

A Web-Based Multidomain Lifestyle Intervention for Older Adults: The eMIND Randomized Controlled Trial

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J Prev Alz Dis 2021;2(8):142-150
Published online December 4, 2020, <http://dx.doi.org/10.14283/jpad.2020.70>

Abstract

IMPORTANCE/OBJECTIVE: To describe the feasibility and acceptability of a 6-month web-based multidomain lifestyle training intervention for community-dwelling older people and to test the effects of the intervention on both function- and lifestyle-related outcomes.

DESIGN: 6-month, parallel-group, randomized controlled trial (RCT).

SETTING: Toulouse area, South-West, France.

PARTICIPANTS: Community-dwelling men and women, ≥ 65 years-old, presenting subjective memory complaint, without dementia.

INTERVENTION: The web-based multidomain intervention group (MIG) received a tablet to access the multidomain platform and a wrist-worn accelerometer measuring step counts; the control group (CG) received only the wrist-worn accelerometer. The multidomain platform was composed of nutritional advices, personalized exercise training, and cognitive training.

MAIN OUTCOMES AND MEASURES: Feasibility, defined as the proportion of people connecting to $\geq 75\%$ of the prescribed sessions, and acceptability, investigated through content analysis from recorded semi-structured interviews. Secondary outcomes included clinical (eg, cognitive function, mobility, health-related quality of life (HRQOL)) and lifestyle (eg, step count, food intake) measurements.

RESULTS: Among the 120 subjects (74.2 \pm 5.6 years-old; 57.5% women), 109 completed the study (n=54, MIG; n=55, CG). 58 MIG subjects connected to the multidomain platform at least once; among them, adherers of $\geq 75\%$ of sessions varied across multidomain components: 37 people (63.8% of 58 participants) for cognitive training, 35 (60.3%) for nutrition, and three (5.2%) for exercise; these three persons adhered to all multidomain components. Participants considered study procedures and multidomain content in a positive way; the most cited weaknesses were related to exercise: too easy, repetitive, and slow progression. Compared to controls, the intervention had a positive effect on HRQOL; no significant effects were observed across the other clinical and lifestyle outcomes.

CONCLUSIONS AND RELEVANCE: Providing multidomain lifestyle training through a web-platform is feasible and well-accepted, but the training should be challenging enough and adequately progress according to participants' capabilities to increase adherence. Recommendations for a larger on-line

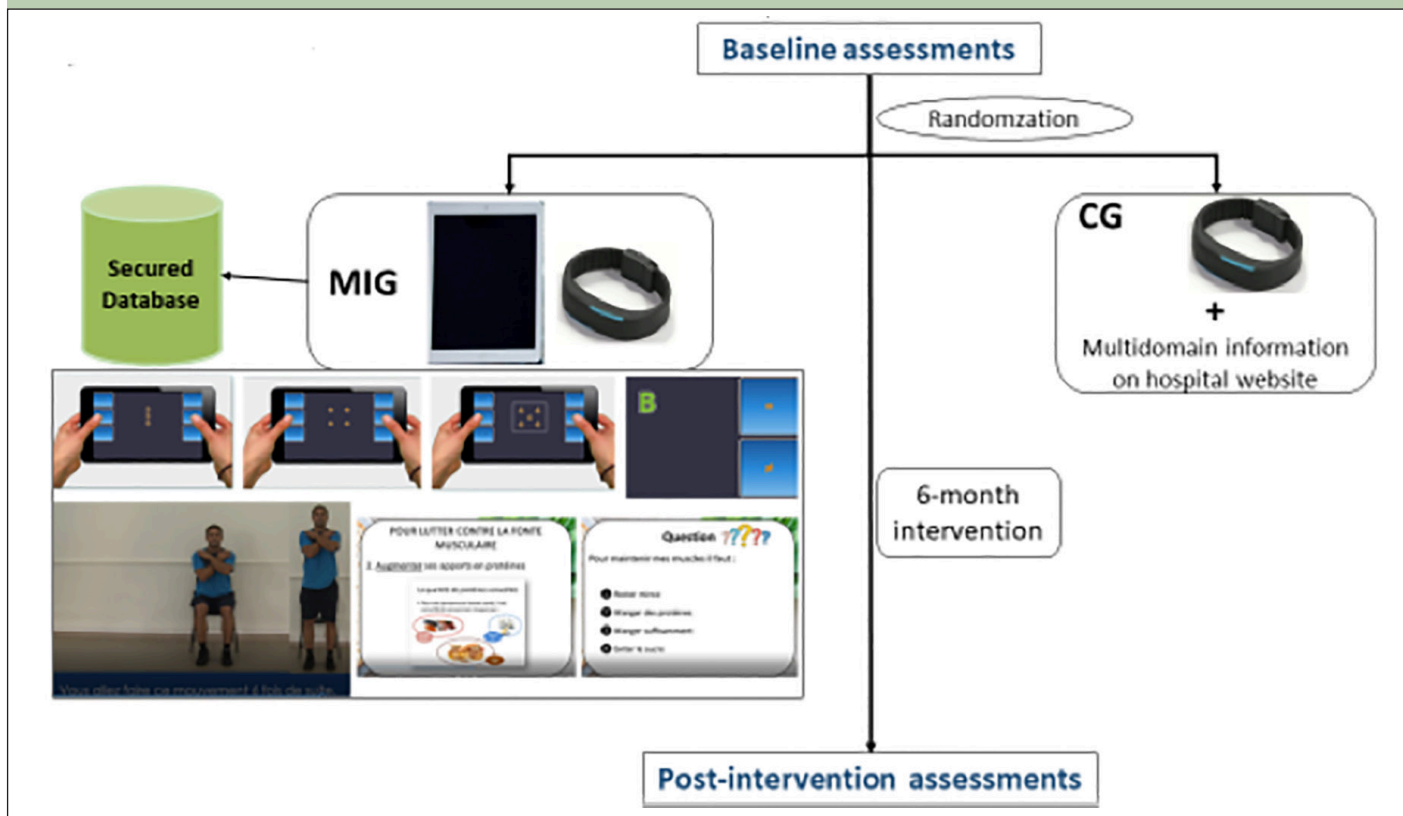
multidomain lifestyle training RCT are provided.

Key words: Multimodal lifestyle intervention, exercise, cognitive stimulation, nutritional advice, web-based intervention.

Introduction

In recent years, the multidomain strategy, an approach characterized by the combination of several lifestyle interventions, have received increasing attention, with the development of large randomized controlled trial (RCT) by our team (1) and others (2, 3). The rationale behind the multidomain lifestyle strategy is simple: if interventions, such as physical exercise, healthy nutrition, and cognitive stimulation, that have already proven their effectiveness for improving/maintaining individual's health during aging are combined, the benefits will then be potentiated.

Although several studies have investigated the effects of multidomain lifestyle strategies on functional-related outcomes during aging (4), mixed findings were obtained. The interventions tested so far are difficult to transpose into actual clinical practice, mainly because they are burdensome (eg, participants must visit research facilities several times a week or month) and expensive (eg, they require specialized professionals, such as exercise instructors). Several multidomain lifestyle platforms exist (5), however, to the best of our knowledge, none of them tested a training (not just health information, counselling or motivation) intervention, dedicated to older adults, through a randomized controlled trial (RCT) design. The advantages of having an online multidomain lifestyle training platform for which the content and procedures have proven their feasibility, acceptability, and efficacy, are multiple, since such a platform may be accessed at any time by the participants, being adapted to individual's time constraints, and does not need the physical presence of

Figure 1. Flow of the eMIND study procedures

After baseline assessments and randomization, MIG received a tablet with access to the multidomain platform for six months and a wrist-worn accelerometer; CG received the wrist-worn accelerometer and information on multidomain activities available in the website of the Toulouse University Hospital. The lowest part of the figure (MIG side) displays examples of how participants received the multidomain lifestyle training in their tablets, with cognitive training (eg, different Stroop tasks and N-back), and videos for both exercise (eg, chair rise – for illustration purposes, we put sit and up-right positions together, but participants had videos) and nutritional advice (eg, proteins).

both participants and specialized professionals. These advantages are still more important in the current context of social isolation and population containment caused by the COVID-19 pandemics.

The main purposes of the present article were to describe the feasibility and acceptability of a 6-month randomized controlled trial (RCT) of a web-based multidomain lifestyle training intervention for community-dwelling older people with spontaneous memory complaint. Secondary objectives were to test the effects of the intervention on both function- (eg, cognition, mobility) and lifestyle-related (eg, PA, food intake) outcomes.

Methods

A detailed description of the eMIND trial has been published elsewhere (6). eMIND is a 6-month pilot, parallel-arm, RCT of a multidomain lifestyle intervention composed of cognitive training, exercise training, and nutritional advices, among community-dwelling older adults from Toulouse area, South-West, France. The protocol was approved by the ethic committee of Tours (CPP Tours; 2017T2-10); the first recruitment occurred in December 2017 and the last study visit in September 2019. The trial was registered in a publicly accessible registry (www.clinicaltrials.gov; NCT03336320). All participants

signed an informed consent before undertaking study procedures.

Participants

Inclusion criteria were: ≥ 65 years-old; Mini-Mental State Examination (MMSE(7)) ≥ 24 ; presenting subjective memory complaints; easy access to internet (Internet access at least twice a week). Exclusion criteria were: illness with life expectancy less than six months; diagnosis of dementia according with DSM-V; diagnosis of neurodegenerative diseases, particularly Parkinson; major depression; any health condition potentially deteriorated by exercise; dependency in ≥ 1 activity of daily living (basic ADL); already participating in exercise or cognitive training ≥ 2 times/week in the last 2 months.

One hundred-twenty participants were enrolled in eMIND (74.2 years-old \pm 5.6; 57.5% women).

Randomization and masking

Participants were randomized after baseline assessments in a 1:1 ratio to either multidomain intervention group (MIG) or control group (CG) using a dedicated at-distance website. Concealment of group

allocation was warranted by using opaque envelopes, stored in a safe and locked place. Outcome assessors were blinded to group assignment.

Intervention

Figure 1 displays the main procedures of eMIND. Participants randomized to MIG received a tablet (model: HP x2 210 G2 - 10.1) providing access to a secured, password-encrypted platform that respected all the laws and regulations in France. Data was stored in an approved database for health data. MIG participants also received a commercial wrist-worn accelerometer (model: FitBit Flex 2) that provides objectively measured step counts. The accelerometer was synchronized with the tablet. Participants could access the platform for as many times as they wanted.

The web multidomain platform focused on three lifestyles: nutritional advice, and exercise and cognitive training. The platform was equipped with a chat, to facilitate communication of participants with the research team, a personalized agenda showing the day-by-day activities (eg, exercise and cognitive training to be done, nutritional advices), a library area where the content of the interventions and educational material on lifestyles were available. Participants were requested to follow both exercise and cognitive training twice a week, and nutritional advices every fifteen days; for that, they should only click on the activities displayed in their personal agenda. The content of each lifestyle is briefly described below.

Exercise training

Three different 6-month exercise programs, with increasingly challenging exercises, were proposed according to individual's baseline physical function (according to the short physical performance battery (SPPB)). Several videos with different exercises were elaborated: eg, chair rise, walking in the line, flexions and extension in the knee, walking backwards, tiptoe standing, etc. Each exercise video had subtitles with big letters to facilitate the understanding. The exercise program was developed by an experienced exercise scientist on the basis of exercise principles (eg, frequency, intensity, load progression), focusing on the lower-body. A typical exercise session was composed of three different types of strength exercises, three balance exercises (the number of both sets and repetitions per set varied according to individual's physical function), a specific advice on aerobic exercise (type, session duration, mode (continuous or in bouts), intensity and how to subjectively reach the self-perceived exertion), and a set of flexibility exercises for warm up and cooling down.

Cognitive training

A computerized cognitive training was provided using Neuropeak (<http://www.lesca.ca/task>), a password encrypted platform developed by researchers from the University of Montreal, Canada. Participants trained on cognitive tasks mainly related with executive functions, with a 6-month cognitive training pre-established personalized program with progressive difficulty; participants received active feedback encouraging them to perform beyond their baseline performances. Three types of tasks were performed: the dual-task, Stroop task, and N-back task. For the dual task (divided attention training), participants had to identify vehicles and fruits, both separately and concurrently (8). For the Stroop task (inhibition and switching training), participants were presented four different conditions: concordant, counting, discordant, and switching. For the N-back (updating training), digits were sequentially presented and the participant had to indicate if the digit was the same than the digit presented "n" steps earlier.

Healthy nutrition advice

Twelve videos (about five-to-eight minutes per video, two videos per month for the 6-month intervention) on nutritional advices were produced for this study by an experienced hospital dietitian from the department of geriatrics (Toulouse University Hospital), being organized under important nutritional topics for older adults, such as, proteins, fat, hydration, fruits and vegetables, calcium and osteoporosis, etc. Advices were based on the French recommendations from the "Programme National Nutrition Santé" (PNNS) (<http://www.mangerbouger.fr/PNNS/Le-PNNS>). A quiz with three questions was used to facilitate the retention of the key messages for each nutritional video. A personalized approach for nutritional advices had been planned for people at-risk of nutritional deficiency (mini-nutritional assessment(9) (MNA) \leq 23.5).

Control group

All controls received the same accelerometer than MIG, but did not have access to the multidomain web-platform. They received a link to information on multidomain activities produced by the research team (<https://www.chu-toulouse.fr/-ateliers-multidomaines->). CG participants were asked to bring their own smartphone/tablet at the baseline visit and the research team helped them to synchronize the accelerometer with the smartphone/tablet.

Main outcome measures

For this pilot RCT, feasibility and acceptability of study procedures and tools were the main outcomes. Feasibility was assessed through the adherence to the multidomain protocol. Participants accessing all the three interventions (clicking on the multidomain contents in their personal agenda in the web-platform) for at least 75% of the requirements were considered adherers, confirming the feasibility of the study procedures. Acceptability was assessed through the content analysis of recorded semi-structured interviews performed at the post-intervention assessments. The main element of acceptability was defined by the question "In your opinion, can this web-platform be used in its current state?", which was anchored by the following responses: No, it requires major changes for improving its easiness-of-use; No, but it requires only minor adaptations; Yes, but a few modifications could render it easier to use; Yes, the platform is easy-to-use in its current state. The main modifications proposed by participants to improve both intervention content and technological aspects were recorded and explored.

Secondary endpoints

Cognitive function

Assessed using the mean of a cognitive composite score (10) combining the Z-scores of four scales: MMSE (7) 10-items orientation, Digit Symbol Substitution Test of Wechsler Adult Intelligence Scale-Revised (DSST, WAIS-R) (11), total recall (up to 48 points) of the Free and Cued Selective Reminding test (FCSRT) (12), and Category Naming test (CNT). The following original scales were investigated separately: MMSE, DSST WAIS-R, total recall of FCSRT, CNT, and Controlled Oral Word Association Test (COWAT) (13).

Physical function

Measured using the SPPB (14), composed of three tests (4-meter usual pace gait speed, 5-repetition chair rise, and balance tests; score range from 0 to 12, higher is better), and the 4-meter gait speed (m/sec).

Depressive symptoms

Measured by the 15-item Geriatric Depression Scale (GDS-15)(15); scores vary from zero to 15, higher is worse.

Nutritional status

Assessed by the MNA (9); scores vary from zero to 30, higher is better.

Health-related quality of life (HRQOL)

Assessed using the Euro-QoL 5D-5L (16). We used two variables: index value (continuous variable varying from -1 to 1, higher is better) for the French population (17) calculated using the EuroQol calculator website (<https://euroqol.org/eq-5d-instruments/eq-5d-5l-about/valuation-standard-value-sets/crosswalk-index-value-calculator/>) and the visual analogue scale (VAS, varying from zero to 100, higher is better).

Physical Activity (PA)

This was assessed subjectively by a self-reported questionnaire (QAPPA (18, 19), continuous values of metabolic equivalent task/week (MET-min/week), higher means higher PA) and using step counts from the accelerometers. We used the mean steps/day from four waves of data collection: first week (baseline measure); first month (excluding the first week); month three; month six. Data on step count were considered valid if captured during $\geq 60\%$ of the exposure (ie, ≥ 18 days/month) and ignoring values ≤ 1000 steps (20–22).

Leisure-time cognitive activities

Assessed through a 14-item self-reported questionnaire asking for the frequency of cognitive stimulating activities (eg, crosswords, cultural outings); scores range from 0 to 56, higher is better.

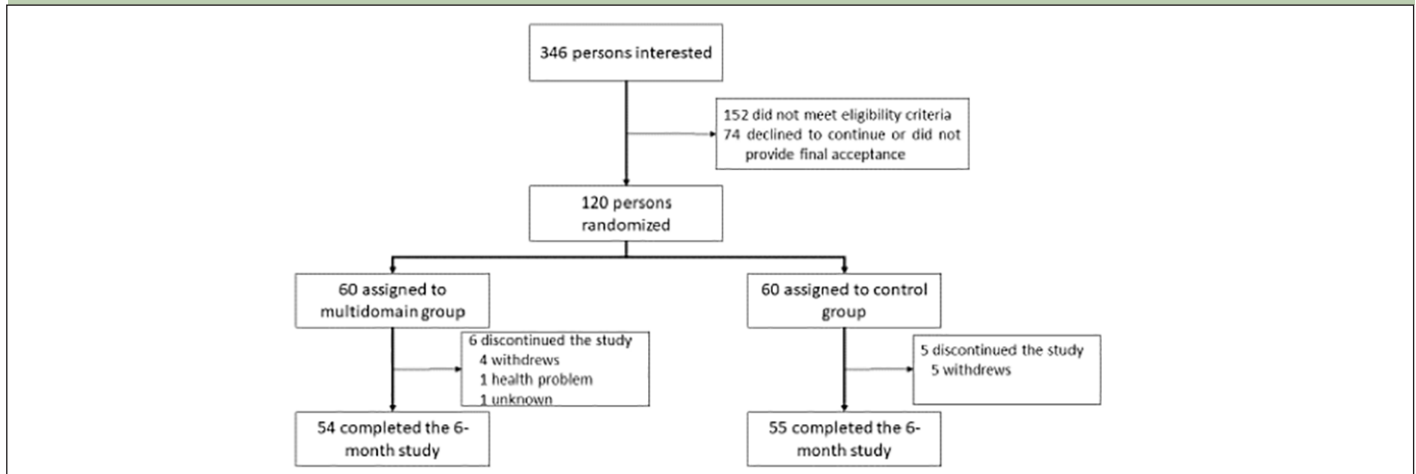
Food intake

Measured by a 21-item food frequency questionnaire (FFQ; scores vary from 0 to 21, higher is better) used in the clinical practice in the frailty day-hospital of the Toulouse University Hospital.

Statistical Analysis

The present pilot study was proposed to inform the development of a future, well-powered RCT of ICT multidomain lifestyle intervention; we estimated having 60 people per study arm, taking into account low adherence to multidomain interventions and 6% dropout, would allow us to have the needed data for a proper sample size calculation on clinical outcomes.

Analyses were performed on an intention-to-treat (ITT) basis. Descriptive statistics (mean (SD) and absolute numbers (%), as appropriate) were used. Content analysis of recorded semi-structured interviews performed at post-intervention were used to identify aspects to be improved in study procedures and tools. Baseline difference between MIG and CG were tested using Student t-test for independent samples and chi-square test, as appropriate. The effects of the intervention on

Figure 2. Flowchart of study participants**Table 1.** Participants' characteristics

Variables	Multidomain lifestyle intervention (n=60)	Controls (n = 60)
Age, years (SD)	75.2 (5.7)	73.2 (5.3)
Sex, women (%)	31 (51.7)	38 (63.3)
Education		
Primary	2 (3.3)	1 (1.7)
Secondary	21 (35)	19 (31.6)
Undergraduate or over	37 (61.7)	40 (66.7)
Geriatric depression scale-15, mean (SD)	2.4 (2.5)	3.2 (2.7)
Mini-mental state examination, mean (SD)	28.5 (1.2)	28.7 (1.1)
Mini-nutritional assessment, mean (SD)	27.6 (2)	27.7 (1.7)
EQ-5D-5L index value, mean (SD)	0.88 (0.12)	0.88 (0.09)
EQ visual analogue scale, mean (SD)	74.6 (12.5)	75.2 (13)
Short physical performance battery, mean (SD)	10.6 (1.2)	10.7 (1.1)
Gait speed, m/sec, mean (SD)	1.19 (0.2)	1.15 (0.2)
FCSRT total recall (/48), mean (SD)	44.8 (4.3)	44.9 (4.1)
COWAT, mean (SD)	20.1 (6.5)	20.8 (6.4)
CNT, mean (SD)	29.9 (9)	28 (7.3)
WAIS-R, mean (SD)	42.8 (12.2)	43.5 (9.6)
Cognitive composite score, mean (SD)	0.04 (0.66)	-0.03 (0.54)
Step count/day (accelerometer), mean (SD)	8874 (3452)	8654 (3493)
Physical activity, MET-min/week, mean (SD)	1524 (1835)	1675 (2131)
Leisure-time cognitive activities, mean (SD)	16.3 (6)	15.2 (5.4)
Food intake, mean (SD)	13 (1.8)	12.6 (2.1)

the secondary outcome measures were assessed using mixed effect linear regressions, with group, time and group-by-time interaction as fixed terms, a random effect at participants' level, and a random slope on time; participant's age was used as a confounder in all analysis due to imbalance between groups.

Statistical significance was determined $p < 0.05$. All analyses were performed using Stata (v.14.0, Texas, USA).

Results

Figure 2 show the flow of study participants. From the 120 participants randomized, 109 were assessed at 6-month (MIG, n=54; CG, n=55). Among the 58 adverse events registered, 12 were serious (eg, heart infarct), being four in MIG (n=3 subjects) and 8 in CG (n=6 subjects); among the 46 non-serious events (eg,

Table 2. Effects of the web-based multidomain lifestyle training intervention on both clinical and lifestyle secondary outcomes using mixed-effect linear regression

Variable	Within-group adjusted mean difference between baseline and 6-month (95% CI; p-value) ^a		Between-group adjusted mean difference (95% CI; p-value) ^a
	Multidomain intervention	Controls	
Cognitive composite score	-0.26 (-0.40, -0.11; 0.001)	-0.05 (-0.20, 0.09; 0.48)	-0.20 (-0.41, 0.002; 0.053)
MMSE	-0.04 (-0.42, 0.34; 0.82)	-0.14 (-0.52, 0.23; 0.45)	0.10 (-0.43, 0.64; 0.71)
FCSRT total recall	-1.71 (-2.83, -0.59; 0.003)	-0.48 (-1.58, 0.62; 0.39)	-1.23 (-2.80, 0.34; 0.13)
COWAT	0.71 (-0.40, 1.81; 0.21)	0.56 (-0.53, 1.64; 0.31)	0.15 (-1.40, 1.70; 0.85)
CNT	-1.41 (-2.89, 0.07; 0.06)	0.25 (-1.21, 1.70; 0.74)	-1.6 (-3.73, 0.42; 0.12)
WAIS-R	-0.46 (-2.56, 1.63; 0.66)	2.08 (0.01, 4.14; 0.05)	-2.54 (-5.48, 0.40; 0.09)
GDS-15	-0.44 (-0.96, 0.07; 0.09)	0.02 (-0.49, 0.53; 0.94)	-0.46 (-1.19, 0.26; 0.21)
MNA	-0.36 (-0.86, 0.13; 0.15)	-0.55 (-1.04, -0.06; 0.03)	0.18 (-0.51, 0.88; 0.61)
SPPB	0.59 (0.26, 0.93; <0.001)	0.35 (0.01, 0.68; 0.04)	0.25 (-0.22, 0.72; 0.30)
Gait speed	-0.007 (-0.05, 0.03; 0.71)	0.04 (-0.001, 0.08; 0.06)	-0.05 (-0.11, 0.10; 0.11)
EQ-5D-5L index value	-0.02 (-0.06, 0.02; 0.36)	-0.08 (-0.11, -0.04; <0.001)	0.06 (0.002, 0.11; 0.04)
EQ visual analogue scale	0.86 (-1.85, 3.57; 0.53)	-5.60 (-8.30, -2.91; <0.001)	6.46 (2.64, 10.3; 0.001)
Step count (Ref.: first week data)			
First month	140 (-320, 600; 0.55)	314 (-181, 810; 0.21)	-174 (-850, 502; 0.61)
Month 3	80 (-449, 605; 0.76)	514 (-31, 1059; 0.07)	-433 (-1190, 323; 0.26)
Month 6	-197 (-832, 438; 0.54)	176 (-497, 850; 0.61)	-373 (-1299, 553; 0.43)
Physical activity (MET-min/week)	51 (-538, 640; 0.86)	-137 (-720, 445; 0.64)	188 (-640, 1016; 0.65)
Leisure-time cognitive activities	1.14 (-0.25, 2.53; 0.11)	0.17 (-1.18, 1.52; 0.80)	0.97 (-0.97, 2.91; 0.33)
Food intake	0.36 (-0.06, 0.78; 0.09)	0.38 (-0.03, 0.79; 0.07)	-0.02 (-0.61, 0.57; 0.94)

a. For all variables, except GDS-15, positive values in the within-group adjusted mean difference indicate improvement over time. For GDS-15, negative values indicate improvement; b. For all variables, except GDS-15, positive values in the between-group adjusted mean difference favor the multidomain intervention. For GDS-15, negative values favor the multidomain intervention

Box 1. Recommendations for developing a large RCT on multidomain lifestyle training: lessons from eMIND^a

Content

Exercise: Diversified exercises; rapid and individually adapted progression; challenging exercises; use of simple materials (eg, therabands; calf weights) may be an option.

Nutrition: The approach by nutritional topic (eg, proteins, hydration, etc) is a good option, but part of the content should be individually tailored according to individuals' interests

Cognitive: long and repetitive sessions should be avoided;

Overall procedures

1. Establish regular contacts between participants and the research team. Two contacts per month in the beginning of the intervention, then one contact per month would probably be enough to adapt the multidomain content to each person and solve most problems participants are facing to keep doing the multidomain program, increasing thus compliance.
2. A rewarding system, for example, with points (gamification) may be an option to increase motivation and reach high compliance levels.
3. A system sending automatic remind messages to participants who did not connect to the multidomain web-platform in the past few weeks may be helpful.

a. These recommendations should be seen as additional elements to the eMIND contents and procedures.

intermittent dizziness), 32 occurred among MIG (n=24 subjects) and 14 in CG (n=10 subjects). No adverse event (both serious and non-serious) was related to study procedures according with study physicians.

Table 1 shows participants' characteristics. Study groups were well-balanced, except that MIG participants were 2-year older than CG (p=0.052).

Regarding feasibility, 58 (out of 60) participants in MIG connected to the multidomain platform at least once during the 6-month trial. Among them, adherers

(≥75% of prescribed sessions) varied across the different components of the multidomain: 37 individuals (63.8%) for cognitive training, 35 (60.3%) for nutrition, and only three (5.2%) for exercise; these same three persons were adherers in all three multidomain components. Regarding exercise, 31 individuals (53.4%) followed ≥50% of the requested frequency (they connected once a week); for cognitive training and nutritional advices, they were 75.8% and 81%, respectively.

Regarding acceptability, we interviewed 53

participants from MIG: four (7.5%) said the multidomain web-platform was not ready to be used and needed major changes; three (5.7%) indicated it required minor changes; 18 (34%) said it was ready to be used, but minor modifications could render it easier to use; and 28 (52.8%) indicated the platform was ready to be used without any change. Among the strengths/weakness of the platform, although most participants interviewed (n=50, 94.3%) indicated the technical/technological aspects were simple, they reported technical interruptions during the cognitive training; one person indicated the letters were too small. Although all individuals interviewed indicated the content was clear, they found weaknesses, the most cited being the physical exercises were too easy (not challenging enough), repetitive (should vary more the exercises proposed), sometimes difficult to perform due to space limitations at home, and progressed slowly. To a lower extent, other weaknesses highlighted were: nutritional advices were lacking novelty; cognitive training was sometimes repetitive and too long. Some participants suggested that having more contacts with the research team would be helpful and a few indicated that the gamification (eg, motivating rewarding system, points) of the intervention could increase interest and adherence.

The effects of the intervention on clinical and lifestyle outcomes are displayed in Table 2. No statistically significant effects were found, except for the two variables (ie, index value and VAS) of HRQOL, showing MIG had an improved HRQOL compared to CG.

A set of recommendations for developing a large RCT on multidomain lifestyle training intervention is provided in Box 1. These recommendations were developed according with the lessons learnt from eMIND.

Discussion

This is the first RCT using a web-based multidomain lifestyle-training intervention for community-dwelling older adults. We showed that study procedures were well-accepted, but expectations regarding participant's adherence to the intervention were not met, in particular for exercise. Moreover, compared to controls, participants of MIG have improved their HRQOL at the end of the 6-month intervention.

Although most participants were not compliant to the protocol to the expected extent, raising questions about the feasibility of a larger trial, a few considerations are worth discussing. We arbitrarily defined good adherence as connecting to $\geq 75\%$ of intervention sessions, which is a high rate, in particular for demanding activities, such as exercise (23). Indeed, the FINGER study, a previous multidomain RCT (2) with supervised exercise training, showed that less than 60% of participants performed at least half of the exercise sessions (24), which is a similar rate than ours (53.4% of MIG connected to half of expected sessions). FINGER also had part of the cognitive

intervention performed at home through a web-based training system; they found that 47.2% of participants did at least half of the training sessions (24), which is much less than 75.8% observed in eMIND. In the multidomain MAPT trial our team conducted (1, 24), 53.5% of participants attended $\geq 75\%$ of multidomain sessions (PA and nutritional counselling and cognitive training performed in the same sessions), which is similar to what we found for nutritional advices and cognitive training in eMIND, but not for exercise. Several methodological differences of FINGER and MAPT, compared to eMIND, must be mentioned: FINGER and MAPT were long-term (2- and 3-year, respectively) trials, with larger samples, and different modalities and frequency for providing the multidomain interventions; eMIND and MAPT have similar population, but were much older than FINGER. In the HATICE (25) web-based multidomain trial (focused on counselling and motivation through a coaching system), participants in the intervention group connected in average 1.8 times per month, during almost 18 months; HATICE's participants were not required to connect on a regular frequency as in eMIND. The fact the study was well-accepted by participants, with clear and, most of time, useful contents is a major result. Therefore, considering the good acceptability and the acceptable adherence rates for cognitive training and nutritional advice, it is plausible to suggest the eMIND findings are promising. Although adherence to exercise was low, compliance of once/week exercise training was acceptable; this is important because doing PA once a week may already bring several health benefits during aging (26, 27).

However, weaknesses must be mentioned and corrected if a larger, well-powered trial should be developed. Indeed, the exercise program should comprise a more diversified set of exercises, with different levels of difficulty in the execution and adapted progression. For this, one possibility is to use a coaching system, like in the HATICE study (25), which would allow participants to interact with the research team through the web-platform in a shorter time interval and adapt the intervention program according to participant's current status; this might lead to providing the most appropriate content to participants, reducing loss of motivation due to repetitive and not challenging enough exercises. Providing participants with inexpensive exercise materials (therabands, calf weights) may facilitate exercise load progression. Adapting the intervention content to avoid demotivation would also improve cognitive training. The coaching system would further help in making more interactive the nutritional advices component. If connected devices are to be used, an important workload should be foreseen to solve technical problems. Problems with the synchronization between accelerometer and tablets/smartphones in eMIND were frequent, being most of time related with participants' low digital literacy; sometimes, problems were related to technical

issues (requiring the support of IT professionals).

The absence of noticeable differences between groups for clinical outcomes was expected, since eMIND has not been powered to test the effectiveness of the intervention. Why MIG participants had a better HRQOL than CG, even if no statistically significant between-group differences were found in any of the clinical and lifestyle outcomes, deserves further investigation. Woo and colleagues (28) showed that a 24-week exercise and nutritional supplementation, compared to controls, improved self-reported health in middle-aged and young older adults. The effects of the isolated components of multidomain are better known, especially exercise, which has shown to improve HRQOL in older adults (29-33). Nutritional support was shown to have a positive effect on quality of life in older hospitalized patients (34). It is possible that alterations in patient-reported outcomes, such as HRQOL, which are subjective and then potentially more sensitive to change in a short-time interval, precede changes in more robust clinical outcomes, such as mobility. However, since the effects of eMIND intervention on HRQOL is of arguable clinical meaningfulness, it is also possible that the HRQOL improvement found would be temporary. A longer and well-powered trial would shed light on this topic.

The main strengths of our study were: the mixed method approach, composed of a RCT design and qualitative semi-structured interviews (for MIG); the use of a wearable step count tracker; and the fact this is the first web-based multidomain lifestyle-training intervention for older adults. Although other web-based multidomain trials (5) were performed, they focused on counselling and motivation or were developed in middle-aged/young older populations; other trials are on-going (35, 36), in particular the large and long-term MYB trial (36), which will provide a training platform for people 55-77 years-old, but all components of the multidomain (performed in short blocks of 10 weeks) will not be available to all participants. eMIND's weaknesses were: the small sample; and short intervention length.

Implementing a web-based multidomain lifestyle-training platform accessible to a large number of older people could have a major positive impact in a public health perspective. This is still more relevant in periods of prolonged social isolation and containment, such as during the COVID-19 pandemics. The preliminary findings of this pilot RCT support the development of a larger, well-powered, long-term RCT to test the effectiveness of an adapted version (in particular, for exercise) of the eMIND platform on clinical outcomes.

Funding: This study is supported by the Fondation pour la Recherche Médicale (FRM DOC20161136208) in the context of the call "Evaluation of the impact of connected devices on health 2016". The Centre Hospitalier Universitaire de Toulouse (CHU-Toulouse) is the sponsor of the study (protocol ID: 17 0071).

Role of Funding Source: None.

Conflict of interest: All authors declare no conflicts of interest related to this article.

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