Supplementary Materials

Treatments in Tables 1-12 have been specified using the Rehabilitation Treatment Specification System [1]. In the RTSS, treatment *ingredients* are clinician actions or objects that are hypothesized to effect a change in some aspect of patient function; and treatment *targets* are those aspects of patient function that the clinician expects to change. There are three groups of targets: 1) organ function (O) targets, in which treatments replace or directly act on organs (e.g., electrical stimulation to the brain); skill and habit (S) targets (e.g., increasing use of communication strategies); and representation (R) targets, which include changes in knowledge, attitudes, and beliefs (e.g., increase knowledge about sleep hygiene). Targets are further specified as direct (D) if the ingredients affect that function directly (e.g., providing exercises to improve verbal recall); volitional (V), if a separate target is required to increase attitude or beliefs that are barriers to achieving the direct target (e.g., increasing motivation to perform exercises to increase verbal recall); or non-volitional (NV), if the patient is not required to actively participate for the treatment to have a benefit (e.g., the treatment is hypothesized to change the patient's function even if the patient is unconscious). See the RTSS manual for further details [2].

Some treatments are divided into *components*. A treatment component is a portion of a clinical treatment that includes one target and selected active ingredients. Treatment components were included in the RTSS because clinicians often name them as a shorthand when planning and describing their intervention (e.g., patient education, caregiver training). Because the tables below summarize a variety of studies, some treatment components have multiple target examples listed.

With the exception of a few manualized treatments, the tables below show typical characteristics of that type of treatment, rather than specific details from an individual study. The tables are intended to be illustrative rather than prescriptive, showing how systematic treatment specification can permit comparison of ingredients, targets, and target categories across studies. This cross-treatment comparison can help identify both similarities across treatments that go by different names, and also active ingredients that are common across effective treatments.

References

1. Hart T, Dijkers MP, Whyte J, et al. A Theory-Driven System for the Specification of Rehabilitation Treatments. *Arch Phys Med Rehabil.* 2019;100(1):172-180.
2. Whyte J. Manual for Rehabilitation Treatment Specification. Moss Rehabilitation Research Institute. http://mrri.org/innovations/manual-for-rehabilitation-treatment-specification/. Published 2018. Accessed July 1, 2018.

Table 1. Cognitive Training

Target population	Target	Target Group (Type)	Ingredients	Dose
Older adults with mild cognitive impairment	Increased knowledge and understanding of age-related changes in cognitive abilities and links with functional independence	R(D)	• Information about age-related changes in cognition included in Participant Information Sheet and provided verbally by researcher • Additional written information about various cognitive abilities and their links with everyday behaviours	• When first expressing interest in the treatment study • Weekly during the intervention period
	Increased capability to use the online training platform	S(D)	• Face-to-face orientation to online training platform • Demonstration of online training platform provided by clinician/trained research staff • Provision of written manual describing all necessary steps to access and complete a training session • Phone-based troubleshooting/technical support	• Once in the first training session • Once in the first training session • Once in the first training session • Once per week
	Improved performance on a composite global measure of cognitive function	S(D)	• Participant to practice on a set of 20-30 computerised tasks targeting multiple cognitive domains	• 30 training sessions (20 min each) over 10 weeks
	Motivation to adhere to the treatment	R(V)	• Verbally delivered information about potential short and long-term gains associated with process training • Feedback on performance delivered by the online training platform • Feedback on performance delivered over the phone by research staff • Written behavioural contract to increase commitment to the training	• Once in the first training session • After each training session • Once per week • Once in the first training session

			• Barrier identification with problem solving	• Once in the first training session

1

Table 2. Cognitive Rehabilitation

Target population	Target	Target Group (Type)	Ingredients	Dose

People with mild to moderate dementia living in the community	Improved performance of activities selected as targets of intervention	S(D)	• Identification of meaningful target(s) expressed as therapy goals
			• Use of one or more of the following:
			  • Enhanced learning techniques
			  • Development and provision of opportunities for structured practice of compensatory strategies
			  • Prompting
			  • Modification of the environment to optimise goal-related performance
			  • Introduction of assistive technology
			  • Development and provision of opportunities for practice of anxiety management techniques
			  • Graded practice
			• Involvement of family or other supporters where possible
				• In initial sessions, goals and strategies identified and practice initiated
				• Typically one to three goals might be fully addressed in 6-8 one-hour sessions conducted in the person's normal place of residence.
				• Practice as needed over several sessions with ongoing review
				• Between-session practice as prescribed

	Increase effectiveness of use of enhanced learning strategies and/or compensatory strategies to manage daily activities	S(D)	• Use of one or more of the following: enhanced learning techniques, prompting, development and provision of opportunities for structured practice of compensatory strategies • Graded practice • Involvement of family or other supporters where possible	• In initial sessions, goals and strategies identified and practice initiated • Practice as needed over several sessions with ongoing review • Between-session practice as prescribed • Can typically be incorporated within a 6-8 session goal-oriented intervention

	Increase propensity to apply problem-solving skills and strategies learned in treatment to improve functioning in other activities	R(V)	• Identification of suitable activities that could benefit from this approach • Guided problem-solving • Involvement of family or other supporters where possible	• As needed, in later sessions

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Table 3. Cognitive Stimulation Therapy

Target population	Target	Target Group (Type)	Ingredients	Dose
Treatment Component: Stimulation of cognitive functioning				
Adults with mild to moderate dementia	Improving semantic recall	S(D)	• Making connections with different objects or materials (e.g. discussing similarities or differences) • Opportunities to practice	• All 14 sessions
	Improving lexical recall	S(D)	• Activities hypothesized to stimulate lexical recall, e.g., naming of people and objects, word association, word categorisation • Opportunities to practice	• All 14 sessions, in particular sessions 4, 5, 6, 7, 9, 12, 13, and 14
	Improving executive function skills	S(D)	• Activities hypothesized to simulate executive function, e.g., categorisation, discussion of similarities and differences, executing stages of a task in creative sessions • Opportunities to practice	• All 14 sessions, in particular sessions 4, 5, 7, 8, 9, and 13
Treatment Component: Orientation to time and place				
	Improved accuracy of identifying time and place	S(D)	• Discussions of orientation information • Implicit cues to time and place	• At the beginning of each session and also within all 14 sessions, in particular sessions 3, 5, 6, 10 and 11
Treatment Component: Increasing adherence				•
	Increasing motivation to attend sessions, increasing motivation to engage in treatment process within the session, increasing	R(V)	• Verbal and/or written information about potential gains associated with CST, particularly with reference to research and strategic guidelines (e.g. NICE) • Providing continuity and consistency between sessions	• Prior to the sessions starting and during and between the intervention as needed. • All 14 sessions • All 14 sessions

	adherence to treatment outside of sessions		• Providing a safe, accepting environment • Demonstrating respect • Ensuring the atmosphere is fun and enjoyable • Providing choice • Adapting sessions according to interest and abilities, co-designing session content • Focusing on opinions rather than facts • Using multi-sensory stimulation to maximise strengths of the individual • Staff available to troubleshoot any concerns	• All 14 sessions • All 14 sessions • All 14 sessions • All 14 sessions • All 14 sessions, particularly 6 and 11 • All 14 sessions, particularly 1, 2, 4, 6, 8, 9 and 11 • Before, after and between sessions as required

Table 4. Physical exercise

Target population	Target	Target Group (Type)	Ingredients	Dose
Treatment Component: Aerobic Fitness				
People with diagnosed mild cognitive impairment living in the community	Increased aerobic fitness (e.g., improved scores on a maximal exercise test or submaximal test such as 6-minute walk)	O(D)	• Use of structured and purposeful moderate intensity physical activities suitable for the individual to reach the recommended level of 150 minutes per week; e.g., walking, stationary cycling, swimming, water-walking, non-contact games or sports	• 150 minutes/week of moderate intensity aerobic exercise; options: 3x 50 minute sessions, 5 x 30 minute sessions, accumulate bouts of 10 minutes or more
			• Adjustments to approach to ensure completion of physical activity	• As needed
			• Choice of training approach that fits the context (e.g., supervised or unsupervised, group or individual, centre or home-based)	• Discuss on first consultation; review progress on a regular basis and modify as needed
			• Service provision by qualified trainers, health professionals and community programs to assist where necessary, e.g., exercise physiologist, physiotherapist, exercise trainer	• Always
			• Use of individualised and progressive approach; e.g., start with approximately 50% of the time and at low intensity and progress over 6-8 weeks at a rate commensurate with the individual's ability to achieve the target dose	• As needed
			• Ongoing monitoring to evaluate safety risk and modify activity accordingly	• Regularly
Treatment Component: Muscle Strength				
People with diagnosed mild	Increased muscle strength (e.g., increase in	O(D)	• Equipment needed to engage in resistance exercises	• 2 sessions per week of between 45-60 minutes of

cognitive impairment living in the community	weight used for one maximum repetition or increase in number of repetitions of a standard weight)		• Provision of resistance via use of one's own body weight, free weights, dumbbells, elastic resistance bands, weight machines or a combination of these • Use of progression in resistance (e.g., weights) , repetitions, and session length (e.g., start with light weights, 2 sets of 6 exercises with 6 repetitions and build to more resistance of 3 sets of 8 exercises at 10 reps; start with 45 minutes and progress to 60 minutes per patient characteristics) • Supervision by qualified trainers and health professionals and in community programs to assist where necessary. • Monitoring of progress to adjust progression • Monitoring of performance to evaluate safety risk and modify activity accordingly	moderate intensity resistance exercises. ***Session:*** • 1 Set = 6-8 exercises • 6, 8 or 10 repetitions • 1 session = 2-3 sets • Always • Ongoing as needed • Ongoing as needed
Treatment Component: Treatment adherence				
People with diagnosed mild cognitive impairment living in the community	Increased propensity to perform physical activity: increased positive attitude toward exercise	R(D)	• Provision of enabling ingredients, e.g., information about sources of support, feedback, choice of activities in line with physical capabilities and preferences • Review of benefits of physical activity • Provision of ingredients that promote positive attitudes about physical activity	• At first session and regularly thereafter.
	Increased propensity to perform physical activity: reduced physical health barriers	R(D)	• Provision of ingredients hypothesized to reduce specific health barriers (e.g., respiratory, muscular, or joint problems; arthritis; risk of falls). • Provision of advice on treatment of mental and physical health problems. • Monitoring of physical and mental health status.	• As needed throughout treatment • As needed throughout treatment • Regularly

			• Provision of information about indicators that physical activity should be stopped.	• As needed throughout treatment

Note: We have specified the two areas of behavior modification as separate targets, but these volition ingredients also should be included in both aerobic fitness and muscle strength treatments.

Table 5. Sleep interventions

Target population	Target	Target Group (Type)	Ingredients	Dose
People with mild, moderate and severe symptoms of dementia living in the community	Increased knowledge in utilizing bright light to strengthen circadian rhythms and regulate sleep-wake cycles	R(D)	• Didactic instruction around impact and benefits of bright light exposure via teach-back • Provide guidelines (environmental modification) on utilizing bright light- when, how long and where to optimize impact on circadian rhythm	• During first 1-2 consultations • From session 1 with ongoing review and repetition of guidelines
	Increased skills utilizing bright light to strengthen circadian rhythms and regulate sleep-wake cycles	S(D)	• Modelling and practice setting up light from skilled professional • Validation and positive reinforcement • Opportunities for practice	• Introduced during session 1. • 1-2 sessions within approximately 8 weeks • Review as needed
	Increased skill in methods to decrease arousal (e.g., agitation or other arousal producing conditions)	S(D)	• Modelling of relaxation strategies to decrease physiological hyperarousal • Validation and positive reinforcement • Opportunities for practice	• 2-3 sessions of approximately 45 minutes per session over approximately 8 weeks • Ongoing review and practice as needed
	Increased knowledge of environmental triggers for nocturnal awakenings (e.g., light, noise, medication-induced nocturia) and strategies for their elimination	R(D)	• Didactic instruction on common dietary, environmental, and lifestyle variables that can lead to nocturnal awakenings • Provision of guidelines on strategies to eliminate triggering events (e.g., removing pets from the sleeping area).	• Once in first 1-2 sessions, with supplementary information provided as needed
People with mild symptoms of cognitive decline	Increased knowledge about sleep and population norms	R(D)	• Didactic instruction • Prompts to process new or previously acquired information via teach-back	• During first 1-2 consultations • From session 1 with ongoing review and repetition of material

living in the community				
	Increased propensity to engage in sleep-promoting behaviours at home	R(D)	• Improved ability to engage in sleep promoting schedules/routines • Providing sleep schedule guidelines (environmental modification) • Instruction on how to complete daily sleep log • Didactic instruction and teach-back around behaviours that promote and/or negatively impact sleep (e.g., sleep hygiene)	• Introduced during session 2. • From session 2 with ongoing review, support and modification as required • Iterative process occurring over 7-8 sessions delivered over a number of weeks (e.g., 8).
	Increased skills in methods to decrease arousal (e.g., worry about sleep or other arousal-producing cognitions)	S(D)	• Normalizing various sleep patterns • Instruction on worry-management techniques • Modelling and role play from skilled professional • Validation and positive reinforcement • Opportunities for practice	• 2-3 sessions of approximately 45 minutes per session over approximately 8 weeks • Ongoing review and practice as needed

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2

Table 6. Meditation

Target population	Target	Target Group (Type)	Ingredients	Dose
Older adults who are cognitively unimpaired (for prevention) or have subjective cognitive decline or mild cognitive impairment.	Increased skill in regulation of attention e.g., increased capacity to: • Direct and sustain attention on a selected object • Detect mind wandering and distractors • Disengagement of attention from distractors and shifting of attention back to the selected object • Cognitive reappraisal of distractors	S(D)	• Training sessions performed with an expert instructor, in a quiet room • Use of focus attention meditation exercises; e.g, instruction to direct attention to: ○ bodily sensations (e.g., breathing exercises, body scan, walking meditation, laying meditation) ○ external sensations (e.g., to sounds, visual object, food odors) ○ emotions (e.g., during physical pain) ○ thoughts (e.g., recognizing that "I am not my thoughts", or that thoughts are labile)	• Mindfulness-based intervention (MBI) programs typically include 2 hours per week with an instructor X 8 weeks, plus 20-40 minutes per day home practice and one day (or more) of intense practice • Dose of specific ingredients is as needed per patient characteristics • Sequence is typically attention/metacognition targets then compassion/loving kindness targets
	Increased skill in meta-cognition e.g., increased capacities for: • Resting the mind • Non-reactive meta-cognitive monitoring • Non-reactive awareness of automatic cognitive	S(D)	• Training sessions performed with an expert instructor, in a quiet room • Use of open-monitoring meditation exercises; e.g, instructions to: ○ rest the mind in the present moment and to keep the field of awareness open and receptive ○ label or notice sensations, emotions, thoughts moment as they arise	• See above

	and emotional interpretations of sensory, perceptual and endogenous stimuli		○ interpret thoughts, feeling and perceptions as mental processes rather than as accurate depictions of reality (e.g., "this is just a thought, no need to act upon it, or to feel emotionally attached to it")	
	Increased compassion/loving kindness e.g.: • Increased wholesome attitude about oneself and others, such as self-compassion, loving-kindness, acceptation • Increased skill in deconstructing maladaptive representations of oneself and others	S(D)	• Training sessions performed with an expert instructor, in a quiet room • Use of compassion and loving-kindness meditation exercises; e.g., instructions to: ○ visualize an image representing love for oneself, then apply that visualization to others • Use of appreciation and gratitude exercises; e.g., anchoring one's attention by repeating: ○ a sentence appreciating one's existence, body, efforts, potential, success, qualities ○ a sentence rejoicing of someone's else existence, qualities, help, kindness	• See above
	Increased propensity to complete home practice during and after intervention	R(V)	• Tools to facilitate daily home practice (e.g., audioguides and audiobooks, instruction sheets, manuals) • Prescribed practice schedule (e.g., formal 10-40 minutes session 1-2 X per day, informal 1-3 minutes exercises several times through the day) • Information about benefits of intervention • Self-reflection exercise to imagine future	• As needed

			state post-training • Credibility and expectancy questionnaire • Opportunity to give feedback	
	Increased experiential knowledge about one's mental habits and one's bodily needs in older age	R(D)	• Didactic instructions on mental and body changes and needs in older age	• As needed
	Increase knowledge about theories and principles of meditation, expected outcomes, and possible obstacles or pitfalls in meditation practices	R(D)	• Didactic instructions on therapeutic benefit/rational for intervention from research data	• As needed

1

Table 7. Reminiscence Therapy

Target population	Target	Target Group (Type)	Ingredients	Dose
People with dementia	Improved cognitive scores on standardized measures (e.g., MMSE, Autobiographical Memory Interview Extended Version)	S(D)	• Materials that prompt memories • Encouragement to actively recall the past	• Weekly from 4 weeks – 24 months with median exposure time of 11.5 hours (range 3-39 hours)
	Increased communication	S(D)	• Inviting the person to share memories of the past • Inviting the person to react to memories shared by others	• As needed within each session
	Increased experience of positive emotions	R(D)	• Asking questions about memories that are usually expected to trigger positive emotions (e.g., their first love, wedding, having a child) • Re-evaluating negative memories/conflict issues • Explicitly welcoming each person and rewarding their input	• During each session • When appropriate • During each session
	Increased feeling of self-identity and self-esteem	R(D)	• Provision of guidance in bringing together experiences into a coherent whole that has positive meaning for participants • Use of activities that are adapted to the needs and capacities of the person with dementia, so that they can engage successfully in activities	• During each session • During each session
	Increased feeling of social connectedness	R(D)	• Inviting the person to share memories with others in the group • Encouraging group members to react to	• During each group session • During each group session

			each others' shared memories	
	Increased motivation to adhere to the treatment	R(D)	• Confirming positive memories, experiences, mood, cognition and self-identity • Providing spoken information about potential short and long-term gains associated with participating in RT sessions	• As indicated • As needed

1

Table 8. Music-based treatments

Target population	Target	Target Group (Type)	Ingredients	Dose*
Treatment Component: Listening to Music				
Adults with dementia	Decreased BPSD (e.g., agitation, anxiety, depression, apathy)	R(V)	• Provide personalised recorded music playlists • Choose music familiar and significant to each participant • Monitor person with dementia during music listening for signs of distress and modify/discontinue music if necessary	• 20-30 mins daily
Adults with dementia	Improved mood	R(V)	• Provide personalised recorded music playlists • Choose music that is familiar and significant to each participant	• 20-30 mins daily
Treatment Component: Group Singing				
Adults with dementia	Decreased BPSD (e.g., agitation, anxiety, depression, apathy)	R(D)	• Provide a calming predictable environment through singing familiar/known songs • Offer choice and control through song selection opportunities.	• 50 mins per weekly singing session
	Improved mood	R(D)	• Provide a supportive group context in which to singing familiar songs • Stimulate a sense of achievement/mastery though supportively teaching new/unfamiliar songs	• 50 mins of each weekly singing session • 20 mins of each weekly singing session
	Improved feelings of social connectedness/peer support within the singing group	R(D)	• Provide targeted group singing program for people with dementia and their care partners • Adapt singing activities to needs of participants, provide easy to follow lyrics, and supportive musical accompaniment	• 90 mins of singing + 30 mins of socialising, weekly • As needed

	Improved cognition (attention, memory and new learning)	R(D)	• Stimulate memory through singing familiar songs • Stimulate learning processes through singing exercises and unfamiliar songs • Offer opportunities for song selection and discussion of memories elicited by familiar songs	• 50 mins of each weekly singing session • 40 mins of each weekly singing session • As needed
	Increased motivation to adhere to treatment	R(D)	• Provide an enjoyable and engaging experience of group singing to generate positive benefits in mood, and cognition and reduce negative symptoms • Provide information to participants about potential short and long-term gains associated with group singing	• 90 mins weekly group singing session • As needed
Treatment Component: Group Songwriting				
Adults with dementia	Improved feelings of social connectedness and sense of belonging within the group	R(D)	• Provide group songwriting program targeted for people with dementia (without caregiver) • Adapt group process to needs of participants	• 10 weekly 1 hour sessions • As needed
	Improved confidence	R(D)	• Stimulate language and learning processes through making contributions to lyric generation and music creation • Adapt group process to needs of participants	• 10 weekly 1 hour sessions • As needed
	Increased sense of accomplishment	R(D)	• Provide participants with copies of the finished song product(s) • Provide feedback and encouragement to group members during songwriting process	• 10 weekly 1 hour sessions • As needed
	Improved cognition (attention, memory and new learning)	R(D)	• Stimulate creativity through supporting participants with dementia to create new lyrics and discuss experiences related to topics of songs	• 16 weekly 1 hour sessions

			• Stimulate learning processes through learning/memorising new lyrics and melodies of participant-created songs	
	Increased motivation to adhere to treatment	R(D)	• Provide an enjoyable and engaging experience of group songwriting to generate positive benefits in mood, sense of belonging, and sense of achievement • Provide information to participants about potential short and long-term gains associated with group songwriting	• 10 weekly 1 hour sessions • As needed
Treatment Component: Individual Music Therapy				
Adults with dementia	Improved non-verbal communication (eye contact, turn taking)	S(V)	• Facilitate musical dialogue (vocal or instrumental) with participant • Use of familiar or extemporised music	• 30 mins twice weekly
	Decreased BPSD (e.g., agitation, anxiety, depression, apathy)	R(V)	• Facilitate musical dialogue (vocal or instrumental) with participant • Use of familiar or extemporised music • Monitor for signs of distress and modify/discontinue session if necessary	• 30 mins twice weekly
	Improved cognition (attention, initiation, organisation of ideas)	S(V)	• Facilitate musical dialogue (vocal or instrumental) with participant • Use of familiar or extemporised music	• 30 mins twice weekly

* Little evidence is currently available to specify optimal dosage for most music-based interventions. A recent Cochrane review reported on studies with music interventions that varied in duration between half an hour and two hours. The total number of sessions ranged from 6-156 with a median total number of 14 sessions (Van der Steen, 2018).

Table 9. Communication Intervention

Target population	Target	Target Group (Type)	Ingredients	Dose
Treatment Component: Direct Treatment of Language				
Adults with mild cognitive impairment/early-stage dementia	Maintenance of performance on lexical-semantic tasks over time (e.g., verbal fluency, naming, identifying words by their definitions)	S(D)	• Lexical, semantic, or phonemic cues to target words, provided in a hierarchy from most-to-least (e.g., from whole words to part words to first letters) or least-to-most • Opportunities for repetitive naming or massed practice naming pictures and objects	• Varies across studies and by individual vs group design. Typically once or twice a week for 1-2 hours.
	Improved recall of specific verbal information (e.g., face-name associations, semantic categories)	S(D)	• Use of error-control techniques (e.g., vanishing cues, errorless learning) • Opportunities to practice	• Varies across studies. Typically multiple per week for 1 hour X weeks or months.
Treatment Component: General Language Stimulation				
Adults with mild cognitive impairment/early-stage dementia	Maintenance of language skills over time (e.g., verbal fluency, oral reading, writing)	S(D)	• Language stimulation activities (e.g., generative naming, object naming, giving opinions, describing pictures, reading aloud) • Cues to begin tasks • Modelling • Encouraging feedback • Error-control strategies (in some studies) • Opportunities to practice • Note: Language activities paired with physical exercise in some studies	• Varies across studies. Typically about twice per week for 2 hours X weeks or months.

Treatment Component: Caregiver Training in Communication Strategies				
Communication partners of adults with mid-late stage dementia	Increased knowledge of supportive communication strategies for people with memory impairments	R(D)	• Written or spoken information about language changes associated with memory decline and reasons to support conversations	• Once at beginning of therapy
	Increased use of supportive communication strategies in conversations with person with dementia	S(D)	• Instruction in use of strategies such as use of two-choice vs. open-ended questions, topic statements at beginning of conversations, restating or reframing what the partner with dementia says, stating information rather than quizzing, talking in the "here and now" vs. about recent past events • Modelling • Corrective feedback • Opportunities to practice	• As needed

1

Table 10. Multisensory interventions

Target population	Target	Target Group (Type)	Ingredients	Dose
Persons with dementia in various stages	Reduce BPSD including agitation, apathy, depression or physical indicators of arousal (heart rate)	O(NV)	• Clinician behaviours, tools, or environmental manipulations that stimulate at least two of the five senses (seeing, hearing, tasting, feeling, smelling) • Delivery of ingredients in individual or group sessions • Ingredients hypothesized to restore sensory deprivation or correct an imbalance in sensory input (not specified)	• Typically, sessions last 15-60 minutes • More continuous exposure possible in adapted versions in which multi-sensory stimulation is used as an approach in daily caregiving • Frequency and duration highly variable • Low fidelity reported with one-to-one supervision by nursing staff
		O(V)	• Providing opportunities for the patient to control aspects of the environment	
	Improve cognition, physical functioning, or communication	O(NV)	• As above (little known about active ingredients)	• As above
	Improve quality of life	R(V)	• As above (little known about active ingredients)	• As above

Table 11. Occupational Therapy

Target population	Target	Target Group (Type)	Ingredients	Dose
People with mild to moderate symptoms of dementia living in the community	Improved initiation of activities of daily living	S(D)	• Modification of environment (e.g., visual and/or written prompts, assistive technology as prescribed) • Cues, prompts • Opportunities to practice	• Modifications usually made in one session • Variable - may take place over several consultations with refinements as needed
	Improved sequencing of activities of daily living	S(D)	• Modification of environment (e.g., visual and/or written prompts, assistive technology as prescribed) • Cues, prompts • Opportunities to practice • Use of errorless learning methods	• Modifications usually made in one session • Variable - may take place over several consultations with refinements as needed
	Increased time spent in leisure and household activities	S(D)	• Identification of suitable activities that are interesting and match the capabilities of the person with dementia • Modification of environment to support capabilities and compensate for deficits • Prompts (verbal or written) to commence or continue activity • Opportunities to practice	• During first two sessions • During first two sessions • As needed • As needed
People with mild to moderate symptoms of dementia living in the community and their families	Increased knowledge about dementia, it's symptoms and effective management strategies	R(D)	• Verbal and written information about dementia, symptoms, and management strategies • Opportunities for conversation among person with dementia, family, and provider	• May be provided over a number of consultations

Note: This describes the intervention that would take place with the person with dementia. Much work in occupational therapy is done with the family who can use changes in communication, changes in routine and changes in the environment to increase overall independence.

Table 12. Neuromodulation

Target population	Target	Target Group (Type)	Ingredients	Dose
Older adults with mild cognitive impairment	Improved declarative memory and other cognitive functions	O(D)	• tDCS equipment • Instructions • Application of tDCS • Tolerability & side effect questionnaire	• 5 consecutive daily sessions • 2mA active tDCS at 20 minutes per session (otherwise sham tDCS) with the anode over F3 and cathode over F4
	Improved declarative memory and other cognitive functions	O(D)	• TMS equipment • Neuronavigation equipment (optional) • Ear plugs • Instructions • Application of TMS • Tolerability & side effect questionnaire	• 5 consecutive daily sessions • 1500 stimuli at 20Hz delivered via figure of eight coil over F3

Note: The approaches noted above are meant to serve as mere examples and focus on neuromodulation in isolation whereas it can be paired with other non-pharmacologic and/or pharmacologic approaches. Although tDCS at 2mA for 20 minutes are the most commonly used current amplitude and session duration, respectively, there is a general lack of dose response data. TMS dosage and targets also vary considerably and could now include theta-burst stimulation. Likewise, these examples

1. **Cognitive Training section + RTSS Table 1**

Treatment specification

Cognitive training (CT) refers to the formal training of cognitive abilities and processes, usually through repeated practice on standardized tasks designed to reflect specific cognitive domains [1, 2]. Practice may focus on a single or on multiple cognitive domains, it may include advice on the use of, as well as practice with, internal cognitive strategies (e.g., mnemonics), and may be conducted individually or in small groups, and be supervised or unsupervised. A common assumption behind CT is that underlying cognitive processes can be improved or maintained through training, and that training-related cognitive gains may be associated with gains in day-to-day activities, or functional cognition. CT is sometimes confused with the related but distinct approaches of general cognitive stimulation and cognitive rehabilitation (described elsewhere in this paper), and unfortunately these terms are still often used interchangeably [3].

Common targets and aims of CT. The primary/immediate target of CT interventions is typically cognition, as reflected in performance on standardized cognitive tests. Depending on the nature of the training, the target may be a specific cognitive ability or process (e.g., divided attention), several inter-related processes, or global cognitive ability. Beyond cognitive ability, additional *aims* of CT treatments have included improvement on measures of mood and wellbeing of the person affected, subjective experience of everyday cognition, functional independence, quality of life, and caregiver burden.

Broader contexts of CT. Process-based cognitive training has a long history of use in clinical and healthy populations, particularly with children and older people [4]. In ageing, interest in cognitive training increased at a rapid rate since the early 1980s, with numerous studies published in cognitively healthy people, people with acquired brain injury (e.g., Stroke), and people with neurodegenerative diseases, particularly dementia due to Alzheimer's or vascular disease.

Amount and quality of evidence in relation to dementia and MCI

Numerus studies and reviews have been published on the effects of cognitive training on cognition and other outcomes in older adults with MCI and dementia. An influential and rigorous meta-analysis from 2017 ([5], AMSTAR=12) found moderate effect on global cognition (k=17, g=0.35, 95% CI= 0.20-0.51), as well as small to moderate effects on several specific cognitive processes, and on "psychosocial function". A recently published Cochrane Review of computerized cognitive training (CCT) in people with MCI ([6], AMSTAR=12.5) that focused on interventions lasting a minimum of 12 weeks, and that applied stricter inclusion criteria and risk of bias rating found, based on meta-analysis of 5 trials, a moderate effect of CCT on global cognition at the end of treatment relative to active control (k=5, g=-0.53, %95 CI= -1.06 to -0.01). Effects of CCT were found in several specific cognitive domains as well

(episodic memory, speed of processing, working memory), but not on any non-cognitive outcome, based on a small number of meta-analyzed trials. Regarding people with mild to moderate dementia, a recent Cochrane Review ([3]; AMSTAR=14), found that relative to active or passive control conditions, CT was associated with gains in global cognition (k=33, g=0.42, %95 CI= 0.23 to 0.62), and verbal category fluency (k= 9, g= 0.52, %95 CI= 0.23 to 0.81) at the end of treatment, and that these gains were maintained in the medium term (up to 12 months post-treatment). CT did not benefit non-cognitive outcomes, and no differences were found when CT was compared with an alternative treatment.

Evidence syntheses efforts of trials of CT in people with MCI and dementia have consistently identified methodological challenges in primary trials, which are often ranked at being at high or unclear risk of bias in several key domains, including lack of randomization concealment, incomplete outcome data, and selective reporting. Large statistical and clinical heterogeneity and imprecision of effect estimates has led authors of recent reviews to grade most of the evidence as being of 'low' or even 'very low' quality.

Main methodological challenges and the most pressing questions to be addressed

Consistent implementation of best practice standards in numerous aspects of trial planning (including registration and protocol publication), implementation (including adequate randomization and appropriate control, as well as selection of outcomes and measures), analysis (including dealing with missing data, protocol deviations, and multiple comparisons), and reporting (clear, detailed and transparent description of all key design features), remain significant barriers in the field of CT.

The methodological challenges discussed above notwithstanding, the weight of the evidence supports the view that structured process-based cognitive training leads to at least modest improvements in cognitive test performance in people with MCI and dementia, and that these improvements may be maintained over a short to medium period. What is now required is a sustained effort to improve our understanding of how to develop more personalized CT interventions that can be better integrated with everyday life and meaningful everyday activities, so that ongoing engagement is more likely and that transfer of gains from performance on standard tests of cognition to relevant functional domains is enabled. In addition, improved knowledge of the structural and functional effects of CT in key brain regions and networks would help ensure that task design and selection, as well as dosing parameters, are informed by such changes.

2. Cognitive Rehabilitation section + RTSS Table 2

Treatment specification

Cognitive rehabilitation (CR) is a person-centered, goal-oriented, problem-solving behavioral therapy aimed at managing or reducing functional disability and mitigating excess disability [7]. CR is a well-established intervention approach for people experiencing cognitive impairments following brain injury [8] and has been adapted for people with dementia.

Core elements are an individualized formulation, collaborative identification of specific realistic and meaningful goals, application of evidence-based behavioral strategies, and adjustment of goals and strategies in response to changes in the person's condition. The rehabilitation therapist assesses the person's current ability and the demands of the activity the person wishes or needs to do, identifies where mismatches arise, and collaboratively develops a therapy plan to support goal attainment [9].

CR focuses on supporting functioning and optimizing the ability to function in everyday life, in relation to the person's individual needs, wishes and preferences. The key targets are the functional disability that results from cognitive impairment and any excess disability resulting from secondary consequences of cognitive impairment, such as loss of confidence or depression. These targets are addressed by working with people on the goals that are important to them and that will make a difference in their daily lives, and addressing these directly in the person's everyday context.

Better management of functional disability may help to support adjustment to living with dementia, promote independence and social inclusion and maintain the quality of relationships with family and friends.

Amount and quality of evidence

There is robust evidence demonstrating the potential for improved functioning and better management of functional disability for people with mild to moderate dementia. Early evidence from robust single-case designs has demonstrated the potential for improvement in functional ability in relation to the specific goals targeted in therapy. This finding was confirmed first in a small randomized controlled trial [10] and more recently in the large-scale GREAT trial [7]. The only other large-scale trial of CR [11] reported that, compared to those receiving usual treatment, CR participants showed less functional decline at 24 months, a six-month delay in institutionalization and lower overall rates of institutionalization. While most research has focused on people with the more common forms of dementia, a recent small trial demonstrated similar benefits for people with Parkinsonian dementias [9] and single-case designs have reported effective interventions for people with front-temporal dementia [9]. Narrative case studies are available to illustrate the approach [7].

Main methodological challenges and most pressing questions to be addressed

While evidence from pilot studies and qualitative evaluations suggests that people with dementia and caregivers can experience a range of benefits such as improved adjustment or coping, such effects have not been captured using quantitative measures in large trials. Typical length of follow up in trials precludes identification of any long-term benefits such as delay in admission to long-term care. It will be important to establish whether and how this approach can be effectively implemented into service provision and care settings, and whether doing so can prove cost-effective through for example preventing crises or delaying admission to long-term care.

3. Cognitive Stimulation Therapy section + RTSS Table 3

Treatment specification

CST is a brief, manualized intervention for people with mild to moderate dementia. Group CST has been developed as a 14 session program, typically delivered over 7 weeks [12]. It is built upon several theories including learning theory and brain plasticity; which suggest that appropriate and targeted mental stimulation can lead to the development of new neuronal pathways. Sessions follow a set of guiding principles which include 'new ideas, thoughts and associations' and 'opinions rather than facts'. A 'maintenance CST' program includes 24 additional sessions to be delivered weekly once the initial CST program is completed[13]. A 75 session 'individual CST' (iCST) manual is also available for delivery by family caregivers [14]. CST aims to improve cognitive function through themed group activities, which implicitly stimulate skills including memory, executive function and language through tasks such as categorization, word association and discussion of current affairs. It also aims to improve quality of life (QOL) and mood. Social theories suggest that creating an optimal and supportive group environment can enhance skills, reduce stigma and increase wellbeing and there is evidence that improved cognition in CST is mediated by improved QOL [15]. CST is typically used within hospital settings, day centers and care homes. Its use for people with Intellectual Disabilities, Traumatic Brain Injury and Parkinson's disease is now being explored, although there is limited published research in these areas and no known RCTs.

Summary of existing evidence

There is now a large, international evidence-base for group CST in dementia, since the seminal RCT [12] which demonstrated significant benefits to cognition and QOL (n=201). The subsequent trial of weekly 'maintenance CST' [13] found significant improvements in QOL at 6 months and in activities of daily living at 3 months (n=237). Despite no changes in cognition or QOL following the caregiver delivered individualized CST (iCST) [14], there were significant improvements in caregiver QOL and in the relationship between the caregiver and person with dementia.

A Cochrane systematic review of 15 RCTs (n=718) [16] found consistent benefits of Cognitive Stimulation on cognitive function (SMD 0.41, 95% CI 0.25-0.57) in mild to moderate dementia, over and above any medication effects. These remained evident 1-3 months after treatment ended. There were also significant benefits to self-reported QOL and wellbeing and to staff reported communication, but no differences in mood or activities of daily living. This review included all interventions described as 'Cognitive Stimulation', which included but was not exclusive to the CST program described above. A more recent systematic review [17] included 12 studies (8 RCTs), all evaluating the same UK CST protocol [12]. Including trials from the US, UK, Hong Kong, Japan, Tanzania and Portugal, it found that

all studies examined impact on cognition, with nine demonstrating statistically significant improvements. Several studies also found significant benefits to QOL, depression and impact on caregivers. Crucially, the review concluded that this CST program can be widely linguistically and culturally adapted, with the benefits to cognition replicated internationally. A synthesis of 22 systematic reviews incorporating 197 studies of psychosocial interventions in dementia [18] concluded that Cognitive Stimulation demonstrates the best evidence for improving cognition amongst all psychosocial interventions. The seminal CST and subsequent 'maintenance CST' papers [12, 13] were fully powered, multi-centered RCTs, producing quality evidence and several subsequent trials were rated as high quality in the Olbia review [19, 20].

Main methodological challenges and most pressing questions to be addressed

Sample sizes have generally been small and underpowered, with the Cochrane review finding that under half the trials provided sufficient details of randomization and many failed to consider the effects of clusters within the analysis. Further, many used proxy raters including care staff to evaluate subjective outcomes such as mood. Although large (n=356) and methodologically robust, the iCST trial was hampered by limitations including high attrition (24%) and lack of adherence, with 22% of the treatment group receiving no sessions at all. Whilst group CST is now widely delivered in practice in the UK and beyond, there appears to be a common deviation from the 14 sessions. Implementation research examining the link between variations in dose and outcome would be of high clinical utility, with the Cochrane review noting an unclear relationship between dose and outcome. No research to date has examined fidelity to the CST manual and it would be of value to understand whether fidelity to specific components infers more or less impact on outcome. Finally, iCST as delivered by non-family caregivers needs to be evaluated in order to understand whether CST is indeed ineffective in an individualized format, or whether failure to find effects was due to poor adherence and/or family caregivers not being equipped to deliver CST.

4. Nutritional interventions section

Treatment specification

Nutrition interventions refer to actions to modify the dietary intake of micronutrients (vitamins and minerals) and/or macronutrients (proteins, fats, carbohydrates), individually through vitamin supplements or in combination through diet.

Common targets and aims. Most nutritional interventions have tested the effects of high dose vitamin supplementation on cognitive change. Interventions that employ entire diet approaches target the impact of multiple nutrients consumed at natural dose levels.

Broader contexts in which this intervention has been used. Nutritional interventions have been investigated extensively for the prevention and treatment of cardiovascular-related conditions, with the most successful strategies in whole diet approaches [21, 22]. These diet intervention trials demonstrated effects on potential bio mechanisms in the development of dementia, including decreased levels of inflammation, oxidative stress, blood pressure, and glucose [23-25].

Amount of evidence in relation to dementia

There are a limited number of randomized-controlled nutritional interventions in individuals with mild cognitive impairment (MCI). A recent Cochrane Review [26] identified five trials (n=879) on B vitamin supplements and showed no overall beneficial effects on cognition, however, in one trial (n=266) of MCI patients with high homocysteine [27], B vitamins supplementation for six to 24 months resulted in improved episodic memory. Another systematic review [28] reported improvements in cognitive performance, especially in memory, by supplementation of DHA and EPA (two studies, n=36 and n=86) [29, 30], DHA (one study, n=240) [31, 32], and flavonols (one study, n=90) [33]. Of note, all of these trials were relatively small in size, and had a high degree of heterogeneity, thus limiting the comparison and pooling of studies.

An even smaller number of trials tested the effects of various dietary interventions on cognition in individuals with cognitive impairment. In these trials, ranging in size from 49 to 80 persons, a low-saturated fat/low-glycemic index diet for four weeks improved delayed visual memory[33]; a low carbohydrate diet improved memory performance [34]; calorie restriction-induced weight loss diet increased cognitive scores [35]; and, 1 cup/day consumption of blueberry drink for 24-weeks resulted in improved memory discrimination versus the placebo group [36].

A Cochrane Review of nutritional interventions in patients with Alzheimer's dementia (AD) [37] reported that two large trials of vitamin E supplementation (2000 IU/d) demonstrated delayed progression in functional decline (n=613) [38] and delayed progression of AD as measured by the time to the occurrence of death, institutionalization, inability to perform basic activities of daily living, or

severe dementia (n=341) [39]. However, in the latter study, significant adverse events, including dental events, falls, and syncopal episodes were reported between the treatment and the placebo groups, albeit non-significant after adjustment for multiple comparisons [38].

Quality of evidence and main methodological challenges

The diet intervention studies were all positive but small in size, short in duration, and tested very different diets. Only one trial each examined the dietary effects of low saturated fat/low glycemic, low carbohydrate, restricted calories, and blueberry consumption. These results need to be replicated in larger trials.

Systematic reviews of trials evaluating the effects of vitamin supplements in patients with MCI and Alzheimer's dementia identified several methodological limitations. Cochrane review rated the overall quality of evidence as moderate, and studies included in the analysis as low to unclear risk of bias [26, 37] Most of the concerns were related to issues concerning open-label, randomization, attrition bias, adequacy of the control group, and selective outcome reporting. In addition, differences in cognitive outcomes together with variation in sample size and duration of the intervention presented overwhelming challenges to conduct meta-analyses of the trial data [28].

What are the most pressing questions that need to be addressed in relation to nutritional interventions?

Although there is limited evidence on the effect of nutritional interventions on cognitive outcomes in MCI patients and significant methodological challenges as mention above, the evidence is promising. The single positive trials of various diets and food (low saturated fat/low glycemic, low carbohydrate, restricted calories, blueberries) warrant additional investigation in much larger, well-controlled trials. Findings of beneficial effects on memory for B vitamins, DHA/EPA, and flavanol supplementation should be replicated in trials of sufficient trial size and duration to observe real effect differences, as well as rigorous procedures for randomization and blinded testing to ensure confidence in the findings. The evidence on vitamin E in slowing disease progression in patients with mild to moderate AD is strong, and may warrant the use of vitamin E supplementation in these patients.

5. Physical exercise training section + RTSS Table 4

Treatment specification

See Table.

'Exercise' refers to planned and/or structured activity which may be aerobic exercise (goal of aerobic fitness), resistance training (goal of muscle strength) [40] or a combination (multimodal) or mind-body exercise (e.g. Tai Chi). A growing body of evidence supports the view that exercise training aerobic and resistance may improve cognition for those with MCI. Systematic reviews and meta-analyses report inconsistent results, some showing positive effects of exercise on cognition [41-43] and others not [44].

Aerobic exercise summary of evidence and quality

The most recent systematic reviews and meta-analyses in MCI report positive effects of aerobic exercise on global cognition [41-43, 45, 46] and memory [42]. Effect sizes for global cognition are small to medium [42, 43, 45] with significant but weak/modest benefits on memory [42]. Evidence for other cognitive domains is less convincing [43].

Aerobic exercise interventions employ session duration ranging 20-60 minutes, frequency between 2-5 times/week and intensity 60-80% of maximum heart rate [42]. Higher adherence results in greater improvement in cognitive function [47]. Home and group-based aerobic programs report higher adherence rates (60%-78%) than multimodal (75%) and resistance training (51%-54%) [43].

Resistance exercise summary of evidence and quality

The evidence for resistance training is more limited with 4 recent reviews [41, 43, 48, 49]. The highest-quality positive evidence is for global cognition with small to moderate [41, 43, 49] with limited effects for executive function [43, 49]. Higher intensity and more frequent sessions appear to be more effective [41, 43, 49] but have low (51%-54%) adherence rates [43].

Common formats include progressive exercise using one's own body weight, free weights, dumbbells, resistance bands, weight machines or a combination (range: 6-8 exercises with 2-3 sets of 6, 8, 10 repetitions), supervised with sessions of 60-75 minutes in duration 2-3 times/week.

Challenges for future work

Treatment specification refinement for optimal cognitive outcomes requires interventions with clearly defined mode, frequency, duration and intensity of exercise. Combinations of aerobic, resistance and the inclusion of mind-body are options needing evaluation. Home-based aerobic regimes as well as

the safety and efficacy of unsupervised resistance training require more evidence. Reporting adherence to the exercise prescription is crucial for recommendations of optimal dose. Adequately powered studies, consistent measures of cognition and long-term follow-up are critical. It is imperative that adverse events are recorded, barriers and enablers to exercise are identified and creative strategies be evaluated to enhance the translation evidence and implementation.

6. Sleep treatments: CBT-I in MCI section + RTSS Table 5

Treatment specification

Insomnia includes problems with sleep initiation, repeated and prolonged awakenings, and/or nonrestorative sleep. Sleep specialists target these symptoms through modulation of emotions, thoughts, and behaviors related to sleep using Cognitive Behavioral Therapy for Insomnia (CBT-I).

The development of insomnia, including in persons with cognitive impairment, can be understood by the neurocognitive model [50]. Building upon the "3-P" behavioral approach [51], the model articulates predisposing, precipitating, perpetuating, and conditioned cortical arousal factors that underlie progression from risk to chronic insomnia.

Summary of existing evidence

Several meta-analyses of CBT–I support the finding that sleep disturbance is very amenable to change in both young and older adults [52-54] with treatment resulting in robust improvements in sleep quantity and quality. Evidence is now emerging that CBT-I is also successfully used in patients with comorbid conditions; modified versions have been successfully delivered to older patients with neurocognitive disorders [55-57].

Overall quality of the evidence and main methodological challenges

Overall quality of the evidence for CBT-I is strong. Methodological challenges include collection of reliable sleep data in persons with cognitive decline, and accessing individuals in medically underserved communities with a shortage of sleep specialists.

Commentary on central challenges and suggestions for next steps

Given the established evidence for CBT-I, future targets include: need for more studies that include participants with a range of cognitive abilities; continued study on the neuronal overlap and causal mechanisms in sleep and cognitive decline to help determine which approaches should be used, for which populations, and at which point in time following diagnosis; and continued exploration into novel interventions targeting sleep in MCI, such as interventions targeting sleep spindles that are connected to improve declarative memory formation [58].

7. Sleep treatments: Behavioral treatments for Sleep in dementia section + RTSS Table 5

Treatment specification

Categories of sleep disturbances in persons with dementia (PWD) include insomnia symptoms, hypersomnia, excessive motor activity at night, and hallucinations or other behavioral problems. Sleep disturbances are common in PWD, and treatment can improve quality of life, ease caregiver burden. Sleep disturbances in PWD have a bio behavioral ethology, including genetic, neuroendocrine, neurodegenerative, personality, and environmental/lifestyle [59]. Sleep specialists target nocturnal neurocognitive symptoms in PWD through implementation of sleep promoting strategies based upon cognitive-behavioral (CBT) theories of sleep, contextual applied behavior analysis models, and environmental modifications.

Summary of existing evidence

Studies have documented the effectiveness of increasing daytime bright light, daily participation in structured activities, and modifications to the sleep environment (e.g., decreasing nocturnal noise and light) to improve sleep-wake rhythms and reduce night-time wakefulness in community-dwelling older adults with dementia [60-63].

Overall quality of the evidence and main methodological challenges

While quality studies have established the effectiveness of various environmental and multi-component interventions to improve sleep in PWD, there are currently no meta-analysis or systematic reviews of non-pharmacological cognitive-behavioral interventions. Use of objective sleep measurements and/or proxy reporters in studies is crucial given participants' memory impairments. Methodological challenges include lack of standard intervention components or measurements; need for caregivers who can oversee treatment recommendations and sleep assessments; and the wide range of cognitive ability in participants with other comorbid conditions that can complicate treatment response.

Commentary on central challenges and suggestions for next steps

Future questions to address include: how dementia diagnostic subtypes and age of dementia onset impact response to interventions; understanding the role of sleep disturbances including obstructive sleep apnea in the pathogenesis of Alzheimer's disease; mechanisms of action underlying impact of behavioral and environmental interventions on sleep; and development of treatment algorithms specifically targeted to particular nocturnal behavioral symptoms and caregiving environments.

8. Meditation section + RTSS Table 6

1. Treatment specification

Meditation corresponds to a family of emotional and attentional regulatory training exercises [64, 65]. A meditation training program usually includes both sessions with an instructor and daily home practice. Each session can combine different types of meditation, such as focused attention, open-monitoring and compassion/loving-kindness meditations [66]. Most of the studies currently rely on 8-weeks mindfulness-based intervention (MBI), while longer interventions have recently been developed [67].

Summary of the existing evidence

To date, only one narrative review focused on the effects of meditation in patients with neurocognitive disorders [68]. The authors selected 10 relevant studies among 102 original articles. Only one was a randomized controlled trial (RCT) with a large sample size [69]. It showed significantly lower cognitive decline over a two-year period in the meditation group compared to either the passive or one of the active control groups in patients with mild to moderate Alzheimer's Disease. The remaining studies were either pilot RCT [70-72] or pilot non-randomized studies. Overall, they showed reduction in perceived stress [71-73] and increased executive functions [73], memory [70, 73, 74], quality of life [72, 75] , sleep quality [72, 74], brain volume [70], cerebral blood flow [76] and functional connectivity [77] with meditation. A few additional interventional studies on meditation in patients with neurocognitive disorders have been published since then and they also overall reported a positive impact of meditation on anxiety, depression, memory complaints and quality of life [78-83]. Two additional systematic reviews have recently been published but they did not specifically focused on meditation as they also include mind-body interventions with physical activity in MCI [84] and in dementia [85].

Other reviews investigated the effects of meditation in both cognitively impaired and unimpaired elderly adults [86-89]. Gard et al. [88] included six RCT and six non-randomized studies and Berk et al. [89] included six pilot studies showing evidence of feasibility of 8-week mindfulness-based interventions in older adults.

Finally, some reviews focused on the potential mechanisms underlying the effects of meditation on telomerase activity [90, 91], cognitive reserve [80, 92-94], brain ageing [95-97] and neurodegenerative diseases [98, 99].

Overall quality of evidence

In Russel et al.'s review [68], most of the studies had small sample sizes, short durations, and/or did not have a control group. In Gard et al.'s [88], and Berk et al.'s reviews [89], the risk of bias assessed with the Cochrane Risk of Bias Tool was high or unclear.

Commentary on central challenges and suggestions for next steps

Research in meditation is still in its infancy. There is a need for more RCT with larger sample sizes, active and passive control groups and an intent-to-treat principle. Studies with longer follow-up period will help to determine if meditation induces long-term brain changes and impacts clinically-meaningful outcomes such as conversion to MCI or dementia. The use of biomarkers will provide more insight into the mechanisms underlying the effects of meditation. A positive aspect is the feasibility and acceptability of meditation in healthy older adults, which remains to be tested in cognitively impaired patients. In conclusion, future studies with longitudinal, randomized and controlled designs and large sample sizes will allow confirming that meditation practice is a relevant approach to prevent or slow down cognitive decline and dementia.

9. Reminiscence section + RTSS Table 7

Treatment specification

Definition

Reminiscence therapy (RT) is a commonly used psychosocial intervention in dementia and "typically described as the discussion of past activities, events, and experiences usually with the aid of tangible prompts from the past such as photographs, music or familiar objects" [100, 101]. The therapy can be offered to individuals or in groups, the latter with people with dementia only or together with families (joint RT groups). The intervention may vary from recollection and sharing of personal memories regarding specific themes in the past, to a more structured approach (a life review, making of a life story book) and more active reminiscence using art [102, 103].

Common targets and aims of RT

Common targets of RT are: to improve cognition, communication, a sense of integrity & personal identity, experience positive emotions, social connectedness, and to improve the quality of the relationship with informal caregivers. The aims are to improve mental health (depression, anxiety), quality of life, well-being, and to diminish BPSD. For joint RT, targets for the informal caregivers may be improved mood, quality of the caring relationship and aims are to improve well-being/ quality of life, and alleviation of stress; and for formal caregivers aims are improved attitudes towards dementia and knowledge about dementia [103-105].

Amount of evidence in relation to dementia

Many studies have been published on the effectiveness and recently various systematic reviews and meta-analyses were published [104-107]. In 2018, a Cochrane review [103], and abridged paper of this review [100] were published. The evidence from this (abridged) Cochrane shows that RT has small but significant positive effects on quality of life, mood, cognition and communication in people with mainly mild to moderately severe dementia. However, these effects were inconsistent across intervention modality (group/individual) and setting (care home/community). Main results from this review were that no overall effect was found on self-reported quality of life but significant positive effects were found on self-reported quality of life for RT in care home settings. For overall communication and interaction, significant differences favoring RT were found at post-treatment and follow-up. For overall depressed mood, no significant differences were found, but for individual reminiscence results were significantly in favor of reminiscence. For overall cognition there was a just significant effect in favor of RT and a significant effect size for individual RT and for RT in care homes (SMD 0.29, 95% CI 0.03 to 0.56, Z= 2.19, p = 0.03).

Furthermore, the meta analyses showed no positive effects of the joint RT interventions, with family caregivers included, on stress related to caring, well-being and quality of life, carer mood or the quality of their relationship with the person with dementia. In total four adverse events were reported in two studies [100, 103]. The adverse events did not lead to withdrawals from the studies.

In the systematic review and meta-analysis of Park et al., 2019, 24 studies were included. Park found significant effect sizes in favor of RT for depression, for quality of life and for BPSD. Other recent systematic reviews had included both qualitative and quantitative studies with small sample sizes [104, 107] , focused more understanding the mechanism of reminiscence [105] or were not in English [108].

Overall quality of the evidence and main methodological challenges

In the Cochrane review [100, 103] 22 RCT studies were included with 1972 participants in total. The Cochrane 'Risk of bias' tool [109] was used and showed no high-risk biases; unclear risks were most often reported for selection bias and detection bias. These biases are rather common in psychosocial research. Six studies (n=223) were excluded from the meta-analysis because of an unclear risk of selection bias. For each effect, GRADE scores were given for the confidence in the quality of the evidence [110]. In the systematic review and meta-analyses of Park et al. [106], the Risk of Bias" tool of the Cochrane Collaboration [109] was used. 18 studies were included with low risk of bias and 6 with high risk of bias.

Both reviews found less positive results in the larger sample sized community-based studies [103, 106]. This could partly be explained by high attrition and Intention-to-treat-analyses which may result in more conservative assessments of effects [100].

What are the most pressing questions that need to be addressed in relation to RT?

There is a large variety in RT interventions which makes it difficult to compare the effects found, also because often treatment protocols are not (detailed) described [103]. There is a need for more large RCTs with detailed treatment protocols and clear description of aims and targets, allowing for better comparison of effects of different types of RT for different subgroups and settings. A complication is that RT is a person-centered care intervention that is intended to be a tailored process, and therefore it is difficult to set a golden standard [104].

10. Music-based treatments section + RTSS Table 8

Music-based treatments for adults living with dementia

There is a growing evidence base supporting the use of music-based NPTs in dementia care. These include *music therapy treatments* (where there is a goal-based therapeutic musical interaction with a trained therapist), as well as *music activities* that can be implemented by other clinicians, caregivers, or even self-administered. A 2017 review of non-pharmacological interventions in dementia care [111] concluded that music therapy was one of just two forms of intervention for which there is convincing evidence of effectiveness in reducing the behavioral and psychological symptoms of dementia (BPSD). Listening to music has been found to activate multiple neurological networks [112], while playing an instrument or singing has been found to have structural and functional impact on neuroplasticity [113]. For this reason, music therapy treatments have the ability to address a range of target areas, including cognitive, physical, emotional and social outcomes, and most treatments will target multiple areas simultaneously. Providing an accessible outlet for emotional expression may reduce negative dementia symptoms such as agitation, aggression, depression and apathy.

Music-based treatments are classified as active or receptive. Active music treatments include instrument playing, singing, songwriting, and moving to music. Receptive music treatments involve listening to recorded or live music. The following sections will discuss and compare common active and receptive music treatments, provide an overview of the existing evidence and discuss methodological and practical challenges reflected in the research literature.

Treatment Specification

A common receptive music-based treatment involves programming personalized playlists of familiar recorded music for a person with dementia to listen to with the aim of stimulating memories and reducing BPSD. Singing is a powerful active music-based treatment tool for facilitating engagement and communication, and group singing offers additional benefits of peer support and reducing isolation [114-116]. Therapeutic group songwriting is another active treatment that involves writing songs in a group context with the support of a qualified music therapist to address cognitive, emotional and/or social goals [117-119]. Individual music therapy might include a number of musical strategies to address non-musical goals as outlined above, including familiar song singing, instrumental/vocal improvisation, movement to music, music listening, and verbal processing [120].

Summary of the Existing Evidence

Literature summary

A recent meta-analysis revealed that receptive music-based treatments had a significant effect on reducing apathy, anxiety, agitation and behavioral challenges [121]. Agitation and aggression may be more effectively addressed in individual music therapy rather than group music interventions [122]. Many studies highlight the importance of using *familiar* music for people with dementia to stimulate memory and maintain a familiar environment [123-128]. Group singing is commonly used in dementia care and can improve quality of life and affect [114], as well as social confidence, relationship quality and cognitive stimulation [115, 116, 129]. More targeted programs such as group songwriting and individual music therapy may have psychosocial benefits as well as addressing cognitive goals, neuropsychiatric symptoms and increased engagement and wellbeing [117-119, 122, 130-134]. Group songwriting may be ideal for people in earlier stages to target communication and cognitive skills and social connections and, whereas individual music therapy may be more useful for people in later stages of dementia as it can be tailored specifically to individual needs and circumstances.

Quality of the evidence

Current evidence for the effectiveness of music-based treatments is compromised by heterogeneity in study designs (e.g. randomization, blinding, dosage) and small sample sizes. Further, there is a lack of consensus and clarity regarding intervention length, optimum time to treat, and treatment protocol (i.e. differential effects of various music-based treatments). Despite limited quantitative evidence to support the benefits of therapeutic group singing and songwriting, qualitative evidence suggests that these treatments are perceived as valuable and beneficial by participants [115, 119, 129, 135]. The 2018 Cochrane review found 7 RCTs providing evidence for the effectiveness of individual music therapy on reducing BPSD and improving wellbeing for people with dementia [122].

Commentary on central challenges and suggestions for next steps:

One of the main challenges for research on music-based treatments in dementia is that many studies are outcome-focused rather than treatment-focused. Accordingly, many studies use multiple music treatments, making it difficult to distinguish the differential effects of various music interventions. Thus, despite multiple meta-analyses reporting beneficial effects [122, 136-141], it is difficult to determine which specific treatment (e.g. playing, singing, listening) or treatment combination is most effective. The exception to this is the distinction between active and receptive treatments, however even here, several meta-analyses disagree on which is more effective [121, 138, 140]. Overall, current evidence indicates that active music interventions have a greater effect on behavioral and cognitive outcomes than receptive interventions [140], however future research needs to explore comparative effects of different music treatments, dosages, and duration of effects.

Receptive music treatments have potential contraindicative effects, especially when provided outside of a music therapy context. Listening to familiar music may trigger emotional responses that require support, and people in advanced stages of dementia may not be able to independently regulate or communicate that they require assistance regulating the musical input [142, 143]. Research indicates that people with dementia who experience high levels of depression may display increased sadness when listening to personalized music playlists; the level of pleasure received from listening to playlists also appears to decline when cognitive impairments increase [144]. Therefore, psychological history and symptoms need to be considered when planning music-based treatments.

Although there is evidence for the effects of both receptive and active music-based treatments on a range of psychological and behavioral variables, the underlying mechanisms for how and why these effects occur are poorly understood and needs exploration. In addition, future research will ideally inform the development of guidelines for which music-based treatments (and dosage) are best indicated for individuals at different stages of the dementia trajectory, for different dementia symptoms, and for different dementia types.

11. Communication interventions section + RTSS Table 9

Treatment Specification

Typical aims and targets. The aim of communication interventions is to increase frequency and quality of communication interactions between individuals with memory impairments and their everyday communication partners. Overall, these interventions aim to improve a construct referred to as "quality of communication life", defined as the extent to which a person's communication acts, in his or her personal environment and from his or her perspective, allow meaningful participation in life situations [145]. Typical providers are speech-language pathologists/speech therapists, and typical targets are measures of increased communication engagement, such as increased talking time, diversity of words and topics expressed, use of nouns rather than pronouns, and initiation and cross-talk among group members (i.e., vs. primarily responding to questions by care staff or family); and decreased negative behaviors such as repetitive questioning and inappropriate or disruptive utterances.

Indirect interventions. Caregiver training is a staple of indirect interventions for this population, particularly for adults with dementia. Caregivers are educated about communication and trained to use relatively simple strategies such as slowing their speech rate, simplifying their syntax, and asking yes/no rather than open-ended questions. A second type of indirect intervention is environmental modification, including ensuring ambient lighting and listening conditions are optimal for communication, and any vision or hearing problems are corrected – a critical consideration for older adults.

Direct interventions. Direct interventions use language stimulation activities to maintain or improve language functions. Targets in MCI and early-stage dementia are mostly related to word retrieval, with ingredients like encouraging self-talk and providing cues. In later stages, targets focus on communication habits and skills, like face-name association training and group reading of simple materials. As in all later-stage interventions, activities are designed to improve comprehension, expressive language, and social communication by maximizing use of intact non-declarative memory processes, including language-related processes such as grammar and phonology, and by reducing demands on declarative and working memory. As a result, these interventions commonly use error-control methods such as vanishing cues and spaced-retrieval training.

Amount and quality of evidence in relation to MCI and dementia

There have been five systematic reviews of interventions to improve communication in adults with dementia [146-150], and two systematic reviews of caregiver training [151, 152], as well as several recent studies of both direct training (e.g. [153, 154]), and career training (e.g. [155, 156]. Overall,

results in MCI suggest that language simulation can reduce the rate of decline early in the disease when language is specifically targeted (e.g., language does not appear to improve incidentally when other cognitive functions are treated [150]. In dementia, results indicate that caregiver training is effective in reducing caregiver stress and burden, reducing negative communication behaviors and increasing signs of engagement, and improving self-reported quality of life. The literature has limitations, however, including small sample sizes and the use of multi-component interventions in which it is impossible to identify essential ingredients.

Methodological challenges and next steps

It is a challenge to determine appropriate designs for interventions that may take months to show effects and are designed to maintain rather than improve performance. The complex nature of the MCI and dementia populations also pose a challenge, as does the tendency for late (or no) recognition of communication problems. The most important next steps are to increase recognition that these interventions can change the lives of persons with MCI and dementia [157] and identify essential ingredients to make that happen.

12. Multisensory interventions section + RTSS Table 10

Treatment specification

Multisensory interventions stimulate at least two of the five senses (sight, hearing, taste, touch, smell). Other interventions may also use massage, music, tasty food, etc. but aims (e.g. establishing connection in Namaste Care [158]) and theoretical foundation differ. The basis for theory around multisensory interventions is increased sensitivity to sensory stimulation, sensory dysfunction [159] or a lowered stress threshold [160]. Interventions should compensate sensory deprivation (Snoezelen [161, 162]) or restore balance ("sensoristasis") by the right pacing of sensory-stimulating and sensory-calming activities [160].

Multisensory interventions mostly aim at improving behavior, quality of life or wellbeing, or functioning; some studies have also examined effects on heart rate [162-164]. They are being used for people with dementia at various stages. Typically they are considered interventions for those in the severe stage [165]; indeed, passively undergoing such intervention does not preclude effectiveness. However, interventions specific to severe dementia (or to mild dementia or MCI) are rare [158, 162]. Usually they cover moderate dementia or moderate to severe dementia.

Snoezelen and sensory gardens involve supervised presence in environments equipped with tools to stimulate the senses. The Sonas structured group program stimulates all senses, additionally using reminiscence and physical activities. It could also be provided as an individual intervention [162, 166]. Snoezelen is usually offered in specially equipped rooms, but also as an approach in nurses' daily caregiving [167].

Summary of existing evidence

All interventions have been studied in some randomized controlled trials and in studies with other designs. Most studies were performed in nursing homes, some in day care centers. Since two Snoezelen trials were identified in a Cochrane review that was last issued in 2009 [168], at least 5 more RCTs studies have been identified [162, 164]. Unlike the first studies with over 100 participants, more recent studies had much smaller sample sizes yet found significant effects on behavior, mood or other outcomes. In practice, Snoezelen mostly uses vision and touch [165, 169]. Implementation studies of Snoezelen and sensory gardens reported problems with adherence and fidelity related to limited staff time and instruction or climate [165, 169, 170].

A scoping review reported inconsistent effects of sensory gardens in studies employing various designs including only 2 RCTs [163, 171]. Goto et al. [171] found more positive effects of an indoor garden (viewing, hearing waterway) compared with Snoezelen.

Three RTCs examined effects of Sonas; two found no effects on behavior, quality of life, or mood and one reported effects on communication in a small subgroup with severe dementia [162, 172].

The overall quality of the evidence of multisensory interventions is insufficient to draw conclusions on effectiveness to improve behavior, quality of life or functioning. RCTs are available, some single-blinded, and some therefore find the overall quality of the evidence adequate [164, 173]. More formal rating systems also indicated that most studies were of sufficient quality [162]. However, variable ways of delivering the interventions, variable control groups (e.g. outdoor versus indoor) and length of follow up preclude pooling of results of the mostly small studies.

Commentary on central challenges and suggestions for next steps

Well-designed RCTs that additionally examine the process of implementation of the complex multisensory interventions could add substantially to a still modest evidence base of effects. There is a need to build up theory on how the interventions may work and the most active ingredients such as through realist review [158] and smart designs. For example, few research groups have compared multisensory with single sensory interventions. A small study suggested effects of viewing a garden only [174] while access to outdoor spaces alone decreased agitation in more studies [170]. Possibly Snoezelen in a multi-sensory environment improves some different symptoms compared with individual music or activity interventions including gardening [161, 175, 176]. Also, some subgroups may benefit more but much larger sample sizes are needed to test moderators. Finally, as with other interventions, one-to-one contact especially with the person supervising or delivering the intervention may mediate or explain part of effects [159, 161]. If future work indicated sensory loss as a modifiable risk factor for dementia rather than a non-causal predictor, people with MCI may be targeted additionally.

13. Occupational therapy section + RTSS Table 11

Treatment specification

The aim of occupational therapy is to optimize occupational performance. Intervention often may include working with the person to improve cognitive, physical and/or psychosocial function and modifying the occupational or environment. The primary aim is to enable people to participate in the activities that they want, need, or are expected to do [177]. Occupational therapists use common theoretical models to work with people of all ages and there is good evidence for the intervention with older people [178] as well as people with dementia specifically [179]. There are a number of theoretical models underpinning occupational therapy. One of the simplest is the Person-Environment-Occupation (PEO) Model [180]. The model portrays the relationship between the capabilities and characteristics of the person; the physical, social and cultural environment; and the target occupation. All three contribute to the level of occupational performance achieved.

Summary of existing evidence

There are now a number of high quality randomized, controlled trials which have tested the efficacy of occupational therapy for dementia (n=15) [179]. Overall, results are positive showing that occupational therapy can improve ADL performance, is associated with reductions in the changed behaviors and associated with increased quality of life.

Existing randomized controlled trials are mostly of moderate to high quality. Most studies are at low risk of bias in relation to random sequence generation, allocation concealment, blinding of outcome assessment and selective reporting. However, some studies are not reported in adequate detail and it is not generally possible to blind participants. Furthermore, many of the outcome measures are self-report (as reported by either the person with dementia or their proxy/carer). Mixed findings and heterogeneity means that overall the body of evidence is considered low to moderate according to GRADE [110].

Commentary on central challenges and recommendations for next step

Despite the increasing number of trials and mostly rigorous methods used there are a number of challenges in the field. The first is the difficulty in pooling studies due to heterogeneity in intervention targets, methods, outcome measures, and terminology across studies. For example, the COT-ID intervention has a strong focus on activities of daily living such as showering and dressing to promote independence within the home [181]. In contrast, the tailored activity program primarily involves engagement in meaningful activities and caregiver education to reduce the impact of changed behaviors such as restlessness or distress [182]. Additional variation exists in the populations involved

in the research studies with some research trials involving people with milder symptoms and some involving people with moderate to severe symptoms of dementia.

While there are a number of established trials which clearly describe the intervention provided as occupational therapy there are many other trial interventions which are either provided by occupational therapists or could be provided by occupational therapists. Such approaches include case management, caregiver psychoeducation or cognitive rehabilitation.

What are the most pressing questions that need to be addressed in relation to the specific NPI?

Given the established evidence for occupational therapy one of the key challenges facing the field is how to implement effective interventions in practice. Audits from a number of countries show that current practice is short and assessment focused and does not reflect the interventions which have been shown to be effective in research trials.

In addition, given the heterogeneity amongst existing studies, more research is needed in order to make recommendations about which approaches should be used, for which populations and at which point in time following diagnosis. For example, very few studies have tested the efficacy of specific occupational therapy interventions for people in residential care facilities.

14. Neuromodulation section + RTSS Table 12

Treatment specification

Neuromodulation uses some form of energy, typically electrical or magnetic fields, to alter the excitability of the brain. To date, we are unaware of any clinically approved uses of neuromodulation for cognitive deficits. Treatment parameters and experimental uses vary across participant populations including stimulation type (e.g., transcranial magnetic stimulation (TMS); transcranial direct current stimulation (tDCS)), targeted brain region(s), dosing (amplitude/intensity, duration, number of sessions), and timing (whether stimulation is performed before, during, and/or after cognitive training/testing). Given the brevity of this section, we have limited to TMS and tDCS as applied to those with mild cognitive impairment (MCI) and dementia of the Alzheimer's type (DAT). Most of the studies to date have focused on cognitive improvement.

Summary of the existing evidence

An initial meta-analysis of 11 studies and about 200 participants found an overall large effect size (ES) benefits for cognitive functioning that favored active neuromodulation versus sham stimulation, even after controlling for potential confounding variables (ES 1.35; 95% CI 0;86-1;84; corrected ES 0.78) [183]. Across the included studies, stimulation during a task resulted in larger effects (ES 1.79) than did offline (ES 1.04), and single session effects were somewhat higher (ES 1.49) than multi-session effects (ES 1.2). Regarding TMS specifically, the authors reported high frequency stimulation was superior (ES 1.64) to low frequency (ES 0.23). A subsequent review paper noted that the majority (12/19) of TMS and tDCS studies targeted the lateral prefrontal cortex with mixed results [184].

A recent meta-analysis of multi-session tDCS specific effects in MCI and (all cause) dementia found no significant effects but was hindered by a small number of total studies (n=8), differing outcome measures (including those that largely focused on global cognition), and small sample individual group sizes (n<20/group) [185]. We previously reviewed the effects of tDCS in those across the dementia spectrum [186, 187] and also found mixed evidence, which we attributed to many of these same factors (see pressing questions). Briefly, efforts to enhance global cognition have only been successful when paired with a pharmacologic agent [188] but not when limited to tDCS [189, 190]. Likewise, there were no significant effects of tDCS when measured using visual attention [191] or psychiatric symptoms [190]. However, multiple studies have reported improved memory test performance after tDCS was applied over the lateral temporal cortex of those with dementia of the Alzheimer's type [189, 191-194]. Two prior studies in those with MCI reported improvements in verbal fluency [195] and subjective impressions of cognitive deficit [196], both of which reported evidence of

accompanying neurophysiologic change using functional magnetic resonance imaging (fMRI) and positron emission tomography (PET), respectively.

Central challenges and next steps

The most pressing needs focus on establishing fundamental dosing parameters and patient specific factors that affect variable responding in larger sample sizes; factors being examined in ongoing studies (e.g., NCT03875326; [197]).

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