Deliverable D4.1
Title: Clinical trial registry

The StayFitLonger Study: an Innovative Computerized Home-based Training to Foster Independent Life at Home (SFL)

ClinicalTrials.gov Identifier: NCT04237519

Recruitment Status : Recruiting
First Posted : January 23, 2020
Last Update Posted : January 23, 2020

See **Contacts and Locations**

Sponsor:
University of Lausanne Hospitals

Collaborators:
HES-SO Valais-Wallis
Centre de Recherche de l'Institut Universitaire de Geriatrie de Montreal
Haute-Ecole Arc

Mindmaze SA
Université Catholique de Louvain
Active and Assisted Living Programme
BRUSANO
Pro-Senectute Vaud

Information provided by (Responsible Party):
Jean-François Démonet, University of Lausanne Hospitals

Study Description

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Brief Summary:

Multimodal training, including physical and cognitive activities, has been associated with a reduction in age-related physical and cognitive decline. Therefore, combining these activities into a home-based computerized training program may represent a powerful approach to foster independent life at home. The StayFitLonger study is a 6-month multi-site randomized controlled, double-blind trial, which tests the efficacy of a home-based computerized intervention that combines physical and cognitive exercises through virtual coaching to enhance motivation.

In Switzerland, Canada and Belgium, a total of 128 older participants will be recruited and randomly assigned to one of two physical and cognitive home-based interventions for 6 months: StayFitLonger or active control training. The StayFitLonger intervention provides physical and cognitive training exercises, feedback and instructions through a virtual coach to optimize motivation. It also offers social and psycho-educational contents. Monthly supervision (home-visits and phone calls) will be provided during this 6-month intervention. Outcomes will be measured at baseline, and after 6 months of training.

This study will demonstrate the feasibility, sustainability and efficacy of a home-based multi-domain intervention program allowing further development and possible commercialization of a scientifically validated training program to slow down cognitive and physical decline.

Condition or disease	Intervention/treatment	Phase
Cognitive Decline Prevention in Robust Older Adults Cognitive Decline Prevention in Pre-frail Older Adults Physical Decline Prevention in Robust Older Adults	Behavioral: SFL training Behavioral: Active controlled training	Not Applicable

Physical Decline Prevention in Pre-frail Older Adults		

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Study Design

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Study Type :	Interventional (Clinical Trial)
Estimated Enrollment :	128 participants
Allocation:	Randomized
Intervention Model:	Parallel Assignment
Intervention Model Description:	Double-blind, parallel-group (intervention A vs B), multicentric randomized control trial (RCT). A stratification will separate robust from pre-frail healthy older adults in each intervention. Note that the study is combined with a further 6-month observational study to test adherence, user experience and acceptability in all participants.
Masking:	Double (Participant, Outcomes Assessor)
Masking Description:	Assessors are blind to the hypotheses and to participants' assignment as they only have access to the testing sessions. Participants are asked not to mention elements of their training program to assessors . Would such circumstance occur, it will be reported but this should have minimal effect on integrity as the assessors are blind to the hypotheses. Team members responsible of the statistical analyses are blind to the training assignment as they only have access to anonymized data set and have no access to neither participants' assignment nor the randomization list. At each study site, study coordinators and trainers responsible for the introductory and refresher courses, and supervision of participants during the home-based training are not blind. Participants are aware that the trial has two different training conditions that are compared to each other and that they are randomly allocated to one of them. However, they are not informed of the study hypotheses.
Primary Purpose:	Prevention

Official Title:	StayFitLonger. Preventive Effects of a Combination of Non-drug Interventions (Physical, Cognitive and Social) in Healthy Elderly Subjects: Multicentre Randomised Controlled Trial.
Actual Study Start Date :	January 11, 2019
Estimated Primary Completion Date :	November 1, 2020
Estimated Study Completion Date :	November 1, 2020

Resource links provided by the National Library of Medicine

MedlinePlus related topics: Health Checkup

U.S. FDA Resources

Arms and Interventions

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Arm	Intervention/treatment
Experimental: SFL training Practice recommendation 3 times per week: • Physical exercises: between 30 to 45 minutes that can be split during the day (e.g. 2x15 or 20 minutes, or 3x10 or 15 minutes during the same day). • Cognitive exercises: minimum of 15 min.	Behavioral: SFL training The SFL training program comprises: • Physical exercises: 50 video exercises to improve balance, muscle strength and physical capabilities in older adults; • Cognitive exercises: Four ludic activities targeting problem solving (4 Images/ 1 word), memory (Quiz and Recall me), speed processing and divided attention (Attention!). In addition, the SFL program includes a series of unique components: • Chat rooms: to share views about topics of interest and tips for common real-life problems; • Psycho-education content: to improve self-management and promoting cognitive transfer though 22 different topics (provide recommendations usually given in psychotherapy sessions); • Virtual coach: to guide participants

Arm	Intervention/treatment
	along the proposed exercises by giving them instructions, reminding them regularly to practice a variety of available activities repeatedly, providing appropriate and timely feedback on participant's performances and rewarding assiduity, perseverance and performance.
Active Comparator: Active control training Practice recommendation 3 times per week: • Physical exercises: between 30 to 45 minutes that can be split during the day (e.g. 2x15 or 20 minutes, or 3x10 or 15 minutes during the same day). • Cognitive exercises: minimum of 15 min.	Behavioral: Active controlled training The active control training program is structured in the same manner as the SFL training program and will also offer different physical and cognitive activities: • Physical exercises: 12 different exercises trains upper and lower extremity strength, mobility and balance offered through a computerized version of a health insurance company physical training program; • Cognitive activities: Four commercially available leisure activities (Sudoku. Cross Words, Pac-Man and Countdown activities) that are appreciated by older adults but do not teach cognitive strategies and are were not designed to improve cognition per se. No chat room, psycho-educational content or virtual coach were included in the active control training program.

Outcome Measures

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Primary Outcome Measures :

1. Timed-Up & Go Test (TUG) [Time Frame: T0 (baseline)]

   To measure lower extremity function, mobility and risk of falls

2. Timed-Up & Go Test (TUG) [Time Frame: T1 (six months following T0)]

   To measure lower extremity function, mobility and risk of falls

Secondary Outcome Measures :

1. Physical domain: Twenty-meter walking test [Time Frame: T0 (baseline)]

   To measure gait speed in sec.

2. Physical domain: Twenty-meter walking test [Time Frame: T1 (six months following T0)]

   To measure gait speed in sec.

3. Physical domain: Five Time Sit to Stand Test (FTSTS) [Time Frame: T0 (baseline)]

   To measure lower extremity strength in sec

4. Physical domain: Five Time Sit to Stand Test (FTSTS) [Time Frame: T1 (six months following T0)]

   To measure lower extremity strength in sec

5. Physical domain: Four Stage Balance Test (FSBT) [Time Frame: T0 (baseline)]

   To measure balance. A total score of 4 is obtained when a participant performs successfully 4 positions (parallel, semi-tandem and tandem). The test is stopped when a participant fails at holding a given position for at least 10 sec.

6. Physical domain: Four Stage Balance Test (FSBT) [Time Frame: T1 (six months following T0)]

   To measure balance. A total score of 4 is obtained when a participant performs successfully 4 positions (parallel, semi-tandem and tandem). The test is stopped when a participant fails at holding a given position for at least 10 sec.

7. Physical domain: motion sensors measures [Time Frame: T0 (baseline)]

   During TUG and 20-m walking test, motion sensors will provide measures on: walking speed, variability in gait, stance phase, foot-flat phase, double support, stride velocity, maximal swing speed, turning angle and variability in toe clearance.

8. Physical domain: motion sensors measures [Time Frame: T1 (six months following T0)]

   During TUG and 20-m walking test, motion sensors will provide measures on: walking

speed, variability in gait, stance phase, foot-flat phase, double support, stride velocity, maximal swing speed, turning angle and variability in toe clearance.

9. Cognitive domain: Global cognition composite score [Time Frame: T0 (baseline)]

   This score is the ZAVEN composite score computed by averaging z-scores from:

   - Total recall of the California Verbal Learning Test (CVLT) and delayed recall of the WMS-IV Logical Memory to measure episodic memory;
   - WAIS-IV Digit Symbol substitution Test (DSST) to measure complex attention;
   - Verbal fluency (VF) to measure executive functions.

10. Cognitive domain: Global cognition composite score [Time Frame: T1 (six months following T0)]

    This score is the ZAVEN composite score computed by averaging z-scores from:

    - Total recall of the California Verbal Learning Test (CVLT) and delayed recall of the WMS-IV Logical Memory to measure episodic memory;
    - WAIS-IV Digit Symbol substitution Test (DSST) to measure complex attention;
    - Verbal fluency (VF) to measure executive functions.

11. Cognitive domain: Memory composite score [Time Frame: T0 (baseline)]

    This score is computed by averaging z-scores from:

    - Delayed recall of the CVLT;
    - Delayed recall of the WMS-IV Logical Memory Test.

12. Cognitive domain: Memory composite score [Time Frame: T1 (six months following T0)]

    This score is computed by averaging z-scores from:

    - Delayed recall of the CVLT;
    - Delayed recall of the WMS-IV Logical Memory Test.

13. Cognitive domain: Executive composite score [Time Frame: T0 (baseline)]

    This score is computed by averaging z-scores from:

    - Verbal fluency (VF);
    - Trail Making Test (condition B - A; shifting - processing speed scores);
    - Victoria Stroop (high interference - naming conditions);
    - Divided attention subtest from the Test of Attention Performance 2.3.1 (number of

total omissions (visual and auditory)).

14. Cognitive domain: Executive composite score [Time Frame: T1 (six months following T0)]

    This score is computed by averaging z-scores from:

    - Verbal fluency (VF);
    - Trail Making Test (condition B - A; shifting - processing speed scores);
    - Victoria Stroop (high interference - naming conditions);
    - Divided attention subtest from the Test of Attention Performance 2.3.1 (number of total omissions (visual and auditory)).

15. Cognitive domain: Speed processing composite score [Time Frame: T0 (baseline)]

    This score is computed by averaging z-scores from:

    - Trail Making Test (time on condition A);
    - DSST (number of correct symbols);
    - Victoria Stroop (time on naming condition).

16. Cognitive domain: Speed processing composite score [Time Frame: T1 (six months following T0)]

    This score is computed by averaging z-scores from:

    - Trail Making Test (time on condition A);
    - DSST (number of correct symbols);
    - Victoria Stroop (time on naming condition).

17. Affective domain: Hospital Anxiety and Depression Scale (HADS) [Time Frame: T0 (baseline)]

    To measure mood.

18. Affective domain: Hospital Anxiety and Depression Scale (HADS) [Time Frame: T1 (six months following T0)]

    To measure mood.

19. Affective domain: Falls Efficacy Scale International (FES-I) [Time Frame: T0 (baseline)]

    To measure fear of falling.

20. Affective domain: Falls Efficacy Scale International (FES-I) [Time Frame: T1 (six months

following T0)]

To measure fear of falling.

21. Psycho-social domain: Older People Quality of Life questionnaire (OPQOL 35). [Time Frame: T0 (baseline)]

    To measure quality of Life (QoL)

22. Psycho-social domain: Older People Quality of Life questionnaire (OPQOL 35). [Time Frame: T1 (six months following T0)]

    To measure quality of Life (QoL)

23. Psycho-social domain: Cognitive Function Instrument (CFI) - [Time Frame: T0 (baseline)]

    To measure subjective difficulties encountered in activities of daily living, related to cognitive functions

24. Psycho-social domain: Cognitive Function Instrument (CFI) - [Time Frame: T1 (six months following T0)]

    To measure subjective difficulties encountered in activities of daily living, related to cognitive functions

25. Psycho-social domain: Everyday Cognition (E-Cog) [Time Frame: T0 (baseline)]

    To measure subjective difficulties encountered in activities of daily living, related to cognitive functions

26. Psycho-social domain: Everyday Cognition (E-Cog) [Time Frame: T1 (six months following T0)]

    To measure subjective difficulties encountered in activities of daily living, related to cognitive functions

27. Psycho-social domain: Ad-hoc questionnaire [Time Frame: T0 (baseline)]

    To measure participant's expectation from the training program. The questionnaire is related to the efficacy of the program and its different components, the expectation (difficulty, agreeableness, motivation) and the quality of the introductory courses.

28. Psycho-social domain: Ad-hoc questionnaire [Time Frame: T1 (six months following T0)]

    To measure participant's expectation from the training program. The questionnaire is related to the efficacy of the program and its different components, the expectation (difficulty, agreeableness, motivation) and the quality of the introductory courses.

29. Cognitive processes manipulated during training: ad-hoc computerized test
[Time Frame: T0 (baseline)]

    To measure divided attention trained during Attention! activity with an ad-hoc computerized test designed specifically for this multitasking activity and provided in the form of a serious game.

30. Cognitive processes manipulated during training: ad-hoc computerized test
[Time Frame: T1 (six months following T0)]

    To measure divided attention trained during Attention! activity with an ad-hoc computerized test designed specifically for this multitasking activity and provided in the form of a serious game.

31. Cognitive processes manipulated during training: Rivermead Behavioural Memory Test - Third edition (RBMT-3). [Time Frame: T0 (baseline)]

    To measure prospective memory trained in the Quiz activity with two subtests ("belonging" and "appointment")

32. Cognitive processes manipulated during training: Rivermead Behavioural Memory Test - Third edition (RBMT-3). [Time Frame: T1 (six months following T0)]

    To measure prospective memory trained in the Quiz activity with two subtests ("belonging" and "appointment")

33. Cognitive processes manipulated during training: Flexibility subtest from the Test battery for Attention Performance [Time Frame: T0 (baseline)]

    To measure concept elaboration trained in the 4images/1 word activity with a "set shifting" computerized task

34. Cognitive processes manipulated during training: Flexibility subtest from the Test battery for Attention Performance [Time Frame: T1 (six months following T0)]

    To measure concept elaboration trained in the 4images/1 word activity with a "set shifting" computerized task

35. Cognitive processes manipulated during training: Similitudes subtest from the WAIS-IV:
[Time Frame: T0 (baseline)]

    To measure concept elaboration trained in the 4images/1 word activity and assess verbal reasoning and the development of concepts.

36. Cognitive processes manipulated during training: Similitudes subtest from the WAIS-IV: [Time Frame: T1 (six months following T0)]

    To measure concept elaboration trained in the 4images/1 word activity and assess verbal reasoning and the development of concepts.

Other Outcome Measures:

1. Effects of moderators on primary and secondary outcomes: Age [Time Frame: Age measured within a month prior to the start of the intervention]

    To see the influence of age on primary and secondary outcomes using 2 age groups defined by the median

2. Effects of moderators on primary and secondary outcomes: Sex [Time Frame: Sex measured within a month prior to the start of the intervention]

    To see the influence of sex on primary and secondary outcomes using 2 sex groups (male and female)

3. Effects of moderators on primary and secondary outcomes: Education [Time Frame: Education measured within a month prior to the start of the intervention]

    To see the influence of education on primary and secondary outcomes using 2 education groups (less or more than 12 years)

Eligibility Criteria

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Information from the National Library of Medicine NIH NLM

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the contacts provided below. For general information, Learn About Clinical Studies.

Ages Eligible for Study:	60 Years to 100 Years (Adult, Older Adult)
Sexes Eligible for Study:	All
Accepts Healthy Volunteers:	Yes

Criteria

Inclusion Criteria:

- Fluent french speaker adults
- Retired, living at home and having a wireless Internet connection in their house;
- Independent for all daily activities (optimal score to the 4-IADL);
- Open to the use of new technologies and electronic tablets;
- Interested in exercising to stay fit;
- Able to walk without a walking aid (e.g. wheelchair, sticks, walker, etc.);
- Available to commit themselves for the time period during which the study takes place;
- No vision deficits that would prevent them to read information on a tablet;
- No current neurological or psychiatric diagnosis (e.g. Parkinson's disease).

Exclusion Criteria:

- MoCA score < 26;
- score ≥ 3 on the Fried's frailty index (Fried et al., 2001)

Contacts and Locations

Go to

Information from the National Library of Medicine NIH NLM

To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.

Please refer to this study by its ClinicalTrials.gov identifier (NCT number): ***NCT04237519***

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Principal Investigator: Stefan Agrigoroaei, PhD

Canada, Quebec

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Mindmaze SA

Université Catholique de Louvain

Active and Assisted Living Programme

BRUSANO

Pro-Senectute Vaud

Investigators

Principal Investigator:	Jean-François Demonet, MD, PhD	Centre Hospitalier Universitaire Vaud
Principal Investigator:	Sylvie Belleville, PhD	Institut universitaire de gériatrie de M
Principal Investigator:	Stefan Agrigoroaei, PhD	Université Catholique de Louvain

More Information

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Publications:

Fried LP, Tangen CM, Walston J, Newman AB, Hirsch C, Gottdiener J, Seeman T, Tracy R, Kop WJ, Burke G, McBurnie MA; Cardiovascular Health Study Collaborative Research Group. Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci. 2001 Mar;56(3):M146-56.

Publications automatically indexed to this study by ClinicalTrials.gov Identifier (NCT Number):

Belleville S, Cuesta M, Bieler-Aeschlimann M, Giacomino K, Widmer A, Mittaz Hager AG, Perez-

Marcos D, Cardin S, Boller B, Bier N, Aubertin-Leheudre M, Bherer L, Berryman N, Agrigoroaei S, Demonet JF. Rationale and protocol of the StayFitLonger study: a multicentre trial to measure efficacy and adherence of a home-based computerised multidomain intervention in healthy older adults. BMC Geriatr. 2020 Aug 28;20(1):315. doi: 10.1186/s12877-020-01709-2.

Responsible Party:	Jean-François Démonet, Professor, University of Lausanne Hospitals
ClinicalTrials.gov Identifier:	NCT04237519 History of Changes
Other Study ID Numbers:	aal-call-2017-068
First Posted:	January 23, 2020 Key Record Dates
Last Update Posted:	January 23, 2020
Last Verified:	January 2020

Individual Participant Data (IPD) Sharing Statement:

Plan to Share IPD:	Undecided

Studies a U.S. FDA-regulated Drug Product:	No
Studies a U.S. FDA-regulated Device Product:	No

Keywords provided by Jean-François Démonet, University of Lausanne Hospitals:

- Multimodal intervention
- Cognitive training
- Physical training
- Social interactions
- Prevention
- Frailty

Additional relevant MeSH terms:

- Cognitive Dysfunction
- Cognition Disorders
- Neurocognitive Disorders
- Mental Disorders

Clinical Study Protocol

StayFitLonger. Preventive effects of a combination of non-drug interventions (physical, cognitive and social) in healthy elderly subjects: multicentre randomised controlled trial.

StayFitLonger (SFL)

Study Type:	Clinical trial with interventions that are neither a therapeutic product nor a transplant product, nor a transplant
Study Categorisation:	Risk category according to HRA: A
Study Registration:	Will be as "StayFitLonger" in ClinicalTrial.gov and in Swiss National Clinical Trials Portal (SNCTP) as soon as the ethics committee has approved this present protocol.
Study Identifier:	2017-068 (AAL number), Prof. Antoine Widmer is the international sponsor/promoteur (Haute Ecole Spécialisée de la Suisse occidentale - HES-SO Valais/Wallis)
Sponsor, Sponsor-Investigator or Principal Investigator in Switzerland:	Prof. Dr Jean-François Démonet, Neurologe, MD, PhD Chef de Service - Directeur du Centre Leenaards de la Mémoire - CHUV Département des neurosciences cliniques Bureau MP16 05/518 Rue du Mont-Paisible 16, Cité Hospitalière CHUV CH-1011 Lausanne Jean-Francois.Demonet@chuv.ch +41 21 314 97 19
Investigational Product:	StayFitLonger: an integrated platform for healthy aging at home
Protocol Version and Date:	Version 2_16.11.2018

CONFIDENTIAL

Signature Page(s)

Study number	Not yet registered
Study Title	Comparison of two Android applications for healthy elderly subjects: protocol for a multi-centre randomised controlled trial.

The study statistics will be compiled by the SFL project supervision committee, including Sylvie Belleville, Jean-François Démonet and Mélanie Bieler.

The Sponsor-Investigator and project supervision committee have approved the protocol Version 2_16.11.2018, and hereby confirm to conduct the study according to the protocol, the current version of the World Medical Association Declaration of Helsinki, the ICH-GCP guidelines or ISO 14155 norm, if applicable, and the local legally applicable requirements.

Promotor and sponsor of the international project: Dr Antoine Widmer

Place/Date	Signature

Sponsor-Investigator in Switzerland: Prof. Dr Jean-François Démonet

Place/Date	Signature

Trial statistician: Project supervision committee, Melanie Bieler-Aeschlimann

Place/Date	Signature

Local Principal Investigator at study site*:
I have read and understood this trial protocol and agree to conduct the trial as set out in this study protocol, the current version (Version 2_16.11.2018) of the World Medical Association Declaration of Helsinki, the ICH-GCP guidelines or ISO 14155 norm and the local legally applicable requirements.

Site	Centre Leenaards de la Mémoire - CHUV Département des neurosciences cliniques Bureau MP16 05/518 Rue du Mont-Paisible 16, Cité Hospitalière CHUV CH-1011 Lausanne
Principal Investigator in Switzerland	Prof. Dr Jean-François Démonet, Neurologe, MD, PhD

Place/Date	Signature

**Note:* In multi-centre studies, this page must be individually signed by all participating Local Principal Investigators.

Site	Centre de recherche, IUGM

4545 chemin Queen-Mary
Montréal, Québec
Canada H3W 1W5

Principal Investigator in Canada	Sylvie Belleville, PhD

Place/Date | Signature

**Note:* In multi-centre studies, this page must be individually signed by all participating Local Principal Investigators.

TABLE OF CONTENTS

STUDY SYNOPSIS

Sponsor / Sponsor-Investigator in Switzerland	Prof. Dr Jean-François Démonet
Study Title:	**English version**: Preventive effects of a combination of non-drug interventions (physical, cognitive and social) in healthy elderly subjects: multicentre randomised controlled trial. **French version**: Les effets préventifs d'une association d'interventions non médicamenteuses (physique, cognitive et sociale) chez le sujet âgé en bonne santé: essai randomisé contrôlé multicentrique.
Short Title / Study ID:	StayFitLonger (SFL)
Protocol Version and Date:	Version 2_16.11.2018
Trial registration:	Trial be registered as "StayFitLonger" in ClinicalTrial.gov and in SNCTP as soon as the ethics committee will approve the present protocol. Registration number: to be defined. Date: to be defined.
Study category and Rationale	Study category A. The integrated platforms with physical and cognitive exercises will be tested in healthy older people, as preventive action to keep their functional capabilities as long as possible.
Clinical Phase:	Phase of development
Background and Rationale:	The *retentions of physical and cognitive activity* are amongst the modifiable factors that can protect seniors from deleterious effects of aging (Norton, Matthews, Barnes, Yaffe, & Brayne, 2014). ● *Physical activity* has a positive effect both on body homeostasis and brain functions by having a mild effect on cognitive functions (Seematter-Bagnoud, Lenoble-Hoskovec, Santos-Eggimann, & Bula, 2012; Sofi et al., 2011). ● The FINGER study also showed cognitive improvement after a 2-year multidomain intervention of diet, physical, cognitive and social interaction training supplied by vascular risk monitoring (Ngandu et al., 2015).

	● *Staying cognitively active* (i.e. exercising stimulating intellectual activities) seems to play an important role, especially when undertaken in a social frame (social activities being a third factor of protection against neurodegenerative disease –(Fratiglioni, Paillard-Borg, & Winblad, 2004). A home solution that integrates both physical and cognitive exercises and reinforces social connections in seniors, including the vulnerable elderly population, is the scope of the StayFitLonger solution.
Objective(s):	The first aim of the study is to compare the effect of two home-based exercise programmes: ● an experimental training composed of an intermix of self-management physical exercises, strategic cognitive learning and on-line guidance with a virtual coach ● an alternative training composed of Helsana programme and some commercial casual cognitive games, in healthy older adults. Therefore, there are two objectives: ● The first objective is to demonstrate the efficacy of the experimental training and its higher benefice compare to the alternative training. ● The second objective of this study is to check whether subject adhere to the experimental training.
Outcome(s):	**Concerning the RCT (over 6 months) - First part of our study** The ***primary outcome***: functional capabilities measured with the Time-Up & Go Test (TUG) (see chapter 5.1.1). The ***secondary outcomes*** are subdivided into 4 domains: physical capacities; global cognition and a set of cognitive sub-processes; affective abilities; specific associated domains (quality of life, daily livings activities (ADL), and expectation from the programme). **1. Physical capacities** will assess the mobility, strength and balance (see chapter 5.2) **2. Cognitive global abilities and its sub-processes** will assess (see chapter 5.2 for details): 2.1 *A global cognition score* (ZAVEN). and specific cognitive tests exploring cognitive sub-components: 2.2 *Memory* 2.3 *Executive & attentional functions* 2.4 *Speed processing* **3. Affective ability** will assess: 3.1 *Mood*

	3.2 *Fear of falling* **4. Specific associated domains** will be assessed with: 4.1 The *Quality of Life* (QoL) 4.2 The *daily living activities (ADLs)* 4.3 The *expectations* on the physical and cognitive programme. **Concerning the longitudinal design (over 12 months) - Second part of our study** The ***primary outcome*** is AAL main interest, i.e. the adherence to the experimental training. It will be measured by monitoring the dose of training (time spent and regularity of training). The ***secondary outcomes*** are aiming at relying, for each individual, its adherence profiles and its relationship with the efficacy of the training performed over periods of 6 months. Some survey will provide additional knowledge on the way subjects will use and appreciate the experimental training: ● The *subject technological and gaming habits* ● The *user experience of the device* ● The *feasibility and acceptability* of the device ● The *final feedback* on StayFitLonger intervention.
Study design:	This multinational study is a combination of: ● A randomised controlled trial (double blind, with two training groups) over 6 months AND ● an observational study over 12 months.
Inclusion / Exclusion criteria:	*Inclusion criteria*: ● Retired seniors of 60+ years old ● Living at home and independent ● Ready to invest time for 1 year ● Open-minded to new technology and interested in exercising to stay fit *Exclusion criteria* (see chapter 7.1 for details): - MoCA < less than 26 - Fried's frailty criterion ≥ 3.
Measurements and procedures:	**First part of the study: RCT over 6 months:** ● RCT design: Time (2) x Intervention (2) ● Double-blind study (subjects are blind to the training as well as assessors). ● Randomisation: allocation to one of the two training conditions:

	- Half of the subject will have StayFitLonger training programme. - Half of the subject will have an alternative (control) training programme. ● Stratification: subjects will be stratified across their physical vulnerability into robust (Fried = 0) and pre-frail (Fried = 1 or 2). ● Measurements will be performed on three time points (at baseline = T0, after 6 months = T1, after 12 months = T2. ● Group A (StayFitLonger training) and group B (alternative or control training) will receive 10 hours of training in group session to learn how to use a tablet and their allocated training. ● For the physical part: participants will be recommended to train 3 times a week between 30-45 minutes that can be split during the day (e.g. 2x15 or 20 minutes, or 3x10 or 15 minutes during the same day). ● For the cognitive part: participant will be recommended to train 3 times a week between 10-15 minutes. ● Monitoring: trainers (physiotherapist and neurologist) will perform one home visit each and 5 phone calls each along the first six months. Second part of the study: longitudinal exploration of adherence to the experimental training ● After 6 months, Group B will also receive the StayFitLonger training with the same intensity of monitoring. Groupe A will continue their training with less monitoring.
Study Product / Intervention:	The StayFitLonger propose an integrated information and communication technology (ICT) platform with an intermix of programme of ecological (simple drawings of living rooms) video-based physical training, a component in process for validation in randomised controlled trial in Switzerland (Swiss CHEF Trial) (Mittaz Hager, Mathieu, & Hilfiker). The target of the physical exercises is to improve gait and to maintain strength, which are well known to play a crucial role in preventing falls and keeping autonomy. Additionally, the platform will have a set of cognitive, social and combined physio-cognitive exercises. The cognitive training is based on providing exercises to improve some facets of memory (prospective memory, concept memory and paired-associate learning), of executive functions (flexibility, inhibition, planning and decision making) and of attentional skills (selective and divided attention) that will be trained in serious games implemented on the platform. Some of the games will be played in dual task during the physical training. A social component will be added by annexing a guide (or virtual coach)

	to drive the seniors' motivation and to dispense some instructions for optimising their training. Furthermore, another social component will be addressed through the opportunity to share interests, to cooperate or to compete against one another in a selection of these serious games. The device provided to the end-user will consist in a tablet. To increase motivation, activities need to be ludic and in adequacy with the expectations of a senior end-user. This will be achieved by giving personalised settings to tailor the environment to the end-user's tastes and wishes (i.e. cooking tasks, following daily news, answering phone call). The cognitive training itself will be monitored to provide a feedback of the end-user's performances. Relevant rewards (using multisensory and/or emotional stimuli) and strategic recommendations (i.e. ways to improve) will be given by a virtual guide. The main goal of the virtual coach is to guide the end-user along the proposed exercises in order to favour support to improve adherence. The implementation of the "StayFitLonger" exercise programme will take place during four sessions of group teaching, two home visits and 10 phone calls.
Control training (if applicable):	The alternative training (AT) will also receive a home-based exercise programme on a tablet to rule out technology as confounding factor. The AT will receive a physical programme created by the Helsana insurance company to improve physical condition. In particular, the Helsana programme provides physical exercises, however in a much less ecological way than the SFL programme. A digitised version of that programme will be provided in PDF format. On the cognitive side, the participants will be advised to train with causal computerised cognitive games (e.g. crosswords, hidden word, solitary, categorisations, Pac-Man, ...). These games engage the same memory, attentional and executive functions but are not considered to be cognitively-stimulating and do not provide strategies. Subjects will be advised to train as suggested in the Helsana programme and the same recommendations as the ET will be followed for the cognitive programme.
Number of Participants with Rationale:	To achieve our objectives, the sample size calculation estimates 128 subjects. We calculated the sample with the Marker Stratified Designs method as we will stratify the groups between robust and pre-frail with the Fried phenotype (more details are given in chapter 11.2). Canada will include 32 subjects, 16 in the ET and 16 in the AT. In Belgium will include 32 subjects, 16 in the ET and 16 in the AT. Finally, Switzerland will include 64 subjects, 32 will be in the ET and 32 in the AT.

Study Duration:	The study duration is 18 months in total. Subjects will be recruited over a period of 3 months and involved in the study for more than a year (about 15 months). The 6 first months is the RCT study and after the 6 months, the group B will do the same intervention as group A and both groups will continue the training over another 6 months which is what we call the longitudinal study (see below).
Study Schedule:	March 2018-February 2019: Android platform development, ethical protocol writing and submission, study preparation (CRFs, recruitment, institution information, physiotherapists and neuropsychologists teaching, coordination between Canada and Belgium) January-May 2019: Screening February-May 2019: First assessment March-June: Training (planned) End of May 2019: Last Participant-In (planned) Middle July 2020: Last Participant-Out (planned) January 2020: Start of the RCT analysis June 2019-August 2020: RCT: Data analysis, publication redaction August 2020: Longitudinal: Data analysis, publication redaction
Investigator(s):	Principal investigator in Switzerland: Prof. Dr Jean-François Démonet, Neurologe, MD, PhD Chef de Service - Directeur du Centre Leenaards de la Mémoire - CHUV Département des neurosciences cliniques Bureau MP16 05/518 Rue du Mont-Paisible 16, Cité Hospitalière CHUV CH-1011 Lausanne e-mail: Jean-Francois.Demonet@chuv.ch Phone number : +41 21 314 97 19 Co-Investigators in Switzerland: Dr Mélanie Bieler-Aeschlimann (PhD) Centre Leenaards de la Mémoire (CLM) Dép. des Neurosciences Cliniques du CHUV Mont-Paisible 16 CH-1011 Lausanne email: melanie.bieler-aeschlimann@chuv.ch, Phone number: +41 79 556 67 18 Prof. Anne-Gabrielle Mittaz Hager (PhD cand.) HES-SO Valais-Wallis Department of physiotherapy Rathausstrasse 8 3954 Leukerbad, email: gaby.mittaz@hevs.ch,

	phone number: +41 79 609 90 63
Study Centre(s):	Multi-national study in 3 countries (Switzerland, Canada, Belgium)
Statistical Considerations:	Descriptive statistics will first be used to describe the sample main characteristics (mean, standard deviation, …). *RCT study statistics*. Then a modified intention-to treat (mITT) analysis will be performed to assess efficacy of the intervention. An effect will be supported for each outcome taken individually if the interaction is significant and if POST change score is larger in the intervention than the alternative group. All analyses will be adjusted for sex, age, and education. *Longitudinal study statistics*. Descriptive statistics will be used to assess adherence to the intervention. It will be restricted to per-protocol subjects. Details of the statistical plan methodology can be found in chapter 11.
GCP Statement:	This study will be conducted in compliance with the protocol, the current version of the Declaration of Helsinki, the ICH-GCP or ISO EN 14155 (as far as applicable), as well as all national legal and regulatory requirements.

ABBREVIATIONS

4-IADL	Alzheimer Cognitive Composite
ADCS-PACC	modified version of the Preclinical Alzheimer Cognitive Composite
ADCS-PACC	-Preclinical Alzheimer Cognitive Composite
AE	Adverse Event
AGMH	Anne-Gabrielle Mittaz Hager
AP	Alexandre Pineaud
AT	Alternative training
AW	Antoine Widmer
BASEC	Business Administration System for Ethical Committees, (https://submissions.swissethics.ch/en/)
BLM	Benedetta Leidi-Maimone
CA	Competent Authority (e.g. Swissmedic)
CEC	Competent Ethics Committee
CFI	Cognitive Function Instrument
CHEF	Comparison of home-based exercise programmes for falls prevention and quality of life in older people
CHUV	Centre Hospitalier Universitaire Vaudois
CI	Confidence Interval
CIUSSS	Centre intégré universitaire de santé et de services sociaux
ClinO	Ordinance on Clinical Trials in Human Research (in German: KlinV, in French: OClin, in Italian: OSRUm)
CLM	Centre Leenaards de la Mémoire
CPG	Good Clinical Practice
CRF	Case Report Form
CT	Control Therapy
CTCAE	Common terminology criteria for adverse events
CVLT	California Verbal Learning Test
DPM	Daniel Perez-Marcos
DSST	Digit Symbol substitution Test

DSUR	Development safety update report
E-Cog	Everyday Cognition
EC	Ethic Committee
eCRF	Electronic Case Report Form
ET	Experimental training
EU	European
FCSRT - 48 words	Free and Cued Selective Reminding Test
FR	Functional Reach test
FSBT	Four Stage Balance Test
FTSTS	Five Time Sit to Stand
GCP	Good Clinical Practice
H1	Alternative hypothesis
HADS	Hospital Anxiety and Depression Scale
HES- SO	Haute Ecole Spécialisée de la Suisse occidentale
Ho	Null hypothesis
HRA	Federal Act on Research involving Human Beings (in German: HFG, in French: LRH, in Italian: LRUm)
IB	Investigator's Brochure
ICT	Information and Communication Technology
IIT	Investigator-initiated Trial
IMP	Investigational Medicinal Product
ISO	International Organisation for Standardisation
ITT	Intention to treat
JFD	Jean-François Démonet
KG	Katia Giacomino
MBA	Mélanie Bieler-Aeschlimann
MC	Marc Cuesta
MCI	Mild cognitive impairment (MCI)
MD	Medical Device
MedDO	Medical Device Ordinance (in German: MepV, in French: ODim)

MEM - story	The logical Memory IIa subtest from the Wechsler Memory Scale
MMSE	Mini–Mental State Examination
MOCA	Montreal Cognitive Assessment
OPQOL-35	Older People Quality of Life questionnaire
PI	Principal Investigator
PV	Pia Vandebergh
QoL	Quality of Life
RBMT-3	Rivermead Behavioural Memory Test – Third Edition
RCT	Randomised controlled trial
REDCap	Research Electronic Data Capture
SB	Sylvie Belleville
SC	Sylvain Cardin
SD	Standard deviation
SDV	Source Data Verification
SFL	StayfitLonger
SG	Stéphane Gobron
SNCTP	Swiss National Clinical Trials Portal
SOP	Standard Operating Procedure
SPC	Summary of product characteristics
STEADI	Stopping Elderly Accidents, Deaths & Injuries
SUSAR	Suspected Unexpected Serious Adverse Reaction
T&E	Test-and-Exercise Home-based Programme
T0	First evaluation
T1	Second evaluation
T2	Third evaluation
TAP	Test battery for Attention Performance
TAP	Test battery for Attention Performance
TGP	Thomas Genoud-Prachex
TJ	Tania Javaux
TMF	Trial Master File

TMT	Trail Making Test
VD	Vaud
VF	Verbal fluency
VS	Victoria Stroop
WAIS-VI	Wechsler Adult Intelligence Scale-VI
WHOQOL-OLD	World Health Organization Quality of Life
WMS-IV	Wechsler Memory Scale-IV
ZAVEN	Z-Scores of Attention, Verbal fluency and Episodic memory for Nondemented older adults

STUDY SCHEDULE

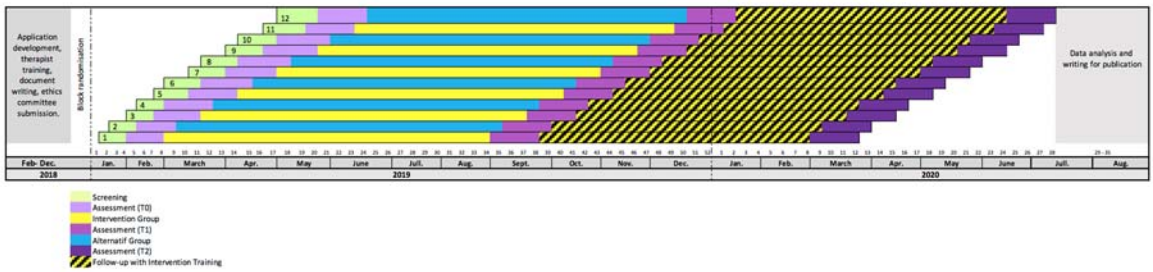


Figure 1: Study schedule

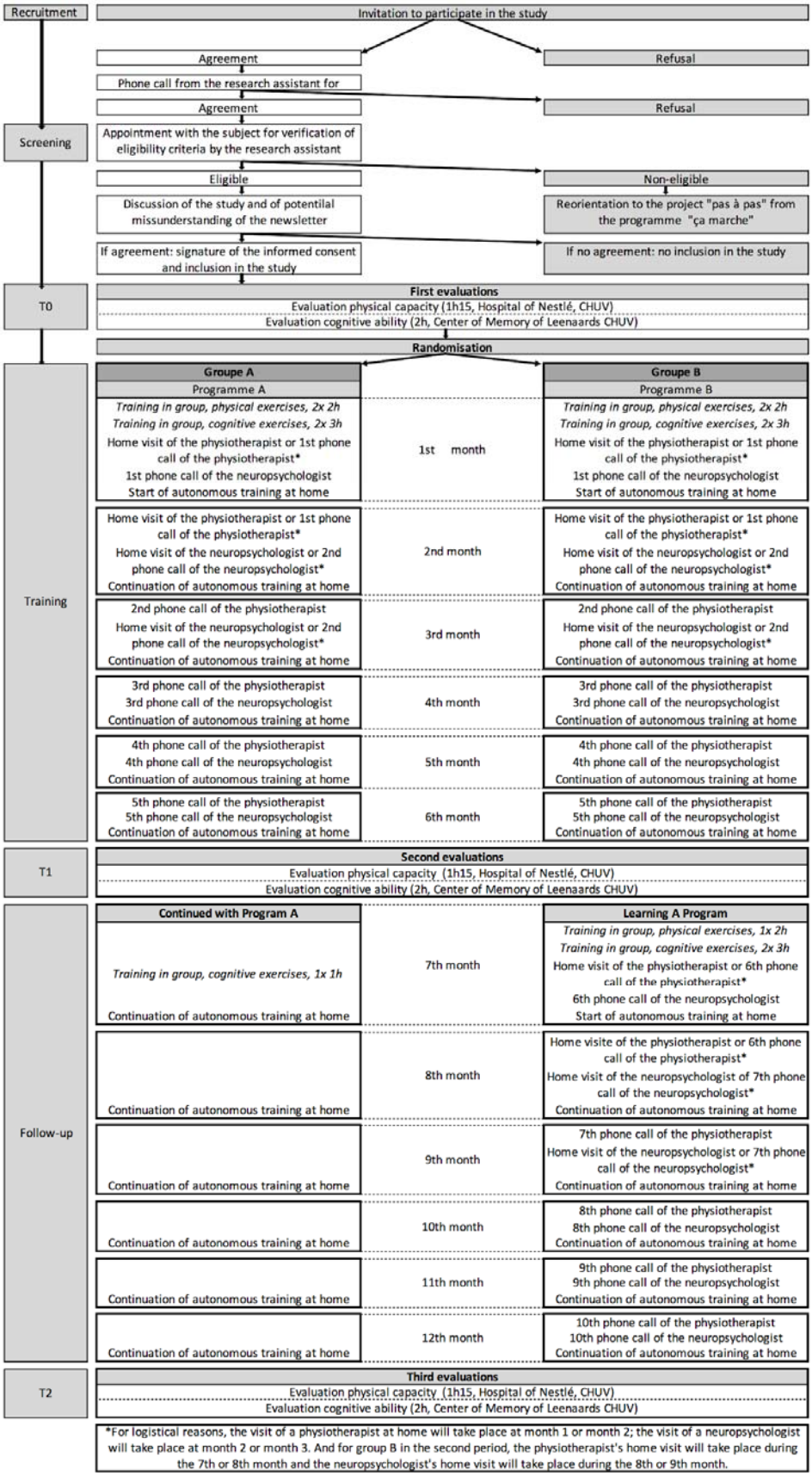


Figure 2: Participant Timeline

1. STUDY ADMINISTRATIVE STRUCTURE

Steering committee	Prof. Dr Jean-François Démonet (JFD)	Investigator	Principal investigator and statistician supervisor in Switzerland	Directeur du Centre Leenaards de la Mémoire – CHUV, Département des neurosciences cliniques, Bureau MP16 05/518, Rue du Mont-Paisible 16, Cité Hospitalière CHUV CH-1011 Lausanne, email: Jean-Francois.Demonet@chuv.ch, tel.: +41 21 314 97 19.
	Dr Mélanie Bieler-Aeschlimann (MBA)	Co-investigator	Clinical study coordination (for Switzerland) and participation in statistics	Centre Leenaards de la Mémoire (CLM), Dép. des Neurosciences Cliniques du CHUV, Mont-Paisible 16, CH-1011 Lausanne, email: melanie.bieler-aeschlimann@chuv.ch, tel.: +41 79 556 67 18.
	Prof. Anne-Gabrielle Mittaz Hager (AGMH)	Co-investigator	Clinical expert	HES-SO Valais-Wallis, Rathausstrasse 8, 3954 Leukerbad, email: gaby.mittaz@hevs.ch, tel.: +41 79 609 90 63.
	Prof. Antoine Widmer (AW)	Member	International sponsor/promotor, and Fund raising	HES-SO Valais-Wallis, TechnoArk, Techno-Pôle 3, 3960 Sierre, email: antoine.widmer@hevs.ch, tel.: +41 27 606 90 78
	Sylvie Belleville (SB), PhD	Member	Investigator in Canada and Statistician supervisor	Centre de recherche de l'Institut Universitaire de gériatrie de Montréal CIUSSS du Centre-Sud-de-l'Île-de-Montréal 4565, Chemin Queen-Mary

				Montréal (Québec) H3W 1W5; email: Sylvie.Bellevielle@criugm.qc.ca tel.: +1 514 340 3540
	Marc Cuesta (MC)	Member	Project Manager in Canada	Centre de recherche de l'Institut Universitaire de gériatrie de Montréal CIUSSS du Centre-Sud-de-l'Île-de-Montréal 4565, Chemin Queen-Mary, Montréal (Québec) H3W 1W5; email: marc.cuesta@criugm.qc.ca, tel.: +1 514 340 3540.
	Pia Vandebergh (PV)	Member	Investigator in Belgium	Belgique vzw Conectar asbl Verenigingstraat, 15, rue de l'Association Brussel 1000 Bruxelles, email: pvandebergh@conectar.brussels
Data management team	Tania Javaux (TJ)	Executive secretary of Prof. J.-F. Démonet	Redcap checker + secretary work (not blind)	Centre Leenaards de la Mémoire (CLM), Dép. des Neurosciences Cliniques du CHUV, Mont-Paisible 16, CH-1011 Lausanne, email: tania.javaux@chuv.ch, tel.: +41 21 314 0509
Therapist in contact with participants	Thomas Genoud-Prachex (TGP)	Neuropsychologist (CHUV)	Neuropsychology assessment (blind) in Switzerland	Centre Leenaards de la Mémoire (CLM), Dép. des Neurosciences Cliniques du CHUV, Mont-Paisible 16, CH-1011 Lausanne, email : laura.manzoni@chuv.ch

	Katia Giacomino (KG)	Member	Protocol writing and CEC application and Physiotherapeutic assessor (blind) in Switzerland	HES-SO Valais-Wallis, Rathausstrasse 8, 3954 Leukerbad, email: katia.giacomino@hevs.ch
	Benedetta Leidi-Maimone (BLM)	Research assistant (CHUV)	Contact, screening, following (blind) in Switzerland	Centre Leenaards de la Mémoire (CLM), Dép. des Neurosciences Cliniques du CHUV, Mont-Paisible 16, CH-1011 Lausanne, email: Benedetta.Leidi-Maimone@chuv.ch
	Alexandre Pineaud (AP)	Scientific mediator (CHUV)	Training subjects on ET & AT (not blind) in Switzerland	Centre Leenaards de la Mémoire (CLM), Dép. des Neurosciences Cliniques du CHUV, Mont-Paisible 16, CH-1011 Lausanne, email: Alexandre.Pinault@chuv.ch
Developer team	Sylvain Cardin (SC)	VR Product Manager	Coordinate development team in Switzerland	Chemin de Roseneck 5, CH-1006 Lausanne, email: sylvain.cardin@mindmaze.ch
	Daniel Perez-Marcos (DPM)	Senior Scientist at MindMaze	Technical Coordinator SFL in Switzerland	Chemin de Roseneck 5, CH-1006 Lausanne, email: daniel.perez@mindmaze.ch
	Stéphane Gobron (SG)	Senior Engineer	Coach Developpement in Switzerland	Haute Ecole Arc / hes-so Espace de l'Europe 11 CH-2000 Neuchatel, Switzerland, email: stephane.gobron@he-arc.ch

Figure 3: Study administrative structure.

1.1 Sponsor, Sponsor-Investigator

The principal sponsor of this trial in Switzerland is Prof. Dr Jean-François Démonet. He is the lead of the steering committee, supervises the protocol writing, the data management team and coordinates the scientific part with Belgium and Canada.
Prof. Dr Jean-François Démonet, Neurologue, MD, PhD, Chef de Service - Directeur du Centre Leenaards de la Mémoire – CHUV, Département des neurosciences cliniques, Bureau MP16 05/518, Rue du Mont-Paisible 16, Cité Hospitalière CHUV
CH-1011 Lausanne, Jean-Francois.Demonet@chuv.ch, tel.: +41 21 314 97 19.

1.2 Principal Investigator(s)

The sponsor is also the principal investigator of this trial in Switzerland.
In addition, there are two co-investigators, namely:
Co-Investigators:
Dr Melanie Bieler-Aeschlimann (PhD). Centre Leenaards de la Mémoire (CLM), Dép. des Neurosciences Cliniques du CHUV, Mont-Paisible 16, CH-1011 Lausanne, email: melanie.bieler-aeschlimann@chuv.ch, tel.: +41 79 556 67 18.

Prof. Anne-Gabrielle Mittaz Hager (PhD cand.), HES-SO Valais-Wallis, Rathausstrasse 8, 3954 Leukerbad, email: gaby.mittaz@hevs.ch, tel.: +41 79 609 90 63.

1.3 Statistician ("Biostatistician")

The study statistics will be compiled by the SFL project supervision committee, including Sylvie Belleville, Jean-François Démonet and Mélanie Bieler-Aeschlimann.

Dr. Melanie Bieler-Aeschlimann, Centre Leenaards de la Mémoire (CLM), Dép. des Neurosciences Cliniques du CHUV, Mont-Paisible 16, CH-1011 Lausanne, email: melanie.bieler-aeschlimann@chuv.ch, tel.: +41 79 556 67 18.

Sylvie Belleville, Ph. D., Centre de recherche de l'Institut Universitaire de gériatrie de Montréal, CIUSSS du Centre-Sud-de-l'Île-de-Montréal 4565, Chemin Queen-Mary, Montréal (Québec), H3W 1W5; email: Sylvie.Bellevielle@criugm.qc.ca, tel.: +1 514 340 3540.

Prof. Dr Jean-François Démonet, Neurologue, MD, PhD, Chef de Service - Directeur du Centre Leenaards de la Mémoire – CHUV, Département des neurosciences cliniques, Bureau MP16 05/518, Rue du Mont-Paisible 16, Cité Hospitalière CHUV
CH-1011 Lausanne, Jean-Francois.Demonet@chuv.ch, tel.: +41 21 314 97 19.

1.4 Laboratory

Not applicable.

1.5 Monitoring institution

The monitoring institution is the Department of neuroscience: Département des Neurosciences Cliniques du CHUV, Mont-Paisible 16, CH-1011.

1.6 Data Safety Monitoring Committee

The clinical data of the participant will be registered in the REDCap during the trial and stay under the responsibility of CHUV. The technical data will be hosted by HES-SO servers. After the trial, the clinical data collected will be backed up and remain at CHUV and the technical data (such as games scores, quiz created by users) will be hosted by HES-SO Valais-Wallis for ten years.

A data and safety monitoring board are not necessary in this type of study.

1.7 Any other relevant Committee, Person, Organisation, Institution

The trial is an international, one collaborating with the geriatrics institute of Montréal (Centre de recherche, IUGM 4545, chemin Queen-Mary, Montréal, Québec, Canada H3W 1W5) and the Conectar centre in Brussels (Conectar asbl**,** avenue Josse Goffin 180, 1082 Bruxelles, Belgium).
Canada will submit a protocol to the Quebec ethics committee for this project (Comité central d'éthique de la recherche 500, rue Sherbrooke Ouest, Montréal (QC) H3A 3C6 and Belgium will also submit their protocol to their ethics committee (Eurostation II, Place Victor Horta, 40 bte 10, 1060 Bruxelles, Belgium).

2. ETHICAL AND REGULATORY ASPECTS

The decision of the CEC and Swissmedic/foreign competent authority concerning the conduct of the study will be made by writing to the Sponsor-Investigator before the commencement of this study. The clinical study can only begin once the approval from all required authorities has been received. Any additional requirements imposed by the authorities shall be implemented.

2.1 Study registration

This trial will be register in the Swiss National Clinical Trials Portal database SNCTP and in ClinicalTrials.gov once accepted by the CEC.

2.2 Categorisation of study

Considering the Risk analysis for Risk-Adapted Monitoring from the Swiss clinical trial organisation, this trial comes under Category A (See Appendix 4: Risk Analysis for Risk-Adapted Monitoring_V1).

2.3 Competent Ethics Committee (CEC)

This study will take place in Lausanne (Vaud), Québec and Belgium. The Competent Ethics Committee (CEC) for this international study is the "commission d'éthique de la recherche sur l'être humain Vaud (CER-VD)." Our partners in Quebec and Belgium will comply with their local Ethical Committee organisation.

2.4 Competent Authorities (CA)

Not applicable.

2.5 Ethical Conduct of the Study

The study will be carried out in accordance with the protocol and with principles enunciated in the current version of the Declaration of Helsinki, the guidelines of Good Clinical Practice (GCP) issued by ICH, in case of medical device: the European Regulation on medical devices 2017/745 and the ISO 14155 and ISO 14971 Norms, the Swiss Law and Swiss regulatory authority's requirements. The CEC and regulatory authorities will receive annual safety and interim reports and be informed about study stop/end in agreement with local requirements.
The "Institut de gériatrie de Montréal" and the "Institute of Conectar" will also carry out the study in accordance with the protocol with principles enunciated in the current version of the Declaration of Helsinki and the guidelines of Good Clinical Practice (GCP) issued by the International Council for Harmonisation (ICH).

2.6 Declaration of interest

This study is co-financed by the European Commission under the Active and Assisted Living (AAL) programme (project "StayFitLonger"). The consortium does not exclude a financial interest in participating in the study, as any Foreground Intellectual Property coming from this research may be integrated in the future commercialisation of related products.

2.7 Patient Information and Informed Consent

The research assistant will explain to each participant the nature of the study, its purpose, the procedures involved, the expected duration, the potential risks and benefits, and any discomfort it may entail. Each participant will be informed that the participation in the study is voluntary and that he/she may withdraw from the study at any time and that the withdrawal of consent will not affect his/her subsequent medical assistance and training.
The participant must be informed that his/her medical records may be examined by authorised individuals other than their treating physician.

All participants in the study will be provided a participant information sheet and a consent form describing the study and providing sufficient information for participant to make an informed decision about their participation in the study. Enough time needs to be given to the participant to decide whether to participate or not. The participation information sheet and the informed consent will be distributed at the end of oral presentation carried out in partnership with Pro senectute Vaud. The person who are interested to participate will be asked to give their contact detail, and the research assistant (BLM) will contact them to fix an appointment to control of the eligibility criteria. The time between subject received the information letter + the informed consent and gets the appointment with BLM will be minimum 2 week and maximum 3 weeks. The research assistant (BLM) will control during the phone call that subjects already received the information letter and the informed consent and if this is not the case, she will send them the document by post.
The formal consent of a participant, using the approved consent form, must be obtained before the participant is submitted to any study procedure.
The participant should read and consider the statement before signing and dating the informed consent form and should be given a copy of the signed document. The consent form must also be signed and dated by the investigator (or his designee) at the same time as the participant signs, and it will be retained as part of the study records.

2.8 Participant privacy and confidentiality

The investigator affirms and upholds the principle of the participant's right to privacy and that they shall comply with applicable privacy laws. Especially, anonymity of the participants shall be guaranteed when presenting the data at scientific meetings or publishing them in scientific journals.
Individual subject medical information obtained as a result of this study is considered confidential and disclosure to third parties is prohibited. Subject confidentiality will be further ensured by using subject identification code numbers corresponding to treatment data in the computer files.
For data verification purposes, authorised representatives of the Sponsor(-Investigator), a competent authority, or an ethics committee may require direct access to parts of the medical records relevant to the study, including participants' medical history.

2.9 Early termination of the study

The Sponsor-Investigator may terminate the study prematurely according to certain circumstances, for example:

- ethical concerns,
- insufficient participant recruitment,
- when the safety of the participants is doubtful or at risk, respectively,
- alterations in accepted clinical practice that make the continuation of a clinical trial unwise,
- early evidence of benefit or harm of the experimental training

2.10 Protocol amendments

Substantial amendments are only implemented after approval from the CEC and CA respectively.
Under emergency circumstances, deviations from the protocol to protect the rights, safety and well-being of human subjects may proceed without prior approval by the sponsor and the CEC/CA. Such deviations shall be documented and reported to the sponsor and the CEC/CA as soon as possible.
All non-substantial amendments are communicated to the CA as soon as possible if applicable and to the CEC within the Annual Safety Report (ASR).

3. BACKGROUND AND RATIONALE

3.1 Background and Rationale

Frailty is a state of high vulnerability, cumulating adverse health outcomes, and that can be defined according to Fried as "a physiologic state of increased vulnerability to stressors that results from decreased physiologic reserves, and even dysregulation, of multiple physiologic systems". Although this state could first be silent, "when loss of reserve reaches an aggregate threshold that leads to serious vulnerability, the syndrome may become detectable by looking at clinical, functional, behavioural, and biological markers". Geriatricians have proposed a frailty index to identify people at high risk of frailty. A senior can be ranged as frail when he/she cumulates at least three of the five following factors: a) generalised weakness, b) poor endurance, c) weight loss and/or undernourished, d) low activity (even homebound), and e) fear of falling and/or unsteady gait. Indeed, falls are particularly common and burdensome in the elderly population (Palumbo, Palmerini, Bandinelli, & Chiari, 2015).

According to WHO, every year 37.3 million falls are severe enough to require medical attention (WHO, 2018). They represent a serious public health and socioeconomic problem due to high healthcare costs (annual cost of $31 Billion in the US only) and have a major impact on affected patients (Hartholt et al., 2011). On the other hand, mild cognitive impairment (MCI) is a state of cognitive functioning that can be classified between healthy aging and dementia. Such a cognitive decline may appear due to pre-dementia symptoms such as memory failure or result from a variety of other aetiologies. The prevalence of MCI is set to lie between 15% and 20% for seniors (60+ years) and the annual rate of progression of MCI towards dementia reaches 8% to 15% (Petersen, 2016).

Preventing aging effect. "Keep a healthy mind in a healthy body!" The gold standard for physical and cognitive healthy aging seems to reside in having preventive interventions. This very active scientific domain means focusing on modifiable factors that could potentially delay the deleterious effects of aging on cognitive functions and delay the apparition of symptoms of neurodegenerative disease (Eustache & Guillery-Girard, 2016). A set of mechanisms, articulated around a concept of "reserve", have been described to explain the observed inter-individual differences. Two kinds of reserves can be distinguished: a static brain reserve caused by determined and unmodifiable mechanisms such as genetic factors and a more dynamic reserve also called cognitive reserve, closely linked to the behaviour adopted by an individual as well as to the set of information he/she manipulates during his/her lifetime (Stern, 2009, 2012). The retentions of physical and cognitive activity are amongst the modifiable factors that can protect seniors from deleterious effects of aging (Norton et al., 2014). Physical activity has a positive effect both on body homeostasis and brain functions by having a mild effect on cognitive functions. Seemater-Bagnoud et al. (2012) have shown for instance that aerobics training of 30 minutes per day three times a week is sufficient to maintain both physical and cognitive faculties of seniors of more than 70 years old (Seematter-Bagnoud et al., 2012). In line with this result, Sofi et al (2011) found in a meta-analysis a decreased risk factor of up to 38% to develop dementia for those seniors that practice a vigorous exercise more than three times per week (Sofi et al., 2011). The FINGER study also showed cognitive improvement on processing speed and executive functioning after a 2 years multi-domains intervention of diet, physical and cognitive training supplied by vascular risk monitoring (Ngandu et al., 2015). Staying cognitively active i.e. exercising stimulating intellectual activities seems to play an important role, especially when undertaken in a social frame (social activities being a third factor of protection against neurodegenerative disease) – (Fratiglioni et al., 2004).

Indeed, it seems possible at any age to warrant a harmonious brain aging and even to compensate for a low educational attainment by enlarging its cognitive reserve (Lachman, Agrigoroaei, Murphy, & Tun, 2010; Reed et al., 2011). However, since retirement, some seniors seems to lack both physical and cognitive activities and to withdraw from their social circle

(Grotz et al., 2016). This lack of activities has negative influence on their health, exposing them to be more vulnerable both physically (becoming frail as per Fried concept, (Fried, Ferrucci, Darer, Williamson, & Anderson, 2004; Fried et al., 2001) and cognitively (starting to develop mild cognitive impairment - MCI - as defined by Peterson in 2004, revised in 2016). Therefore, a home solution that integrates both physical and cognitive exercises and reinforces social connections in seniors, including the vulnerable elderly population, is the scope of the StayFitLonger solution.
A personalised home solution tailored for seniors. The ultimate goal of the StayFitLonger training programme is to perpetuate independent living at home by maintaining and where possible improving good physical and intellectual shape while staying at home. We broadly target retired seniors who are 60 or older, and who are robust or who are defined as pre-frail.
We will validate the solution with a selected population (128 end-users) considered as healthy senior and pre-frail. During the trial period we will explore (a) clinical relevance in prevention; (b) perceived usefulness of the solution; (c) Integration into everyday life; (d) User experience and acceptance over long-term periods (1 year); (e) Security and reliability of the system; and (f) business development for market penetration in EU countries.

3.2 Investigational Product (treatment, device) and Indication

We are currently creating an integrated ICT platform in collaboration with Mindmaze, HE-arc, HES-SO Valais-Wallis and Pro Senectute. We propose an integrated ICT platform with a video-based ecological programme (simple drawings of living house rooms) for physical training, a component already validated in a pilot project, with a set of cognitive, social and combined physio-cognitive exercises.
We focus on building solutions to delay the onset of these related symptoms which have a demonstrably higher cost. One of the most effective solutions to prevent/delay motor and cognitive deficits is to exercise regularly. We develop an evidence-based solution that provides motivation and monitors deteriorating/improving symptoms. We distinguish ourselves from the existing competition in being the first solution which incorporates both motor-cognitive activities, with a social component, backed by research.
In the physical part, the physical exercises target the improvement of gait and strength, which are well known to play a crucial role in preventing falls. This part is based on a previous project for physical training and ongoing study validation (Mittaz Hager et al.). The Test-and-Exercise home-based programme (T&E) was created by physiotherapists and researchers of the HES-SO Valais/Wallis and includes 50 video-based guided exercises where users imitate a senior model. The number of repetitions and series of exercises is specified for each exercise. This platform was developed by HES with the help of Leenaards Foundation.
The cognitive part is aiming at providing efficient strategies to improve memory, attention and executive control. Memory training aims at improving strategic learning by teaching individuals to use different techniques that improve the storage and retention of information in episodic and semantic memories (Dresler et al., 2017). Dual tasks will be trained using Sylvie Belleville multitasking strategy (Belleville, Mellah, de Boysson, Demonet, & Bier, 2014), i.e. modulating the rate of attention provided to each task, a strategic mean to improve flexibility. Part of the exercises will also concern cognitive-motor exercises where seniors end-users have to perform a cognitive task (using prospective memory for instance) while doing the physical activities. Furthermore, ADL activities are aimed at being the support of some cognitive activities in order to favour optimal transfer to real life (Simons et al., 2016). At the end of cognitive training, the system will also provide prevention messages to improve end-user's literacy on how to keep on maintaining cognitive functions.
To favour social aspect and optimise motivation, seniors will be encouraged to create their own learning material to learn new associations, or relearn forgotten ones, in their domains of interest. They will have the possibility to share learning material with other subjects of the

study. Subjects would also have the choice to play in a cooperative or competitive way (Cameirao, Smailagic, Miao, & Siewiorek, 2016); (Gorsic, Cikajlo, & Novak, 2017)) and at least some cognitive tasks will adapt the level of difficulty to the individual performance. Moreover, scores of the cognitive part will be recorded to give end-users a feedback on their performance. A light version of chat rooms addressing different topics of interest (such as cooking, do-it yourself) will also give the opportunity to seniors to talk together and find solutions to common real -life problems.
The device provided to the end-user will consist of a tablet. Activities will allow end-users to train at home, alone or with (remote) end-users. The adherence to physical exercises will be recorded through one sensor from Gait-Up, placed at the pelvis.
To further increase motivation, activities have to be ludic and in adequacy with the expectations of a senior end-user. This will be achieved by providing personalised settings to tailor the environment to the end-user's tastes and wishes (i.e. following daily news, topic of interest, adapted coach settings to provide a light or strong guidance according to the subject preferences). The physical training itself will be monitored to provide a feedback on the end-user's performances. Relevant rewards (using multisensory and/or emotional stimuli) and strategic recommendations (i.e. ways to improve) will be given by a virtual coach. The virtual coach's main job will be to guide the end-user along the proposed exercises in order to favour support to improve adherence. The virtual coach uses non-verbal communication: emotional-based rendering & behaviour will be created by HE-arc institute of computer engineering.

3.3 Preclinical Evidence

In 2014-2015, HES-SO Valais/Wallis conducted a pilot study and compared the T&E and the OTAGO home-based exercise programmes (Mittaz Hager et al.).
The sample characteristics were: 17 women and 2 men, average age of 78 y.o. (Standard deviation, SD=8.41). 26.3% without falls in the last 12 months, 36.8% with one fall in the last 12 months and 36.8% with two or more falls in the last 12 months.
This pilot study showed the feasibility of the present study against the participation agreement (86.3%, 95% Confidence Interval (CI) 72.8% to 99.8%), the exercise adherence (84.2%, 95% CI 67.8% to 100%), the costs (+6.63%) and the missing values (87.2%, 95% CI 72.2% to 100%).
In addition, the sample showed the characteristics we were looking for, namely characteristics of older adults, identified at risk of falling regarding the cut-off value of the these outcomes: Questionnaire Short Fall Efficacy Scale-International (average of 11.32), Time up and Go test (average of 17.21 sec.), Five Time Sit to Stand (average of 17.73 sec.), Four Test Balance-scale (median = 2) and an average of the walking speed of 0.72 m/s. Quality of life, measured with the Older People Quality of Life Questionnaire (OPQOL-35) shows an average score of 121.89 on the maximum value of 175.
The statistical power was not adequate to evaluate the effects of both home-base exercise programmes in the pilot-study. However, comparing the differences between training groups, before - after, the average of all measured outcomes was improved in both training groups, T&E and Otago, after six months of intervention. The results showed better improvement in balance outcomes for T&E and better improvement in strength outcomes for Otago.
One participant experienced a fall. This fall was not attributed to the intervention. The participant was not excluded from the trial; she just interrupted the intervention for four weeks.
Therefore, the Swiss CHEF trial shows preclinical evidence for the use of the StayFitLonger programme as the physical part is based for on the T&E programme.

3.4 Clinical Evidence to Date

There are many studies exploring the effect of cognitive and physical training in elderlies with different support (some examples are cited below).

- Doniger et al. (2018) studied in an RCT the effect of virtual reality - cognitive training to improve cognition and cerebral blood flow in middle-aged individuals at high AD risk Alzheimer's disease. They concluded that a more ecologically valid cognitive-motor VR setting that better mimics complex daily activities may increase transfer of trained skills (Doniger et al., 2018)
- McEwen et al. (2018) studied the relative effectiveness of simultaneous performance of memory training and aerobic exercise to a sequential performance intervention on memory functioning in older adults. Their findings showed promising result, a 4-week simultaneous memory training and aerobic exercise program was sufficient to improve memory, attention, and reasoning abilities in older adults (McEwen et al., 2018).
- Zhu et al. (2016) performed a meta-analysis and assessed the efficacy of combined intervention on cognition by comparing combined intervention to control group, cognitive intervention and physical exercise. Authors found that combined intervention demonstrates advantages over control group and physical exercise. However, evidence is still lacking for superiority when compared combined intervention to cognitive intervention.

But there are only few studies looking at the effect of a home-based training including cognitive and physical training through on an application support.

3.5 Dose Rationale: Rationale for the intended purpose in study (pre-market MD)

Rationale for drug dose is not applicable in our study as there is no drug.
However, the rationale for dose of physiotherapy training for seniors is given by the international guidelines (Paterson, Jones, & Rice, 2007).
There is currently no recommendation on cognitive brain training dose and it is still not clear whether dose increases the longevity of training benefits (Simons et al., 2016). In FINGER study (Ngandu et al., 2015)[1], participants were asked to train individually with a computer-based training three times a week during 10 to 15 minutes. They performed a total of 72 training sessions in 6 months. Thus, both groups will be encouraged to cognitively train as long as they want but at least 10 to 15 minutes.

3.6 Explanation for choice of comparator (or placebo)

We believe that comparing the StayFitLonger programme to no comparison might not be adequate.
For the physical part, we chose to compare the "StayFitLonger" programme with the Helsana programme that created a programme of physical activities for the elderly. Helsana proposes these exercises in booklet, free of charge, in which 12 different exercises trains upper and lower extremity strength, mobility and balance. Advices and tips are given to stay physically active such as to go shopping on foot. It also contains information about which exercise to choose, the frequency to train and precautionary measures to follow.
Helsana programme, that conceived an adapted a programme for the elderly, is an adequate intervention for the alternative training and, therefore, we consider it as a "standard care."

For the cognitive part, we will use free computer-based games (e.g. sudoku, crosswords, hidden word, solitary, memory, categorisations, Pac-Man) that are training the same cognitive skills (memory, executive control and attention), however, without providing associate cognitive

[1] one of the most recent cohort study with positive cognitive efficacy outcome

strategies. Although usually played with paper and pencil, these kinds of casual games are known to be appreciate by elderly people (Chesham, Wyss, Muri, Mosimann, & Nef, 2017). Thus, it is a convenient alternative cognitive therapy because both the experimental and alternative therapy will be provided with the same informatic support. However, the "fun" of the games of the alternative therapy should be counterbalanced by motivational factors in the experimental therapy. This is the reason why the alternative therapy will not provide social aspects (coach plus possibility to play with or against other players).

3.7 Risks / Benefits

Risks:

The practice of home-based exercise presents minimal risk when the participant follows the recommendations of the physiotherapist.

Participants will be instructed by the physiotherapist and the neuropsychologist in how to perform the tests and the exercises in order to prevent falls.

In case of serious injury (requiring an emergency or inpatient treatment) due to a fall occurred during an exercise or for another reason, the subject will be asked to inform his/her physiotherapist (See Chapter 10.3.2: Reporting of Safety related events).

The participants might feel a little bit the muscles or joints discomfort after the training, which is normal. These sensations will disappear with time and become less frequent with the training. We recommend to the participants for whom the disagreement persists to contact their physiotherapist in order to take the appropriate measures.

Benefits:

All participants will benefit from a personalised home-based programme free of charge conceived by trained physiotherapists and neuropsychologists.

The benefits of these home-based exercise programmes are:

- Programme exercises conceived for fall prevention are considered effective at reducing the number, the risk and the rate of falls in elderly community-dwelling individuals (Gillespie et al., 2009; Gillespie et al., 2012; Gine-Garriga, Roque-Figuls, Coll-Planas, Sitja-Rabert, & Salva, 2014; Karlsson, Magnusson, von Schewelov, & Rosengren, 2013), appear to prevent falls-related injuries (Clemson et al., 2012; El-Khoury, Cassou, Charles, & Dargent-Molina, 2013), and show a significant improvement of frail older adults' quality of life (Langlois et al., 2013), such as in women with osteoporosis and osteopenia (Cesarec, Martinec, Basic, & Jakopic, 2014),
- Home-based exercise programmes seem to reduce the number of falls, risk of falling and risk of death (Thomas, Mackintosh, & Halbert, 2010),
- It seems to improve balance, leg strength, function, physical activity in older people (Hill, Hunter, Batchelor, Cavalheri, & Burton, 2015) and balance confidence in older adults living in the community (Cyarto, Brown, Marshall, & Trost, 2008),
- Regular physical activities appear to be a way to slow down the decline and keep or even increase personal autonomy and quality of life (Pernambuco et al., 2012).

All the study-participants will benefit from the StayFitLonger programme, indeed at six month the alternative training with Helsana programme and no specific cognitive programme will have the experimental training programme for five months. The experimental training starting with the StayFitLonger programme will continue the programme the next five months with less follow-up. Furthermore, subjects we will be informed that they participate in a research project

limited in time and that, at the end of the research, the platform may be discontinued but, if the project is successful, they will have the possibility to continue the programme.

Describe, if applicable and relevant, the potential threats to the study, e.g. competing trials, and anticipate risk minimisation.
Not applicable.

3.8 Justification of the choice of study population

The population we focus on are independent elderly in the all days living activities, willing to stay fit and contribute actively to maintain a good health condition. This population is at risk of frailty in the future and might benefit from a training programme to prevent cognitive and functional decline.
We will include retired volunteers still living at home that are ready to invest time for a training programme on a tablet.
As the StayFitLonger programme is as training programme and not a therapy, we will exclude frailty participants (Fried's criterion ≥ 3) and those needing a walking aid in the house for safety reasons. Moreover, the subject having a MoCA score (Nasreddine et al., 2005) less than 26 might not benefit from the training because it may already be too difficult for them to achieve.

4. STUDY OBJECTIVES

4.1 Overall Objective

For pure scientific rationales, the **first part of the study** is a random control trial over six months, aiming at comparing the effect of two home-based exercise programmes, i.e. an experimental training composed of a combination of self-management physical exercises, cognitive training and on-line guidance with a virtual coach WITH an alternative training composed of Helsana programme and some commercial casual cognitive games, in healthy older adults. The objective is to demonstrate the superiority of the experimental training on the alternative training on physical capabilities, cognitive abilities, affective ability (such as mood, fear of falling), and specific associated domains (such as quality of life daily life, daily living activities, subject's expectation).

The **second part of our study** is more dedicated to observational rationales.
Therefore, there are three complementary objectives

- First, we need to align with the Active and Assisted Living (AAL) European association principal requirements, demanding (for ethical reasons) that the overall lots of inserted seniors have the opportunity to use the experimental training for one year. A compromise has then been found by giving the opportunity to the alternative training group to use the experimental training. Therefore, adherence of the training therapy will be studied over one year (for experimental training group) and six months (for the alternative training group).
- Second, getting back to the superiority of the experimental training, if it happen, we want to know whether this gain will concern all category of healthy seniors (robust and vulnerable) or mainly vulnerable ones (the one mainly aimed at with such training programmes)!
- Third, new cognitive applications have been designed specifically for this study and their efficacy should be investigated into more details.

They will be described into details in the "other objectives of interest" section.

4.2 Primary Objective

The objective of the scientific part of the study (RCT) is to evaluate if the experimental program will be associated with better performance 6 months later than the alternative training programme (i.e. control training) on a functional physical task (Timed Up & Go) used to measure strength, balance and gait while walking. We are claiming that, relative to the control training programme, the experimental training programme will yield better gain of performance than the control programme in healthy older seniors.

4.3 Secondary Objectives

The second scientific objective (RCT) is to verify whether the experimental training programme is associated with better physical and cognitive abilities after 6 months, whether it reduces fear of falling and improves mood, quality of life, daily living activities (ADL), the sustainability and exercise-adherence over (6 months) time compared to the alternative training.

4.4 Other objectives of interest

First, the stratification will allow to compare the effect or the training on robust and pre-frail seniors. We are claiming that the benefits of the experimental training would be smaller for the robust healthy older adults than for the pre-frail ones. Our hypothesis is that such a program will be particularly interesting and efficient for reducing cognitive decline in pre-frail older adults.

Second, to fill out AAL requests and to remain ethical for each invested senior, another critical objective is to measure adherence to the experimental training over time. This will be done by analysing whether the adherence to the experimental training is maintained over time under less supervision (no more visit and phone call during the second part of the experience). On the other hand, for the group switching therapy, the adherence to the alternative and experimental training will be compared and reported.

Third, in AAL project, new cognitive applications have been designed to complete the lot of physical activities. Testing their efficacy on the experimental group is another objective of interest.

4.5 Safety Objectives

Not applicable.

5. STUDY OUTCOMES

If the experimental training has an advantage over the alternative training, it should be visible with specific tools assessing physical and cognitive performance that should show a differential benefit over a six months period of the RCT study. Both interventions could lead to a benefit (due to test-retest, placebo effect, intervention effect, …). However, we are claiming that the gain that will be emerged from the experimental training should be bigger than the one measured for the alternative training. This differential benefit could decrease over the 6 last months of the experience as both groups will have the experimental training since the middle of the experience.
Therefore, all measures will be taken over three time points: T0, T1 (after 6 month) and T2 (after 12 months) and the different outcomes will be assessed with the following tools.
On table 1 is a summary of all the executed test according the analysis (i.e. RCT and Longitudinal analysis)

5.1 Primary Outcome

5.1.1 For the 6th month RCT, our primary outcome are physical capacities. It will be measured with the «Time-Up & Go» (TUG) test, a global test recognised for its efficacy to measure the lower extremity function, mobility and the risk of fall. We will assess the total time in second needed to perform the TUG.

5.1.2 For the longitudinal study over the 12 months of the project, our primary outcome is the adherence to the experimental training. It will be measured only for subjects that have the experimental training by monitoring the tablet usage during the whole trial and a mean adherence curve will provide a valuable feedback on the success of our programme (if correctly followed people should have a straight adherence curve with a flat slope and an average of 3h of training per week (as recommendation are to respect a frequency of 3 sessions of 45' per week of physical training and a minimum of 15' for cognitive training).

5.2 Secondary Outcomes

5.2.1 For the 6th month RCT, assuming that training might have an impact on other functional domains and habits, some relevant changes should also be measurable. Secondary outcome is therefore subdivided into 4 domains: physical capacities; cognitive abilities; affective abilities (including mood and fear of falling); specific associated domains, such as quality of life, ADL activities, subjective expectation from the intervention and finally adherence to the training. For each of these domains, the most relevant tools (i.e. tools that can highlight a benefit from the training) have been chosen.

Physical capacities: The first domain of secondary outcomes would consist in completing the report of the physical potential changes by assessing gait speed (Timed 25-Foot Walk in metre/second), lower extremity strength (Five Time Sit to Stand Test: time to perform 5 sit to stand in second) and balance (Four Stage Balance Test, total score). Moreover, to obtain more accurate measures, the TUG will be measured via two wearable captors that will provide specific movement parameters (see Table 1 for details). All these parameters will give a more precise extraction of the movement performance, some of them being specifically linked to frailty.

Cognition: The second domain of secondary outcomes is cognition: *self-management* training of physical activity and providing cognitive *strategies* only to the experimental group should differentiate the cognitive performance of our subject according to their group attribution. Global cognition will be measured with a composite of Z-Scores on Attention, Verbal fluency and Episodic memory assessment. This modified version of the Preclinical Alzheimer

Cognitive Composite (ADCS-PACC) (Donohue et al., 2014), called ZAVEN score, was shown to be particularly sensitive to performance of nondemented older adults (Lim et al., 2016). Some cognitive sub-components will be assessed with specific cognitive tests currently used for assessing cognition in older adults (all details are provided in Table 1).

Affective sphere: The third domain of the secondary outcome concerns the affective sphere which could also be affected positively by such trainings. Therefore, affective measures will be collected in both groups for fear of falling (measured through the Falls Efficacy Scale-International score) and for subjective mood (measured with the HADS).

Specific associated domains: A fourth and last domain of interest concerns the effect of the training on specific associated domains such as quality of life (measured through the OPQOL-35 score), personal habits of the subject such as ADL activities (measured with the CFI and completed with part of the E-Cog) and expectation of the subject from the training programme (assessed with a Pre/Post home-made questionnaire).

5.2.2 For the longitudinal study over the 12 months of the project, our secondary outcome is aiming at relying, for each individual, its adherence profiles and its relationship with the efficacy of the training performed over periods of 6 months.

5.3 Other Outcomes of Interest

5.3.1 Another question of interest concern whether the differential benefits we hope to find for the whole lot of subjects on primary and secondary outcomes will be the same for robust and pre-frail seniors. The stratification will permit to separate our subjects into two populations and measure the same primary and secondary outcomes for robust and pre-frail subject independently.

5.3.2 Adherence to the experimental training by using a technological device is AAL main interest. As a definition, we will set that adherence is not only the time spent using the dedicated training, but also the regularity of training. Therefore, the curve of the time spent training will be measured (by cumulating the time spent to train over a week for each week of training) will be the other outcome of interest. Furthermore, each of the above first and secondary outcomes could have an impact on the time of training. A factorial analysis is needed to perform an observational study of the device usage. Into more details, it is planned to measure the overall time of training (dose outcome), the number of repetitions made in using the different applications (intensity outcome), and the distribution of training over time (regularity outcome). We will also analyse the general profile and individual profiles of adherence to see whether subjects trained regularly on a long-term period and whether they can be classified into good-adherent and bad-adherent participants according to different factors (for instance, their expectation of the efficacy of the therapy). As AAL is only interested in the adherence profile of the participants to the experimental intervention, adherence profile will be measured from baseline (T0) to the end the study for Group A and from T1 to T2 for the Group B, as they only have the experimental therapy during the 6 last months of the study.

5.3.3 To cover our last objective (testing the efficacy of the delivered new cognitive applications), some specific cognitive tests have been added to the lot of cognitive assessment. Concept elaboration, prospective memory and multitasking will be addressed with specific cognitive tools (for the two first functions) and with a new designed assessment (for the last one).

Concerning the RCT (over 6 months) - First part of our study		
Primary outcome		
1. Physical capacities	1.1 Mobility and balance	Time of the Time-Up & Go Test (TUG) (Podsiadlo & Richardson, 1991)
Secondary outcomes		
1. Physical capacities	1.1 Mobility and balance	● Timed 25-Foot Walk (20-meter walking test) (Fischer, Jak, Kniker, Rudick, & Cutter, Revised in October 2001) ● Five Time Sit to Stand Test (FTSTS) (Bohannon, 2006) ● Four Stage Balance Test (FSBT) (CDC, Centers for Disease Control and Prevention, National Center for Injury Prevention and Control) ● Captors while assessing the TUG will also provide measures on: walking speed, variability in gait, stance phase, foot-flat phase, double support, stride velocity, maximal swing speed, turning angle and variability in toe clearance).
2. Cognitive global abilities and its sub-processes	2.1 Global cognition	ZAVEN composite score is composed of: ● Episodic memory composite: total recall of the California Verbal Learning Test and delayed recall of the Logical Memory of the Wechsler Memory Scale (WMS-IV, French version) (Wechsler, 2012) ● Complex attention composite: Digit Symbol substitution Test (DSST) of the 4th version of the Wechsler Adult Intelligence Scale (WAIS-IV) (Wechsler, 2011) ● Executive function composite: Verbal fluency (VF) (Cardebat, Doyon, Puel, Goulet, & Joanette, 1990)
	2.2 Memory composite	● Delayed recall of the California Verbal Learning Test (CVLT) (Delis et al., 2010) (Poitrenaud, Deweer, Kalafat, & Van Der Linden, 2017). ● Delayed Recall of the Logical Memory Test (IIa Subtest of the Wechsler Memory Scale – WMS-IV, french version) (Wechsler, 2012)
	2.3 Executive & attentional functions composite	● Verbal fluency (VF) (Cardebat et al., 1990) ● Trail Making Test (condition B – A; shifting – processing speed scores) (Tombaugh, 2004) ● Victoria Stroop (high interference – naming conditions)(Bayard, Erkes, & Moroni, 2011) ● Divided attention from Zimmermann & Fimm, 2002 in the book of (Leclercq, Zimmermann, & H. van Zomeren, 2002) (naming condition)
	2.4 Speed processing composite	● Trail Making Test, condition A (Tombaugh, 2004) ● Digit Symbol Substitution Test (from Wechsler Adult Intelligence Scale or WAIS-IV)(Wechsler, 2011) ● Victoria Stroop (naming condition) (Moroni & Bayard, 2009)

3. Affective ability	3.1 Mood 3.2 Fear of falling	● Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983) ● Falls Efficacy Scale International (FES-I) (Delbaere et al., 2010)
4. Specific associated domains	4.1 Quality of Life (QoL) 4.2 Cognition in Activities of Daily Living (ADLs) 4.3 Expectation questionnaire	● The Older People Quality of Life questionnaire (OPQOL 35)(Bowling, 2009) ● Cognitive Function Instrument (CFI) (Walsh, Raman, Jones, & Aisen, 2006) - Self report (Amariglio et al., 2015) + Three subdomains of the Everyday Cognition (E-Cog) (Farias et al., 2008) ● Home-made Pre/Post questionnaire on subject expectation of the training programme
Longitudinal design (over 12 months) - Second part of our study		
Primary outcome		
1. Adherence	Adherence to the experimental training programme measured by monitoring the curve of mean training dose over time and the regularity of training.	
Secondary outcomes		
2. Adherence profiles will be separated into good and bad-adherent (in function of their individual profile curve)	2.1 Technology and gaming profile 2.2 User experience of the product 2.3 Acceptability of the programme 2.4 Final Feedback questionnaire on SFL intervention All these data will provide variables that will be used as moderator factors of adherence	Home-made questionnaire to address the usage and habits of the subject concerning games & technology AttrakDiff scale (performed at T1 and T2) (Lallemand et al., 2015), comparing Pre/Post ratings for Group A and Product 1/Product 2 for Group B) Home-made questionnaire (performed at T1 and T2) to obtain ratings on different components (enjoyment, appropriateness, safety, self-evaluation and motivation) Home-made questionnaire (performed at T2), closing the study and studying impact of various specificity of SFL programme (virtual guide, social interactions, preferences, gamification, psycho-education & self-management, and SFL usability). Effects of adherence profiles on the experimental programme efficacy will be investigated using clinical (RCT) primary and secondary outcomes.
Other outcomes of interest:		
Stratification	● Robust vs Pre-frail	Primary and secondary outcomes will be measured for Robust & Pre-Frail populations independently (see chapter 6.2 for more details).
Moderators	● Age ● Level of education ● Adherence to training	Analysis of the impact on the primary and secondary outcome of the besides moderators.

	• Cognitive status (MoCA)	
Effects on specific cognitive functions	● Multitasking: ● Prospective memory: ● Concept elaborations	● Home-made computerized Multitasking Test (Belleville et al., 2014) ● Prospective Memory Items of the third version of the Rivermead Memory Test (Wilson, 2018) ● Flexibility (from the Test battery for Attention Performance or TAP) from Zimmermann & Fimm, 2002 in (Leclercq et al., 2002) ● Similitudes (from the 4th version of the Wechsler Adult Intelligence Scale or WAIS-IV) (Wechsler, 2011)

Table 1: Outcomes summary.

5.4 Safety Outcomes

Not applicable.

6. STUDY DESIGN

6.1 General study design and justification of design

The methodology of this trial follows the recommendations of SPIRIT 2013 (Chan et al., 2013). Our study is an international multi-centre trial performed in three sites: Switzerland, Canada and Belgium. Both part of the study will be conducted in these three countries.

As already explained in chapter 4, StayFitLonger design is divided into two part:

1. A double-blind random control trial (RCT), with parallel groups, with pure scientific rationale, will be conducted over six months (between T0 and T1), aiming at comparing the effect of two home-based exercise programmes, i.e. an experimental training and an alternative training (see chapter 4.1 for details on the training programmes).
2. A longitudinal observation design over 12 months (between T0 and T2 for Experimental Group; between T1 and T2 for Alternative Group that switch from alternative training programme to the experimental training programme after the 6 first months of RCT), devoted to address AAL rationales, i.e. measure the adherence of the subjects to the experimental training programme.

The 128 healthy older adults (see sample size in chapter 11.2) should be enrolled in the protocol, half of these subjects should be recruited in Switzerland. The aimed population is seniors over 60+ years; robust or pre-frail seniors according to Fried's frailty scale, a physical test that will be perform at screening time (before T0). Among other inclusion criteria, enrolled seniors should have a strong interest to stay fit, be timely available the next 12 months, and motivated to engage in a 12 months training programme.

As the subject will receive an information letter, they are considered as blinded because they do not know which training can provide the best benefit. The assessors will be blinded to the group assignment, the allocation process will be blinded too. Allocation to the groups will be

performed through the programme REDCap in which the list of randomisations will be previously implemented.

The participants will be randomly assigned to either the experimental training ("StayFitLonger" programme) or the alternative training (the digitised training programme of Helsana) with a cognitive self-maintenance. The randomisation will be stratified according to the participants' score on the Fried's phenotype scale (Fried et al., 2001).

Participant will be assessed at three time point: baseline (T0), 6 months (T1) and after 12 months (T2).

Potential problems and limitation of the design:

- AAL requests prevents us to fulfil more conventional designs such as a cross-over design study over 12 months (each group changing therapy after 6 months) or an RCT including a follow up at 12 months. Conventional comparison among the two groups at T2 is thus not possible. However, the advantage of our combined design is that the whole lot of seniors will have up to 12 months of training, which is more equitable in an ethical point of view.
- Another limitation of the study is the timing of the study that needs to be fulfilled in only 16 months (March 2019 to July 2020) with an inclusion period of only 3 months. It will be particularly challenging to include up to 64 patients in such short time to reach Switzerland effectives.

6.2 Methods of minimising bias

6.2.1 Randomisation

The programme REDCap (Harris, 2009) will be used for the randomisation process. The randomisation criteria will be predefined and entered into REDCap. Daniel Damian (the CLM computer scientist, not involved in the trial) will be in charge for creating the list of randomisations and the sequence list will be implemented in REDCap by an HES-SO engineer who is not involved in the trial. The same engineer (of the HES-SO) will also be in charge of giving selective access of the different instruments in REDCap to the trial contributors (according to their specific function).

Groups of subjects will progressively enter the study. The secretary (TJ) will randomise the participant with REDCap. A block randomisation will be realised including 12 subjects per training group. Each of these 12 subjects will be attributed randomly to the experimental or alternative trainings. Furthermore, subjects will be stratified according to their results to the Fried's phenotype (Fried et al., 2001). Robust seniors will be the one having no fragility (no frailty criterion on Fried's phenotype) and pre-frail seniors will be subjects having some signs of frailty (i.e. pre-frail score at Fried's phenotype with the presence of 1–2 criteria).

6.2.1 Blinding procedures

The participants are considered as blind even if they will be aware that the trial has two different training groups and that they will be randomly allocated to one of the two training groups. Indeed, participants are not aware which training might be better.

The research assistant (BLM), responsible for the screening, will be blinded to the participants' assignment, firstly because the randomisation will be done only after the first assessment and

secondly because she will have only access to the participants' personal data and the assessment sheet screening parameters of the eligibility criteria in REDCap (Harris, 2009) .

The physiotherapists assessor (KG) and the neuropsychologist assessor (TGP) responsible for the three assessment sessions will be blinded to the participant's assignment, as they will only have access to the different tests in REDCap (Harris, 2009) and will not be aware of the list of the randomisation sequences. For the T1 and T2 assessment, participants will be asked not to tell assessors which programme they have followed.

The secretary (TJ) will not be blinded, as she will control the data implemented in the REDCap (the screening and the informed consent) in order to control that no data are missing.

The statistician is blinded to the training assignment as he/she will only have access to anonymised data results and will neither see the participants' assignment nor the randomisation list.

The scientific mediator (AP) and the physiotherapist (still to be defined) will be responsible for the participants' instruction of the StayFitLonger training as well as the alternative training. As the physiotherapist and the scientific mediator give both training, they will not be blinded.

6.2.2 Other methods of minimising bias

The questionnaires and the assessment tests used in this trial are validated versions or in process of translation validation. To assess the specific usage of the experimental training programme, some home-made questionnaire has been added to have a feedback on our new device. To ensure that all tests and questionnaires are applied in the same way by all assessors (in Switzerland, Canada and Belgium), a guideline will be provided to all stakeholders to explain how to proceed the tests and questionnaires. In the same vein, a document concerning the procedure to be followed when explaining the application to the subjects (for the experimental training group and the alternative training group) will be provided to all people having this function.

The missing values during assessments will be limited due to the use of the REDCap software (Harris, 2009). Moreover, the validation is a safety measure as the results cannot be modified. Access permission will be delivered, depending on the stakeholder's role, by an engineer not involved in the trial.

A modified intention to treat method will be used to be conservative in case of missing data due to drop-outs or incomplete assessment.

6.3 Unblinding Procedures (Code break)

Not applicable.

7. STUDY POPULATION

7.1 Eligibility criteria

Participants fulfilling all of the following inclusion criteria are eligible for the study:

Inclusion criteria:

- Age (minimum 60 years old)
- Retired
- Living at home
- Independent (4-IADL: score optimum (Barberger-Gateau, Fabrigoule, Rouch, Letenneur, & Dartigues, 1999))
- Ready to invest time during 1 year
- Open-minded to use a tablet
- Interested in exercising to stay fit
- Able to walk at home without an walking aid (wheelchair, sticks, walker, etc.)
- Fluent French speaker
- Sufficient visual capacity to read the information on the tablet

Exclusion criteria:

The presence of any one of the following exclusion criteria will lead to exclusion of the participant:

- MoCA < less than 26 (Nasreddine et al., 2005)
- Fried's frailty criterion ≥ 3 (Fried et al., 2001)

(See downloaded documents "Vérification des critères d'éligibilité_SFL_V2, Screen: 6/14/5),

7.2 Recruitment and screening

The recruitment of the participants will be done through the organisation Pro Senectute Vaud by the neuropsychologists Mélanie Bieler-Aeschlimann (MBA) and Benedetta Leidi-Maimone (BLM), assistant in research from CHUV. Publicity will be made by Pro Senectute communication channels (putting an ad in their yearly journal, sending information via their newsletter, sending a letter to Pro Senectute members living close from Lausanne and through social media (i.e. Facebook, LinkedIn, Twitter). Oral communications will be performed via Pro Senectute events where flyers will be distributed (See downloaded documents "flyers SFL", Screen: 6/14/11). After the oral presentation, the interested seniors will receive the information letter and the informed consent. Moreover, they will be invited to come at the end of the presenter to the presenter in order to give their telephone details. The research assistant (BLM) will contact them to set an appointment for the control of the eligibility criteria. The research assistant (BLM) will control during the phone call that subjects already received the information letter + the informed consent and if this is not the case, she will send them the document by post.

At the end of the screening session, a member of the CLM (BLM or TJ) will plan the appointments for the first assessment (physical and cognitive). If subjects are not able to come to the screening appointments or the assessments (T0, T1, T2) or one of the training sessions, they can contact the secretary (TJ) to fix a new appointment.

Screening:

The screening period of participants is over 3 months in order to reach the target sample size *(See Figure 4)*.

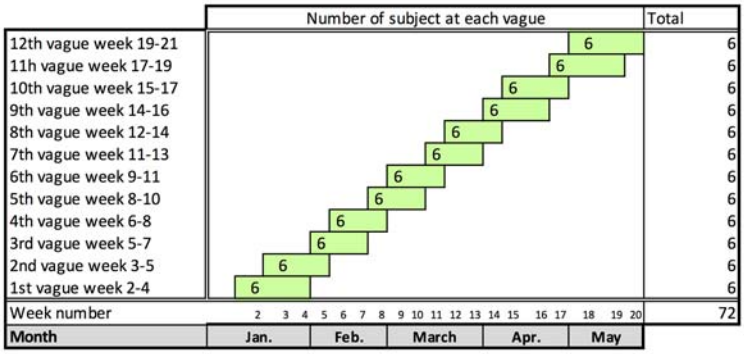


Figure 4: Distribution of the subjects

The research assistant (BLM) has already skills to complete each point of the screening tests (MoCA score and the Fried's phenotype) as she was engaged in previous research studies involving the same screening tests. If the participant is eligible to the trial, an ID number will be created, and personal data will be directly registered in REDCap. BLM will only have access to the screening sheet and the personal data in REDCap. Moreover, she will also be responsible for phone calls and visits follow-up of both training groups. At this point of the trial this, she will not be blind anymore, but it has only minimal impact as she will not be involved in the randomisation process.
The ID number will be created with the two capital letters designating the country (i.e.: CH: Switzerland; BE: Belgium; CA: Canada) followed by a number (i.e.: CH004).
The people interested to participate to the trial and who did not reach a MoCA score (Nasreddine et al., 2005) of 26 or have a Fried phenotype ≥ 3 (Fried et al., 2001), will be addressed to a more adapted training proposed by the programme called "ça marche" which have an adapted programme for sedentary seniors called "pas à pas" (http://www.ca-marche.ch/projet/pas-a-pas/).

7.3 Assignment to study groups

The software REDCap (Harris, 2009), will be used to register the participant details, ID number and the participants data.
After the screening (first appointment) and each assessment (physical and neuropsychological), the secretary (TJ) will control the data implemented of the screening and if the informed consent was filled properly in the REDCap in order to control that no data are missing. She will validate the data and will randomise participants. The validation is a safety measure so that data cannot be modified. After the randomisation, TJ she will contact participants and fix the appointments of the physical and cognitive training.

7.4 Criteria for withdrawal / discontinuation of participants

The participants are free to withdraw their consent and abandon the trial at any time if they want to.

The investigator may also decide to exclude a subject from the study if training would be dangerous for the subject.

As this is an intention-to-treat approach, we will document, the reasons for withdrawing and participants withdrawing from the study will be invited to come to the 6-month post-test.

8. STUDY INTERVENTION

8.1 Identity of Investigational Products (training)

We are currently creating an integrated ICT platform in collaboration with Mindmaze, HE-arc, HES-SO Valais/Wallis and Pro Senectute. We propose an integrated ICT platform with an ecological video-based programme (simple drawings of living house rooms) for physical training that will be enlarged with a set of cognitive and physio-cognitive exercises. Some social aspects will complete the whole lot.

8.1.1 Experimental training

The StayFitLonger programme is composed of a physical and cognitive training. The participant will have the choice between these 2 trainings possibilities.
The physical training aim is to increase balance, muscle strength and physical capabilities in older adults. Exercises were developed by HES-SO Valais/Wallis in a previous ongoing trial "Tests & Exercises or T&E" programme. This is a home-based exercise programme which is composed of 50 tests and 50 exercises. The participants receive a tablet-computer with videos demonstrating each test and each exercise. This programme is based on the concept of *self-efficacy* and of *Empowerment*.
As opposed to alternative training programmes that prescribe exercises to participants, our programme let the participants choose the exercise they want to do. In order to help them select what they are able to perform, a scale was created to evaluate the perceived difficulty. The scale is ranged from 0 to 4 (0: no difficulty; 4: very/too difficult). The exercises judged as "0" or "1" are exercises we suggest performing for the warm-up or to maintain the present physical condition. Exercises evaluated as "2" are exercises good for the training. Finally, exercises ranged between "3" and "4" are exercises that must not be done, because they are too difficult and trigger a high risk of falling *(Figure 5: Scale for perceived difficulty)*.

Difficulté perçue	Que faire ?
« Aucune difficulté »	Faites-le en tant qu'échauffement.
« Légèrement difficile »	Faites-le pour entretenir vos capacités
« Difficile »	Idéal pour vous. Faites-le souvent.
« Très difficile »	Ne faites pas cet exercice.
« Trop difficile »	Ne faites pas cet exercice.

Figure 5: Scale for perceived difficulty

The test assesses the physical performance of the subject namely: strength, balance, mobility, and coordination. Every exercise category suggests 4 types of exercises of different difficulty. Each exercise suggests a way to increase by either modifying the body position or by increasing the workload.

The cognitive part of the SLF programme will be composed of several applications devoted to increase memory, executive functions and attention performances by providing a set of strategic learning methods. Subjects will be trained, at their level of performance, to learn or relearn new information by using different strategic learning methods such as errorless learning or visuo-spatial binding (Dresler et al., 2017; Warmington & Hitch, 2014) or to vary their attentional focus to gain flexibility in dual tasks (Belleville et al., 2014). Some cognitive-motor tasks will also be provided such as training prospective memory (Hering, Rendell, Rose, Schnitzspahn, & Kliegel, 2014) in an ecological way during the physical exercises (subjects will for example be asked to fetch and drink a glass of water after a certain amount of time of physical training). Sylvie Belleville multitasking game is, in a way, also a cognitive-motor task as the subjects have to answer partly with their feet (a Physilog sensor being attached to their waist). Each cognitive or physio-cognitive app will be available directly on the tablet. People will be free to train but encouraged to play at least three times a week for a minimum of 15 minutes.

8.1.2 Control alternative training

The alternative training (AT) will be also based on a tablet to rule out technology as a confounding factor. Different applications will be provided, a digitised version of Helsana's physical training programme in PDF format. Helsana proposes 12 different exercises training *viz*. upper and lower extremity strength and mobility, and balance. Advices and tips are given to stay physically active such as to go shopping on foot. It also contains information about which exercise to choose, which training frequency and the precautionary measures.

On the cognitive side, the participants will be advised to train with computerised cognitive games (e.g. crosswords, hidden word, solitary, categorisations, Pac-Man, ...). These games engage the same memory, attentional and executive functions but are not considered to be cognitively-stimulating and do not provide strategies.

8.1.3 Packaging, Labelling and Supply (re-supply)

Not applicable.

8.1.4 Storage Conditions

Not applicable.

8.2 Administration of experimental and control training/interventions

Both programmes of the physical part will be explained by 1 physiotherapist (to be defined). The two different programmes on the neurocognitive part will be explained by a scientific mediator (AP). Moreover, the scientific mediator (AP) responsible for the cognitive training will explain that the two trainings were created specially to train the elderly and that we do not know yet the effects of these trainings. However, a scientific mediator (AP) has no neuropsychological background (he is biologist specialised in molecular biology and has recognised skills a scientific mediator), he will neither be explained nor has the needed background to understand the differences between the two cognitive trainings, which makes him an impartial trainer.
Both instructors will present and explain both programmes with the same enthusiasm in order to minimise the contamination bias.
A document will be distributed in both groups to remind how to use the sensor (See downloaded documents "Manuel d'utilisation du physilog_V1", Screen: 6/14/11).

8.2.1 Experimental Training

The implementation of the experimental training programme will be done through four sessions of teaching group, two home visits and ten phone calls. For an ideal training session, the participant should perceive the activity as moderate, not too easy and not too difficult.

For the physical training the subject's will be advised to practice the same exercises during at least 3 weeks, 3 to 4 sessions per week with as day of rest between the training sessions. Participants will be recommended to train between 30 to 45 minutes that can be split during the day (e.g. 2x15 or 20 minutes, or 3x10 or 15 minutes during the same day).
For the cognitive training the subject's will be advised to practice 3 times per week for 15 minutes. Ten hours of training in groups are dedicated for the instruction on the use of the tablet. For an adequate training session, the perceived intensity should be neither too difficult nor too easy, but moderate.

The home visits are conducted to control that subjects are able to use the device, answer their questions and see if exercises should be adapted to the subject's environment.

The calls are conducted to answer the subjects' potential questions, ask if they encounter difficulties with their exercise programme and take care of their general health.

Month 1: Two group's sessions of 2 hours with 5-6 subjects will be organised by one physiotherapist and 2 sessions of 3 hours with the neuropsychologist. These sessions are intended for subjects to learn how to use a tablet (handling, charging), learn how to navigate in the application, instruct participants to create their own programme, explain neurocognitive exercises and explain how to place the sensor.
At the end of month one, the neuropsychologist will make the first call.

Month 1 or 2:
At the end of the first month or at the beginning of the second month, the physiotherapist will visit the patient at home for 1 hour. If the physiotherapist visits the subject during the second month, then the first month the physiotherapist will make the first call and vice versa.

Month 2 or 3: The neuropsychologist will visit the subject at home during either month 2 or 3 for 1 hour. If the neuropsychologist visits the subject during the third month, then the second month, the neuropsychologist will make the second call and vice versa.

Months 3: The physiotherapist will make the second call.

Month 4 to 6: Each month, the physiotherapist and the neuropsychologist will phone the subject independently.

8.2.1 Alternative training

In the physical part, the therapist will deliver the recommendations made by Helsana, namely: the choice of the exercice does not matter but they recommend privileging the exercises in a standing position as they request more strength than in a sitting position; exercises may take a little effort, but the participant should always feel good; the exercises should be repeated two or three times a week. First, each exercise should be repeated several times and then gradually increase the number of repetitions; the participant should always feel good and not force himself/herself. Subject's will be asked to train as recommended by The Helsana programmes:

- For the exercise in a standing position, the participant should lean on a stable support if he/she lacks confidence. He/she can lean against a sink or the kitchen worktop. They should not lean against a chair, as it may slip or tip,

- He/she should wear non-slip shoes or socks or walk barefoot,
- Always keep control of his/her movements and start slowly,
- He/she should avoid sudden or jerky movements,
- He/she should have a relaxed breathing and exhale when an effort is made,
- If discomfort or pain is experimented while exercising, the training should be stopped, and the physical therapist should be called.

Ten hours of training are dedicated to the instruction in training groups for the use of the tablet.

In the cognitive part, subjects will be free to play the alternative training if wanted. They will also be encouraged to play a minimum amount of time, i.e. three times a week for a minimum of 10 to 15 minutes.
The exact same follow-up procedure will be executed in the alternative training group as in the SLF experimental training group (see chapter: 8.2.1 Experimental Training).

8.3 Dose / Device modifications

During the instruction sessions, the physiotherapist will explain that it is normal, after a training session, to feel some muscles- and/or joints-pain and that it will disappear in the following days. These sensations will disappear with time and become less frequent with the training.

If disagreement persists or unexpected muscles- and/or joints pain appears or if they experience any other disease, the participants will be informed to contact their physiotherapist.

If during phone calls (either from the subject or from the physiotherapist), subjects report unexpected muscles- and/or joints pain or if they experience any other disease, she/he will analyse the situation and suggest measures to decrease the pain. If the problem does not disappear or has unclear origins, the physiotherapist will recommend the subject to contact this/her physician.

8.4 Compliance with study intervention

In order to improve adherence to exercises, the subjects will be asked to fill up an electronic diary after the physical and cognitive training sessions which will directly be implemented in the application. When the subject wants to stop this training, the application will ask him/her how long (in minutes) he/she trained during this session. The physiotherapists will explain how to access to the exercises and how to fill in these electronic diaries. Concerning the cognitive exercises, the software will record the responses of executed cognitive exercises. During the visits or phone calls, the therapist will ask and control if the participants encounter problems with the diaries.

8.5 Data Collection and Follow-up for withdrawn participants

Not applicable.

8.6 Trial specific preventive measures

Not applicable.

8.7 Concomitant Interventions

Participants with simultaneous treatment in physiotherapy will be asked to inform the physiotherapist of the trial. The physiotherapist will record the information in order to analyse it as a confounding factor.

8.8 Study Drug / Medical Device Accountability

Not applicable.

8.9 Return or Destruction of Study Drug / Medical Device

At the beginning of the project, we will inform each participant that the application was created for this project and that it is limited in time. At the end of the trial, participants will be offered the tablet, but the training application will be uninstalled. The Gmail account linked to the application (specially created for the trial) will be deleted. In case of success, the participant will be informed that Mindmaze might commercialise the product at one point.

9. STUDY ASSESSMENTS

The assessors (KG and TGP) will be trained to perform the assessment and to use the REDCap (Harris, 2009) software before the start of the trial.
The subjects will be assessed three times and location of the assessment will centralised in the CHUV building:

- assessment before randomisation (T0)
- assessment at six months (T1)
- assessment at twelve months (T2).

The physical assessment will be done in a room of the neurological rehabilitation department of the CHUV in the building so called "Nestlé" on the fifth floor (Hôpital Nestlé CHUV, Av. Pierre-Decker 5, CH-1011 Lausanne). The assessment will start with general question about their health, falls, followed by a questionnaire of quality of life and the questionnaire of fear of falling. After that, the physical examination will be performed as following, TUG, Timed 25-FooT WALK, FTBS, FTSTS. The physical assessment will take 90 minutes. At T1 and T2, we general question about their health will not repeated.

The cognitive assessment will be conducted by a neuropsychologist in an office of the neuroscience department (Centre Leenaards de la Mémoire, Dép. des Neurosciences Cliniques du CHUV, Mont-Paisible 16, CH-1011 Lausanne). The overall assessment should last two hours.
For planning reasons, a period of 1 month is planned for the 3 assessment periods (physical and neuropsychology).
After the first assessment (T0), KG and TGP will directly fix the next appointment for T1, and at T1 they will fix with the subject an appointment for T2.
If subject have to change their appointment for the assessment at T1 and T2, they will have to contact the CLM secretary (TJ) to change the appointment.

9.1 Study flow chart(s) / table of study procedures and assessments

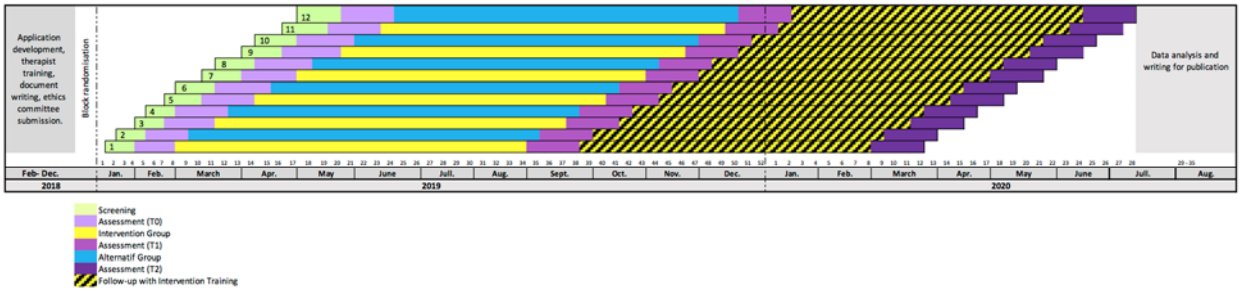


Figure 1: Study schedule

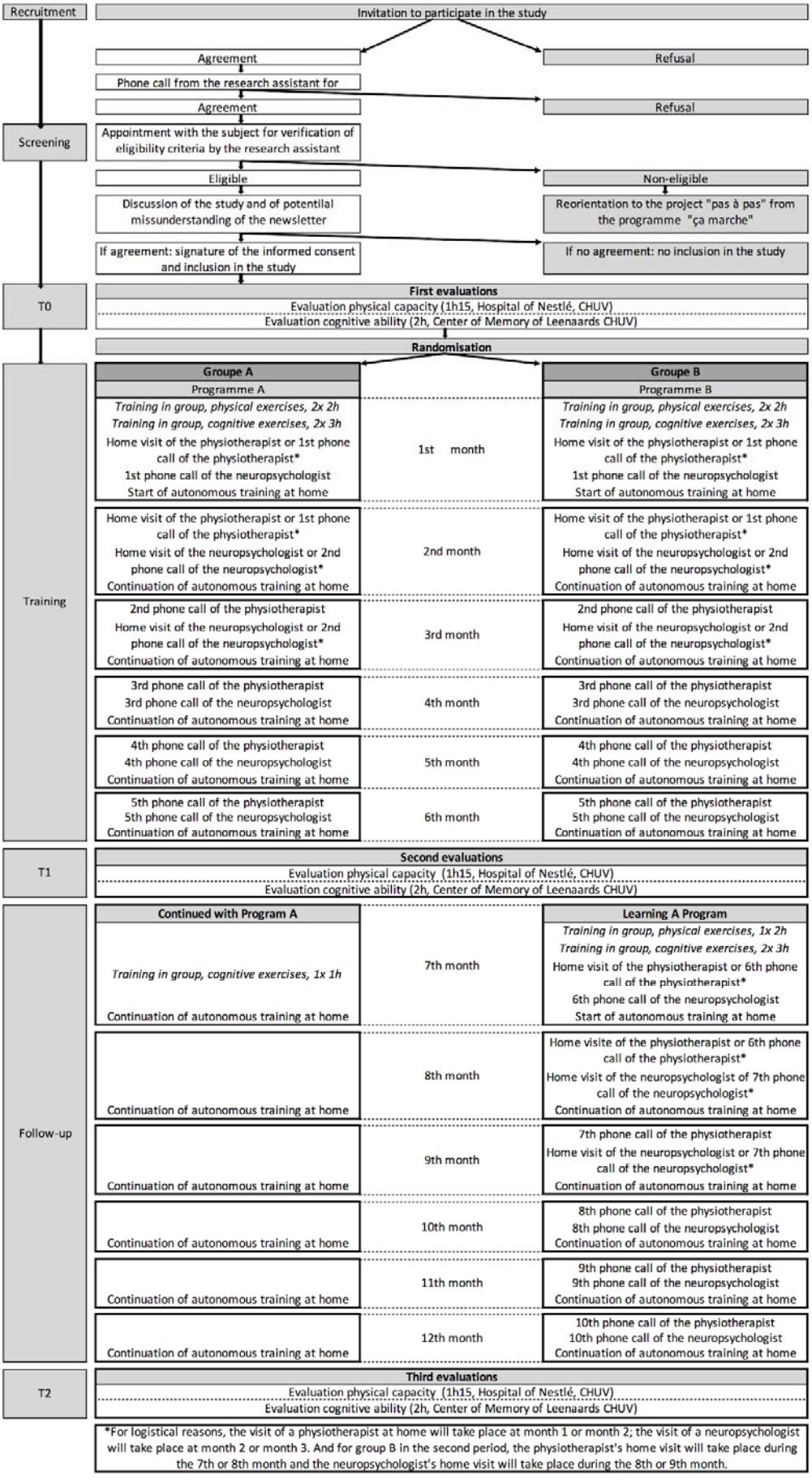


Figure 2: Participant Timeline

9.2 Assessments of outcomes

9.2.1 Assessment of primary outcome

To assess the primary outcome, the Time-Up & Go (TUG) (Podsiadlo & Richardson, 1991) test will be used to measure the lower extremity function, mobility and fall risk. The TUG will be assessed at T0, at six months (T1) and after twelve months (T2) (See Figure 2). In the TUG, the person sits on a chair and at the command "Go", he/she has to stand up, walk three metres at a comfortable and safe pace, turn, walk back to the chair and sit down. The time is measured twice in seconds and averaged, begins at "Go" and ends when the person is seated. This time is not only associated with motor performance but also with cognitive functions (Herman, Giladi, & Hausdorff, 2010) and the history of past falls. Furthermore, it seems that the velocity of walk is directly correlated with the risk of fall (Samah, Mohd Nordin, Shahar, & Ajit Singha, 2016))
.

The subject will have one sensor on each foot which will record motion parameter. The Gait Analysis Desktop Package provided by Gait Up SA is a portable gait lab providing 25 spatio-temporal parameters based on inertial sensing technology. It contains two Physilog®5 sensors and a dedicated software featuring a patented fusion algorithm based on gait events detection, signal de-drifting, strap-down integration, and biomechanical modelling (Bregou Bourgeois, Mariani, Aminian, Zambelli, & Newman, 2014; Dadashi et al., 2013; B. Mariani, 2012; B. Mariani et al., 2010; B. Mariani, Jimenez, Vingerhoets, & Aminian, 2013; B. Mariani, Rouhani, Crevoisier, & Aminian, 2013). The Physilog®5 sensor is a stand-alone 7 degree-of-freedom MEMS inertial measurement unit with wireless synchronisation, including 3D accelerometer, 3D gyroscope and a barometric pressure sensor. The system is non-invasive: sensors are directly strapped on the shoe/feet with Velcro®.

This simple and accurate system is used in clinical routine for gait assessment or clinical test instrumentation (Dadashi et al., 2013). Subjects can be measured in natural condition i.e. in hospital, at home or outside, with a wide range of protocols without time nor volume limitation. The Gait Analysis Package has been validated against Optical Motion Capture and Pressure Insoles with patients suffering from different pathologies (Healthy young and Elderly subjects (B. Mariani et al., 2010), Parkinson's Disease patients (B. Mariani, Jimenez, et al., 2013), Children with Cerebral Palsy (Bregou Bourgeois et al., 2014), Patients before and after Osteoarthritis treatment (B. Mariani, Rouhani, et al., 2013), …).

9.2.2 Assessment of secondary outcomes

The secondary outcomes can be subdivided into assessing five domains: physical capacities; cognitive abilities; affective abilities (including mood and fear of falling); specific associated domains, such as quality of life, ADL activities and finally adherence to treatment and technology. (see chapter 5.2). The tests described below will be conducted at T0, after six months (T1) and after twelve months (T2) (See Figure 2).

The physiotherapist will be in charge of testing physical capacities and will also conduct part of the assessment of related domains (fear of falling for the affective domain and quality of life for the associated domains). The order of the testing is the following:

General question about heath and falls:

The general question about heath will be asked only at T0 and concern their life situation, usual activities, if they take a medication and which one, if they have vision or hearing problems, etc… (See downloaded document: Evaluation physique_T0-1-2_V1, Screen: 6/14/5).

We will also ask them if in the previous 12 months, they fell and will record the severity of the fall according to the categories defined by Schwenk et al. (Schwenk et al., 2012) (see Chapter 9.2.3). At 6 months and 12 months, we will ask them if they if they fell down the past 6 months.

Quality of life assessment:
The quality of life modification will be assessed with the older people's quality of life questionnaire (OPQOL 35). This questionnaire is composed of 35-items assessment the quality of life by elderlies. Following items are reviewed: life overall (4 items), health (4 items), social relationships and participation (7 items in QoL follow-up survey, 8 items in Omnibus surveys), independence, control over life, freedom (5 items), area: home and neighbourhood (4 items), psychological and emotional well-being (4 items), financial circumstances (4 items), and religion/culture (2 items; asked in Omnibus surveys only). The scale has 5-point Likert-scales going from "strongly agree" to "strongly disagree". The coding is reversed so that high scores is high QoL and vis and versa. The scale range goes from 35 points (QoL so bad could not be worse) to 175 (QoL so good could not be better) (Bowling, 2009).
Mittaz-Hager et al. validated the french translation of the OPQOL-35, the paper is not published yet (Butikofer, Rausis, & Mittaz Hager, 2017)(See the three timepoints downloaded document of the physical assessment, Screen: 6/14/5. Bowling et al. 2009 reported that the OPQOL had acceptable levels of reliability and validity in British population samples of older people (Bowling, 2009).

Fear of falling:
It was demonstrated that FES-1 has a good reliability and validity and was validated for use in older adults with cognitive impairment (Hauer et al., 2010). FES-I can be administered as self-completion questionnaires, or administered verbally through an assessor, we decided to do it verbally for this project. The score is calculated by adding up all results. The minimum score (16) correspond to no concern about falling and the maximum score (64) is severe concern about falling. Delbaere et al. established 2 cut-points for low, moderate and high concern of falling (low concern: 16-19, moderate concern: 20-27, high concern: 28-64) (Delbaere et al., 2010).

Physical assessment:
A series of three additional physical tests will complete the proof of the effect of the physical training of the IG on gait, strength and balance.
The gait speed will be assessed through the Timed 25-FooT WALK (20 meters walking test) (Fischer et al., Revised in October 2001), this test also evaluates the lower extremity function. The participant is asked to walk a 20 meter as fast as possible but safely when the assessor says "GO". The test will be performed twice, and the mean of both tests will be calculated. Physilog will also be placed on each foot to analyse 25 gait parameters (See the three timepoints downloaded document of the physical assessment, Screen: 6/14/5).

Balance will be assessed through the Four Stage Balance Test (FSBT) or (ability to stand in four progressively more difficult stances: 1. Feet side-by-side; 2. Partial tandem; 3. Tandem and 4. On one foot) (Sarmiento & Lee, 2017)(See the three timepoints downloaded document of the physical assessment, Screen: 6/14/5).

The functional lower limb muscle strength will be assessed with the Five Time Sit to Stand Test (FTSTS) (Bohannon, 2006). The subject is asked to stand up and sit down 5 times as quickly as he can when the assessor says "Go". The subject will keep arms crossed on the chest and should stand up completely and sit on the chair without leaning on the backrest of the chair. The chair is against a wall to avoid of the risk of slipping. The assessor starts the chronometer when he says "GO" and stops when the participant touches the chair after the fifth rising up. A blank test must be done before carrying out the test twice by timing (See the three timepoints downloaded document of the physical assessment, Screen: 6/14/5).

Cognitive assessment:
The neuropsychologist (TGP) will be in charge of the cognitive assessment, completed by some questionnaire to provide data for related domains such as mood and daily living activities, as well as acceptability and user experience of the developed product. To be consistent, testing should have a specific order that provide enough distracting tasks between the learning phase of memory tests and their recall phase. Different memory tasks should also be conducted one after the other to avoid interference. Here is a table summarizing the order of the cognitive test, the function assessed, a brief overview of the procedure and an estimation of the time to complete each test (overall pure cognitive assessment should take ~80').

Order	**Test's name**	**Cognitive function**	**Description**	**Estimated time**
1	Verbal fluency (Cardebat et al., 1990)	Executive function	The subject should produce as many words as possible in 2' time both on a categorial task (provide as many animals as possible) and in a literal task (find as more word as possible beginning with letter "M")	Twice 2' = 4'
2	RBMT-3 (Wilson, 2018)	Prospective memory - 2 items presentation (Meeting and Personal objects)	Subject is asked to provide two personal objects and should ask for them back once a minuterie will ring (25' later). Then subject should recall to do an action once the testing will be over	5'
3	CVLT (Delis et al., 2010)	Episodic memory - Learning phase	Subject is asked to learn a list A of article to buy in a supermarket. He will be presented 5 times with the same list and will be asked to remember as many articles as possible (free recall) and then will be helped with cues (semantic cues recall). Then he should learn a list B (distractors) with the same procedure. Immediate recall measures its ability to recall a many items of list A by preventing misleading use of items from list B.	15'
4	Stroop Victoria (Bayard et al., 2011)	Speed processing (language) and executive functions	This test is separated in three sub-parts: ● Colour condition (C) ● Word condition (W) ● Interference condition (I) In each condition, the subject is asked to name the colour of the items but in the word and interference condition, he will be presented with words (different from colours for M condition; colours name for I condition) and should	3'

			inhibit to read the written word.	
5	TMT (Tombaugh, 2004)	Speed processing and executive function	The first part of TMT is assessing speed processing: subject need to join bullet-points with numbers inside on alphabetic order. Second part is devoted to providing a measure of flexibility by adding bullet-points with letters and asking the subject to switch systematically between letters and numbers on his way of joining the bullet in both the alphanumeric and alphabetic orders.	4’
6	Digit Symbol Substitution Test (DSST, WAIS IV) (Wechsler, 2011)	Complex, sustained attention	A code linking digit from 1 to 9 with symbols is presented to the subject. After a first learning phase, a table with a first row filled in by digit in random order is presented to the subject. He is asked to fulfil the underneath second row with the matching symbol.	3’
7	RBMT-3 (Wilson, 2018)	Prospective memory - Meeting recall	Once the bell is ringing, the subject is supposed to ask spontaneously two questions to the assessor.	3’
8	Similitudes	Conceptualisation	Subject is asked to find the common concept shared between two words (ex: what shared a horse and a tiger?)	7’
9	CVLT (Delis et al., 2010; Poitrenaud et al., 2017)	Episodic memory - Delayed recall	Recall from list A is asked both on a free and cued mode.	5’
10	Logical memory 1 (Wechler. D, 2008)	Episodic memory - Immediate recall	Two stories are read to the subject that should immediately recall as much elements as possible.	3’
11	TAP - Mental flexibility from Zimmerman and H. van Zomeren in (Leclercq et al., 2002)	Mental flexibility	A digit and a letter are appearing simultaneously on a computer screen and the patient needs to answer as quickly as possible on a specific order (letter first, digit second); they need to switch that order from one trial to the other. (Visit the TAP dedicated website: https://www.psytest.net/index.php?page=Flexibilitaet&hl=en_US)	6’
12	TAP - Divided	Divided attention	Subject has to perform two tasks at the same time: a visual task where	6’

	attention from Zimmerman and H. van Zomeren in (Leclercq et al., 2002)		you need to identify square targets among distractors and an auditory task where you need to detect oddball's sounds (Visit the TAP dedicated website: https://www.psytest.net/index.php?page=Geteilte-Aufmerksamkeit&hl=en_US)	
13	Logical memory 2 (Wechler. D, 2008)	Episodic memory - Delayed recall	Subject is asked to provide a delayed recall of the two stories he was read about 15' ago.	3'
14	RBMT-3 (Wilson, 2018)	Prospective memory - Personal objects recall	As soon as the examiner is saying the that the testing part is over, then the subject is supposed to ask spontaneously for his belongings back. He should recall both the object and its location.	3'
15	Multi-tasking Game assessment	Divided attention and flexibility	To directly assess the effect of the multi-tasking game, a complementary computerized version has been developed where participants are asked to pick up items while walking in a city with different obstacles and distractors.	10'

Related domains questionnaires: total estimated time ~ 25 additional minutes (giving a total of 1h45).

Order	**Name & Reference**	**Assessed function**	**Description**	**Estimated time**
1	HADS	Mood	Anxiety and depression can be addressed with this 2-dimensions questionnaire	7'
2	CFI & part of E-Cogn (home-made french translation)	Both assessing cognition in activity of daily living (ADLs)	The Cognitive Function Instrument (CFI; 14 questions on memory, language and ADLs difficulty) will be completed with three cognitive sub-domains of the Everyday Cognition (E-Cog; Planing- 5 items, Organization - 6 items, Divided attention - 4 questions).	7'
3	Only at T1/T2: Home-made Q1	Acceptability of the intervention	Home-made questionnaire with 9 items on enjoyment (1), appropriateness (4), safety	5'

			(2), self-evaluation (1) and motivation (1) provided by the intervention.	
4	Only at T1/T2: AttrakDiff (french version) (Lallemand, Koenig, Gronie, & Martin, 2015)	User experience	A standardised visual tool aiming at evaluating the user experience and design of an interactive product. It consists in rating on a Likert scale 28 opposite adjectives (ex: ugly - attractive). It allows to compare two interventions (Group B) and provide a Pre/Post for updated version of the same product (Group A).	6'

Assessment adherence to treatment and technology:
The adherence to exercise will be measured by monitoring automatically the time of use of the device and periodically transmit data via the network (internet) to the technical database. Furthermore, the time of use will be cross-checked with subjective reports that each subject will provide at the end of its activities via an electronic diary of the training throughout the twelve months of training. This information recorded in the table will be the date of the training session and the duration of the training session in minutes and the repetitions.

The technology profile of each subject will be provided by filling in a *technological and gaming habits,* a home-made questionnaire that will be administered during the screening (See downloaded "Vérification des critères d'éligibilité_SFL_V2, Screen: 6/14/5). And a final questionnaire will collect a *final feedback* on the features provided by StayFitLonger intervention (virtual guide, social interactions, preferences, gamification, psychoeducation & self-management and SFL usability). A detailed description of when which questionnaire is performed can be found in Table 1.
A document recording the drop outs and question about satisfaction will be a conducted only if subjects agrees to answer (See downloaded documents: Drop out_V1; Screen: 6/14/5).

9.2.3 Assessment of safety outcomes

9.2.3.1 Adverse events
We defined the adverse event in chapter 10 (See chapter: 10.3 Medical Device Category A studies). Falls is one of the adverse events that we defined, and they will be recorded as the population sample is not a fallers' population. At T0, the subject will be asked if they fell in the past 12 months and the severity of the fall will be recorded using the categories defined by Schwenk et al. (Schwenk et al., 2012):

1: No injury
2: Minor injury (reduction in physical function for at least three days)
3: Moderate injury (requiring a medical/health professional examination)
4: Serious injury (requiring accident and emergency or inpatient treatment)

Moreover, we will ask them more precision about the fall; the location and the description of the falls:

- Where? Inside OR outside
- When? Day OR night

- How? Describe shortly the event.

At 6 and 12 months of training, subjects will be asked if, in the previous 6 months, they fell, and, in the case of a fall, the severity of the fall will be recorded using the Schwenk categories (Schwenk et al., 2012).

Between the first and third months of the training, the physiotherapists (to be defined) and the neuropsychologist (AP) will visit the subjects at their home. In the course of the 6 months, the physiotherapist (to be defined) and the neuropsychologist (BLM) will call them (five times each). The subjects will be asked how they feel and if they encounter any health problem.
If the therapists note an AE like:

- Falls that require medical attention,
- Exacerbation of a pre-existing illness,
- Increase in the frequency or intensity of a pre-existing episodic event or condition,
- Condition detected or diagnosed after the intervention, even though it may have been present prior to the start of the study,
- Continuous persistent disease or symptoms present at T0 that worsened following the start of the study,

the therapists will inform the co-investigator (AGMH) the same day.

In case of AE, AI or SAE occurred during an assessment, after a home visit or a phone call, it will be reported to the co-investigator and she will follow the predefined procedure (See Appendix 2: Process and procedure_Risk management pathway_V1). The detailed steps are described in chapter 10.3.1.

9.2.3.2 Laboratory parameters
Not applicable.

9.2.3.3 Vital signs
Not applicable.

9.2.4 Assessments in participants who prematurely stop the study

The subjects have the right to stop their participation in the study without adverse event. In this case, we will ask them if they agree to participate in the expected T2 assessment at twelve months. The withdrawal of subjects will be recorded. We will ask them some questions if they agree to respond (See downloaded documents: Drop out_V1; Screen: 6/14/5).

If the subject withdraws because of an AE, we will record and monitor the AE until resolution, stabilisation, or until it is shown that the study is not the cause of the AE.

9.3 Procedures at each visit

9.3.1 Visit for screening

During the appointment of the inclusion criteria verification, the research assistant (BLM) will explain the goal and proceedings of the study. She will explain the benefits and potential risks. Participant will be told that all partners in the consortium, including Mindmaze Holding and its affiliated Entities, will have access only to the anonymised data from the tablet and sensors and can make any use of the collected data as well as the obtained reports that does not contain any private information by which a participant can be identified.

When eligible criteria are controlled and if the participant fulfils all inclusion criteria and have no exclusion criteria (See downloaded documents: Vérification des critères d'éligibilité_V2, Screen: 6/14/5), BLM will explain the informed consent and collect their signature.
If the subject is eligible and the informed consent is signed, BLM will explain the following steps of the trial. Someone from the CLM team (either BLM or TJ) will fix with them the appointment of the first physical and cognitive assessment (T0). If the subject is not eligible, she/he will be reoriented to a more adapted programme.
After the appointment, the research assistant (BLM) will inform per e-mail the secretary (TJ) that on subject was screened. The secretary (TJ) will control that the screening and the informed consent were filled appropriately. After the control, she we will randomise the participant through the REDCap software.

9.3.2 Visit for assessment sessions

The assessments will be performed at the hospital CHUV, which is centred in the city and easily accessible in public transport.
Three assessment sessions will be done: before starting the training (T0), after six months (T1) and after twelve months (T2) (See downloaded documents: Evaluation physique_T0-1-2_V1: 6/14/5; Evaluation cognitive_T0-1-2_V1, Screen: 6/14/5). A physiotherapist (KG) and a neuropsychologist (TGP), specially trained and blinded to the participant's training-group attribution, will do the assessments.

9.3.3 In-home visits and phone calls of the physiotherapist and the neuropsychologist during the training period

Subjects of the experimental and alternative training group will have the same protocol with 1 in-home visits of each therapist and five phone-calls from each therapist. Physical and cognitive trainers responsible for home and telephone follow-up are asked to address the below described points in their meeting with the subject. Trainers will not necessary be asked to read the questions as they are, but it is important to cover all the points. The different point to be discussed are listed in REDCap (See downloaded document "Suivi à domicile et suivi téléphonique_V1", Screen: 6/14/5), and the answers are collected and registered during the meeting/phone call.

Before contacting the subject, the physical and cognitive trainers will have the opportunity to check the tablet usage by the participant from the stored server data. This will allow them to see the frequency and duration of the subjects' training sessions during the last weeks. In case of abnormalities, it is important to understand where the subject encounters difficulties.

10. SAFETY

10.1 Drug studies

The chapter 10.1 it is not applicable.

10.1.1 Definition and assessment of (serious) adverse events and other safety related events

Assessment of Causality
Not applicable.

Suspected Unexpected Serious Adverse Reactions (SUSARs)
Not applicable.

Assessment of Severity
Not applicable.

10.1.2 Reporting of serious adverse events (SAE) and other safety related events

Reporting of SAEs
Not applicable.

Reporting of SUSARs
Not applicable.

Reporting of Safety Signals
Not applicable.

Reporting and Handling of Pregnancies
Not applicable.

Periodic reporting of safety
Not applicable.

10.1.3 Follow up of (Serious) Adverse Events

Not applicable.

10.2 Medical Device Category C studies

The chapter 10.2 is not applicable.

10.2.1 Definition and Assessment of (Serious) Adverse Events and other safety related events

Adverse Event (AE)
Not applicable.

Adverse Device Effect (ADE)
Not applicable.

Serious Adverse Event (SAE)
Not applicable.

Device deficiency
Not applicable.

Health hazards that require measures
Not applicable.

10.2.2 Reporting of (Serious) Adverse Events and other safety related events
Reporting to Sponsor-Investigator:
Not applicable.

Pregnancies
Not applicable.

Reporting to Authorities
Not applicable.

Periodic safety reporting:
Not applicable.

10.2.3 Follow up of (Serious) Adverse Events
Not applicable.

10.3 Medical Device Category A studies
Device deficiencies and all **adverse events (AE)** including all **serious adverse events (SAE)** are collected, fully investigated and documented in the source document and appropriate case report form (CRF) during the entire study period, i.e. from the patient's informed consent until the last protocol-specific procedure, including a safety follow-up period. Documentation includes dates of events, treatment, resolution, assessment of seriousness and causal relationship to device and/or study procedure [ISO 14155, 6.4.1.].

10.3.1 Definition and Assessment of safety related events
To define the adverse events (AE) in this trial, we inspired us from the AE typology developed by Iliffe et al. (Iliffe et al., 2014) and published in HEALTH TECHNOLOGY ASSESSMENT. Adverse events (AE) are defined as "any unfavourable and unintended sign, symptom, syndrome or illness that develops or worsens during the period of observation in the trial. This include:

1. exacerbation of a pre-existing illness
2. increase in frequency or intensity of a pre-existing episodic event or condition
3. condition detected or diagnosed after the intervention, even though it may have been present prior to the start of the study
4. continuous persistent disease or symptoms present at T0 that worsen following the start of the study."
5. Falls severity 2 or 3

We will consider the Adverse Event that will not require medical attention adverse incidents (AI). See above the list of potential AI related to a physical and cognitive training:

1. Tiredness
2. Muscle contractures

3. Falls severity 0 or 1
4. Dizziness
5. Headaches

We also inspired us from the study of Iliffe et al. (2014) for the definition of the serious adverse event (SAE) which is "any AE occurring following study-mandated procedures, having received the IT or the AT programme that results in any of the following outcomes:

1. death,
2. a life-threatening AE,
3. inpatient hospitalisation or prolonging of existing hospitalisation,
4. a disability/incapacity.

Participants or family member will be asked to contact immediately the co-investigator Ann-Gabrielle Mittaz Hager in case of any SAE. The co-investigator Ann-Gabrielle Mittaz Hager will follow the predefined procedure (See Appendix 2: Process and procedure_Risk management pathway_V1) and she will immediately determine the seriousness and consulting if necessary the principal investigator Prof. Démonet. The causality of the SAE in conjunction with the ET or the AT programme will be determined by the principal investigator Prof. Démonet. A SAE that will deemed directly related to, or suspected to be related to, the trial intervention was reported to the Steering Committee and to the local Ethics Committee within 2 opening day.

All AEs will be assessed for seriousness, expectedness and causality. All AEs will be recorded and closely monitored until resolution, stabilisation, or until it will be shown that the study intervention was not the cause.

The analysis of causal relationship of Adverse Events is also inspired from Iliffe et al. (2014) and is as followed:

- Unrelated: The event is definitely not associated with study procedure; a relationship can be ruled out.
- Possible related: The relationship between the study procedures and the event is possible, but other causes cannot definitely be ruled out. Under this definition, we can find Adverse Reaction, Possible Adverse Reaction and Unrelated serious Event.
- Related: This event is definitely associated with the study procedure. Because the participants of this study are older adults at risk of falling, they can experience falls or other health diseases due to the old age."

The AE, SAE, AI will be recorded (See Appendix 1: Collection AI_AE_SAE_SLF_V1).

10.3.2 Reporting of Safety related events

Reporting to Prof. Démonet (Sponsor-Investigator) :
For participant from Canada or in Belgium, we will ask them to call the physiotherapist in case of falls that causes injury that need physician visit or admission in a hospital or in an emergency unit. Any member of the trial team, participants themselves or family of the participant have to report any adverse event or health hazards to the local coordinator and to the Sponsor-Investigator within 24 hours.

Health hazards that require measures are reported to Prof. Démonet (Sponsor-Investigator) within 24 hours upon becoming aware of the event:

Pregnancies

Not applicable.

Reporting to Authorities:
In Category A studies, the sponsor is subject to the notification requirements specified in Art. 15 of the MedDO of 17 October 2011 (SR 812.213).

- **Health hazards** that require measures are reported within 2 opening days [ClinO Art. 37].

Periodic safety reporting:
A yearly safety update-report is submitted by the Investigator to the Ethics Committee via BASEC. A report is submitted to Swissmedic by the Sponsor-Investigator, as defined in Art. 15a,b of the MedDO of 17 October 2011 (SR 812.213).

10.4 Assessment, notification and reporting on the use of radiation sources

Not applicable.

11. STATISTICAL METHODS

The statistical methods planned for the analysis of primary, secondary and safety variables are described in this chapter.

In general, continuous variables will be summarized using the following standard descriptive statistics: number of observations, arithmetic mean, standard deviation, minimum, median and maximum. If appropriate, the lower and upper quartile will be added. Ordinal and categorical data will be described using absolute and relative frequencies.

All individual data as well as results of statistical analyses will be extracted of REDCap and presented in individual participant data listings and statistical summary tables. A significance level alpha of 5% will be used.

11.1 Hypothesis

11.1.1 RCT over 6 months (between T0 and T1):

The study hypothesis is that, in opposition with the baseline assessment at T0 where the two groups should have the same performance, the experimental training group (using the StayFitLonger training) will show greater relative physical and cognitive performance at the post-test assessments than the Alternative training group (i.e. Self-Directed Prescribed Physical Exercises and Casual Cognitive Game group). This should be set by measuring the velocity of walk with the TUG at baseline (T0) and after 6 months (T1) for the two groups. A statistical effect will be set as significant if a relative difference, across groups, over time is found.

Formally speaking, applying the so called "gold standard design" for the test of a new experimental versus an alternative training, it means that we have the following pair of hypotheses:

Null hypothesis: H_0: there is no difference on the relative variation of the TUG over 6 months or a difference is observed in favour of the alternative training.
Alternative hypothesis: H_1: there is a difference on the relative variation of the TUG over 6 months and this difference is in favour of StayFitLonger programme.

Our aim is then to reject the H_0 hypothesis. The same pair of hypotheses can be adapted to each of the secondary outcomes of the RCT.

11.1.2 Adherence study (between T0 and T2 for experimental group & T1 to T2 for alternative group):

AAL programme requirement is to provide a proof of adherence to the developed IT platform.
For the Experimental Group, our main adherence hypotheses are that: (i) seniors invested in SFL programme will train the required number of hours a week at the beginning of the training (i.e. 3h per week as recommended at T0); (ii) the adherence will decrease with time but stay higher than half of the required dose (i.e. 1,5h per week in mean at T2 for), even though the they will have less supervision during the six last months of the experiment.
For the Alternative Group, adherence hypotheses are a bit different: (i) it is not certain that subjects will train the recommended time because they could lack motivation after having to change training programme (we assume that some seniors will adhere and some will not); the time of training at the beginning of the SFL training will be measured (at T1); (ii) the adherence will decrease with time but stay higher at T2 than half of the measured dose at T1.

11.2 Determination of Sample Size

As we are planning to stratify our subjects into two categories (pre-frail and robust), a Marker Stratified Design should be used to calculate the sample size of our RCT (see: http://www.bigted.org/NonAdaptiveDesigns/MarkerStratifiedDesigns.html). By using a Marker-by-treatment interaction, we will base our sample size calculation on the results of 2 studies corresponding to our population (pre-frail and robust seniors): (1) for pre-frail subjects, we based us on the results of an ongoing study called the Swiss CHEF trial which enrols patients reporting at least one fall and (2) For the robust subject, we based us on the results of a Japanese study Uemura et al. (2018) that had the same kind of intervention than us and the recruited subjects were devoted of illness and had normal cognitive skills (Uemura, Yamada, & Okamoto, 2018).

Based on the results of the T&E pilot study, we estimated the minimal sample size required to conduct a valid study on pre-frail subjects. For a 2-arm study (experimental training vs. alternative training) and taking TUG (Time-UP & Go) as primary outcome, 16 participants per group are required to detect a difference of 3.22 seconds using a two-sided t-test (alpha=0.05) with a power of 80%. Since data might not be normally distributed, the non-parametric Wilcoxon-Mann-Whitney test should be used for the analysis. To account for this, additional 15% of participants should be enrolled, which results in a sample size of 18.4 participants per training group. Assuming a dropout rate of 25%, the number increases to 24.5 participants per group, and overall 50 participants should be enrolled.

Based on the results of Uemura et al. (2018), the same estimation will provide the minimal sample size required for robust subjects. For a 2-arm study (experimental training vs. alternative training) and taking TUG (Time-UP & Go) as primary outcome, 23.5 participants per group are required to detect a difference of 0.82 seconds using a two-sided t-test (alpha=0.05) with a power of 80%. Since data might not be normally distributed, the non-parametric Wilcoxon-Mann-Whitney test should be used for the analysis. To account for non-parametric distribution (Wilcoxon-Mann-Whitney), an additional 15% of participants should be enrolled, leading to a sample size of 27 participants per training group. Assuming a dropout rate of 25%, the number increases to 36 participants per group, and overall 72 participants should be enrolled.

Therefore, according to the previous sum of sample sizes (122) and for a homogeneous distribution among the different involved countries, we will recruit a total sample of 128 participants (64 for Switzerland, 32 for Canada and 32 for Belgium).

11.3 Statistical criteria of termination of trial

We have no specific stopping rules established because we are not expecting risks that are different in the two training groups (i.e. no adverse event stopping criteria) and we are not planning to stop the trial based on superiority criteria. Thus, the screening phase will stop when the required sample size will be achieved, i.e. when 128 subjects will have been enrolled in the trial. The trial will stop when the last enrolled subject will have had his third assessment (T2: physical and cognitive assessment).

11.4 Planned Analyses

Each of the two parts of the project will involve its own planned analysis with specific statistical method.

Efficacy. The **first part of the study,** i.e. the double-blind RCT methodology will allow to compare the *efficacy* of the two training programmes, for seniors in general. It will be done by measuring the performance of the two groups at two time-point: baseline (T0) and after 6

months of training (T1). The potential difference of effects on robust and pre-frail seniors will be kept for secondary analysis by applying the same method to robust and pre-frail seniors independently.

Adherence to SFL programme. As requested by AAL, the **second part of the study** is dedicated to measure the adherence to StayFitLonger programme over the usage time (i.e. 12 months for the Experimental Group and 6 months for the Alternative Group). The methodology used here will be a more qualitative approach, as used in longitudinal studies. Primary analysis will focus on a way to validate the product, based on a mean adherence curve. Secondary analysis will be based on individual profile characteristics and descriptive statistics will be used to explore the different factors having an effect on the observed adherence curve (slope of adherence profile, cumulated dose, efficacy, …).

A detailed statistical analysis plan will be written as a separate document after finalisation of the protocol.

11.4.1 Datasets to be analysed, analysis populations

Efficacy of the training programmes. Concerning the *efficacy objectives* of the study, we will use a modified intention to treat analysis, i.e. performed on the entire set of participants except the one that never started the intervention, with mixed linear model as these are robust to missing data (Schulz, Altman, & Moher, 2011). The primary analysis will be done with treating strata as random effects. For secondary analysis, adjustment for centre will be done by adjusting for senior type (robust vs vulnerable).

Adherence to SFL programme. Concerning the *adherence objectives* of the study, we will limit our analysis to the per-protocol participants who had StayFitLonger programme, as required by AAL.

11.4.2 Primary Analysis

Efficacy of the training programmes. Concerning the *first part* of the study (*RCT over 6 months*), the *primary efficacy analysis* will be based on a modified intention-to treat (mITT) analysis. Efficacy analysis will be conducted using mixed linear models. The fixed effects will be intervention (experimental, alternative), time (Pre, Post), and their interaction. A significant interaction is expected if the intervention is more beneficial than the alternative condition. When an interaction is found, we will examine whether there is a significant difference between Pre and Post in each group and assessed change scores at post-training (Experimental [Pre_Post]/|Pre|, Alternative [Pre_Post]/|Pre|). Efficacy will be supported if the Post change score is larger in the experimental than the alternative group. All analyses will be adjusted for sex, age, and education. Group differences on baseline characteristics of the mITT sample will be assessed using separate analysis of variance. All analyses should be adjusted for sex, age and education, and normalized scores will be used to facilitate comparison across variables. This method will be applied to each of our primary and secondary outcomes.

Concerning the *second part* of the study (**longitudinal observations on adherence** over 12 months for experimental/6 months for alternative groups), we will limit our individual adherence factors analysis to the per-protocol participants. A mixed linear model will be used to find the mean curve of adherence, based on all per-protocol participants data. The slope of this experimental curve will be compared to the theoretical expected adherence curve (i.e. a flat curve with an intercept of 3 hours of training a week) and provide a first visual overview of the training adherence. Different scenarios might be envisaged; however, this experimental adherence curve will undoubtedly decrease with time with an intercept close from 3h/week (in general, subjects will start to apply the required dose at the beginning of the training and will

lose motivation with time). Then, assuming an intercept of 3h/week at the beginning of the training, the training adherence will be qualified as Over expectation/ Perfect/Sufficient/Insufficient if the slope is Positive/Null/Slightly negative/Steeply negative with Slightly negative being $0 < \text{slope} \leq -0.125$ and Steeply negative a slope<-0.125 (i.e. subjects are still training in mean half of the required time at 12 months or not). If the assumption of an intercept of 3h/week at the beginning of the training is not obtained, then the area under the curve will be measured (= cumulated dose) and compared to that of the theoretical adherence curve. The training adherence will be qualified as Over expectation/Good/Sufficient/Insufficient if the cumulated dose is Higher/Equal/Higher than half/Lower than half of the theoretical cumulated dose.

Excel and SPSS tables will be prepared up to the end of year 2019. Efficacy analyses will start in February 2020, once all the subject will have had their T1 assessment. Adherence will be computed at that time too to have an overview of the 6th first month of adherence. Data from the 6th last months will be added as soon as T2, the last assessment, will be completed (i.e. beginning of August 2020). It will be done by MBA in cooperation with Sylvie Belleville and Prof. Jean-François Démonet.

11.4.3 Secondary Analyses

Efficacy of the training programmes (RCT over 6 months):

- ***Robust vs pre-frail stratification***: the secondary efficacy analysis is aiming at using the stratification to separate the subjects into robust and pre-frail seniors and apply the same analysis than the one described above. Our hypothesis is that pre-frail seniors will obtain a higher benefit of the training. By being less conservative than in a mITT, we will also compare per-protocol group of robust and vulnerable subject and apply stepwise regression analyses to see whether there is a significant differ
- ***Moderators***: Age, level of education, cognitive status (MoCA), expectation from therapy, adherence (cumulated dose), and other characteristic of the training profile could be set as moderator factors. We will use stepwise regression analyses with the per-protocol participants from the experimental training group to explore whether the moderators predict efficacy (i.e. change scores on primary and secondary outcomes).

Adherence to SFL programme (over 12/6 months for experimental/alternative group):
Adherence factors analysis: Individual adherence curve (set as the cumulated time of training over a week of the experiment) will be computed and analysed via linear regressions. Both the slope and intercepts will provide individual adherence factors. The area underneath the curve (= cumulated dose) will provide another factor of adherence. Regularity (i.e. how many sessions of at least 30 minutes were made per week) and intensity (i.e. how many repetitions per time) of the physical training will be considered as two another one. The correlation between these different factors will be studied and a primary component analysis will allow to find the best common factor.
Defining good and bad adherent profile. By using extreme quartile method, we will separate our subject into good and bad adherents and describe their profile according to the above factors. Then mixed linear model will help defining the characteristics of good and bad adherents.
Effects on efficacy. For each subject, we will thus test whether these adherence factors are correlated with the subject efficacy. It will be done with t-test performed on each primary and secondary outcomes to check whether the good adherent profile will have a higher benefits from the therapy than the bad adherent profile.
Separating physical and cognitive training. The same analysis will be made by separating the time spent to perform physical exercises from the time spent playing cognitive games.

Adherence with less supervision. The adherence pattern of the experimental group will be compared over the six first months of training (supervised SFL training) and the six last months of training (unsupervised SLF training). It will provide insight on the role of keeping high or low supervision.

Cognitive app. validation. Last but not least, specific effects of the cognitive applications, specifically developed for the SFL programme, will be analysed by using the analyses design than described on the primary analysis but on specific cognitive test linked to the trained cognitive function.

Secondary analysis will be addressed once primary analysis will be over, by the same persons and by using the same software as the one described in the previous paragraph.

11.4.4 Interim analyses
Not applicable.

11.4.5 Safety analysis
The proportion of adverse events will be compared between the training groups by the blinded statisticians.

11.4.6 Deviation(s) from the original statistical plan
Any deviations from planned analyses, the reasons for such deviations, and all alternative or additional statistical analyses that may be performed before database close, will be described in amendments and in the clinical investigation report.

11.5 Handling of missing data and drop-outs
As settled in a mITT approach, i.e. the reasons and characteristics of drop-outs will be recorded and all participants will be invited to complete the post-tests. We will use a mixed linear model and include all participants who completed the pre-test.
All data of the patients will be used as available. All endpoints will be analyzed, dropping patients with impossible values. Percentages will be based on participants with non-missing values only.

12. QUALITY ASSURANCE AND CONTROL

To implement and assure the quality of this trial, the Steering Committee will stay in close contact with all stakeholders in Switzerland as well as with the investigator in Canada and in Belgium (See *Figure 3: Study administrative structure*).
We regularly perform meetings in Switzerland and video conferences with the Canada and the Belgium all together to prepare this study and later to the follow-up.
Katia Giacomino and Mélanie Bieler-Aeschlimann will train all therapists in the three countries to implement the home-based exercise programmes and to execute the assessment examinations. An explanatory brochure will be distributed at each site for the assessors to explain how to perform the assessments. In order to ensure that the tests are carried out properly, we ask that assessors to film themselves during an evaluation session with a fake subject. These videos will be viewed and judged by Katia Giacomino for the physical part and Mélanie Bieler-Aeschlimann for the cognitive part.

A brochure for the usability of the application will be distributed for the trainers to each site and a Workshop will be organised through video conferences in order to explain how to use the application.

12.1 Data handling and record keeping / archiving

The clinical data will be collected and managed by using the REDCap electronic data capture tools that is hosted in HES-SO servers. REDCap (Harris, 2009) (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies, providing 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources.

Data form the Physilog during assessment: During two assessments (TUG and the 25 Feet Walking test) subjects will wear 2 the Physilog. The raw technical data in ".bin" format will be transferred in the Gait up software program to interpret the data. The Excel file coming from the software will be saved under the ID number of the participant in REDCap.

Data from the Physilog during home training: The technical data of the Physilog, used during the training session, will be sent via Bluetooth to the tablet and the technical encrypted data from the tablet will be sent to a secure server in the HES-SO. All registered data by the different devices is anonymised.

12.1.1 Case Report Forms

Some Case Report Forms will only be electronic (e-CRF) and other will be paper recorded (p-CRF) as subjects have to write down answers for some tests.

The paper sheets will be "named" with the subjects' identity code (see below). The score of the test of the paper records (i.e. MoCA test (Nasreddine et al., 2005)) will be registered in REDCap directly.
All paper records, as well as the signed informed consent, will be scanned and registered on a secured server in the CLM with specific read/write options. For example, the assessor will only have written option to specific sub-files in order to load the scanned document (i.e.: CH007/T0/neuropsychology assessment/ or CH007/Informed consent/). The paper forms will

be destroyed after scanning through the CHUV system for confidential paper. The same procedure will be followed at T0, T1 and T2.

Once all the data are exported from REDCap and data are analysed, theses Excel files will be kept on the secured servers of the HES-SO. Ten years after the end of the trial, the results will be destroyed by the Informatic Office Service.
The identity code (CI) includes two letters and seven numbers. The letters will design the country with the two capital letters (CH: Switzerland; BE: Belgium; CA: Canada). The numbers are the order of entry in the study as soon as the coordinator received the consent, (i.e.: CH001, BE006).
All assessors (KG & AP) will use a computer from their institution to fill the assessments (T0, T1 and T2 assessment) and a link will be given to them to have access to REDCap. All assessors will be trained to ensure the quality, the rigour and the standardisation of the assessment sessions and the use of the REDCap software. REDCap will be configured to minimise the missing data. It will be impossible to enter the next data if the precedent is not entered. When possible, we also will set minimal and maximal bounds (i.e. Height (cm) expected range is 130-215 cm). The "closed" questions will propose the possible answers, the "open" questions will allow enter text.

12.1.2 Specification of source documents

As described above, electronic CFR are registered on REDCap, and paper sheets will be scanned and stored in a secured server of HES-SO.

12.1.3 Record keeping / archiving

After the trial, the clinical data collected will be backed up and kept on a secured servers of the CLM for ten years.
The technical data (such as games scores, quiz created by users) will be hosted by HES-SO Valais-Wallis for ten years.

12.2 Data management

12.2.1 Data Management System

This table give the detail of who has access to which document in REDCap.

Instrument	Right to enter data	Right of consultation	Export duty
Code d'identification	Benedetta Leidi-Maimone	Tania Javaux, Jean-François Démonet, Murielle Bortolotti	Statisticians, Mélanie Bieler-Aeschlimann Jean-François Démonet, Sylvie Belleville

Consentement éclairé	Benedetta Leidi-Maimone	Tania Javaux, Jean-François Démonet, Murielle Bortolotti	Statisticians, Mélanie Bieler-Aeschlimann Jean-François Démonet, Sylvie Belleville
Données personnelles	Benedetta Leidi-Maimone	Tania Javaux, Benedetta Leidi-Maimone, les physiothérapeutes désigné-e pour les en groupe et à domicile, Jean-François Démonet, Murielle Bortolotti	
Eligibilité	Benedetta Leidi-Maimone	Tania Javaux, Jean-François Démonet, Murielle Bortolotti	Statisticians, Mélanie Bieler-Aeschlimann Jean-François Démonet, Sylvie Belleville
Evaluation T0, (physique et cognitive)	Katia Giacomino and Thomas Genoud-Prachex	Tania Javaux, Jean-François Démonet, Murielle Bortolotti	Statisticians Mélanie Bieler-Aeschlimann Jean-François Démonet, Sylvie Belleville
Randomisation	Automatically generated	Tania Javaux	
Evaluation T1 (physique et cognitif)	Katia Giacomino and Thomas Genoud-Prachex	Tania Javaux, Jean-François Démonet, Murielle Bortolotti	Statisticians, Mélanie Bieler-Aeschlimann Jean-François Démonet, Sylvie Belleville
Expectation questionnaire - PRE	Alexandre Pinaud or physiotherapeutic trainer (to be defined)	Tania Javaux, Jean-François Démonet, Murielle Bortolotti	Statisticians, Mélanie Bieler-Aeschlimann Jean-François Démonet,

			Sylvie Belleville
Suivi téléphonique	Benedetta Leidi-Maimone and physiotherapeutic trainer assigned to home visits	Tania Javaux, Jean-François Démonet, Murielle Bortolotti	Statisticians, Mélanie Bieler-Aeschlimann Jean-François Démonet, Sylvie Belleville
Evaluation T2 (physique and cognitive)	Katia Giacomino and Thomas Genoud-Prachex	Tania Javaux, Jean-François Démonet, Murielle Bortolotti	Statisticians Mélanie Bieler-Aeschlimann Jean-François Démonet, Sylvie Belleville
Adverse Event	Anne-Gabrielle Mittaz Hager Jean-François Démonet	Tania Javaux, Jean-François Démonet, Murielle Bortolotti	Statisticians Mélanie Bieler-Aeschlimann Jean-François Démonet, Sylvie Belleville
Drop out	Mélanie Bieler-Aeschlimann	Tania Javaux, Jean-François Démonet, Murielle Bortolotti	Statisticians Mélanie Bieler-Aeschlimann Jean-François Démonet, Sylvie Belleville

Figure 6: REDCap Access

To manage the data, we will use REDCap software.

An engineer from the HES-SO specialised in REDCap, will be mandated from CHUV and will implement all instruments in REDCap.

Alexandre Cotting is the IT project manager responsible for software REDCap. His service will responsible to make sure that REDCap is working by testing the implemented documents of these trial several times.

Mélanie Bieler-Aeschlimann is responsible for the Data Management.

The physiotherapist and neuropsychologist assessors are responsible to collect the data on REDCap.

Mélanie Bieler-Aeschlimann is responsible to export of the data from REDCap the selected

statistical software.

12.2.2 Data security, access and back-up

The REDCap software allows to give access to specific "instrument" depending on the function of the persons (See *Figure 6: REDCap Access)*. An engineer of the HES-SO, which is not involved in the trial will give access to each person involved in the study and give him/her only access on what he/she is allow on REDCap.
REDCap software will be programmed so that every change in data will be described (what was changed, when and who did the changes). The IT project manager responsible for software REDCap will be responsible to perform regular backup of the REDCap software. The technical data registered in on a secure server of the HES-SO Valais-Wallis will perform backups on a daily basis.

12.2.3 Analysis and archiving

Mélanie Bieler-Aeschlimann will be responsible to download the clinical data from REDCap to in an Excel file. This Excel will then be downloaded in a statistical software such as SPSS, R or Stata.
The clinical data (in an Excel file), which will be downloaded in the selected statistical software, will be backed up and registered on a secured server of the CLM. Only persons involved in the statistical analysis will be allowed to access to this secured file.

12.2.4 Electronic and central data validation

The secretary (TJ) will control all the data (screening and informed consent) entered in REDCap to avoid the missing data (see chapter 9.3.1 Visit for screening).

12.3 Monitoring

In order to ensure the proper conduct of the study and to certify that the study respects what has been defined in the protocol, we will conduct internal audits. They will be performed by the study coordinator of CLM (actually Mrs Murielle Bortolotti, MB) that will be mandated to control that the predefined method to manage the data in the protocol are respected. The study coordinator of CLM has the knowledge and skills required for research and monitoring of clinical trials, therefore we think that the necessary skills to carry out this internal audit are filled out. The study coordinator of CLM (MB) works at the CLM but is not involved in this research project.

The audit will be conducted as follows:
In March 2019, the data of 5 subjects will be taken at random and the study coordinator of CLM (MB) will check that these people have signed the informed consent, that eligibility criteria have all been filled in correctly in REDCap and that all the tests of the physical and cognitive evaluations have been filled correctly. She will also check that the scanned PDF documents have been registered on the secured server of CLM.
In July 2020, the study coordinator of CLM (MB) will randomly take 5 other subjects, she will check that the cognitive and physical tests have been completed correctly for the T1 and T2 assessment (both cognitive and physical assessments). Finally, the study coordinator of CLM will also check that the scanned PDF documents have been registered on the secured CHUV server.

12.4 Audits and Inspections

The source data/documents (clinical data) will be accessible to auditors/inspectors from CEC in the HES-SO Valais-Wallis in Techno-Pôle 1, 3960 Sierre. Antoine Widmer will answer the

questions during the inspections. All involved parties will keep the participant data strictly confidential.

The technical data will also be accessible to auditors/inspectors from CEC in the HES-SO Valais-Wallis research offices in Sierre, Techno-Pôle 1, 3960 Sierre. Antoine Widmer will answer the questions during the inspections. All involved parties will keep the participant data strictly confidential.

12.5 Confidentiality, Data Protection

The data are protected by the steering committee and all data management procedure (See Chapter 12.2.2). Direct access to source documents will be permitted for purposes of monitoring, audits and inspections. During and after the study,

- The steering committee and the expanded steering committee have access to protocol,
- The data management team have access to the dataset and all changes will be recognised and noted (date, who and what),
- Auditors and inspectors from CEC will have access to the protocol and the datasets.

12.6 Storage of biological material and related health data

Not applicable.

13. PUBLICATION AND DISSEMINATION POLICY

During the study, we will send two Newsletters to the participants and the field partners (recruitment institutions, physiotherapists and neuropsychologists who train the subjects).

The first results will be communicated as soon as possible to participants, to different partners and health care professionals. A report will be communicated to the public health and social politicians, as well as to health insurances, the National funding agencies and the AAL Central management unit to promote this kind of trainings to prevent functional and cognitive decline in older people.

We forecast to participate in international professional meetings and congresses, present the overall results on the SFL website (http://www.stayfitlonger.eu) as well as in the social media and publish this protocol and the results of the trial in medical journals focussing on geriatrics rehabilitation (such as The Lancet, Physical neurorehabilitation, Neuropsychological Rehabilitation or Journal of the American Geriatrics society) or public health.

Regarding the dissemination of results, and as agreed in the Consortium Agreement, any planned publication shall be communicated to the other Parties at least forty-five (45) calendar days before the publication. If no objection is made within thirty (30) calendar days after the receipt of the notice, the publication is permitted.

14. FUNDING AND SUPPORT

14.1 Funding

The development of this project is funded by the "ACTIVE AND ASSISTED LIVING PROGRAMME " (AAL programme). The budget of the application development and the trial is: 2'517'847 CHF.

14.2 Other Support

The application development, hardware's such as tablets and gait up sensors, as well as salaries are included in the above budget.

15. INSURANCE

Even if this study is a category A, the insurance of the CHUV (Centre Hospitalier Universitaire Vaudois) will cover the costs (See Appendix 3: Attestation_assurance_recherche_2018). The CHUV insurance will cover any costs that may arise in Switzerland. The geriatric institution of Montreal and the Conectar centre in Belgium will operate the insurances of their respective institution.

With regard to any damage caused by participants to the tablet or the sensors during training and the assessments, the CHUV will be liable for the latter in its capacity as promoter in accordance with the applicable legal provisions. This information was also confirmed by Mrs Kaeser (See Appendix 3: Attestation_assurance_recherche_2018).

16. REFERENCES

16.1 References from the Ethics Committee:

1. Declaration of Helsinki, Version October 2013, (http://www.wma.net/en/30publications/10policies/b3/index.html)
2. International Conference on Harmonization (ICH, 1996) E6 Guideline for Good Clinical Practice. (http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R2__Step_4.pdf)
3. International Conference on Harmonization (ICH, 1997) E8 Guideline: General Considerations for Clinical Trials http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E8/Step4/E8_Guideline.pdf)
4. Humanforschungsgesetz, HFG Bundesgesetz über die Forschung am Menschen (Bundesgesetz über die Forschung am Menschen, HFG) vom 30. September 2011/ Loi fédérale relative à la recherche sur l'être humain (loi relative à la recherche sur l'être humain, LRH) du 30 septembre 2011 / Legge federale concernente la ricerca sull'essere umano

(Legge sulla ricerca umana, LRUm) del 30 settembre 2011

5. Verordnung über klinische Versuche in der Humanforschung (Verordnung über klinische Versuche, KlinV) vom 20. September 2013 / Ordonnance sur les essais cliniques dans le cadre de la recherche sur l'être humain (Ordonnance sur les essais cliniques, OClin) du 20 septembre 2013. Ordinanza sulle sperimentazioni cliniche nella ricerca umana

(Ordinanza sulle sperimentazioni cliniche, OSRUm) del 20 settembre 2013

6. Heilmittelgesetz, HMG Bundesgesetz über Arzneimittel und Medizinprodukte (Heilmittelgesetz, HMG) vom 15. Dezember 2000 / Loi fédérale sur les médicaments et les dispositifs médicaux (Loi sur les produits thérapeutiques, LPT) du 15 décembre 2000 / Legge federale sui medicamenti e i dispositivi medici (Legge sugli agenti terapeutici, LATer)
7. ISO 14155:2011 Clinical investigation of medical devices for human subjects -- Good clinical practice (www.iso.org)
8. ISO 10993 Biological evaluation of medical devices (www.iso.org)
9. MEDDEV 2.7/3 revision 3, May 2015
10. Medizinprodukteverordnung (MepV) vom 17. Oktober 2001 / Ordonnance sur les dispositifs médicaux (ODim) du 17 octobre 2001 / Ordinanza relativa ai dispositivi medici (ODmed) del 17 ottobre 2001
11. WHO, International Clinical Trials Registry Platform (ICTRP) (http://www.who.int/ictrp/en/)
12. European regulation on medical devices 2017/745.
13. Strahlenschutzverordnung (StSV) vom 26. April 2017 / Ordonnance sur la radioprotection (ORaP) du 26 avril 2017 / Ordinanza sulla radioprotezione (ORaP) del 26 aprile 2017.

16.2 Other references

17. APPENDICES

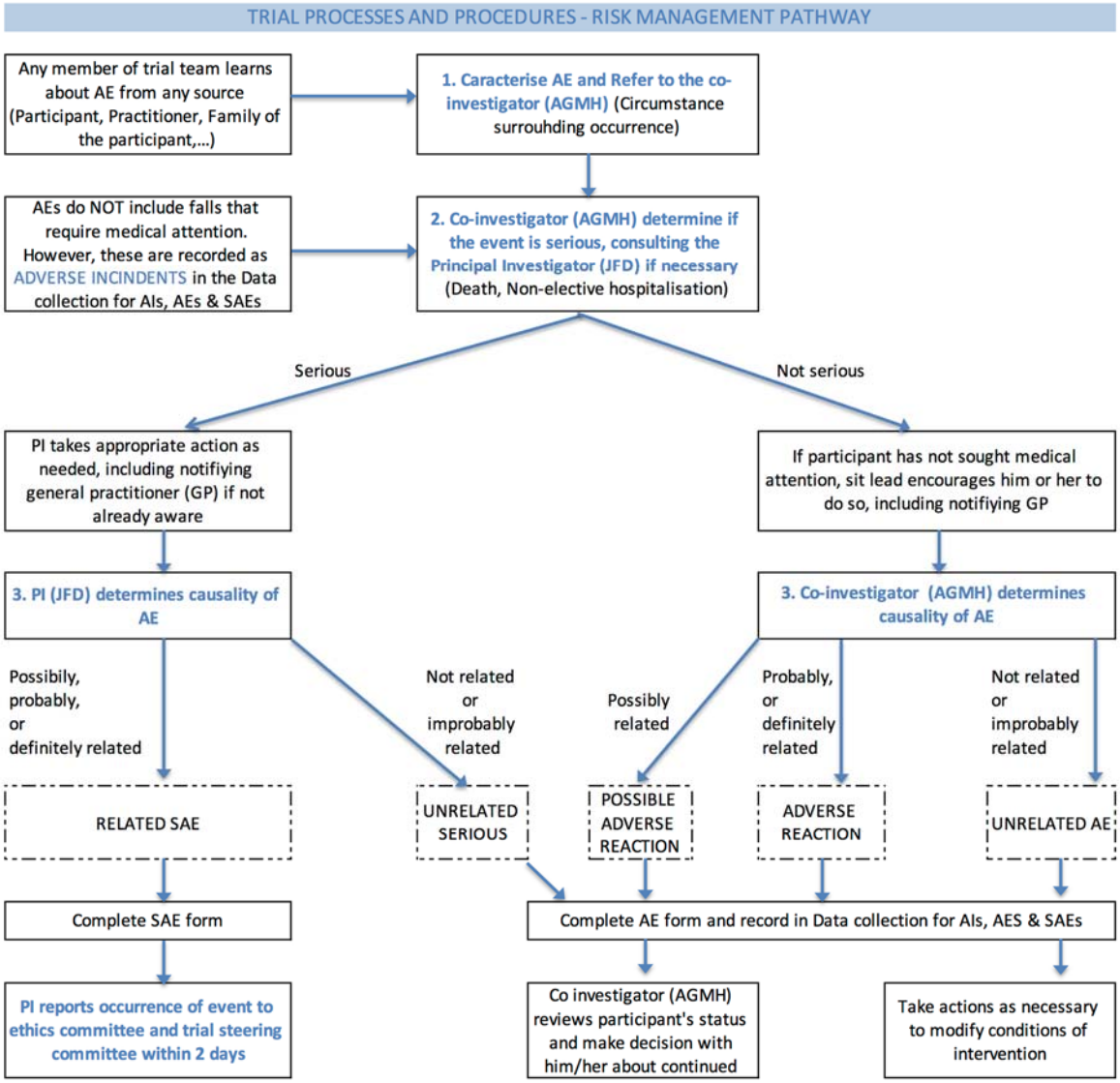
Appendix 1: Collection AI_AE_SAE_SLF_V1

19. Recueil des données des Lost of follow up, AIs, AEs et des SAEs _ StayFitLonger Trial_Swiss

AI (Adverse Incident): AE qui ne requière pas d'intervention médicale (ni visite médicale ni hospitalisation)
AE (Adverse Event): Tout signe, symptôme, syndrome ou maladie défavorable ou non-intentionnel, qui se développe ou qui se péjore durant l'étude et qui requiert une attention médicale
SAE (Serious Adverse Event): Tout AE dont les conséquences sont : Décès, Situation de mise en danger, Hospitalisation, Invalidité-Incapacité

CI Participant	Type d'événement	Annoncé par	Date de l'événement	Description de l'événement	Catégorie:			Conclusion de l'événement :			Mesure(s) prise(s)
					AI	AE	SAE	Sans lien avec la précédure	Lien possible mais d'autres causes ne sont pas à exclure	En lien avec la procédure	

Appendix 2: Process and procedure_Risk management pathway_V1



Appendix 3: Attestation_assurance_recherche_2018

Centre hospitalier
universitaire vaudois
Direction générale
Rue du Bugnon 21
1011 Lausanne

Commission cantonale vaudoise
d'éthique de la recherche sur l'être
humain
Professeur Patrick Francioli
Président
Avenue de Chailly 23
1012 Lausanne

Référence : PFL/PS

Lausanne, le 8 décembre 2017

Responsabilité et garantie 2018

Monsieur le Président,

Vous trouverez ci-après l'attestation du CHUV concernant sa responsabilité en qualité de promoteur, compte tenu des dispositions légales en vigueur, en particulier l'Ordonnance relative à la recherche sur l'être humain à l'exception des essais cliniques, (ci-après « ORH ») et à l'Ordonnance sur les essais cliniques dans le cadre de la recherche sur l'être humain (ci-après « OClin ») pour ce qui concerne l'année 2018.

Tout comme le document y relatif établi l'année passée, dite attestation confirme que le CHUV, lorsqu'il est promoteur d'une recherche au sens de l'article 3 ORH, respectivement article 2 litt. c. OClin, répondra du dommage conformément aux articles 12 et 13 ORH ainsi que 10 à 14 OClin et que son obligation de garantie sera conforme aux montants décrits dans l'Annexe 1 ORH, respectivement dans l'Annexe 2 OClin.

Nous profitons de ces lignes pour vous confirmer en outre que pour les projets de recherche de catégorie A au sens de l'article 13 al. 1 ORH ainsi que article 12 litt. b OClin, le CHUV assumera sa responsabilité en application des dispositions de la Loi vaudoise sur la responsabilité de l'Etat, des communes et de leurs agents (LRECA, RSV 170.11), en particulier son article 4.

Comme dit plus haut, dite attestation est valable pour tout projet relevant des dispositions précitées, et ce dès le premier janvier 2018, pour la durée d'une année.

Enfin, nous vous proposons que tout investigateur soumettant un projet de recherche ou une étude clinique dont le CHUV est le promoteur, comme défini plus haut, continue à faire figurer dans le protocole la phrase suivante :

« En ce qui concerne les dommages éventuels causés aux participants, le CHUV répondra de ces derniers en sa qualité de promoteur conformément aux dispositions légales applicables ».

En vous remerciant d'avance de prendre bonne note de ce qui précède, nous vous transmettons, Monsieur le Président, nos meilleures salutations,

Philipp Müller
Directeur administratif et financier

Pierre-François Leyvraz
Directeur général

canton de vaud

Appendix 4: Risk Analysis for Risk-Adapted Monitoring_V1.

Risk Analysis for Risk-adapted Monitoring.

Risk Analysis for Risk-Adapted Monitoring

Title of Protocol: StayFitLonger Trial Sponsor's Name: Centre Hospitalier Universitaire Vaudois (Centre Leenaards de la Mémoire)
Principal Investigator: Prof. Jean-François Demonet Date: 01.10.2018
Ethics Committee No.:
Trial Site(s): Vaud
Project No.:
Signature:

Completed by: Anne-Gabrielle Mittaz Hager
Function: Member of the Steering Committee

Monitoring Class (resulting from the risk analysis below; if no risk analysis has been conducted, a high risk will be assumed)

To complete the questionnaire please use "Tab" for navigation.
Please type **"1"** in the corresponding field.

Potential risk of therapeutic intervention in comparison to standard of medical care

Type of clinical trial	**Comparable** (see also ClinO Art. 19, 20, 61, category A)	1
	Higher (see also ClinO Art. 19, 61, category B)	
	Markedly higher (see also ClinO Art. 19, 20, category C)	

Please type **"1"** for Yes and "0" for No.

Potential trial participant-related critical indicator

Participant-related indicators (P)	Yes / No	If Yes, specify its nature.			If Yes, which QA measure can control the risk?	If no QA measure, can monitoring control the risk?
		Participant safety	Participant rights	Data validity		
P1 Will a vulnerable population be included?	No					
P2 Will adult participants who are temporarily unable to provide informed consent be included into the trial?	no					
P3 Will trial participants be recruited within the scope of emergency medical treatment?	no					
P4 Are there any critical eligibility criteria?	no					
P5 Is there a lack of previous experience on the (combination of) medications and/or therapies being studied?	no					
P6 Is it likely that participants receive additional medication for concomitant diseases/symptoms?	Yes					participants are cogntively healthy but may benefit from medical treatment of frequent chronic conditions e.g. HTA, diabetes, hypercholesterlomia
P7 Is there only very limited knowledge about at least one of the investigational drugs?	no					
P8 Are there any additional risks of the therapies being tested not yet taken into account?	no					
P9 Are there any additional risks associated with trial-related procedures (other than the therapy being tested)?	no					
P10 Are trial procedures (therapy and/or diagnostics) clinically unusual and complex?	no					
P11 Are there any risks of coincidental or deliberate unblinding?	no					
P12 Are there any risks of (informative) withdrawals or drop-outs?	no	no				
P13 Are there any sources of bias or variance with regard to the primary endpoint?	no					
P14 Are there any potential trial protocol deviations that could have a negative impact on participant safety and/or the validity of the trial?	no					
P15 Are there any further risks that could have a negative impact that haven't been answered adequately in questions P1-P14?	no					
Summary of participant-related indicators						0

Robustness-related indicators (R)	Yes / No
R1 Is a "hard" primary endpoint being investigated?	0
R2 Are the clinical trial procedures (design) very simple?	1
Summary of robustness-related indicators	**1**

Site-related indicators (S) (No influence on risk category.)	Yes / No	If Yes, specify its nature.			If Yes, which QA measure can control the risk?	If no QA measure, can monitoring control the risk?
		Participant safety	Participant rights	Data validity		
S1 Are there any technical requirements for the trial sites?	no					
S2 Are there any essential personnel requirements for the trial sites?	yes			yes	Training, monitoring and monthly reports	
S3 Are there any essential storage requirements for the investigated product?	no					
S4 Are there any essential documentation requirements for the investigated product?	yes	1			Adverse event documentation, monitored by Steering committee	
S5 Are there any essential transport and/or storage requirements for material samples?	0					
S6 If the trial is randomised but not blinded, is randomisation performed locally at the trial sites (e.g. by envelopes)?	yes			yes		
Summary of site-related indicators						0

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Centre intégré
universitaire de santé
et de services sociaux
du Centre-Sud-
de-l'Île-de-Montréal
Québec

Direction de l'enseignement universitaire et de la recherche

PAR COURRIER ÉLECTRONIQUE

Le 14 décembre 2018

Sylvie Belleville, Ph.D.
Directrice scientifique
Centre de recherche - Institut universitaire de gériatrie de Montréal
4545, Chemin Queen Mary, Montréal, Québec H3W 1W5

Objet **: Autorisation de réaliser la recherche suivante :**
Titre : *«Les effets préventifs d'une association d'interventions non médicamenteuses (physique, cognitive et sociale) chez le sujet âgé en bonne santé»*
Numéro attribué au projet par le CÉR évaluateur : CER VN 18-19-29

Madame,

Il nous fait plaisir de vous autoriser à réaliser la recherche identifiée en titre sous les auspices du Centre intégré universitaire en santé et services sociaux du Centre-Sud de l'île de Montréal. Cette autorisation vous permet de réaliser la recherche au sein du centre de recherche de l'institut universitaire de gériatrie de Montréal.

Pour vous donner cette autorisation, notre établissement reconnaît l'examen éthique qui a été effectué par le Comité d'éthique de la recherche vieillissement-neuroimagerie:

- qui agit comme CER évaluateur pour ce projet, conformément au Cadre de référence des établissements publics du RSSS pour l'autorisation d'une recherche menée dans plus d'un établissement (le Cadre de référence);
- qui a confirmé dans sa lettre du 3 décembre 2018 le résultat positif de l'examen scientifique et du 13 décembre 2018 de l'examen éthique du projet; et
- qui a approuvé la version réseau du formulaire de consentement en français utilisé pour cette recherche.

Cette autorisation vous est donnée à condition que vous vous engagiez à :
- respecter les dispositions du Cadre de référence se rapportant à votre recherche;
- respecter le cadre réglementaire de notre établissement sur les activités de recherche, notamment pour l'identification des participants à la recherche;
- utiliser la version des documents se rapportant à la recherche approuvée par le CER évaluateur, les seuls changements apportés, si c'est le cas, étant d'ordre administratif et identifiés de façon à ce que le CER évaluateur puisse en prendre connaissance; et
- respecter les exigences fixées par le CER évaluateur pour le suivi éthique continu de la recherche.

…/2

L'autorisation qui vous est donnée ici de réaliser la recherche sous les auspices de notre établissement sera renouvelée sans autre procédure à la date indiquée par le CER évaluateur dans sa décision de renouveler son approbation éthique de cette recherche.

Vous consentez également à ce que notre établissement communique aux autorités compétentes des renseignements personnels qui sont nominatifs au sens de la loi en présence d'un cas avéré de manquement à la conduite responsable en recherche de votre part lors de la réalisation de cette recherche.

La personne à joindre pour toute question relative à cette autorisation ou à son renouvellement ou au sujet de changements d'ordre administratif qui auraient été apportés à la version des documents se rapportant à la recherche approuvée par le CER évaluateur, est madame Karima Bekhiti (karima.bekhiti.ccsmtl@ssss.gouv.qc.ca).

En terminant, nous vous demandons de toujours mentionner dans votre correspondance au sujet de cette recherche le numéro attribué au projet de recherche par le CER évaluateur.

Veuillez agréer nos sentiments les meilleurs.

Annie-Kim Gilbert, Ph. D.
Directrice de l'enseignement universitaire et de la recherche
Personne mandatée par l'établissement pour autoriser la réalisation des projets de recherche

AKG/pl

c. c. : Johane de Champlain, Présidente du CER vieillissement-neuroimagerie
Corinne Benquet, Ph. D., Chef de Service, Centre de recherche - Institut universitaire de gériatrie de Montréal

Université Catholique de Louvain
Faculté de médecine

Cliniques universitaires SAINT-LUC UCL BRUXELLES

Comité d'Éthique Hospitalo-Facultaire

Bruxelles, ce 15 octobre 2019

A l'investigateur responsable:
M. Stefan AGRIGOROAEI
IPSY
Place Cardinal Mercier 10 boite L3.05.01
1348 Louvain-la-Neuve

AVIS FAVORABLE DEFINITIF

Concerne : 2019/18SEP/408 - N° Enregistrement Belge : B403201941535

N° Protocole : 1
Acronyme : n/a
Intitulé : STAYFITLONGER - Preventive effects of a combination of non-drug interventions (physical, cognitive and social) in healty elderly subjets; a multicenter randomized controlled trial.

Cher Collègue,

Le Comité d'Éthique Hospitalo-Facultaire Saint-Luc - UCL a pris connaissance de l'étude susmentionnée. Nous avons examiné l'ensemble des documents concernant cette étude, y compris les documents modifiés suite aux remarques :

- Document 1 version 2 reçu le 07/10/2019
- Résumé version 1 reçu le 12/09/2019
- Document d'information et de consentement patient, version 2 reçu le 07/10/2019
- Protocole version 1 reçu le 12/09/2019
- CV daté et signé de l'investigateur principal et co-investigateur + certificat GCP
- Attestation d'assurance Ethias dd 11/09/2019
- Conditions financières
- Questionnaires 1 RGPD
- Annexes :
    - Annonce de recrutement : flyer recrutement version 2 reçu le 07/10/2019
    - Détails évaluation cognitive reçu le 12/09/2019
    - Détails évaluation physique reçu le 12/09/2019
    - Contrats qui lient les différents sites de l'étude reçu le 12/09/2019

En tant que comité d'éthique principal désigné par le promoteur (unique en Belgique), selon les directives de la loi du 07 mai 2004, nous donnons un avis favorable définitif à ce projet.

Nous rappelons à l'investigateur qu'il est personnellement responsable de cette étude et au promoteur qu'il est responsable de la conformité linguistique des formulaires d'information et de consentement.

Aucun participant ne peut être admis dans une expérimentation ou un essai clinique avant que le comité d'éthique (IRB/IEC) n'ait donné un avis écrit favorable au projet.

Aucune modification ni changement au protocole ne peut être mis en route sans l'approbation préalable écrite du comité d'éthique à l'amendement approprié excepté les situations prévues dans les bonnes pratiques cliniques (BPC/GCP).

Promenade de l'Alma 51 bte B1.43.03 - 1200 Bruxelles
Tél. : 02/764.55.14 - Fax : 02/764.55.13 E-mail : commission.ethique-saint-luc@uclouvain.be

Comité d'Éthique Hospitalo-Facultaire

Le comité d'éthique principal déclare qu'il procède selon les directives ICH/GCP, les lois et règlements applicables, et ses propres procédures écrites.

Le comité d'éthique principal déclare qu'aucun de ses membres ayant une affiliation avec l'étude ou le sponsor n'a voté pour cette étude.

Une liste des membres actuels est jointe en annexe.

Le comité d'éthique principal sera continuellement informé de tous les SUSAR et déviations liés à ce protocole et qui se sont produits en Belgique.

Le comité d'éthique sera également informé du statut de l'étude sur base continue (comme requis par les directives ICG-GCP 4.10.1).

Nous vous prions d'agréer, cher Collègue, l'expression de nos sentiments les meilleurs.

I. de Hemptinne

I. de HEMPTINNE
Membre du CE

Prof. J.-M. MALOTEAUX
Président

Promenade de l'Alma 51 bte B1.43.03 - 1200 Bruxelles
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Cliniques universitaires SAINT-LUC UCL BRUXELLES	Composition du Comité d'éthique hospitalo-facultaire nominatif	UCLouvain
CEHF-FORM-006-5.0		**Commission d'éthique hospitalo-facultaire**
		Date d'application : 24/06/2019

Comité d'éthique hospitalo-facultaire (CEHF)

COMPOSITION (cfr CEHF-DSQ-005_Description fonctionnement CEHF)

▪ Président	▪ Jean-Marie MALOTEAUX, Docteur en médecine
▪ Vice-président	▪ Véronique DUVEILLER – Pharmacien ▪ Marc MAES - Docteur en médecine ▪ Geneviève SCHAMPS – Juriste
▪ Secrétaire	▪ Marie-Chantal LIESSE - Infirmière
▪ Docteurs en médecine attachés aux Cliniques universitaires Saint-Luc ou à la Faculté de Médecine de l'UCL	▪ Martine BERLIERE ▪ Yves HORSMANS ▪ Laurent HOUTEKIE ▪ Yves HUMBLET ▪ Raymond READING ▪ Luc ROEGIERS ▪ Jean-Bernard OTTE[i] ▪ Marie-France van den HOVE – VANDENBROUCKE[i]
▪ Médecins omnipraticiens ou extérieurs aux Cliniques universitaires Saint-Luc	▪ Dominique LAMY ▪ Patrick EVRARD (Cliniques Mont-Godinne)[i]
▪ Ethicien	▪ Eric GAZIAUX
▪ Juriste	▪ Emmanuelle VAN HELLEPUTTE
▪ Infirmières (Cliniques universitaires Saint-Luc) et assistante sociale	▪ Cécile COUPEZ ▪ Claire DETIENNE[i] ▪ Carine VANDEUREN - Assistante sociale, représentante des patients*
▪ Psychologue	▪ Guibert TERLINDEN[i]
▪ Pharmacien hospitalier des Cliniques universitaires Saint-Luc	▪ Pascale de PIERPONT[i] ▪ Séverine HALLEUX[i]
▪ Méthodologiste, PhD	▪ Isabelle de HEMPTINNE[i] ▪ Anne GABRIEL[i]
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Rationale and protocol of the StayFitLonger study: a multicentre trial to measure efficacy and adherence of a home-based computerised multidomain intervention in healthy older adults

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Abstract

Background: In older adults, multidomain training that includes physical and cognitive activities has been associated with improvement of physical and cognitive health. The goal of the multisite StayFitLonger study is to assess a home-based computerised training programme, which combines physical exercises, stimulating cognitive activities and virtual coaching.

Methods: One hundred twenty-eight cognitively healthy older adults will be recruited from the community in Switzerland, Canada and Belgium. The study will comprise (1) a 26-week double-blind randomized controlled efficacy trial and (2) a 22-week pragmatic adherence sub-study. In the efficacy trial, participants will be randomly assigned to an experimental or an active control intervention. In the experimental intervention, participants will use the StayFitLonger programme, which is computerised on a tablet and provides content that combines physical activities with a focus on strength and balance, as well as divided attention, problem solving and memory training. Outcomes will be measured before and after 26 weeks of training. The primary efficacy outcome will be performance on the "Timed-Up & Go" test. Secondary outcomes will include measures of frailty, cognition, mood, fear of falling, quality of life, and activities of daily living. Age, sex, education, baseline cognition, expectation, and adherence will be used as moderators of efficacy. Following the 26-week efficacy trial, all participants will use the experimental programme meaning that participants in the control group will 'cross over' to receive the StayFitLonger programme for 22 weeks. Adherence will be measured in both groups based on dose, volume and frequency of use. In addition, participants' perception of the programme and its functionalities will be characterised through usability, acceptability and user experience.

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Discussion: This study will determine the efficacy, adherence and participants' perception of a home-based multidomain intervention programme and its functionalities. This will allow for further development and possible commercialization of a scientifically validated training programme.

Trial registration: ClinicalTrials.gov, NCT04237519 Registered on January 22, 2020 - Retrospectively registered.

Keywords: Cognitive training, Physical activity training, Social interactions, Home-based training, Computerised training, Multidomain intervention, Adherence, Frailty, Cognition

Background

Finding ways to improve and maintain functional abilities and quality of life in older adults has become a worldwide priority. It is well recognized that a reduced engagement in physical, cognitive and social activities has a negative influence on the health of older adults, exposing them to being more vulnerable both physically and cognitively. Sedentary behaviours can ultimately lead to physical frailty, which is defined as a state of high vulnerability with cumulation of adverse health outcomes [1, 2]. Fear of falling and/or unsteady gait is a common component of physical frailty and falls are particularly frequent in older adults [3, 4]. In addition to mobility limitation and falls, cognitive decline has been identified as a major cause of disability and dependency in older populations [5, 6].

Expert recommendations propose that non-pharmacological interventions focusing on modifiable lifestyle factors can be used to protect older people from the deleterious effects of physical and brain aging that can lead to disability [7, 8]. Keeping a healthy mind in a healthy body might be the approach of choice for healthy aging. Several studies have shown that physical activity induces many beneficial effects on general health, cognition and quality of life in healthy older adults but also in frail individuals [9–14]. In parallel to studies on physical activity, increasing evidence shows that cognitive training can also have a positive impact not only on cognition but also on physical status [15–23]. This is consistent with findings indicating that cognitive deficits, mainly impairment of executive functions and attentional control, are associated with falls [24] and abnormal gait [25].

Because aging is complex and different interventions are likely to potentiate their effects, an increasing number of studies have relied on combined interventions targeting two or more modifiable factors (for a review see [26]). For instance, the FINGER study, which combined face-to-face physical exercises and diet guidance with a home-based computerised-cognitive training, showed cognitive improvement on processing speed and executive functions [27]. The MAPT study used a multidomain intervention, which combined face-to-face cognitive training, diet and physical exercises guidance [28]. However, as these programmes were provided face-to-face for the most part, accessibility remains a potential barrier, as older adults may experience mobility challenges or may not have easy access to resources or facilities that can provide those programmes in their community or nearby environment.

Relying on computerisation to deliver lifestyle interventions has several advantages: it can be used to support home-based training, which reduces costs and increases access; training can be self-paced and repeated as wished; it helps provide immediate feedback; it allows scaling up for wider use if efficacy is proven; and it provides an excellent interface for active control interventions [29–31]. Surprisingly, whereas many studies assessed computerised cognitive training programmes, very few have combined at-home computerised cognitive and physical activity training [32–35]. Furthermore, few studies have integrated and assessed the user viewpoint. Adoption of technology by older adults depends on whether it responds to their needs and whether it is adapted to their capabilities [36, 37]. Barriers of technical nature (e.g., difficulty logging in or navigating) are often raised by older adults when measuring their interest for computerised brain health programmes [38]. This stresses the importance of collecting data on the perception of the programme and its functionalities and working with developers to adapt programmes to end users. This will be done in the present study by measuring usability, acceptability and user experience.

The StayFitLonger study was designed to test efficacy, adherence and perception of a home-based computerised training programme, which combines physical exercises and cognitive training in both robust and pre-frail older adults. The ultimate goal of the training programme is to maintain independent living at home by upholding and when possible improving physical and cognitive capacities in older adults. The programme comprises easily implemented videos of physical exercises focusing on gait and strength (Test-and-Exercise home-based programme, T&E, [39]). It also includes a series of ludic activities to increase cognitive functions. These cognitive activities train attentional control through dual-task exercises that were found to increase divided attention capacities and frontal lobe function [40], general knowledge learning and problem-solving capacities. Other features of the programme include: 1) prospective memory exercises embedded in the physical

exercises; 2) social functionalities (i.e., creating and sharing learning material with peers; chatting with peers about topics of interest and sharing solutions to common real-life problems) to encourage social engagement, as it is positively related to health status and cognitive functions in older adults and helps counteract isolation [41, 42]; 3) psychoeducational content on cognition, physical health, nutrition and on ways to apply newly learned strategies in real life to empower participants and promote self-management (e.g., [43]); 4) a virtual coach to improve adherence by guiding participants, reminding them to use the programme regularly, and providing feedback and rewards through a system of virtual credits; 5) possibility to personalise the application settings to tailor the environment to the participant's tastes and wishes (e.g. virtual coach apparence); and 6) wearable motion sensors, which are used during the physical exercises and one cognitive exercise in which a motor response is required, and as a complement to secondary outcomes.

Objectives and hypotheses

The StayFitLonger study has two major objectives that will be addressed in the trial and the sub study. The **efficacy trial** will test the effect of the training on physical, cognitive, affective, and psychosocial outcomes using a 26-week double-blind parallel-group randomised control trial (RCT). Participants will be allocated randomly to either the StayFitLonger training home-based computerised programme (experimental intervention) or a home-based computerised comparator (active control). The primary objective is to assess whether the StayFitLonger programme leads to larger pre-post improvement than the active control condition on the Timed-Up & Go (TUG), a broadly used and validated functional physical task to measure lower extremity function, mobility and balance. Participants allocated to the experimental intervention are expected to show larger post-training improvement on the TUG than participants in the control intervention. As a secondary objective, we will assess whether the StayFitLonger programme improves physical, cognitive, affective, and psychosocial secondary outcomes. We will also explore whether gains differs in robust vs. pre-frail seniors since some studies suggest that changes in response to training might depend on frailty status [11, 14].

The **adherence sub-study** will rely on a pragmatic quasi-experimental design. At the end of the 26-week RCT, participants in the experimental group will be asked to continue using the programme and participants in the control group will 'cross-over' to the StayFitLonger programme. This sub-study will last 22 weeks and indicators of adherence will be recorded throughout the entire duration of the StayFitLonger study (48 weeks). This will allow us to assess whether adherence is maintained over time and whether it is influenced by personal characteristics, the presence or not of supervision and the type of intervention. Usability, acceptability and user experience will also be evaluated.

Methods

The study is registered with the US National Institutes of Health clinical trials registry (ClinicalTrials.gov Identifier: NCT04237519). This trial report follows the recommendations of SPIRIT 2013 [44].

Efficacy trial

Design

The design of the efficacy trial and adherence sub-study is illustrated in Table 1. The efficacy trial will be a double-blind parallel group multicentric RCT. It will be completed in three sites: Centre Leenaards de la mémoire – Centre hospitalier universitaire Vaudois (CHUV) in Switzerland; Institut universitaire de gériatrie de Montréal (IUGM) of the Centre intégré universitaire de santé et de services sociaux Centre-Sud-de-l'Île-de-Montréal (CIUSSS-CSMTL) in Canada; and Brusano and Centre Public d'Action Sociale (CPAS) of Woluwe-Saint-Lambert in Belgium. Participants will be randomised to one of two home-based computerised intervention conditions, the StayFitLonger training programme (experimental) or the comparator, an active control training programme. Outcome measures (Table 2) will be collected at two timepoints: pre-training (T0; within 6 weeks prior to the start of the intervention) and post-training (T1, within 4 weeks following the end of the 26-week training). Of note, a second exploratory post-training assessment (T2), not part of the RCT, will be performed within 4 weeks following the end of the adherence sub-study. At each timepoint, there will be two assessment visits. Within a month following the T0 assessment, introductory courses in groups of a maximum of six people will take place to introduce the features of the programme and describe the different physical and cognitive exercises. This will mark the beginning of the training that will take place at home for 26 weeks (see Table 1 for details). Participants will be supervised through home visits and monthly phone calls to monitor their use in relation to recommendation and address problems with the use of the programme.

Study population

One hundred and twenty-eight French-speaking healthy participants will be recruited, 64 in Switzerland, 32 in Canada and 32 in Belgium. Participants will be community-dwelling older adults. They will be recruited through diverse sources including ads, newsletters, social media, and flyer distribution during various events.

Table 1 Schedule of enrolment, assessments and interventions

Time points	T-1	T0	T1	T2
Enrolment				
Invitation to participate to the study	X			
Pre-screening by phone	X			
Informed consent and eligibility screening	X			
Randomisation	X			
Assessments				
RCT assessments (see Table 2)		X	X	
Adherence sub-study assessments (see Table 3)		X	X	X
Interventions				
Experimental group				
Introductory courses in group		X		
StayFitLonger (normal supervision)		←	→	
Refresher course in group			X	
StayFitLonger (no supervision)			←	→
Control group				
Introductory courses in group		X		
Active Control (normal supervision)		←	→	
Introductory courses in group			X	
StayFitLonger (normal supervision)			←	→

Recruitment will be carried out with the help of two community associations, Pro Senectute in Switzerland and Brusano in Belgium, and from the bank of participants of the IUGM research centre in Canada.

Inclusion criteria Included participants will be fluent French-speaking adults aged 60 years and over, retired and living at home. They will have access to a wireless Internet connection at home and will be open to the use of new technologies including electronic tablets. They will be independent for daily activities based on a normal score on the 4-Instrumental Activities of Daily Living (4-IADL) scale [45]. They will be interested in exercising to stay fit and able to walk at home without a walking aid (e.g., wheelchair, cane, walker, etc.). They will be available to commit themselves for the time period during which the study will take place, with no vision deficits that would prevent them to read information on a tablet and with no current neurological or psychiatric diagnosis (e.g., Parkinson's disease).

Exclusion criteria Participants with a MoCA score < 26 [46] or a score ≥ 3 on the Fried's frailty index [2] will be excluded from the study.

Procedure and data management

A two-stage screening process will be used to select participants (timepoint T-1; Table 1). Initial contact will be made by phone by research team members with expertise in recruitment. At this stage, only participants who report no major physical, medical, or sensory limitations will be invited to come to the laboratory for further investigation. During the on-site visit, participants will be presented with the information and consent form. In Switzerland, participants will be offered to receive the information and consent form prior to their visit. Once they sign the consent form, inclusion and exclusion entry criteria will be measured for the second-stage screening. The Fried's phenotype scale [2] will be used to exclude frail individuals and to determine frailty level among other participants who will be identified as either robust (score of 0) or pre-frail (score of 1 or 2). In addition, the participant's technology (e.g., use of tablet, email, social network) and gaming profile will be established with an ad-hoc questionnaire. Eligible participants will receive an ID number. All data will be anonymized and maintained in REDCap, a secure online database [47]. Access to data will be restricted by type of data (e.g., assessors will only have access to assessment data). Furthermore, data collected directly by the programme will be transmitted and maintained in a secured server

Table 2 List of outcomes measured for the RCT

RCT Outcomes				Timepoints		
Domain	***Primary outcome***			T0	T1	T2[a]
Physical	Mobility/gait	Timed-Up & Go (TUG) task		X	X	X
Domain	***Secondary outcomes***					
Physical	Mobility/balance	20-m Walking task		X	X	X
		Five Time Sit to Stand Test		X	X	X
		Four Stage Balance Test		X	X	X
		Gait Up sensor measurements: several walking parameters		X	X	X
Cognitive	Global cognition: ZAVEN Composite Score	Episodic memory composite	California Verbal Learning Test (CVLT): free delayed recall	X	X	X
			Wechsler Memory Scale (WMS-IV) Logical Memory Test: delayed recall	X	X	X
		Complex attention composite	Wechsler Adult Intelligence Scale (WAIS-IV) Digit Symbol Substitution Test (DSST)	X	X	X
		Executive function composite	Verbal Fluency task	X	X	X
	Memory Composite Score	CVLT: free delayed recall		X	X	X
		WMS-IV Logical Memory Test: delayed recall		X	X	X
	Executive and attentional functions Composite Score	Verbal Fluency test		X	X	X
		Trail Making Test: Part B- Part A		X	X	X
		Victoria Stroop Test (VST): high interference		X	X	X
		Test of Attention Performance (TAP): Divided Attention		X	X	X
	Speed processing Composite Score	Trail Making Test: Part A		X	X	X
		WAIS-IV DSST		X	X	X
		VST: "naming" condition		X	X	X
	Divided attention	Ad-hoc computerised multitasking task		X	X	X
	Prospective memory	Prospective memory items of the Rivermead Behavioural Memory Test (RBMT-3)		X	X	X
	Concept elaboration	Test of Attention Performance (TAP): Flexibility		X	X	X
		WAIS-IV Similarities		X	X	X
Affective	Mood	Hospital Anxiety and Depression Scale (HADS)		X	X	X
	Fear of falling	Falls Efficacy Scale International (FES-I)		X	X	X
Psycho-social	Quality of Life	The Older People Quality of Life questionnaire (OPQOL 35)		X	X	X
	Subjective difficulties encountered in activities of daily living	Cognitive Function Instrument (CFI)		X	X	X
		Everyday Cognition (E-Cog)		X	X	X
	Expectation questionnaire	Ad-hoc questionnaire on participant's expectation on the programme		X	X	X

[a]T2 assessment is listed here but it is not technically part of the RCT

located at the Haute École Spécialisée de Suisse Occidentale (HES-SO).

Randomisation and blinding procedure

A randomisation list will be generated in Switzerland, independently from the research project and implemented using REDCap. In each site, a team member not involved in assessment or monitoring will assign participants by pressing a "randomisation" button on REDCap. A stratification will be done according to the frailty status. Within each stratum (robust and pre-frail), participants will be assigned to one of the two conditions (StayFitLonger or active control) according to separate randomisation schedules with a 1:1 ratio. Couples (e.g., married individuals) who participate in the study will be assigned to one of the two conditions as a pair: the first member of the couple will be randomised, and the second will be assigned to the same intervention. This has been implemented to avoid contamination in cases where two individuals living in the same household would be randomized to different training programmes.

Assessors will be blind to the hypotheses and to participants' assignment, as they will only have access to the testing sessions. Participants will be asked not to discuss their training programme with assessors. If such a circumstance were to occur, it will be reported but should

have minimal effect on data integrity, as assessors will be blinded to the hypotheses. Research team members responsible for the statistical analyses will be blind to the training conditions. Study coordinators and instructors involved in the introductory courses and supervision of home-based training will not be blind. Participants will be aware that the trial has two different training conditions and that they will be randomly allocated to one of them. However, they will not be informed of the study hypotheses and therefore will not know which one is the experimental condition. Both programmes will have a similar main screen layout and name, and the wording of the recruitment documents and consent forms will not convey the notion that one condition is hypothesised as inferior in terms of its effects on physical capacities and cognition [48].

Interventions

Introductory courses Four face-to-face introductory sessions will be provided to familiarise participants with the material and the assigned application (Table 1). Two sessions of 3 h will present how to use the tablet and accessories (e.g., handling, charging), how to navigate in the application and how to complete the cognitive exercises. Two sessions of 2 h will present the physical exercises and teach participants how to place the motion sensor (Physilog®5, GaitUp, Switzerland) that will be used to record bodily measurements. In both programmes, physical activity instructors will ask participants to practice physical exercises for a total of 30 to 45 min distributed over the day. They will be recommended to train using the same physical exercises for at least 3 weeks with three sessions per week and a day of rest between each session. Cognitive training instructors will encourage participants to practice the cognitive exercises at least 3 times per week for 15 min each time. Participants will be made aware that during an ideal training session, activity should be perceived as of moderate difficulty. Instructions on physical and cognitive activities will be provided by a different instructor, the same for both programmes. Instructors will specifically be asked to present and explain the two programmes in similar ways.

StayFitLonger training programme The StayFitLonger programme will be accessible through the application *RestonsEnForme,* which will be available on a tablet (Galaxy Tab S2, Samsung) that will be provided to each participant. When launched, the main screen of the application provides access to different physical and cognitive activities (Fig. 1a) as well as other features listed below.

The physical exercise activity (*Exercises*) will be based on the T&E home-based programme using the concept of self-efficacy and empowerment [39]. Participants will be invited to create a personalised 8-exercise programme (Fig. 1b). Those will be selected from 50 available exercises, which vary as function of themes (e.g., on a chair, with a pillow) and difficulty level (e.g., different body position or workload). Participants will try the exercises before including them in their programme. Exercices will only be included if judged as not too difficult by the participant. More details on the T&E programme can be found in [39]. During the intervention, participants will be allowed to add new exercises to their 8-exercise programme after a period of at least 3 weeks to introduce variety and increase challenge.

There will be four cognitive training activities which target problem solving, semantic memory, prospective memory, and divided attention. The *Quiz* activity will teach different strategies [49, 50] to learn new vocabulary and semantic repertoires (e.g., mushrooms, trees, flowers, dogs, etc.; Fig. 1c). Participants will choose first a repertoire of interest and will be asked to perform word-image associations related to the repertoire. Based on their level of proficiency in the selected repertoire, participants will then be offered different learning techniques: *completing* (relying on cues for help) or *copying/completing* (copying the word while using pure errorless learning and then completing while using encoding cues). Participants will continue to explore the repertoire through practice using an optimal number of cues to obtain the best performance while limiting the production of errors. This practice will be completed once participants reach at least 60% of correct responses without cues. Then, participants will be invited to a final evaluation without any help. Feedback will be provided with the option of continuing training using the repertoire or choosing another one. The *4 Images/1 Word* activity will train cognitive flexibility (Fig. 1d). Participants will be shown four images that are associated with an overarching concept and will be asked to find and write down the associated concept. Two types of cues will be provided to help them solve the task: number of letters in the target and some of the target letters mixed with distractors. The *Attention!* activity will train participants to vary their attentional priority in dual-tasks [40] while exploring a city on a two-wheel vehicle (Fig. 1e). The dual-task will involve detecting different targets in the environment (i.e., people, 4-wheel vehicles or buildings) by pressing a button on the screen (task A), and at the same time detecting sewer covers with foot taping (task B). The foot response will be recorded by a motion sensor attached to the waist or shoe. The activity will comprise 30 levels with a progressive increase in the degree of difficulty. Difficulty will be increased by manipulating

Fig. 1 Illustration of the different activities of the StayFitLonger training programme

the number of targets, the number of distractors and the speed of the vehicle driven by the player (i.e., bicycle, scooter, motorcycle) and by introducing a response contingency condition (if/then). Participants will complete first each task (detection of targets in the environment and detection of sewer covers) in focused attention. They will then be asked to combine the tasks with different priority levels during a series of trials: one trial in which they will devote 80% of their attention to task A and 20% of attention to task B, one with 20% on task A and 80% on task B, and one with 50% of their attention on each task. Each priority trial will last about 1 min and will be repeated twice in random order. The *Recall you* activity will be embedded into the physical exercises to train prospective memory [51] (Fig. 1f). On every 3 to 4 sessions, the *Exercises* activity will start with an instruction asking participants to complete a casual task (e.g., to get and drink a glass of water or to open a window, etc.) after a certain amount of time in the physical training. A timer will appear on the top left corner so that participants can track time while doing their exercises. For safety reasons, participants will be instructed to complete the exercise they are engaged in before performing the cognitive task.

In addition to the physical and cognitive activities, the StayFitLonger programme will include the following features:

A *Chat room* will provide a venue for participants to share views about topics of interest and tips for common real-life problems (Fig. 2a). Pre-established themes will be available (e.g., cooking, gardening, handiwork, etc.) and participants will have the opportunity to enrich this setting and create their own themes. When entering the chat room, a moderator message will inform participants to be respectful while chatting and to avoid revealing sensitive information (e.g., address, name, credit card information).

Creation of material. Participants will be invited to create material for the *4 Images/1 Word* and *Quiz* activities. Once validated by the research team through a moderation platform, the material will be shared with all participants who will have the opportunity to use it for

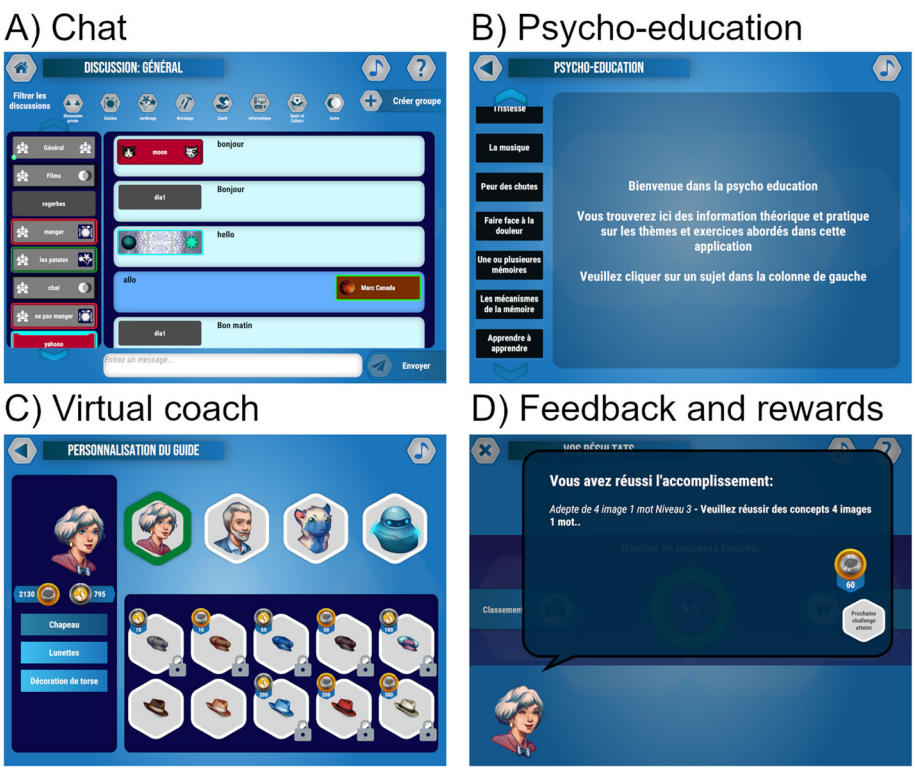

Fig. 2 Illustration of the unique features of the StayFitLonger training programme

their own training and to rate the material created by other participants. This feature has been implemented to foster social interactions across participants.

Psychoeducation. From the application homepage, participants will have access to psychoeducational content (Fig. 2b) on different topics related to physical, psychological and cognitive health. Twenty-two topics will be available (e.g., divided attention improvement; stress regulation; fatigue management, etc.).

Virtual coach. A customisable virtual coach using verbal (but written) and non-verbal communication (Fig. 2c, d) will guide participants along the proposed exercises by giving them instructions, reminding them to practice a variety of available activities repeatedly, providing appropriate and timely feedback (through congruent facial expressions) on participant's performances (e.g., encouraging messages) and rewarding assiduity, perseverance and performance with achievements and virtual credits ("physio-coins" and "cogni-coins"). Some achievements will unlock new icons, backgrounds and frames to modify the user interface, and by spending the coins obtained, it will be possible to get additional icons, background, frames and equipment to customise the virtual coach appearance (e.g., hat, glasses, etc.). These different functions of the virtual coach have been implemented to improve adherence by helping participants through a direct interlocutor (rather than neutral messages) and to keep them motivated [43].

Active control training programme The active control programme will be similar in structure and layout to the StayFitLonger programme (Fig. 3a) and will include physical and cognitive exercises.

The physical exercise activity (*Exercises*) will be a computerised version of Helsana's physical training programme (Fig. 3b). Helsana, a Swiss health insurance company, offers this programme in a booklet. The computerised version will include advice and tips to stay physically active (e.g., to go shopping by foot) and 12 exercises to train upper and lower extremity strength, mobility and balance. It will also provide information about which exercises to choose, the training frequency and precautionary measures to follow. This programme has been judged close to "standard care", as it is similar to a large range of programmes and recommendations available to the general public. It will differ from the *Exercise* activity available on the StayFitLonger programme, as it only contains a limited number of exercises and does not benefit from interactive content (e.g., videos of exercises), self-management, personalization features, and rewards from the virtual coach.

The four cognitive activities provided in the active control programme will be commercially available leisure activities that do not target specific cognitive processes and do not teach cognitive strategies [52–56]. The *Crosswords* activity will include 219 puzzles with

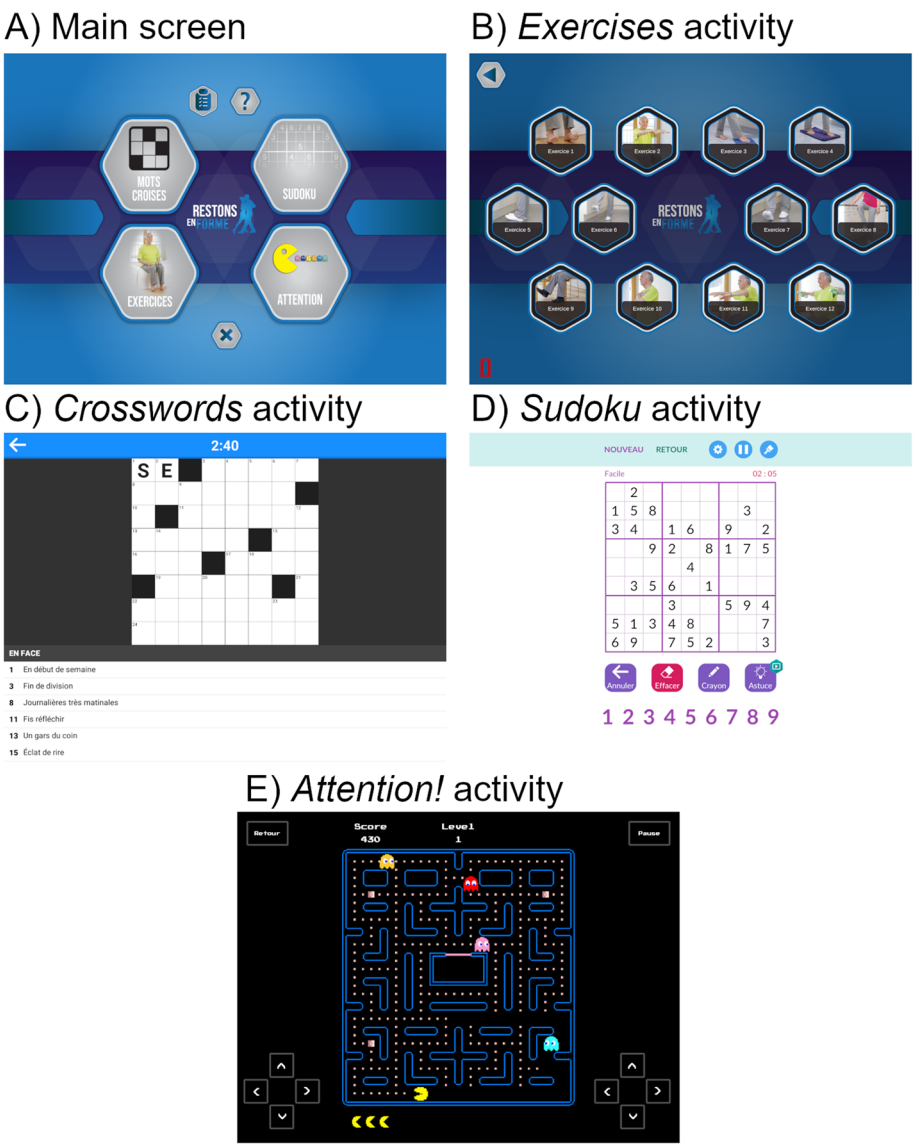

Fig. 3 Illustration of the different activities of the active control training programme

five different sizes (Fig. 3c). The *Sudoku* activity will include around 5000 puzzles with four levels of difficulty (Fig. 3d). The *Attention!* activity will be a maze arcade game inspired from Pac-Man in which participants eat dots in a maze while trying to avoid coloured ghosts (Fig. 3e). The *Countdown* activity will be embedded into the *Exercises* activity and triggered randomly every 3 to 4 days. It will require that participants count backward from 100 to 1 or recite the alphabet from Z to A while doing their exercise.

There will be no chat room, psycho-educational content or virtual coach included in the active control training programme.

Supervision during the intervention Participants will receive a phone call and a home visit on week four and on week eight. Then, they will receive two phone calls (one from the physical activity instructor and one from the cognitive activity instructor) every four weeks. These will serve to identify and help participants to resolve difficulties with the programme, devices or exercises, and to obtain information about their health.

Outcome variables

Primary outcome The primary outcome will be the performance on the TUG test [57]. In this test, the person will be sitting on a chair and will be asked to stand-up,

walk three meters, turn around, walk back to the chair, and sit down. Time will be measured from the moment the person stands up until s/he sits down. Participants will perform the TUG twice providing two measures that will be averaged.

Secondary outcomes Measures in four domains will be used as secondary outcomes (Table 2).

Physical domain. 1) Walking speed will be measured over a 20-m distance. Participants will be instructed to walk as quickly as possible without running and in a safe manner. Time will be measured in seconds using a smartwatch. The task will be carried out twice, and measures will be averaged. 2) Lower extremity strength will be measured with the Five Time Sit to Stand Test (FTSST) [58]. Participants will sit on a chair with arms folded across their chest and will be asked to stand up and sit as quickly as possible five times while keeping their arms folded. The task will be administered twice, and the two measures averaged. 3) In the Four Stage Balance Test (FSBT) [59], participants will be asked to perform four progressively more challenging positions and to hold each of them as long as they can for a maximum of 10 s (parallel, semi-tandem and tandem positions) or as long as possible (one-leg stance position). The test will be stopped if a participant fails at holding a given position. 4) A smartwatch (Huawei Watch 2) connected to two motion Physilog®5 sensors worn by participants will be used during the TUG and the 20-m Walking task to collect additional specific gait movement parameters (Table 2). These sensors are a standalone 7 degree-of-freedom MEMS inertial measurement unit with wireless synchronisation, including 3D accelerometer, 3D gyroscope, and a barometric pressure sensor. The system is non-invasive, as sensors will be directly strapped on right and left shoe/foot.

Cognitive domain. 1) Global cognition will be measured with the ZAVEN composite score [60, 61] computed by averaging z-scores from the following tests: delayed free recall of the California Verbal Learning Test (CVLT); delayed recall of the WMS-IV logical memory subtest [62]; number of correct symbols reported in the WAIS-IV digit symbol substitution test (DSST) [63]; and letter fluency of the verbal fluency task [64]. 2) An executive composite score will be computed by averaging z-scores from the following tests: letter fluency of the verbal fluency task; time to complete the Trail Making Test part B-A (TMT) [65]; interference index of the Victoria Stroop Test (VST) [66]; number of total visual and auditory omissions of the divided attention subtest (Test of Attention Performance 2.3.1; TAP [67];). 3) A memory composite score will be obtained by averaging z-scores from the delayed free recall score of the CVLT [68, 69] and the delayed recall of the logical memory task. 4) A processing speed composite score will be obtained by averaging z-scores from the following tests: time to complete the TMT part A; number of correct symbols reported in the DSST; time to complete the "naming condition" of the VST [70]. 5) Divided attention will be measured with a customized computerised task performed on a tablet [40]. Participants will be asked to deliver newspapers by pressing on a screen button while on a bicycle that moves forward automatically. At the same time, they will have to follow the road traffic regulation to ensure their safety (e.g., stopping when traffic lights go from green to red and avoiding animals crossing the road). The tasks will involve different distractors to vary participants' attentional demand. Participants will be made aware that they should prioritize their safety as they would in real life. Each task will be done first in focused attention and then both tasks will be combined and performed using three levels of speed. The number of delivered items, reaction time, and errors will be recorded. 6) Prospective memory will be measured with two subtests of the Rivermead Behavioural Memory Test (RBMT-3) [71]. In the "belonging" subtest, participants will be instructed to remember asking for two personal belongings at the end of the session. In the "appointment" subtest, participants will be asked to remember asking two questions when an alarm rings 25 min later. 7) Concept elaboration will be assessed with the TAP flexibility sub-test, a "set shifting" computerised task [67] and the WAIS-IV Similarities subtest [63]. In the Similarities subtest, participants will be presented with pairs of words (e.g.: apple and peach) and will be asked how the two words are alike.

Affective domain. Mood will be assessed using the Hospital Anxiety and Depression Scale (HADS) [72]. Fear of falling will be measured with the Falls Efficacy Scale-International (FES-I) [73].

Psychosocial domain. Quality of life will be assessed with the 35-item Older People Quality of Life questionnaire (OPQOL 35) [74]. Cognition in everyday life will be measured with the self-reported Cognitive Function Instrument (CFI) [75] and Everyday Cognition scale (E-Cog) [76]. The CFI will include 14 questions to measure subjective concerns regarding cognition and activities of daily living over the last year. The E-Cog will measure how cognitive functions in different domains (everyday memory, language, visuospatial abilities, planning, organisation, divided attention) impact activities of daily living compared to 10 years ago. Participant's expectation toward the efficacy of the training programme will be assessed with an ad-hoc 17-item questionnaire.

Statistical analyses

Sample size calculation Given that our secondary analyses will stratify participants into two categories (robust

and pre-frail), we determined our sample size to ensure that we have the capacity to test the hypotheses related to this stratification. This was done with a Marker Stratified Design using the following plan: marker-by-treatment interaction using separate test (see: http://www.bigted.org/NonAdaptiveDesigns/MarkerStratified-Designs.html). For pre-frail participants, it was estimated that 16 participants per group (StayFitLonger vs. active control) would be required to detect a significant difference of 3.22 s in the TUG test using a two-sided t-test (alpha = 0.05) based on the T&E pilot study. As data might not be normally distributed, a non-parametric test was required resulting in a sample size of about 18 participants per group. Considering a dropout rate of about 25% based on prior studies, a sample size of 24.5 pre-frail participants should be enrolled for each group. For robust older adults, a sample size of 23.5 participants per group would allow to detect a difference of 0.82 s on the TUG test using a two-sided t-test (alpha = 0.05) with a power of 80% based on the study by Uemura et al. [77]. By accounting for the non-normality of data (using a non-parametric test) and the dropout rate, we targeted recruiting 36 robust participants per group. Thus, a total sample of 122 participants was determined as sufficient to have the appropriate power based on sample size calculation. To have a balanced distribution in the three countries, the total N targeted for recruitment was set at 128 participants.

Analysis of efficacy on primary and secondary outcomes All statistical tests will be two-tailed and a p value < .05 will indicate statistical significance. Effect sizes will also be assessed. Standard descriptive statistics will be provided with means and standard deviation for demographics and baseline characteristics. Group comparisons will be made using t-tests for continuous variables and chi-square analyses for discrete variables.

The primary efficacy analysis will be done with a modified intention-to treat (mITT) approach. All participants will be included in the analyses and the characteristics of those who withdrew will be analysed, as well as the causes leading them to leave the study. A linear mixed model will be used to analyse the data, as it handles correlated data and unbalanced designs and are robust against missing values. The fixed effects will be Intervention (StayFitLonger vs. active control), Time (T0, T1) and their interaction. If the StayFitLonger training is more beneficial than the active control training, a significant interaction will be expected. In such case, the presence of a significant difference between T0 and T1 in each group will be evaluated, as well as group difference on change scores at post-training using the pre-training and control group as reference points. The same analysis will be used with primary and secondary outcomes. To examine the effect of frailty status on efficacy, participants will be stratified into robust and pre-frail seniors and data will be analyzed separately in these two populations using the same method described above.

Analysis of moderators Age, sex, education and score on MoCA, four variables considered as time-invariant for the duration of the study, will be assessed as potential moderators of the impact of training on primary and secondary outcomes. Prior to their use, we will verify that they are independent from each other with a chi-squared test or correlations.

Adherence sub-study

Design

The adherence sub-study will be a pragmatic quasi-experimental study including all participants from the Swiss and Canadian sites (about 96). Following the 26-week efficacy trial, participants in the experimental group will be asked to continue to use the StayFitLonger programme with no supervision and will be invited to a refresher course to answer questions and discuss potential issues that occurred during the RCT. Participants in the control group will cross-over to use the experimental programme for 22 weeks (Table 1).

Variables

Adherence. For the entire duration of the study (between T0 and T1, and T1 and T2), three measures of adherence in relation to the device usage will be recorded directly from the application (Table 3): dose measured by the time (min) spent on the programme per week; volume corresponding to the total number of repetitions performed per week within each activity (e.g., 3 quizzes completed while using the Quiz activity); and frequency corresponding to the number of sessions per week. These will be recorded separately for the physical and cognitive activities. Adherence will be calculated for each individual by plotting weekly data over the entire training period.

User experience. The AttrakDiff 2 scale [78] will evaluate user experience (Table 3) with a 28-item questionnaire given at T1 and T2. It will measure attractiveness, pragmatic quality and hedonic qualities (stimulation and identity) of the application. Pragmatic quality corresponds to usability for instance efficiency, effectiveness and learnability. Hedonic qualities refer to the programme's originality and beauty. In addition, a 9-item questionnaire will be given at T0 to ask participants' knowledge regarding the effects of cognitive and physical interventions and the quality of the introductory courses.

Table 3 List of variables measured during the adherence sub-study

Adherence sub-study variables		Timepoints		
Domain	***Variable***	T0	T1	T2
Adherence	Dose variable: total time of training for each activity	During training		
	Volume variable: number of times each activity is carried out			
	Frequency variable: number of training sessions of at least 30 min performed per month			
User experience	Ad-hoc questionnaire exploring the quality of the introductory course	X		
	AttrakDiff 2 scale		X	X
Acceptability	Ad-hoc questionnaire to obtain ratings on different components (enjoyment, appropriateness, safety, self-evaluation)		X	X
Usability	Ad-hoc questionnaire exploring the impact of unique features of the programme (virtual coach, social interactions, preference, gamification, educative content, self-management, usability)			X

Acceptability. A 9-item ad-hoc questionnaire will be used at T1 and T2 to measure acceptability (Table 3) that is, the participants' feeling toward the programme (enjoyment, safety, efficacy, motivation to use other programmes) and its appropriateness (for older adults, to improve physical and cognitive health and to maintain a social circle).

Usability. A 16-item ad-hoc questionnaire will be used at T2 to measure usability (Table 3). Participants will be asked to rate the virtual coach, social interactions, gamification, educative content, and self-management.

Statistical analyses

Dose, frequency and volume variables will be analysed with polynomial regression models including linear and non-linear trajectories. This will allow to establish the best fitting model describing the use of the programme over time. Regression analyses will examine whether the cumulative values on adherence variables are predicted by personal characteristics, and the group to which they were assigned. We will also examine adherence dichotomously by classifying participants as a function of whether they maintain or not the recommended dose of the programme over time. Finally, we will evaluate whether change scores on primary and secondary measures of efficacy are correlated with adherence.

Qualitative analyses will be used to characterize usability, acceptability and user experience. In addition, correlations analyses between these parameters and a series of variables (age, sex, education, cognitive profile, participant's technology and gaming profile) will be performed.

Quality control and monitoring

Several strategies will be implemented to ensure quality control of the data and intervention. The introductory sessions will be standardised to ensure consistency between sites and between instructors. Assessors will be trained on the tasks with videos and will complete mock testing sessions that will be used to assess adherence to the protocol. Regular controls will be done regarding recruitment and assessment by site coordinators. Any modification to the protocol will be shared with the investigators and among sites and reported to the ethics committee. Internal audits will be conducted to ensure the proper conduct of the study and to certify that it complies with the protocol. Shortly after the beginning of the study and again once the study is completed, data from five participants will be selected randomly and verified by a researcher not involved in data collection. This person will ensure that informed consents have been signed, that eligibility criteria have been respected, and that all the tests relative to the assessments have been properly completed and original documents scanned and uploaded in REDCap.

Potential harms

Falls are one of the adverse events that could occur during the study. Participants will be asked to report the occurrence of a fall and its severity in the last year for T0, and in the T0-T1 and T1-T2 periods [79]. In addition, participants will be asked to report and discuss any potential adverse event during home visits and phone calls. These will be classified according to the typology developed in [80]: falls that require medical attention; exacerbation of a pre-existing illness; increase in the frequency or intensity of a pre-existing episodic event or condition; condition detected or diagnosed after the intervention, even though it may have been present prior to the start of the study; continuous persistent disease or symptoms present at T0 that worsened following the start of the study. All adverse events will be assessed for severity, expectedness and causality and will be recorded and closely monitored until resolution or stabilisation or until it is shown that the study intervention was not the cause.

Access to data

All site coordinators and principal investigators will be given access to the cleaned data sets. They will have direct access to their own site's data sets, and will have access to other sites data by request. To ensure confidentiality, data dispersed to research team members will be blinded of any identifying participant information.

Dissemination of study results

Study results will be published in international journals with peer-reviewed committees. They will also be

presented to the research community in national and international conferences and to the public through lay audience talks and press releases. Interim analyses will be conducted once a site has completed the RCT as required by one of the funding organization (the Active and Assisted Living Programme).

Trial status

Protocol CER-VD 2018–01898 version number 2, December 2018. Recruitment began in January 2019 in Switzerland and Canada and in January 2020 in Belgium. Recruitment was on hold between March and July 2020 in Belgium due to COVID-19. As of August 7, 2020, recruitment has been completed in Canada and Switzerland and has resumed in Belgium. Date of recruitment completion is anticipated to be October 2020.

Discussion

This study will measure the effect of the StayFitLonger programme, a computerised home-based training, which combines physical and cognitive activities and includes elements to favour social life as well as feedback and instructions from a virtual coach to enhance motivation and adherence. The overarching objectives of the study are: 1) to provide scientific evidence that such a programme can promote physical and cognitive health while staying at home; 2) to examine the level and determinants of adherence to a home-based computerised programme as well as assessing participants' perception of the programme and its functionalities.

The StayFitLonger programme includes several innovative features. First, while most physical activity interventions designed for older adults rely on aerobic training, the StayFitLonger programme focuses on balance and strength and was originally designed for older adults at risk of falling. Encouraging pilot results (T&E study, unpublished data) indicated an improvement in balance after 6 months compared to home-based exercise programme. Therefore, we believe that this approach could be beneficial to older adults at risk of frailty and that it could improve strength and reduce falls. The inclusion of pre-frail and robust participants will offer the opportunity to assess the impact and relevance of the programme for older adults with a range of physical capabilities. If necessary, there will be an opportunity to adjust the content in terms of difficulty so that it can broaden the targeted population of the programme for future use or studies. Another innovation is the use of motion sensors during physical exercises and as an outcome, which will provide precise and objective measurements on mobility for a better characterisation of how participants complete the exercises and on physical improvements.

Although the StayFitLonger intervention focuses on cognitive and physical training, it includes complementary approaches that could potentiate its effect, in particular the possibility for participants to interact with other players, promoting an active social life [42], and the inclusion of psychoeducational content. In addition, the virtual coach will provide some elements of feedback and reward, which is expected to increase motivation and adherence [43]. This is innovative, as participants in home-based training benefit from limited training assistance and coaching and this negatively impacts use over the long-term.

One important aspect of the study is to provide a direct measure of adherence, and to follow participants beyond the RCT, which will provide adherence data under unsupervised and more pragmatic conditions. To our knowledge there is no consensus on a method to assess adherence and therefore many different approaches are used in the literature with varying limitations [81]. Precise measurement of adherence to a home-based exercise programme is limited by the need to rely on self-reported measures. However, the use of a computer programme makes it possible to measure the use of the tablet and different exercises to the minute. This will provide a rich set of accurate data on dose, volume and frequency of training.

While the efficacy of a computerised training programme is essential, one prerequisite to its use by the population is that the programme is easy to use and matches the needs of older adults.

The StayFitLonger study will provide critical information on usability, acceptability and user experience, which are inter-related concepts providing insights on the potential long-term use of a technology [36, 37]. Usability refers to the ease of use of a technology and is characterized as a person's perception of its efficacy, efficiency and satisfaction [82]. Acceptability is an a priori willingness to use a tool, while acceptance is an a posteriori pragmatic evaluation of a tool after its use [83]. They are known to be influenced by usability but also by other factors, such as perceived usefulness by the user and others, and this is particularly true among seniors [82]. User experience, which refers to a person's perceptions and responses that result from the technology use and/or anticipated use is also dependant on usability and has an impact on acceptability [84]. Results obtained on these parameters are important to determine the factors that influence future use, but they can also help improving the application or designing new solutions to provide the best experience for end users.

The design includes an active control training as a comparator that mirrors the structure of the StayFitLonger training. Using an active control condition will allow us to attribute the improvement to the particular

content and format of the StayFitLonger programme. Relying on an active control condition as a comparator is a methodological strength compared to other studies that used a no-contact or wait-list control condition. However, this comes with additional challenges in terms of design and power. One of these challenges is that we need to ensure that participants in each group have the same expectation regarding the capacity of their assigned training to yield improvement [48]. To control for this effect, we included an expectation scale and will assess whether it differs among groups and whether expectations are related to pre-post changes.

We are aware of the potential limitations associated with this study. First, the StayFitLonger study spans over a full year and it is hard to predict whether participants will commit for such an extended period of time. Note, however, that we rely on a two-part design, with the RCT portion only lasting 26 weeks, and that attrition will be examined separately for the two portions. Second, while the use of feedback and rewards in the programme was meant to boost motivation, the frequency at which they appear has been set as a fixed parameter to avoid a bias between participants. Hence, this aspect was not personalized. In order to take into account that some participants may dislike receiving regular feedback, they will be able to deactivate this feature during the adherence sub-study. Adherence will be measured from the tablet application, but it is possible that some participants, intentionally or not, start an activity and let the application run in the background while they are actually not doing the activity. To counteract this possibility, the StayFitLonger programme includes a function that stops the application after 10 min of inactivity. However, it has not been implemented in the active control programme. This will be monitored as carefully as possible during data analysis to assess possible outliers in the time of use data of the active control group.

In conclusion, the StayFitLonger study will examine the efficacy, adherence and perception of a home-based computerised multi-modal training programme in robust and pre-frail older adults. Positive results on the StayFitLonger study will pave the way to further development and commercialisation of a scientifically grounded and empirically validated application which will improve the physical and cognitive health associated with independent life at home.

Abbreviations

4-IADL: 4-Instrumental Activities of Daily Living; AD: Alzheimer's Disease; ANOVA: ANalysis Of VAriance; CFI: Cognitive Function Instrument; CHUV: Centre Leenaards de la mémoire – Centre hospitalier universitaire Vaudois; CIUSSS: Centre intégré universitaire de santé et de services sociaux; CVLT: California Verbal Learning Test; DSST: Digit Symbol Substitution Test; E-Cog: Everyday Cognition Scale; FES-I: Falls Efficacy Scale-International; FSBT: Four Stage Balance Test; FTSST: Five Time Sit to Stand Test; HADS: Hospital Anxiety and Depression Scale; HES-SO: Haute École Spécialisée de Suisse Occidentale; IUGM: Institut universitaire de gériatrie de Montréal; MCI: Mild Cognitive Impairment; mITT: Modified Intention-To Treat; OPQOL 35: Older People Quality of Life questionnaire; RBMT-3: Rivermead Behavioural Memory Test – Third edition; RCT: Randomised Control Trial; TAP: Test of Attention Performance 2.3.1; T&E: Test-and-Exercise home-based programme; TMT: Trail Making Test; TUG: Timed Up & Go; VST: Victoria Stroop Test; WMS-IV: 4th version of the Wechsler Memory Scale; WAIS-IV: 4th version of the Wechsler Adult Intelligence Scale; ZAVEN: Z-scores of Attention, Verbal fluency, and Episodic memory for Nondemented older adults

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Authors' contributions

All authors have participated in the conceptualization of the study and design. MC wrote the first version of the manuscript. SB revised and contributed to the writing of the first version. JFD revised a subsequent version of the manuscript. All authors carefully revised the final manuscript and accepted the final submitted version.

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Availability of data and materials

Not applicable.

Ethics approval and consent to participate

The study has been performed in accordance with the Declaration of Helsinki. It has been approved by the Research Ethics Board (REB) in each country: Switzerland: REB Canton de Vaud (application #2018–01898, last approval December 4 2018); Canada: REB vieillissement-neuroimagerie of the CIUSSS-CSMTL (application #18–19-29, last approval December 14 2018); Belgium: REB Cliniques Universitaires Saint-Luc, UCLouvain, Bruxelles (application #B403201941535, last approval October 15 2019). Any modifications to the protocol which may impact on the conduct of the study, potential benefit of the patient or may affect patient safety, including changes of study objectives, study design, patient population, sample sizes, study procedures, or significant administrative aspects will require a formal amendment to the protocol. Such amendment will be approved by the different REB before implementation.
Participants and their informants will sign an informed consent form at their first visit for screening.

Consent for publication
Not applicable.

Competing interests
SB has been a consultant for research development on the prevention of Alzheimer's disease for the Fondation IUGM (2016) and for Sojecci (2017 to current), and for the development of a cognitive stimulation programme for the Centre de promotion de la Santé Avant Âge (2015). She has intellectual property rights on the 'Programme de Stimulation pour une santé cognitive, Memoria, Batterie d'évaluation de la mémoire Côte-des-Neiges' and 'MEMO, Méthode d'Entrainement pour une Mémoire Optimale'.
MBA, DPM and SC are employees of MindMaze SA.
The remaining authors declare that they have no competing interest.

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