov/books/NBK285319/

Contreras-Somoza, L. M., Irazoki, E., Toribio-Guzmán, J. M., De La Torre-Díez, I., Diaz-Baquero, A. A., Parra-Vidales, E., Perea-Bartolomé, M. V., & Franco-Martín, M. Á. (2021). Usability and user experience of cognitive intervention technologies for elderly people with MCI or dementia: a systematic review. *Frontiers in Psychology*, *12*, 636116. https://doi.org/10.3389/fpsyg.2021.636116

Cotelli, M., Manenti, R., Brambilla, M., Gobbi, E., Ferrari, C., Binetti, G., & Cappa, S. F. (2019). Cognitive telerehabilitation in mild cognitive impairment, Alzheimer's disease and frontotemporal dementia: a systematic review. *Journal of Telemedicine and Telecare*, *25*(2), 67–79. https://doi.org/10.1177/1357633X17740390

Cummings, J., Lee, G., Ritter, A., Sabbagh, M., & Zhong, K. (2019). Alzheimer's disease drug development pipeline: 2019. *Alzheimer's & Dementia: Translational Research & Clinical Interventions*, *5*(1), 272–293. https://doi.org/10.1016/j.trci.2019.05.008

De Marchi, F., Contaldi, E., Magistrelli, L., Cantello, R., Comi, C., & Mazzini, L. (2021). Telehealth in neurodegenerative diseases: opportunities and challenges for patients and physicians. *Brain Sciences*, *11*(2), 237. https://doi.org/10.3390/brainsci11020237

De Wit, L., Marsiske, M., O'Shea, D., Kessels, R. P. C., Kurasz, A. M., DeFeis, B., Schaefer, N., & Smith, G. E. (2021). Procedural learning in individuals with amnestic mild cognitive impairment and Alzheimer's dementia: a systematic review and meta-analysis. *Neuropsychology Review*, *31*(1), 103–114. https://doi.org/10.1007/s11065-020-09449-1

Derbie, A. Y., Dejenie, M. A., & Zegeye, T. G. (2022). Visuospatial representation in patients with mild cognitive impairment: Implication for rehabilitation. *Medicine*, *101*(44), e31462. https://doi.org/10.1097/MD.0000000000031462

Desai, R., Leung, W. G., Fearn, C., John, A., Stott, J., & Spector, A. (2024). Effectiveness of cognitive stimulation therapy (CST) for mild to moderate dementia: A systematic literature review and meta-analysis of randomised control trials using the original CST protocol. *Ageing Research Reviews*, *97*, 102312. https://doi.org/10.1016/j.arr.2024.102312

Di Lorito, C., Bosco, A., Rai, H., Craven, M., McNally, D., Todd, C., Booth, V., Cowley, A., Howe, L., & Harwood, R. H. (2022). A systematic literature review and meta-analysis on digital health interventions for people living with dementia and mild cognitive impairment. *International Journal of Geriatric Psychiatry*, *37*(6), gps.5730. https://doi.org/10.1002/gps.5730

Ding, D., Zhao, Q., Wu, W., Xiao, Z., Liang, X., Luo, J., & Hong, Z. (2020). Prevalence and incidence of dementia in an older Chinese population over two decades: the role of education. *Alzheimer's & Dementia*, *16*(12), 1650–1662. https://doi.org/10.1002/alz.12159

Dunn, A. R., & Kaczorowski, C. C. (2019). Regulation of intrinsic excitability: Roles for learning and memory, aging and Alzheimer's disease, and genetic diversity. *Neurobiology of Learning and Memory*, *164*, 107069. https://doi.org/10.1016/j.nlm.2019.107069

Elser, H., Horváth-Puhó, E., Gradus, J. L., Smith, M. L., Lash, T. L., Glymour, M. M., Sørensen, H. T., & Henderson, V. W. (2023). Association of early-, middle-, and late-life depression with incident dementia in a Danish cohort. *JAMA Neurology*, *80*(9), 949-956. https://doi.org/10.1001/jamaneurol.2023.2309

Espinosa, A., Hernández-Olasagarre, B., Moreno-Grau, S., Kleineidam, L., Heilmann-Heimbach, S., Hernández, I., Wolfsgruber, S., Wagner, H., Rosende-Roca, M., Mauleón, A., Vargas, L., Lafuente, A., Rodríguez-Gómez, O., Abdelnour, C., Gil, S., Marquié, M., Santos-Santos, M. A., Sanabria, Á., Ortega, G., … Ruiz, A. (2018). Exploring genetic associations of Alzheimer's disease loci with mild cognitive impairment neurocognitive endophenotypes. *Frontiers in Aging Neuroscience*, *10*, 340. https://doi.org/10.3389/fnagi.2018.00340

European Parliament & Council of the European Union. (2017). *Regulation (EU) 2017/745 on medical devices*. https://eur-lex.europa.eu/eli/reg/2017/745/oj

Felix, R. A., Chavez, V. A., Novicio, D. M., Morley, B. J., & Portfors, C. V. (2019). Nicotinic acetylcholine receptor subunit α_7-knockout mice exhibit degraded auditory temporal processing. *Journal of Neurophysiology*, *122*(2), 451–465. https://doi.org/10.1152/jn.00170.2019

Fillit, H. M., Vellas, B., & Hara, Y. (2023). The state of Alzheimer's research and the path forward. *The Journal of Prevention of Alzheimer's Disease*, *10*(4), 617–619. https://doi.org/10.14283/jpad.2023.102

Forte, L., Despini, G., Quartarone, M., Calabrese, L., Brigiano, M., Trolese, S., Annini, A., Chirico, I., Ottoboni, G., Casagrande, M., & Chattat, R. (2025). Cognitive and non-cognitive predictors of response to cognitive stimulation interventions in dementia: A systematic review aiming for personalization. *Behavioral Sciences*, *15*(8), 1069. https://doi.org/10.3390/bs15081069

García-Casal, J. A., Loizeau, A., Csipke, E., Franco-Martín, M., Perea-Bartolomé, M. V., & Orrell, M. (2017). Computer-based cognitive interventions for people living with dementia: A systematic literature review and meta-analysis. *Aging & Mental Health*, *21*(5), 454–467. https://doi.org/10.1080/13607863.2015.1132677

Gardner, R. C., Bahorik, A., Kornblith, E. S., Allen, I. E., Plassman, B. L., & Yaffe, K. (2023). Systematic review, meta-analysis, and population attributable risk of dementia associated with traumatic brain injury in civilians and veterans. *Journal of Neurotrauma*, *40*(7–8), 620–634. https://doi.org/10.1089/neu.2022.0041

Gavelin, H. M., Lampit, A., Hallock, H., Sabatés, J., & Bahar-Fuchs, A. (2020). Cognition-oriented treatments for older adults: a systematic overview of systematic reviews. *Neuropsychology Review*, *30*(2), 167–193. https://doi.org/10.1007/s11065-020-09434-8

Ge, S., Zhu, Z., Wu, B., & McConnell, E. S. (2018). Technology-based cognitive training and rehabilitation interventions for individuals with mild cognitive impairment: a systematic review. *BMC Geriatrics*, *18*(1), 213. https://doi.org/10.1186/s12877-018-0893-1

Gherman, A., Andrei, D., Popoiu, C. M., Stoicescu, E. R., Levai, M. C., Stoian, I. I., & Bloancă, V. (2025). Multidisciplinary telemedicine in healthcare during and after the COVID-19 pandemic: a narrative review. *Life*, *15*(5), 783. https://doi.org/10.3390/life15050783

Gonzales, M. M., Garbarino, V. R., Pollet, E., Palavicini, J. P., Kellogg, D. L., Kraig, E., & Orr, M. E. (2022). Biological aging processes underlying cognitive decline and neurodegenerative disease. The *Journal of Clinical Investigation*, *132*(10), e158453. https://doi.org/10.1172/JCI158453

Gopi, Y., Wilding, E., & Madan, C. R. (2022). Memory rehabilitation: restorative, specific knowledge acquisition, compensatory, and holistic approaches. *Cognitive Processing*, *23*(4), 537–557. https://doi.org/10.1007/s10339-022-01099-w

Graham, A., Livingston, G., Purnell, L., & Huntley, J. (2022). Mild traumatic brain injuries and future risk of developing Alzheimer's disease: Systematic review and meta-analysis. *Journal of Alzheimer's Disease*, *87*(3), 969–979. https://doi.org/10.3233/JAD-220069

Griffiths, T. D., Lad, M., Kumar, S., Holmes, E., McMurray, B., Maguire, E. A., Billig, A. J., & Sedley, W. (2020). How can hearing loss cause dementia? *Neuron*, *108*(3), 401–412. https://doi.org/10.1016/j.neuron.2020.08.003

Habes, M., Janowitz, D., Erus, G., Toledo, J. B., Resnick, S. M., Doshi, J., Van Der Auwera, S., Wittfeld, K., Hegenscheid, K., Hosten, N., Biffar, R., Homuth, G., Völzke, H., Grabe, H. J., Hoffmann, W., & Davatzikos, C. (2016). Advanced brain aging: relationship with epidemiologic and genetic risk factors, and overlap with Alzheimer disease atrophy patterns. *Translational Psychiatry*, *6*(4), e775–e775. https://doi.org/10.1038/tp.2016.39

Haile, L. M., Kamenov, K., Briant, P. S., Orji, A. U., Steinmetz, J. D., Abdoli, A., Abdollahi, M., Abu-Gharbieh, E., Afshin, A., Ahmed, H., Ahmed Rashid, T., Akalu, Y., Alahdab, F., Alanezi, F. M., Alanzi, T. M., Al Hamad, H., Ali, L., Alipour, V., Al-Raddadi, R. M., … Chadha, S. (2021). Hearing loss prevalence and years lived with disability, 1990–2019: findings from the Global Burden of Disease Study 2019. *The Lancet*, *397*(10278), 996–1009. https://doi.org/10.1016/S0140-6736(21)00516-X

Hanseeuw, B. J., Betensky, R. A., Jacobs, H. I. L., Schultz, A. P., Sepulcre, J., Becker, J. A., Cosio, D. M. O., Farrell, M., Quiroz, Y. T., Mormino, E. C., Buckley, R. F., Papp, K. V., Amariglio, R. A., Dewachter, I., Ivanoiu, A., Huijbers, W., Hedden, T., Marshall, G. A., Chhatwal, J. P., … Johnson, K. (2019). Association of amyloid and tau with cognition in preclinical Alzheimer disease: a longitudinal study. *JAMA Neurology*, *76*(8), 915-924. https://doi.org/10.1001/jamaneurol.2019.1424

Harding, A. J. E., Morbey, H., Ahmed, F., Opdebeeck, C., Elvish, R., Leroi, I., Williamson, P. R., Keady, J., & Reilly, S. T. (2021). A core outcome set for nonpharmacological community-based interventions for people living with dementia at home: a systematic review of outcome measurement instruments. *The Gerontologist*, *61*(8), e435–e448. https://doi.org/10.1093/geront/gnaa071

Harrison, J. K., Noel-Storr, A. H., Demeyere, N., Reynish, E. L., & Quinn, T. J. (2016). Outcomes measures in a decade of dementia and mild cognitive impairment trials. *Alzheimer's Research & Therapy*, *8*(1), 48. https://doi.org/10.1186/s13195-016-0216-8

Hassenzahl, M., & Tractinsky, N. (2006). User experience-a research agenda. *Behaviour & Information Technology*, *25*(2), 91–97. https://doi.org/10.1080/01449290500330331

Hill, N. L., Kolanowski, A. M., & Gill, D. J. (2011). Plasticity in early Alzheimer disease: an opportunity for intervention. *Topics in Geriatric Rehabilitation*, *27*(4), 257–267. https://doi.org/10.1097/TGR.0b013e31821e588e

Hill, N. T. M., Mowszowski, L., Naismith, S. L., Chadwick, V. L., Valenzuela, M., & Lampit, A. (2017). Computerized cognitive training in older adults with mild cognitive impairment or dementia: a systematic review and meta-analysis. *American Journal of Psychiatry*, *174*(4), 329–340. https://doi.org/10.1176/appi.ajp.2016.16030360

Huntley, J. D., Gould, R. L., Liu, K., Smith, M., & Howard, R. J. (2015). Do cognitive interventions improve general cognition in dementia? A meta-analysis and meta-regression. *BMJ Open*, *5*(4), e005247. https://doi.org/10.1136/bmjopen-2014-005247

Hyun, J., Hall, C. B., Katz, M. J., Derby, C. A., Lipnicki, D. M., Crawford, J. D., Guaita, A., Vaccaro, R., Davin, A., Kim, K. W., Han, J. W., Bae, J. B., Röhr, S., Riedel-Heller, S., Ganguli, M., Jacobsen, E., Hughes, T. F., Brodaty, H., Kochan, N. A., … Lipton, R. B., & Cohort Studies of Memory in an International Consortium (COSMIC). (2022). Education, occupational complexity, and incident dementia: a COSMIC collaborative cohort study. *Journal of Alzheimer's Disease, 85*(1), 179–196. https://doi.org/10.3233/JAD-210627

Iconfinder. (n.d.). *Iconfinder – Organic icon set (free icons search results)*. Iconfinder. https://www.iconfinder.com/search/icons?family=organic-1&price=free&license=gte__1

International Electrotechnical Commission. (2015). *Medical devices—Part 1: Application of usability engineering to medical devices (IEC 62366-1:2015). IEC.* https://webstore.iec.ch/en/publication/21863

International Organization for Standardization. (2018). *Ergonomics of human-system interaction—Part 11: Usability: Definitions and concepts (ISO 9241-11:2018). ISO.* https://www.iso.org/obp/ui/#iso:std:iso:9241:-11:ed-2:v1:en

International Organization for Standardization. (2019). *Ergonomics of human-system interaction—Part 210: Human-centred design for interactive systems (ISO 9241-210:2019)*. ISO. https://www.iso.org/standard/77520.html

Irazoki, E., Contreras-Somoza, L. M., Toribio-Guzmán, J. M., Jenaro-Río, C., Van Der Roest, H., & Franco-Martín, M. A. (2020). Technologies for cognitive training and cognitive rehabilitation for people with mild cognitive impairment and dementia. A systematic review. *Frontiers in Psychology*, *11*, 648. https://doi.org/10.3389/fpsyg.2020.00648

Islam, Q. M. (2021). Innovation in primary healthcare in the twenty-first century. *Journal of Health Management*, *23*(1), 129–142. https://doi.org/10.1177/0972063421994987

Jenkinson, B., Maxwell, J., Bell, A., Young, A., Smith, A. C., Christoffersen, A., Trevor, D., Young, L., & Russell, T. (2025). Bringing researchers to the consumer table: the process and outcomes of a consumer

roundtable on telehealth. *Journal of Telemedicine and Telecare*, *31*(3), 430–436. https://doi.org/10.1177/1357633X231188536

Jeon, H., Kim, D. Y., Park, S.-W., Lee, B.-S., Han, H.-W., Jeon, N., Kim, M., Kang, M., & Kim, S. (2025). A systematic review of cognitive telerehabilitation in patients with cognitive dysfunction. *Frontiers in Neurology*, *15*, 1450977. https://doi.org/10.3389/fneur.2024.1450977

Jessen, F., Amariglio, R. E., Buckley, R. F., Van Der Flier, W. M., Han, Y., Molinuevo, J. L., Rabin, L., Rentz, D. M., Rodriguez-Gomez, O., Saykin, A. J., Sikkes, S. A. M., Smart, C. M., Wolfsgruber, S., & Wagner, M. (2020). The characterisation of subjective cognitive decline. *The Lancet Neurology*, *19*(3), 271–278. https://doi.org/10.1016/S1474-4422(19)30368-0

Jia, J., Zhao, T., Liu, Z., Liang, Y., Li, F., Li, Y., Liu, W., Li, F., Shi, S., Zhou, C., Yang, H., Liao, Z., Li, Y., Zhao, H., Zhang, J., Zhang, K., Kan, M., Yang, S., Li, H., … Cummings, J. (2023). Association between healthy lifestyle and memory decline in older adults: 10 year, population based, prospective cohort study. *BMJ*, *380*, e072691. https://doi.org/10.1136/bmj-2022-072691

Jiao, M., Ding, Z., Huang, C., Xu, Y., Zhong, B., & Chen, H. (2025). The effects of computerized cognitive training via tablet and computer platforms on cognitive function in patients with mild cognitive impairment: a systematic review and meta-analysis. *Behavioral Sciences*, *16*(1), 40. https://doi.org/10.3390/bs16010040

Jogie, P., Rahja, M., Van Den Berg, M., Cations, M., Brown, S., & Laver, K. (2021). Goal setting for people with mild cognitive impairment or dementia in rehabilitation: a scoping review. *Australian Occupational Therapy Journal*, *68*(6), 563–592. https://doi.org/10.1111/1440-1630.12758

Juul Rasmussen, I., Rasmussen, K. L., Nordestgaard, B. G., Tybjærg-Hansen, A., & Frikke-Schmidt, R. (2020). Impact of cardiovascular risk factors and genetics on 10-year absolute risk of dementia: risk charts for targeted prevention. *European Heart Journal*, *41*(41), 4024–4033. https://doi.org/10.1093/eurheartj/ehaa695

Kang, S., Lim, J.-I., Stenzel, L., Kim, K. Y., Kim, E., Jeon, H. J., Park, D.-H., Lim, H. K., Shim, Y., Jang, J.-W., Kim, Y., Lee, S., & Park, K. H. (2026). Efficacy and safety of mobile app–based metamemory cognitive training for mild cognitive impairment: multicenter randomized clinical trial. *JMIR mHealth and uHealth*, *14*, e73464. https://doi.org/10.2196/73464

Kleim, J. A., & Jones, T. A. (2008). Principles of experience-dependent neural plasticity: implications for rehabilitation after brain damage. *Journal of Speech, Language, and Hearing Research*, *51*(1). https://doi.org/10.1044/1092-4388(2008/018)

Kolb, B., & Whishaw, I. Q. (1998). Brain plasticity and behavior. *Annual Review of Psychology*, *49*(1), 43–64. https://doi.org/10.1146/annurev.psych.49.1.43

Kourtis, L. C., Regele, O. B., Wright, J. M., & Jones, G. B. (2019). Digital biomarkers for Alzheimer's disease: the mobile/wearable devices opportunity. *Npj Digital Medicine*, *2*(1), 9. https://doi.org/10.1038/s41746-019-0084-2

Kremen, W. S., Elman, J. A., Panizzon, M. S., Eglit, G. M. L., Sanderson-Cimino, M., Williams, M. E., Lyons, M. J., & Franz, C. E. (2022). Cognitive reserve and related constructs: a unified framework across cognitive and brain dimensions of aging. *Frontiers in Aging Neuroscience*, *14*, 834765. https://doi.org/10.3389/fnagi.2022.834765

Kueider, A. M., Parisi, J. M., Gross, A. L., & Rebok, G. W. (2012). Computerized cognitive training with older adults: a systematic review. *PLoS ONE*, *7*(7), e40588. https://doi.org/10.1371/journal.pone.0040588

Lampit, A., Hallock, H., & Valenzuela, M. (2014). Computerized cognitive training in cognitively healthy older adults: a systematic review and meta-analysis of effect modifiers. *PLoS Medicine*, *11*(11), e1001756. https://doi.org/10.1371/journal.pmed.1001756

Li, R., Geng, J., Yang, R., Ge, Y., & Hesketh, T. (2022). Effectiveness of computerized cognitive training in delaying cognitive function decline in people with mild cognitive impairment: systematic review and meta-analysis. *Journal of Medical Internet Research*, *24*(10), e38624. https://doi.org/10.2196/38624

Liu, T., Spector, A., Mograbi, D. C., Cheung, G., & Wong, G. H. Y. (2021). Changes in default mode network connectivity in resting-state fMRI in people with mild dementia receiving cognitive stimulation therapy. *Brain Sciences*, *11*(9), 1137. https://doi.org/10.3390/brainsci11091137

Liu, Y., Lu, G., Liu, L., He, Y., & Gong, W. (2024). Cognitive reserve over the life course and risk of dementia: a systematic review and meta-analysis. *Frontiers in Aging Neuroscience*, *16*, 1358992. https://doi.org/10.3389/fnagi.2024.1358992

Livingston, G., Huntley, J., Liu, K. Y., Costafreda, S. G., Selbæk, G., Alladi, S., Ames, D., Banerjee, S., Burns, A., Brayne, C., Fox, N. C., Ferri, C. P., Gitlin, L. N., Howard, R., Kales, H. C., Kivimäki, M., Larson, E. B., Nakasujja, N., Rockwood, K., … Mukadam, N. (2024). Dementia prevention, intervention, and care: 2024 report of the Lancet standing Commission. *The Lancet*, *404*(10452), 572–628. https://doi.org/10.1016/S0140-6736(24)01296-0

Livingston, G., Huntley, J., Sommerlad, A., Ames, D., Ballard, C., Banerjee, S., Brayne, C., Burns, A., Cohen-Mansfield, J., Cooper, C., Costafreda, S. G., Dias, A., Fox, N., Gitlin, L. N., Howard, R., Kales, H. C., Kivimäki, M., Larson, E. B., Ogunniyi, A., … Mukadam, N. (2020). Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. *The Lancet*, *396*(10248), 413–446. https://doi.org/10.1016/S0140-6736(20)30367-6

Lövdén, M., Bäckman, L., Lindenberger, U., Schaefer, S., & Schmiedek, F. (2010). A theoretical framework for the study of adult cognitive plasticity. *Psychological Bulletin*, *136*(4), 659–676. https://doi.org/10.1037/a0020080

Lynch, B. (2002). Historical review of computer-assisted cognitive retraining: *Journal of Head Trauma Rehabilitation*, *17*(5), 446–457. https://doi.org/10.1097/00001199-200210000-00006

Ma, L.-Z., Zhang, Y.-R., Li, Y.-Z., Ou, Y.-N., Yang, L., Chen, S.-D., Dong, Q., Feng, J.-F., Cheng, W., Tan, L., & Yu, J.-T. (2023). Cataract, cataract surgery, and risk of incident dementia: a prospective cohort study of 300,823 Participants. *Biological Psychiatry*, *93*(9), 810–819. https://doi.org/10.1016/j.biopsych.2022.06.005

Maggio, M. G., De Bartolo, D., Calabrò, R. S., Ciancarelli, I., Cerasa, A., Tonin, P., Di Iulio, F., Paolucci, S., Antonucci, G., Morone, G., & Iosa, M. (2023). Computer-assisted cognitive rehabilitation in neurological patients: state-of-art and future perspectives. *Frontiers in Neurology*, *14*, 1255319. https://doi.org/10.3389/fneur.2023.1255319

Manenti, R., Gobbi, E., Baglio, F., Macis, A., Ferrari, C., Pagnoni, I., Rossetto, F., Di Tella, S., Alemanno, F., Cimino, V., Binetti, G., Iannaccone, S., Bramanti, P., Cappa, S. F., & Cotelli, M. (2020). Effectiveness of an innovative cognitive treatment and telerehabilitation on subjects with mild cognitive impairment:

a multicenter, randomized, active-controlled study. *Frontiers in Aging Neuroscience*, *12*, 585988. https://doi.org/10.3389/fnagi.2020.585988

Manera, V., Ben-Sadoun, G., Aalbers, T., Agopyan, H., Askenazy, F., Benoit, M., Bensamoun, D., Bourgeois, J., Bredin, J., Bremond, F., Crispim-Junior, C., David, R., De Schutter, B., Ettore, E., Fairchild, J., Foulon, P., Gazzaley, A., Gros, A., Hun, S., … Robert, P. (2017). Recommendations for the use of serious games in neurodegenerative disorders: 2016 Delphi panel. *Frontiers in Psychology*, *8*, 1243. https://doi.org/10.3389/fpsyg.2017.01243

Maramba, I., Chatterjee, A., & Newman, C. (2019). Methods of usability testing in the development of eHealth applications: a scoping review. *International Journal of Medical Informatics*, *126*, 95–104. https://doi.org/10.1016/j.ijmedinf.2019.03.018

Maresca, G., Maggio, M. G., De Luca, R., Manuli, A., Tonin, P., Pignolo, L., & Calabrò, R. S. (2020). Tele-neuro-rehabilitation in Italy: state of the art and future perspectives. *Frontiers in Neurology*, *11*, 563375. https://doi.org/10.3389/fneur.2020.563375

Mattson, M. P., & Arumugam, T. V. (2018). Hallmarks of brain aging: Adaptive and pathological modification by metabolic states. *Cell Metabolism*, *27*(6), 1176–1199. https://doi.org/10.1016/j.cmet.2018.05.011

McDonald, A. P., D'Arcy, R. C. N., & Song, X. (2018). Functional MRI on executive functioning in aging and dementia: a scoping review of cognitive tasks. *Aging Medicine, 1*(2), 209 219. https://doi.org/10.1002/agm2.12037

Menegon, F., De Marchi, F., Aprile, D., Zanelli, I., Decaroli, G., Comi, C., & Tondo, G. (2024). From mild cognitive impairment to dementia: the impact of comorbid conditions on disease conversion. *Biomedicines*, *12*(8), 1675. https://doi.org/10.3390/biomedicines12081675

Mosca, I. E., Salvadori, E., Gerli, F., Fabbri, L., Pancani, S., Lucidi, G., Lombardi, G., Bocchi, L., Pazzi, S., Baglio, F., Vannetti, F., Sorbi, S., & Macchi, C. (2020). Analysis of feasibility, adherence, and appreciation of a newly developed tele-rehabilitation program for people with MCI and VCI. *Frontiers in Neurology*, *11*, 583368. https://doi.org/10.3389/fneur.2020.583368

Nielsen, J. (1994). *Usability engineering*. Morgan Kaufmann. https://books.google.com/books?id=95As2OF67f0C

Ohly, S., & Bastin, L. (2023). Effects of task interruptions caused by notifications from communication applications on strain and performance. *Journal of Occupational Health*, *65*(1), e12408. https://doi.org/10.1002/1348-9585.12408

Optale, G., Urgesi, C., Busato, V., Marin, S., Piron, L., Priftis, K., Gamberini, L., Capodieci, S., & Bordin, A. (2010). Controlling memory impairment in elderly adults using virtual reality memory training: a randomized controlled pilot study. *Neurorehabilitation and Neural Repair*, *24*(4), 348–357. https://doi.org/10.1177/1545968309353328

Osareme, J. O., Muonde, M., Maduka, C. P., Olorunsogo, T. O., & Omotayo, O. (2024). Demographic shifts and healthcare: a review of aging populations and systemic challenges. *International Journal of Science and Research Archive, 11*(1), 383–395 https://doi.org/10.30574/ijsra.2024.11.1.0067

Otero, I., Salgado, J. F., & Moscoso, S. (2022). Cognitive reflection, cognitive intelligence, and cognitive abilities: a meta-analysis. *Intelligence*, *90*, 101614. https://doi.org/10.1016/j.intell.2021.101614

Ouanes, S., & Popp, J. (2019). High cortisol and the risk of dementia and Alzheimer's disease: a review of the literature. *Frontiers in Aging Neuroscience*, *11*, 43. https://doi.org/10.3389/fnagi.2019.00043

Paggetti, A., Druda, Y., Sciancalepore, F., Della Gatta, F., Ancidoni, A., Locuratolo, N., Piscopo, P., Vignatelli, L., Sagliocca, L., Guaita, A., Secreto, P., Stracciari, A., Caffarra, P., Vanacore, N., Fabrizi, E., Lacorte, E., the Italian Dementia Guideline Working Group, Caffarra, P., Guaita, A., … Porrello, M. C. (2024). The efficacy of cognitive stimulation, cognitive training, and cognitive rehabilitation for people living with dementia: a systematic review and meta-analysis. *GeroScience*, *47*(1), 409–444. https://doi.org/10.1007/s11357-024-01400-z

Perez, K., Wisniewski, D., Ari, A., Lee, K., Lieneck, C., & Ramamonjiarivelo, Z. (2025). Investigation into Application of AI and Telemedicine in Rural Communities: a Systematic Literature Review. *Healthcare*, *13*(3), 324. https://doi.org/10.3390/healthcare13030324

Perkins, L., Fisher, E., Felstead, C., Rooney, C., Wong, G. H., Dai, R., Vaitheswaran, S., Natarajan, N., Mograbi, D., Ferri, C. P., Stott, J., & Spector, A. (2022). Delivering Cognitive Stimulation Therapy (CST) Virtually: developing and Field-Testing a New Framework. *Clinical Interventions in Aging*, *Volume 17*, 97–116. https://doi.org/10.2147/CIA.S348906

Pixabay. (n.d.). *Vectors*. https://pixabay.com/vectors/

Prince, J. B., Davis, H. L., Tan, J., Muller-Townsend, K., Markovic, S., Lewis, D. M. G., Hastie, B., Thompson, M. B., Drummond, P. D., Fujiyama, H., & Sohrabi, H. R. (2024). Cognitive and neuroscientific perspectives of healthy ageing. *Neuroscience & Biobehavioral Reviews*, *161*, 105649. https://doi.org/10.1016/j.neubiorev.2024.105649

Pu, F., Hu, Y., Li, C., Cao, X., Yang, Z., Liu, Y., Zhang, J., Li, X., Yang, Y., Wang, W., Liu, X., Hu, K., Ma, Y., & Liu, Z. (2023). Association of solid fuel use with a risk score capturing dementia risk among middle-aged and older adults: a prospective cohort study. *Environmental Research*, *218*, 115022. https://doi.org/10.1016/j.envres.2022.115022

Qu, J. (2025). Factors affecting patients' use of telehealth services: cross-sectional survey study. *Journal of Medical Internet Research*, *27*, e63295–e63295. https://doi.org/10.2196/63295

Quaglini, S., Panzarasa, S., Alloni, A., Sacchi, M., Sinforiani, E., Bottiroli, S., & Bernini, S. (2019). HomeCoRe: bringing cognitive rehabilitation at home. *Studies in health technology and informatics*, *264*, 1755-1756. https://doi.org/10.3233/SHTI190632

Rai, H. K., Schneider, J., & Orrell, M. (2020). An individual cognitive stimulation therapy app for people with dementia: development and usability study of thinkability. *JMIR Aging*, *3*(2), e17105. https://doi.org/10.2196/17105

Rai, H. K., Schneider, J., & Orrell, M. (2021). An individual cognitive stimulation therapy app for people with dementia and their carers: protocol for a feasibility randomized controlled trial. *JMIR Research Protocols, 10*(4), e24628. https://doi.org/10.2196/24628

Ranson, J. M., Bucholc, M., Lyall, D., Newby, D., Winchester, L., Oxtoby, N. P., Veldsman, M., Rittman, T., Marzi, S., Skene, N., Al Khleifat, A., Foote, I. F., Orgeta, V., Kormilitzin, A., Lourida, I., & Llewellyn, D. J. (2023). Harnessing the potential of machine learning and artificial intelligence for dementia research. *Brain Informatics*, *10*(1), 6. https://doi.org/10.1186/s40708-022-00183-3

Reijnders, J., Van Heugten, C., & Van Boxtel, M. (2013). Cognitive interventions in healthy older adults and people with mild cognitive impairment: a systematic review. *Ageing Research Reviews*, *12*(1), 263–275. https://doi.org/10.1016/j.arr.2012.07.003

Reilly, S. T., & Harding, A. J. E. (2025). Making outcome measures matter: why should "what matters to people living with dementia" matter to dementia researchers? *Alzheimer's & Dementia*, *21*(6), e70359. https://doi.org/10.1002/alz.70359

Reilly, S. T., Harding, A. J. E., Morbey, H., Ahmed, F., Williamson, P. R., Swarbrick, C., Leroi, I., Davies, L., Reeves, D., Holland, F., Hann, M., & Keady, J. (2020). What is important to people with dementia living at home? A set of core outcome items for use in the evaluation of non-pharmacological community-based health and social care interventions. *Age and Ageing*, *49*(4), 664–671. https://doi.org/10.1093/ageing/afaa015

Reuter-Lorenz, P. A., & Park, D. C. (2014). How Does it STAC up? Revisiting the scaffolding theory of aging and cognition. *Neuropsychology Review*, *24*(3), 355–370. https://doi.org/10.1007/s11065-014-9270-9

Rodero, E., & Lucas, I. (2023). Synthetic versus human voices in audiobooks: the human emotional intimacy effect. *New Media & Society*, *25*(7), 1746–1764. https://doi.org/10.1177/14614448211024142

Rosenberg, A., Mangialasche, F., Ngandu, T., Solomon, A., & Kivipelto, M. (2020). Multidomain interventions to prevent cognitive impairment, Alzheimer's disease, and dementia: From FINGER to World-Wide FINGERS. *The Journal of Prevention of Alzheimer's Disease*, *7*(1), 29–36. https://doi.org/10.14283/jpad.2019.41

Rossi, M., & Rehman, S. (2025). Integrating artificial intelligence into telemedicine: evidence, challenges, and future directions. *Cureus*, *17*, e90829. https://doi.org/10.7759/cureus.90829

Rotenberg, S., Anderson, N. D., Binns, M. A., Skidmore, E. R., Troyer, A. K., Richardson, J., Xie, F., Nalder, E., Bar, Y., Davids-Brumer, N., Bernick, A., & Dawson, D. R. (2024). Effectiveness of a meta-cognitive group intervention for older adults with subjective cognitive decline or mild cognitive impairment: the ASPIRE randomized controlled trial. *The Journal of Prevention of Alzheimer's Disease*, *11*(6), 1534–1548. https://doi.org/10.14283/jpad.2024.166

Saenz, J. L., Adar, S. D., Zhang, Y. S., Wilkens, J., Chattopadhyay, A., Lee, J., & Wong, R. (2021). Household use of polluting cooking fuels and late-life cognitive function: a harmonized analysis of India, Mexico, and China. *Environment International*, *156*, 106722. https://doi.org/10.1016/j.envint.2021.106722

Salari, N., Lotfi, F., Abdolmaleki, A., Heidarian, P., Rasoulpoor, S., Fazeli, J., Najafi, H., & Mohammadi, M. (2025). The global prevalence of mild cognitive impairment in geriatric population with emphasis on influential factors: a systematic review and meta-analysis. *BMC Geriatrics*, *25*(1), 313. https://doi.org/10.1186/s12877-025-05967-w

Schneider, L. S., Mangialasche, F., Andreasen, N., Feldman, H., Giacobini, E., Jones, R., Mantua, V., Mecocci, P., Pani, L., Winblad, B., & Kivipelto, M. (2014). Clinical trials and late-stage drug development for A lzheimer's disease: an appraisal from 1984 to 2014. *Journal of Internal Medicine*, *275*(3), 251–283. https://doi.org/10.1111/joim.12191

Schwedler, K.-J., Ehlers, J., Ostermann, T., & Hohenberg, G. (2026). The role of telemedicine centers and digital health applications in home care: challenges and opportunities for family caregivers. *Healthcare*, *14*(1), 136. https://doi.org/10.3390/healthcare14010136

Seblova, D., Berggren, R., & Lövdén, M. (2020). Education and age-related decline in cognitive performance: systematic review and meta-analysis of longitudinal cohort studies. *Ageing Research Reviews*, *58*, 101005. https://doi.org/10.1016/j.arr.2019.101005

Seblova, D., Fischer, M., Fors, S., Johnell, K., Karlsson, M., Nilsson, T., Svensson, A. C., Lövdén, M., & Lager, A. (2021). Does prolonged education causally affect dementia risk when adult socioeconomic status is not altered? A Swedish natural experiment in 1.3 million individuals. *American Journal of Epidemiology*, *190*(5), 817–826. https://doi.org/10.1093/aje/kwaa255

Shams, L., & Seitz, A. R. (2008). Benefits of multisensory learning. *Trends in Cognitive Sciences*, *12*(11), 411–417. https://doi.org/10.1016/j.tics.2008.07.006

Shang, X., Zhu, Z., Wang, W., Ha, J., & He, M. (2021). The association between vision impairment and incidence of dementia and cognitive impairment. *Ophthalmology*, *128*(8), 1135–1149. https://doi.org/10.1016/j.ophtha.2020.12.029

Shnitzer, H., Chan, J., Yau, T., McIntyre, M., Andreoli, A., Kua, A., Bayley, M., Leochico, C. F., Guo, M., & Munce, S. (2025). The safety of telerehabilitation: systematic review. *JMIR Rehabilitation and Assistive Technologies*, *12*, e68681–e68681. https://doi.org/10.2196/68681

Simons, D. J., Boot, W. R., Charness, N., Gathercole, S. E., Chabris, C. F., Hambrick, D. Z., & Stine-Morrow, E. A. L. (2016). Do "brain-training" programs work? *Psychological Science in the Public Interest*, *17*(3), 103–186. https://doi.org/10.1177/1529100616661983

Sohlberg, M. M., & Mateer, C. A. (1987). Effectiveness of an attention-training program. *Journal of Clinical and Experimental Neuropsychology*, *9*(2), 117–130. https://doi.org/10.1080/01688638708405352

Song, S., Stern, Y., & Gu, Y. (2022). Modifiable lifestyle factors and cognitive reserve: a systematic review of current evidence. *Ageing Research Reviews*, *74*, 101551. https://doi.org/10.1016/j.arr.2021.101551

Spinelli, E. G., Mandelli, M. L., Miller, Z. A., Santos-Santos, M. A., Wilson, S. M., Agosta, F., Grinberg, L. T., Huang, E. J., Trojanowski, J. Q., Meyer, M., Henry, M. L., Comi, G., Rabinovici, G., Rosen, H. J., Filippi, M., Miller, B. L., Seeley, W. W., & Gorno-Tempini, M. L. (2017). Typical and atypical pathology in primary progressive aphasia variants. *Annals of Neurology*, *81*(3), 430–443. https://doi.org/10.1002/ana.24885

Stern, Y. (2002). What is cognitive reserve? Theory and research application of the reserve concept. *Journal of the International Neuropsychological Society: JINS*, *8*(3), 448–460.

Stern, Y., Arenaza-Urquijo, E. M., Bartrés-Faz, D., Belleville, S., Cantilon, M., Chetelat, G., Ewers, M., Franzmeier, N., Kempermann, G., Kremen, W. S., Okonkwo, O., Scarmeas, N., Soldan, A., Udeh-Momoh, C., Valenzuela, M., Vemuri, P., Vuoksimaa, E., & and the Reserve, Resilience and Protective Factors PIA Empirical Definitions and Conceptual Frameworks Workgroup. (2020). Whitepaper: Defining and investigating cognitive reserve, brain reserve, and brain maintenance. *Alzheimer's & Dementia*, *16*(9), 1305–1311. https://doi.org/10.1016/j.jalz.2018.07.219

Stevenson, J. S., Clifton, L., Kuźma, E., & Littlejohns, T. J. (2022). Speech-in-noise hearing impairment is associated with an increased risk of incident dementia in 82,039 UK Biobank participants. *Alzheimer's & Dementia*, *18*(3), 445–456. https://doi.org/10.1002/alz.12416

Taler, V., & Phillips, N. A. (2008). Language performance in Alzheimer's disease and mild cognitive impairment: a comparative review. *Journal of Clinical and Experimental Neuropsychology*, *30*(5), 501–556. https://doi.org/10.1080/13803390701550128

Toosi, R., Tomraee, S., Khodabin, M., & Sakhaei, S. (2025). Telemedicine: An AI solution at last? *Code, Cognition and Society*, *1*(1). https://doi.org/10.22034/ccsr.2025.526987.1002

Tortora, C., Di Crosta, A., La Malva, P., Prete, G., Ceccato, I., Mammarella, N., Di Domenico, A., & Palumbo, R. (2024). Virtual reality and cognitive rehabilitation for older adults with mild cognitive impairment: a systematic review. *Ageing Research Reviews*, *93*, 102146. https://doi.org/10.1016/j.arr.2023.102146

Van Balkom, T. D., Van Den Heuvel, O. A., Berendse, H. W., Van Der Werf, Y. D., & Vriend, C. (2020). The effects of cognitive training on brain network activity and connectivity in aging and neurodegenerative diseases: a systematic review. *Neuropsychology Review*, *30*(2), 267–286. https://doi.org/10.1007/s11065-020-09440-w

Virzi, R. A. (1992). Refining the test phase of usability evaluation: how many subjects is enough? *Human Factors: The Journal of the Human Factors and Ergonomics Society*, *34*(4), 457–468. https://doi.org/10.1177/001872089203400407

Wajman, J. R., Mansur, L. L., & Yassuda, M. S. (2019). Lifestyle patterns as a modifiable risk factor for late-life cognitive decline: a narrative review regarding dementia prevention. *Current Aging Science*, *11*(2), 90–99. https://doi.org/10.2174/1874609811666181003160225

Wang, K.-C., Huang, P.-S., Wang, Y.-L., Hoe, Z.-Y., Noor, A. A., & Chen, P.-T. (2025). Bridging the gap: healthcare practitioners' insights on overcoming telemedicine barriers and optimal strategies for implementation. *Technology in Society*, *82*, 102899. https://doi.org/10.1016/j.techsoc.2025.102899

Wang, R., Qiu, C., Dintica, C. S., Shang, Y., Calderón Larrañaga, A., Wang, H., & Xu, W. (2021). Shared risk and protective factors between Alzheimer's disease and ischemic stroke: a population-based longitudinal study. *Alzheimer's & Dementia*, *17*(2), 191–204. https://doi.org/10.1002/alz.12203

Wilson, S. A., Byrne, P., Rodgers, S. E., & Maden, M. (2022). A systematic review of smartphone and tablet use by older adults with and without cognitive impairment. *Innovation in Aging*, *6*(2), igac002. https://doi.org/10.1093/geroni/igac002

Woods, B., Rai, H. K., Elliott, E., Aguirre, E., Orrell, M., & Spector, A. (2023). Cognitive stimulation to improve cognitive functioning in people with dementia. *Cochrane Database of Systematic Reviews*, *2023*(1), CD005562. https://doi.org/10.1002/14651858.CD005562.pub3

World Health Organization. (2015). *World report on ageing and health*. https://www.who.int/publications/i/item/9789241565042

Wu, H., Song, Y., Chen, S., Ge, H., Yan, Z., Qi, W., Yuan, Q., Liang, X., Lin, X., & Chen, J. (2022). An activation likelihood estimation meta-analysis of specific functional alterations in dorsal attention network in mild cognitive impairment. *Frontiers in Neuroscience*, *16*, 876568. https://doi.org/10.3389/fnins.2022.876568

Xiang, C., & Zhang, Y. (2024). Comparison of cognitive intervention strategies for individuals with Alzheimer's disease: a systematic review and network meta-analysis. *Neuropsychology Review*, *34*(2), 402–416. https://doi.org/10.1007/s11065-023-09584-5

Yang, L., Deng, Y.-T., Leng, Y., Ou, Y.-N., Li, Y.-Z., Chen, S.-D., He, X.-Y., Wu, B.-S., Huang, S.-Y., Zhang, Y.-R., Kuo, K., Feng, W., Dong, Q., Feng, J.-F., Suckling, J., Smith, A. D., Li, F., Cheng, W., & Yu, J.-T. (2023). Depression, depression treatments, and risk of incident dementia: a prospective cohort study of 354,313 participants. *Biological Psychiatry*, *93*(9), 802–809. https://doi.org/10.1016/j.biopsych.2022.08.026

Yang, T., Liu, W., He, J., Gui, C., Meng, L., Xu, L., & Jia, C. (2024). The cognitive effect of non-invasive brain stimulation combined with cognitive training in Alzheimer's disease and mild cognitive impairment: a systematic review and meta-analysis. *Alzheimer's Research & Therapy*, *16*(1), 140. https://doi.org/10.1186/s13195-024-01505-9

Yao, S., Liu, Y., Zheng, X., Zhang, Y., Cui, S., Tang, C., Lu, L., & Xu, N. (2020). Do nonpharmacological interventions prevent cognitive decline? A systematic review and meta-analysis. *Translational Psychiatry*, *10*(1), 19. https://doi.org/10.1038/s41398-020-0690-4

Yin, F. (2023). Lipid metabolism and Alzheimer's disease: clinical evidence, mechanistic link and therapeutic promise. *The FEBS Journal*, *290*(6), 1420–1453. https://doi.org/10.1111/febs.16344

Zhang, W., & Wang, A.-p. (2025). Functional ability of older adults based on the World Health Organization framework of healthy ageing: a scoping review. *Journal of Public Health*, *33*(7), 1513–1531. https://doi.org/10.1007/s10389-023-02121-x

Zhang, Z., Liu, X., Zhang, S., Song, Z., Lu, K., & Yang, W. (2024). A review and analysis of key biomarkers in Alzheimer's disease. *Frontiers in Neuroscience*, *18*, 1358998. https://doi.org/10.3389/fnins.2024.1358998

Ziegler, G., Dahnke, R., Jäncke, L., Yotter, R. A., May, A., & Gaser, C. (2012). Brain structural trajectories over the adult lifespan. *Human Brain Mapping*, *33*(10), 2377–2389. https://doi.org/10.1002/hbm.21374

Zuschnegg, J., Schoberer, D., Häussl, A., Herzog, S. A., Russegger, S., Ploder, K., Fellner, M., Hofmarcher-Holzhacker, M. M., Roller-Wirnsberger, R., Paletta, L., Koini, M., & Schüssler, S. (2023). Effectiveness of computer-based interventions for community-dwelling people with cognitive decline: a systematic review with meta-analyses. *BMC Geriatrics*, *23*(1), 229. https://doi.org/10.1186/s12877-023-03941-y