Official Title: Improving Physical Activity with Cognitive Impairment

NCT Number: NCT05370118

Document Date: January 29, 2025

1. Study Introduction

The proposed research study examines the feasibility of a telerehabilitation physical activity behavioral (TPAB) 12-week intervention to improve physical activity (i.e., daily steps) for individuals with probable amnestic mild cognitive impairment (MCI) and caregivers. Improving physical activity may promote physical independence, slow the transition from MCI to dementia, and reduce health care costs. This study addresses two significant clinical gaps for amnestic MCI rehabilitation: 1) lack of evidence-based rehabilitation strategies to improve habitual physical activity; and 2) barriers to remotely promote habitual physical activity. We hypothesize that the intervention will be deemed feasible and that individuals with MCI will have greater daily steps after completing the intervention.

2. Background

The prevalence of MCI in older adults is approximately 3-25%,[1-3] of which 11-49% will transition to dementia (mainly AD) within two years.[2, 4] Delaying the transition to dementia by five years is estimated to save $500,000 per patient.[5, 6] Addressing modifiable risk factors of dementia, such as physical inactivity, is an approach to delay dementia onset and improve cognitive outcomes and quality of life.[1, 7-9] Previous reports suggest that more daily steps are linked to better cognition[1, 7, 10] and less neurodegeneration in individuals with cognitive impairment.[10, 11] However, there is little literature regarding approaches to increase daily steps in individuals with amnestic MCI (MCI with the domain of memory specifically impaired). Secondly, there is a lack of methods to remotely promote daily steps, which may be especially pertinent for individuals with barriers to participation in standard settings (e.g., those living in rural and underserved areas or those with functional limitations).

A small body of literature has utilized caregivers with physical activity interventions.[12] This will be the first study to our knowledge to engage individuals with probable amnestic MCI and the primary caregiver to facilitate a behavioral intervention targeting improvement in daily steps. Caregivers of individuals with cognitive impairment play a crucial role in daily routines of patients. Involving a primary caregiver has been shown to reduce technology barriers[13] and improve self-reported physical activity intervention outcomes.[14, 15] In addition, most caregivers for individuals with cognitive impairment do not engage in regular physical activity.[16] Involving caregivers in the TPAB intervention may improve their physical activity, help them better cope with demands of caring for a loved one, and reduce depression and burnout associated with caregiving.[15, 17] In addition to the caregiver benefits, approaching physical activity from a dyadic perspective has been suggested as a strategy to maximize effectiveness in individuals with cognitive impairment.[18-20]

This will be the first study to examine the TPAB intervention that combines health behavior theories/techniques and is remotely delivered to improve daily steps for individuals with probable amnestic MCI and caregivers (patient-caregiver dyads). Prior work has utilized self-reported physical activity,[21] which suffers from floor effects and recall bias.[22-24] A Fitbit (Fitbit Inc., Boston, MA) wearable sensor will be utilized in this study to self-monitor, objectively set goals, and assess goal achievement throughout the

Table 1. Telerehabilitation Physical Activity Behavioral (TPAB) Intervention Outline

Behavior Change Technique	Application	Theoretical Base
Self-monitoring of Behavior (1)	Utilize Fitbit for daily step monitoring	Control Theory
Action Planning (2)	Weekly action planning (goal setting) based on participant step count/identified individual targets	Control Theory
Graded Tasks (3)	Connection to self-monitoring and noted differences with higher/lower step count days	Social Cognitive Theory
Restructuring the Physical (4)/ Social Environment (5)	Discussion of personal barriers/facilitators to exercise and discussion of environmental components that can change	Social Cognitive Theory
Problem-Solving (6)	Discussion of reducing personal barriers and leveraging personal facilitators to increase daily steps	Social Cognitive Theory
Prompts/Cues (7)	Identification of cues that will be useful in self-management of daily steps moving forward and long-term	Operant Conditioning

intervention. The Fitbit wearable sensor is designed specifically to provide visual physical activity feedback through the Fitbit application. The Fitbit sensor will already be connected to a de-identified account created by the research team prior to distribution to study participants. No GPS data is collected. Fitbit use instructions will be provided verbally and in written form. The Fitbit application will provide the participant feedback on the number of steps he/she has taken during daily living activity and progress toward physical activity goals. The research team will monitor the Fitbit physical activity data through the Fitabase platform (see attachment for Fitabase data security and privacy information).

Research-grade accelerometers (ActivPAL, PAL Technologies, Glasgow, UK)[25] will be used to objectively measure physical activity (i.e., daily steps) before and after the 12-week intervention.

Enrolled patient-caregiver dyads (individual with probable amnestic mild cognitive impairment and caregiver) will be randomly assigned to either the intervention group (12-week TPAB intervention) or the control group (usual care/no intervention over 12 weeks). Individuals in the TPAB group will participate in virtual 30-minute weekly sessions for 12 weeks with their primary caregiver and the research interventionist (Dr. Hoffman). Established behavior-change techniques will be used in the TPAB intervention (**Table 1**), based largely on the combination of the Social Cognitive Theory, Control Theory, and Operant Conditioning,[26] including behavioral techniques, and patient-centered communication (e.g., motivational interviewing).[27] The behavior-change techniques are designed to target and improve daily steps. The patient-caregiver dyads in the control group will receive usual care and no intervention (no Fitbit) over the 12 weeks.

3. Research Objectives

Aim 1: Determine the feasibility of the TPAB intervention for individuals with probable amnestic MCI and their primary caregivers by measuring 1) participant retention, 2) attendance, 3) acceptability (Intrinsic Motivation Inventory)[28], 3) safety (adverse event tracking), 4) semi-structured interviews.

Aim 2: Examine the preliminary effects of TPAB on physical activity engagement (daily steps) among MCI participants when compared with the control group.

4. Study Population:

Thirty-six individuals with probable amnestic MCI between the ages of 50-85 years old and informal caregivers (19+ years of age) from the Omaha metro and surrounding areas will be recruited to participate in this study. The spectrum of amnestic MCI allows individuals that may or may not be able to give consent and is needed for this study to best reflect individuals with amnestic MCI. If the patient is unable to give consent per research team assessment, a legally authorized representative will be present and sign the consent form and the patient will verbally assent. Additionally, patients will be monitored and withdrawn if they appear to be unduly distressed from participating in the study. Due to anticipated attrition, we plan on recruiting 36 patient-caregiver dyads (18 dyads per group) to meet the necessary 15 dyads per group for statistical purposes. A sample size of 15 patient-caregiver dyads per group will meet our aim to determine a statistically significant change in activity from baseline to post-intervention (13 weeks) with adequate power ($\alpha = .05$, $1-\beta = .8$) ability to detect an effect size of approximately $d = 1.06$.

5. Inclusion/Exclusion Criteria

Inclusion criteria for participants with probable amnestic MCI are: 1) 50-85 years old, 2) memory impairment as demonstrated with deficits in the memory domain scores on the Montreal Cognitive Assessment (MoCA), 3) a score of 18-24 on the MoCA indicating possible MCI,[29] 5) not currently categorized as “Active” on the Rapid Assessment of Physical Activity,[30] 6) have a primary caregiver willing to participate in physical activity and assist the patient with participation in the study Inclusion criteria for both the patient and caregiver include: 1) self-reported household ambulator, 2) on stable doses of medication at least for the previous 30 days at baseline, 3) have a computer/wireless device with Internet access, 4) English-speaking. Caregiver must additionally score 24 or higher on the Mini-Mental Status Exam (MMSE) indicating no impairment to be included in the study[31] and be 19+ years of age. If the caregiver does not meet this requirement the patient will be asked if there is another caregiver willing to participate in the study.

Exclusion criteria for the patients and caregivers are: 1) limitations due to disability, illness, or pain that may affect the patient’s walking safety during the study, 2) unstable heart conditions (e.g., unstable angina, acute pericarditis) 3) uncontrolled hypertension in the last six months, 4) known neurological diseases. All medical criteria will be assessed via self-report.

6. Subject Recruitment:

Investigators will use the UNMC Mind Brain Health Registry (398-15) and distribute fliers at locations that treat individuals with amnestic MCI. Participants on the registry who are care partners of individuals with MCI or individuals with MCI will be contacted. Fliers may also be distributed on social media platforms (e.g., Facebook, Twitter). Fliers will be distributed to share basic study information. Participants will voluntarily identify if interested in this study and will communicate (e.g. call, email) with Dr. Hoffman from the contact information provided on the fliers. Potential participants will be pre-screened via

a standardized phone screen that includes an exercise medical clearance questionnaire (PAR-Q+). If the results of the PAR-Q+ indicate consultation with the individual's primary care provider prior to starting the physical activity intervention proposed in this study, then the individual will be asked for PCP contact information and the research team will receive PCP medical clearance prior to consent and baseline testing. During the consent process, individuals with probable amnestic MCI will be asked a series of questions (Capacity Screening Questions attachment) to determine if he/she has the capacity to consent. If the individual with probable amnestic MCI can answer the capacity screening questions it will be determined they have the ability to consent to the study. If the individual with probable amnestic MCI, is unable to answer the capacity screening questions then the individual's LAR will be contacted prior to completing the consent process. At the initial visit, the remaining screening will occur for the patient: 3) a score of 18-24 on the Montreal Cognitive Assessment indicating possible MCI,[29] 5) not currently categorized as "Active" on the Rapid Assessment of Physical Activity, and the caregiver: score 24 or higher on the Mini-Mental Status exam.

Additionally, potential research participants will be recruited by snowball sampling, enrolled participants referring the research team to others that may qualify.

7. Risks

Our patient population (aged 50-85 years) and the possibility of older caregivers (19+) may include individuals that have medically complex conditions that still meet inclusion/exclusion criteria. To improve the safety of all participants in TPAB intervention, the intervention includes discussion about safety with physical activity throughout.

In the TPAB intervention group, we anticipate the risk of muscle soreness and exposure to falls due to increased exposure to walking (dependent on the efficacy of TPAB intervention). Falls are defined as "inadvertently coming to rest on the ground, floor or other lower level, excluding intentional change in position."[32] Fall risk will be mitigated in the study by discussing walking safety and determining appropriate stepping goals throughout the TPAB intervention. The occurrence of falls will be recorded for the patient-caregiver dyads that are in the TPAB intervention group and the control group at all outcome testing sessions and TPAB intervention sessions. In addition, the control group will be contacted each week to determine if any falls or other adverse events have occurred. As such, study progress and adverse events (falls or other adverse events) will be reviewed on a case-by-case basis and the IRB will be notified. If the number of injurious falls for the TPAB intervention group exceeds that of the control group by 5 (7% of enrollment) at any time, the study will be suspended until an evaluation of study relatedness for each incidence is performed.

Also, some questions may make subjects feel uncomfortable. There is a rare but significant risk of loss of confidentiality. There may also be risks that are unknown at this time.

8. Benefits

Individuals with mild cognitive impairment in the TPAB intervention group may improve physical activity (daily steps). Some possible benefits of improving physical activity in individuals with MCI include greater independence, better cognitive performance, and greater quality of life.[1, 7-9]

Caregivers that are in the TPAB intervention group may also improve physical activity. Benefits associated with increased physical activity for caregivers could include decreased symptoms of depression and less caregiver burnout.[15, 17]

No benefits are anticipated for individuals in the control group.

The success of this remotely administered TPAB intervention can provide data for a larger-scale efficacy study that may ultimately advance reach to rural and underserved areas.

9. Assessment of Potential Risks and Benefits

The study is considered minimal risk since all data collection will occur in non-invasive methods (e.g., questionnaires, audio recordings, and thigh worn activity monitor). The intervention poses no more than minimal risk. The individuals in the intervention group will likely engage in more physical activity (dependent on the efficacy of the intervention) than the control group. The intervention is targeted at improving daily steps and does not specifically target an intensity (e.g., moderate intensity). Considering walking is an activity all our enrolled participants do every day this study poses no more than minimal risk. Common risks associated with walking include mild muscle soreness and falls. The benefits outlined in section 8 outline the moderate impact of the intervention on patients and caregivers. These outcomes can drive future larger clinical trials examining the TPAB intervention and ultimately can make substantial positive impacts on individuals with cognitive impairment and their caregivers.

10. Study Duration

The study duration will be approximately one year as specified by the grant-awarding agency.

11. Participant Duration

Both groups will undergo testing at baseline (before randomization to TPAB intervention or control group) and post-intervention. Consent and baseline testing will be conducted entirely in person (e.g. home setting). Post-testing will at a minimum involve cognitive testing (Trails A & B) done in person with an option for remaining outcomes completed in their preferred setting (e.g., home setting, via phone, or video call (Creighton's Zoom platform)). Research personnel will be present to assist with any questions or issues with questionnaire completion. Phone and video outcomes testing sessions will not be recorded except for the semi-structured interviews for individuals that underwent the intervention. All study personnel will act as mandatory reporters, if events or circumstances are witnessed during baseline, post, or intervention sessions. If

undergraduate students assisting with the research witness events, they deem reportable, they will discuss with the PI (Dr. Hoffman) to determine what agency should receive the report, if necessary. The testing procedures are detailed below and will take approximately 2 hours to complete at each testing time point (baseline and post-intervention). The TPAB intervention will involve weekly 30-minute sessions with Dr. Hoffman for 12 weeks. The details of information covered during the TPAB intervention sessions are outlined in the Intervention Checklist attachment. For the TPAB intervention group, all participants (patients and caregivers) will be provided a Fitbit. Directions on how to interact with the Fitbit app will be discussed during the first intervention session and are detailed in the Patient-Workbook attachment. It is expected that participants will return the provided Fitbit at the end of their study participation. Due to the 7-day activity monitor data collection prior to and following the 12-week TPAB intervention, participants will be enrolled in the study for approximately 14 weeks.

To assess Aim 1, we will measure retention, attendance, acceptability, safety, and qualitative feasibility perspectives. Based upon previous research, we expect to retain at least 85%[33] and attendance of at least 80%[34] to deem the study a success. The TPAB intervention will be regarded as acceptable with a mean of >5.0 (null value)[35] on the Intrinsic Motivation Inventory – Interest / Enjoyment Subscale.[28] The number of adverse events in the TPAB intervention group will be similar to that of the control group and will not exceed five adverse events related to the TPAB intervention. Finally, qualitative feasibility data will be gathered via audio recorded semi-structured interviews.

To assess Aim 2, we will measure daily steps at baseline and post-intervention. Daily steps will be measured across seven days at each time point (from the activPAL). Refer to ActivPAL instructions attachment for more details about activity monitor placement. Previous work has shown individuals with MCI can reliably and feasibly wear activity monitors.[7, 36, 37] We hypothesize that the TPAB intervention group will make significant gains in daily steps from baseline to post-intervention compared to the control group.

Baseline descriptive measures will include demographics (age, sex, education level), and anthropometrics (height, weight, BMI). Patient-caregiver dyads will additionally be assessed on the following outcome measures to determine associations with Aim 1 and Aim 2 outcomes: comorbidities (Functional Comorbidity Assessment[38]) self-reported mobility (International Physical Activity Questionnaire,[39] Physical Activity Scale for Elderly,[40] PROMIS HAQ[41]), global cognitive function (Montreal Cognitive Assessment[29] and Mini-Mental Status Exam [31]), perceptual-motor function (Trails Making Test A[42]), executive function (Trails Making Test B[42]), depression (Geriatric Depression Scale[43]), quality of life (Logsdon QOL-AD Scale[44, 45] and Short Form-36[46]), and caregiver burden (Caregiver Burden Inventory[47, 48]). Theory-based determinates[49] of knowledge (Apathy Scale[50, 51]), self-efficacy (Self Efficacy for Exercise Scale[52], Self-Efficacy of Managing Chronic Disease[53]), outcome expectations (semi-structured interview), goals (semi-structured interview, % weekly goal attainment), and perceived facilitators (Multidimensional Scale of Perceived Social Support[54]) will be assessed to explore the TPAB intervention behavioral targets. Collection methods for the above-stated outcomes are outlined in Table 2.

12. Compensation

Patients and caregivers will each be compensated with a $30 gift card for each testing session (2 testing sessions per participant). Compensation will be provided at the end of each testing session. This gives the opportunity for each participant to be compensated $60 total in amazon gift cards ($120 total for the patient-caregiver dyad). Additionally, all participants that complete the post-testing will be given a Fitbit at the end of the study for both the intervention and control groups.

Table 2. Data Collection Source Information

Data Collection Method	Outcomes
Questionnaires (electronically completed via tablet or laptop)	Acceptability (IMI) Comorbidities (Comorbidities Index) Mobility (IPAQ) Depression (GDS) Quality of Life (QOL-AD & SF-36) Caregiver burden (Caregiver Burden Inventory) Determinates of knowledge (Apathy Scale) Self-efficacy (SEE & self-efficacy for managing chronic disease) Perceived facilitators (MSPSS) Goals/Outcome expectations (PSFS, located on page 8 of the Patient-Workbook Attachment)
Participant Self-Reported	Demographics Frequency of Fitbit interaction
Semi-structured interview (TPAB intervention group participants only)	Qualitative feasibility of TPAB intervention (identification of themes across participants)
Researcher reported	Retention (keep track of subject drop out) Attendance (keep track of number of TPAB sessions attended) Safety (Weekly Health Problem Tracking Sheet) Blood Pressure/Heart Rate
ActivPAL (research grade activity monitor)	Daily steps
Fitbit/Fitabase	Weekly step goal attainment
Tests	Global Cognitive Function (MoCA & MMSE) Perceptual-motor function (Trails A Test) Executive Function (Trails B Test)

13. Confidentiality and Privacy

We will keep all research records that contain identifiable health information, confidential to the extent allowed by law. Paper records will be kept in a locked filing cabinet in Dr. Hoffman's office at Creighton University while electronic records will be stored on password-protected computers and user-restricted drives. A description of this clinical trial and a summary of the results will be available on http://www.clinicaltrials.gov, as required by U.S. law. Additionally, the research team and appropriate governing agencies will have access to the data. Each patient and caregiver will be assigned a study identifier (e.g. MCIBC_01) that will be associated with all research data. Participants' identifiable information (e.g. name, address, phone number) will be stored separately from research data and kept per contract of the funding agency. Deidentified research data will be securely kept indefinitely.

14. Informed Consent Process

We will e-mail or mail potential participants the consent form prior to the first study visit (baseline). This will allow participants ample time to review forms in advance should they desire. At the consent meeting, before reviewing the consent forms, patients and caregivers will be assessed to determine if they meet the remaining inclusion and exclusion criteria. If the remaining criteria are met, patients and caregivers will complete individual/separate consent forms. If a study investigator is unable to attend the baseline testing, remote consent will be conducted via HIPAA Zoom (voice call will be used if video conference is not possible) with the study investigator and potential participants. The consent will be electronically signed via DocuSign. This virtual consent process was previously approved in protocol 2003401. In this circumstance, student investigators will conduct the remaining components of the baseline testing session. During the consent process, the research personnel will review the purpose of the project, details of study participation, potential benefits/risks, and compensation. During this process, any questions will be answered regarding the study. It will be made verbally known that participation in this research is voluntary. If the potential participant chooses not to participate, it will not affect their relationship with the investigative team. The participant is free to withdraw consent and discontinue participation at any time without prejudice. During the consent process, individuals with probable amnestic MCI will be asked a series of questions (Capacity Screening Questions attachment) to determine if he/she has the capacity to consent. If the individual with probable amnestic MCI is able to answer the capacity screening questions it will be determined, they have the ability to consent to the study. If the individual with probable amnestic MCI, is unable to answer the capacity screening questions then the individual's LAR will be contacted prior to completing the consent process. If a legally authorized representative (LAR) is necessary, the LAR will sign the consent form and the patient will verbally assent for enrollment of the study to occur. The target population for this study is individuals with probable amnestic MCI as clinically determined by cognitive testing and will not include individuals with severe cognitive deficits (e.g., dementia, Alzheimer's disease). After signing consent forms patients and caregivers will be formally entered into the study and study-related questionnaires will follow (baseline testing). Copies of the signed consent forms will be provided to all participants. Vulnerable populations such as children, prisoners, non-English speakers, and severe cognitive impairment will not be enrolled in this study.

15. HIPAA

HIPAA authorization is required given the PHI that is acquired during the study procedures. The HIPAA form will be discussed verbally after it is determined the participant is eligible from the phone screen inclusion and exclusion criteria. The HIPAA form will be electronically signed via DocuSign at this time.

16. Data Analysis Plan

Our enrollment goal is 36 patient-caregiver dyads over a 9-month enrollment period. We expect attrition will occur over the 12-week intervention period. Given a sample size of 15 patient-caregiver dyads, our aim to detect a statistically significant change in physical activity from baseline to POST will be adequately powered ($\alpha = .05$, $1-\beta = .8$) to detect an effect size of approximately $d = 1.06$. Assuming a SD of approximately 36% and stable control group activity, this would reflect an approximate 35% increase in steps from baseline to post-intervention. Daily step changes between groups will be compared using a 2 x 2 repeated measures ANOVA, testing for main effects of group and time, and the interaction effect between groups across time. This analysis assumes no missing data for the 15 patient-caregiver dyads – in the event of greater than expected attrition occurs, we will use a mixed model to estimate from all available data on an 'intent to treat' basis. Similar analyses will be performed for all other quantitative outcomes described in the Participant Duration section.

Directed content analysis[55] will be used to assess the qualitative data gathered from semi-structured interviews. Savin-Baden[56] outlined three steps to qualitative research: (1) visually familiarize yourself with the data by reading the transcripts, then identify primary categories, (2) generate conclusions, and (3) check the results. will be analyzed by determining common themes across. The 14 domains of the Theoretical Domains Framework (TDF) will be used as a priori codes to classify the barriers and facilitators discussed by participants. The 14 domains in the TDF are: knowledge; skills; social/professional role and identity; beliefs about capabilities; optimism; beliefs about consequences; reinforcement; intentions; goals; memory, attention, and decisions processes; environmental context and resources; social influences; emotion; and behavioral regulation.[57] The TDF domains will be used as the "primary categories" (i.e. a priori codes) to capture participants' responses to the feasibility of the intervention to achieve improvement in daily stepping (step 1). The researcher will then read through the coded data as well as the data that was not coded to generate conclusions and construct themes related to the feasibility of the intervention to achieve improvement in daily stepping (step 2). Finally, the themes and raw data supporting each theme will be reviewed by the researcher with attention to an accurate representation of participants' perceptions of intervention feasibility (step 3). To enhance rigor, we will consider procedures to promote credibility, consistency, and transferability.[58] First, to ensure credibility we will triangulate between data sources (interviewers notes, transcripts, and interdisciplinary discussion). Secondly, to enhance consistency, the researcher who is coding will keep an audit trail of all decisions related to coding, interpretation, and constructed themes.

REFERENCES

1. Petersen RC, Lopez O, Armstrong MJ, et al. Practice guideline update summary: Mild cognitive impairment: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. *Neurology*. 2018;90(3):126-135. doi: 10.1212/WNL.0000000000004826 [doi].

2. Gauthier S, Reisberg B, Zaudig M, et al. Mild cognitive impairment. *Lancet*. 2006;367(9518):1262-1270. doi: S0140-6736(06)68542-5 [pii].

3. Colautti L, Baldassini D, Colombo V, et al. CREC: the role of serious games in improving flexibility in thinking in neuropsychological rehabilitation. *British Journal of Educational Technology*. 2018;49(4):717-727.

4. Bondi MW, Edmonds EC, Jak AJ, et al. Neuropsychological criteria for mild cognitive impairment improves diagnostic precision, biomarker associations, and progression rates. *J Alzheimers Dis*. 2014;42(1):275-289. doi: 10.3233/JAD-140276 [doi].

5. Ton TGN, DeLeire T, May SG, et al. The financial burden and health care utilization patterns associated with amnestic mild cognitive impairment. *Alzheimers Dement*. 2017;13(3):217-224. doi: S1552-5260(16)32889-8 [pii].

6. Zissimopoulos J, Crimmins E, St Clair P. The Value of Delaying Alzheimer's Disease Onset. *Forum Health Econ Policy*. 2014;18(1):25-39. doi: 10.1515/fhep-2014-0013 [doi].

7. Nickerson GY, Shade K. Effect of Increasing Physical Activity on Cognitive Function in Individuals With Mild Cognitive Impairment: A Knowledge Translation to Practice Pilot Project. *J Gerontol Nurs*. 2021;47(5):14-18. doi: 10.3928/00989134-20210401-01 [doi].

8. Livingston G, Sommerlad A, Orgeta V, et al. Dementia prevention, intervention, and care. *Lancet*. 2017;390(10113):2673-2734. doi: S0140-6736(17)31363-6 [pii].

9. Song D, Yu DSF, Li PWC, Lei Y. The effectiveness of physical exercise on cognitive and psychological outcomes in individuals with mild cognitive impairment: A systematic review and meta-analysis. *Int J Nurs Stud*. 2018;79:155-164. doi: S0020-7489(18)30002-6 [pii].

10. Chang YT. Physical Activity and Cognitive Function in Mild Cognitive Impairment. *ASN Neuro*. 2020;12:1759091419901182. doi: 10.1177/1759091419901182 [doi].

11. Rabin JS, Klein H, Kirn DR, et al. Associations of Physical Activity and β-Amyloid With Longitudinal Cognition and Neurodegeneration in Clinically Normal Older Adults. *JAMA Neurol*. 2019;76(10):1203-1210. doi: 10.1001/jamaneurol.2019.1879 [doi].

12. Anderson-Hanley C, Stark J, Wall KM, et al. The interactive Physical and Cognitive Exercise System (iPACES™): effects of a 3-month in-home pilot clinical trial for mild cognitive impairment and caregivers. *Clin Interv Aging*. 2018;13:1565-1577. doi: 10.2147/CIA.S160756 [doi].

13. Alexander NB, Phillips K, Wagner-Felkey J, et al. Team VA Video Connect (VVC) to optimize mobility and physical activity in post-hospital discharge older veterans: baseline assessment. *BMC Geriatr*. 2021;21(1):502-w. doi: 10.1186/s12877-021-02454-w [doi].

14. Jenkins E, Koirala B, Rodney T, et al. Home/community-based interventions to improve function in persons with mild cognitive impairment/early dementia. *Geriatr Nurs*. 2021;42(5):1109-1124. doi: S0197-4572(21)00240-8 [pii].

15. Patnode CD, Perdue LA, Rossom RC, et al. Screening for cognitive impairment in older adults: updated evidence report and systematic review for the US Preventive Services Task Force. *JAMA*. 2020;323(8):764-785.

16. Farran CJ, Staffileno BA, Gilley DW, et al. A lifestyle physical activity intervention for caregivers of persons with Alzheimer's disease. *Am J Alzheimers Dis Other Demen*. 2008;23(2):132-142. doi: 10.1177/1533317507312556 [doi].

17. Teri L, Gibbons LE, McCurry SM, et al. Exercise plus behavioral management in patients with Alzheimer disease: a randomized controlled trial. *JAMA*. 2003;290(15):2015-2022. doi: 290/15/2015 [pii].

18. Vidoni ED, Watts AS, Burns JM, et al. Feasibility of a Memory Clinic-Based Physical Activity Prescription Program. *J Alzheimers Dis*. 2016;53(1):161-170. doi: 10.3233/JAD-160158 [doi].

19. Burton LC, Newsom JT, Schulz R, Hirsch CH, German PS. Preventive health behaviors among spousal caregivers. *Prev Med*. 1997;26(2):162-169. doi: S0091-7435(96)90129-2 [pii].

20. Liffiton JA, Horton S, Baker J, Weir PL. Successful aging: how does physical activity influence engagement with life?. *European Review of Aging and Physical Activity*. 2012;9(2):103-108.

21. Schwartz HEM, Bay CP, McFeeley BM, Krivanek TJ, Daffner KR, Gale SA. The Brain Health Champion study: Health coaching changes behaviors in patients with cognitive impairment. *Alzheimers Dement (N Y)*. 2019;5:771-779. doi: 10.1016/j.trci.2019.09.008 [doi].

22. Tudor-Locke CE, Myers AM. Challenges and opportunities for measuring physical activity in sedentary adults. *Sports Med*. 2001;31(2):91-100. doi: 10.2165/00007256-200131020-00002 [doi].

23. Fioranzato M, Comoretto RI, Lanera C, et al. Improving Healthy Aging by Monitoring Patients' Lifestyle through a Wearable Device: Results of a Feasibility Study. *Int J Environ Res*

Public Health. 2021;18(18):9806. doi: 10.3390/ijerph18189806. doi: 10.3390/ijerph18189806 [doi].

24. Makarewicz A, Jamka M, Wasiewicz-Gajdzis M, et al. Comparison of Subjective and Objective Methods to Measure the Physical Activity of Non-Depressed Middle-Aged Healthy Subjects with Normal Cognitive Function and Mild Cognitive Impairment-A Cross-Sectional Study. *Int J Environ Res Public Health*. 2021;18(15):8042. doi: 10.3390/ijerph18158042. doi: 10.3390/ijerph18158042 [doi].

25. Taraldsen K, Askim T, Sletvold O, et al. Evaluation of a body-worn sensor system to measure physical activity in older people with impaired function. *Phys Ther*. 2011;91(2):277-285. doi: 10.2522/ptj.20100159 [doi].

26. Carey RN, Connell LE, Johnston M, et al. Behavior Change Techniques and Their Mechanisms of Action: A Synthesis of Links Described in Published Intervention Literature. *Ann Behav Med*. 2019;53(8):693-707. doi: 10.1093/abm/kay078 [doi].

27. Keefe FJ, Main CJ, George SZ. Advancing Psychologically Informed Practice for Patients With Persistent Musculoskeletal Pain: Promise, Pitfalls, and Solutions. *Phys Ther*. 2018;98(5):398-407. doi: 10.1093/ptj/pzy024 [doi].

28. McAuley E, Duncan T, Tammen VV. Psychometric properties of the Intrinsic Motivation Inventory in a competitive sport setting: a confirmatory factor analysis. *Res Q Exerc Sport*. 1989;60(1):48-58. doi: 10.1080/02701367.1989.10607413 [doi].

29. Yang C, Wang L, Hu H, Dong X, Wang Y, Yang F. Montreal Cognitive Assessment: Seeking a Single Cutoff Score May Not Be Optimal. *Evid Based Complement Alternat Med*. 2021;2021:9984419. doi: 10.1155/2021/9984419 [doi].

30. Topolski TD, LoGerfo J, Patrick DL, Williams B, Walwick J, Patrick MB. The Rapid Assessment of Physical Activity (RAPA) among older adults. *Prev Chronic Dis*. 2006;3(4):A118. doi: A118.

31. Lopez MN, Charter RA, Mostafavi B, Nibut LP, Smith WE. Psychometric Properties of the Folstein Mini-Mental State Examination. *Assessment*. 2005;12(2):137-144. doi: 10.1177/1073191105275412.

32. World Health Organization, World Health Organization. Ageing, Life Course Unit. *WHO global report on falls prevention in older age.* World Health Organization; 2008.

33. Cox KL, Clare L, Cyarto EV, et al. A Randomized Controlled Trial on the Effects of a 6-Month Home-Based Physical Activity Program with Individual Goal-Setting and Volunteer Mentors on Physical Activity, Adherence, and Physical Fitness in Inactive Older Adults at Risk of Cognitive Decline: The INDIGO Study. *J Alzheimers Dis*. 2021;84(1):207-226. doi: 10.3233/JAD-210479 [doi].

34. Xu Z, Zhang D, Lee ATC, et al. A pilot feasibility randomized controlled trial on combining mind-body physical exercise, cognitive training, and nurse-led risk factor modification to reduce cognitive decline among older adults with mild cognitive impairment in primary care. *PeerJ*. 2020;8:e9845. doi: 10.7717/peerj.9845 [doi].

35. Christiansen CL, Miller MJ, Kline PW, et al. Biobehavioral Intervention Targeting Physical Activity Behavior Change for Older Veterans after Nontraumatic Amputation: A Randomized Controlled Trial. *PM R*. 2020;12(10):957-966. doi: 10.1002/pmrj.12374 [doi].

36. Lyons EJ, Swartz MC, Lewis ZH, Martinez E, Jennings K. Feasibility and Acceptability of a Wearable Technology Physical Activity Intervention With Telephone Counseling for Mid-Aged

and Older Adults: A Randomized Controlled Pilot Trial. *JMIR Mhealth Uhealth*. 2017;5(3):e28. doi: 10.2196/mhealth.6967 [doi].

37. van der Wardt V, Hancox JE, Burgon C, Bajwa R, Goldberg S, Harwood RH. Measuring Physical Activity Levels in People With Mild Cognitive Impairment or Mild Dementia. *J Aging Phys Act*. 2020;29(1):10-16. doi: japa.2019-0234 [pii].

38. Groll DL, To T, Bombardier C, Wright JG. The development of a comorbidity index with physical function as the outcome. *J Clin Epidemiol*. 2005;58(6):595-602. doi: S0895-4356(05)00021-1 [pii].

39. Craig CL, Marshall AL, Sjöström M, et al. International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc*. 2003;35(8):1381-1395. doi: 10.1249/01.MSS.0000078924.61453.FB [doi].

40. Washburn RA, Smith KW, Jette AM, Janney CA. The Physical Activity Scale for the Elderly (PASE): development and evaluation. *J Clin Epidemiol*. 1993;46(2):153-162. doi: 0895-4356(93)90053-4 [pii].

41. Crins MHP, van der Wees, P. J., Klausch T, van Dulmen SA, Roorda LD, Terwee CB. Psychometric properties of the PROMIS Physical Function item bank in patients receiving physical therapy. *PLoS One*. 2018;13(2):e0192187. doi: 10.1371/journal.pone.0192187 [doi].

42. Strauss E, Sherman EM, Spreen O. *A compendium of neuropsychological tests: Administration, norms, and commentary.* American chemical society; 2006.

43. Hoyl MT, Alessi CA, Harker JO, et al. Development and testing of a five-item version of the Geriatric Depression Scale. *J Am Geriatr Soc*. 1999;47(7):873-878. doi: 10.1111/j.1532-5415.1999.tb03848.x [doi].

44. Logsdon RG, Gibbons LE, McCurry SM, Teri L. Assessing quality of life in older adults with cognitive impairment. *Psychosom Med*. 2002;64(3):510-519. doi: 10.1097/00006842-200205000-00016 [doi].

45. Villars H, Cantet C, de Peretti E, Perrin A, Soto-Martin M, Gardette V. Impact of an educational programme on Alzheimer's disease patients' quality of life: results of the randomized controlled trial THERAD. *Alzheimers Res Ther*. 2021;13(1):152-3. doi: 10.1186/s13195-021-00896-3 [doi].

46. Ware JE,Jr, Gandek B. Overview of the SF-36 Health Survey and the International Quality of Life Assessment (IQOLA) Project. *J Clin Epidemiol*. 1998;51(11):903-912. doi: S0895-4356(98)00081-X [pii].

47. Marvardi M, Mattioli P, Spazzafumo L, et al. The Caregiver Burden Inventory in evaluating the burden of caregivers of elderly demented patients: results from a multicenter study. *Aging Clin Exp Res*. 2005;17(1):46-53. doi: 2810 [pii].

48. Novak M, Guest C. Application of a multidimensional caregiver burden inventory. *Gerontologist*. 1989;29(6):798-803. doi: 10.1093/geront/29.6.798 [doi].

49. Bandura A. Health promotion by social cognitive means. *Health Educ Behav*. 2004;31(2):143-164. doi: 10.1177/1090198104263660 [doi].

50. Starkstein SE, Mayberg HS, Preziosi TJ, Andrezejewski P, Leiguarda R, Robinson RG. Reliability, validity, and clinical correlates of apathy in Parkinson's disease. *J Neuropsychiatry Clin Neurosci*. 1992;4(2):134-139. doi: 10.1176/jnp.4.2.134 [doi].

51. Ito D, Kawakami M, Narita Y, Yoshida T, Mori N, Kondo K. Cognitive Function is a Predictor of the Daily Step Count in Patients With Subacute Stroke With Independent Walking Ability: A

Prospective Cohort Study. *Arch Rehabil Res Clin Transl*. 2021;3(3):100132. doi: 10.1016/j.arrct.2021.100132 [doi].

52. Resnick B, Jenkins LS. Testing the reliability and validity of the Self-Efficacy for Exercise scale. *Nurs Res*. 2000;49(3):154-159. doi: 10.1097/00006199-200005000-00007 [doi].

53. Bodenheimer T, Lorig K, Holman H, Grumbach K. Patient self-management of chronic disease in primary care. *JAMA*. 2002;288(19):2469-2475. doi: 10.1001/jama.288.19.2469.

54. Zimet GD, Powell SS, Farley GK, Werkman S, Berkoff KA. Psychometric characteristics of the Multidimensional Scale of Perceived Social Support. *J Pers Assess*. 1990;55(3-4):610-617. doi: 10.1080/00223891.1990.9674095 [doi].

55. Hsieh HF, Shannon SE. Three approaches to qualitative content analysis. *Qual Health Res*. 2005;15(9):1277-1288. doi: 15/9/1277 [pii].

56. Savin-Baden M, Howell-Major C. Qualititative research: The essential guide to theory and practice. *Qualitative Research: The Essential Guide to Theory and Practice.Routledge*. 2013.

57. Atkins L, Francis J, Islam R, et al. A guide to using the Theoretical Domains Framework of behaviour change to investigate implementation problems. *Implement Sci*. 2017;12(1):77-9. doi: 10.1186/s13012-017-0605-9 [doi].

58. Merriam SB, Tisdell EJ. *Qualitative research: A guide to design and implementation.* John Wiley & Sons; 2015.