Effects of a long-term exercise programme on functional ability in people with dementia living in nursing homes: Research protocol of the LEDEN study, a cluster randomised controlled trial

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ABSTRACT

Background: Exercise may lead to improvements on functional ability, physical function, and neuropsychiatric symptoms (particularly depression) in people with dementia (PWD). However, high-quality randomised controlled trial (RCT), controlling for the socialisation aspect of group-based exercise interventions, and designed to delay the declines on the functional ability of PWD in the nursing home (NH) setting is almost inexistent. This article describes the protocol of the LEDEN study, an exercise RCT for PWD living in NHs.

Methods/design: LEDEN is a cluster-randomised controlled pilot trial composed of two research arms: exercise training (experimental group) and social/recreational activity (control group). Both interventions will be provided twice a week, for 60 min, during the 6-month intervention. The total duration of the study is 12 months, being six months of intervention plus six months of observational follow-up. Eight French NHs volunteered to participate in LEDEN; they have been randomised to either exercise intervention or social/recreational intervention in a 1:1 ratio.

Results: The primary objective is to investigate the effects of exercise, compared to a social/recreational intervention, on the ability of PWD living in NHs to perform activities of daily living (ADL). Secondary objectives are related with the cost-effectiveness of the interventions, and the effects of the interventions on patients’ physical function, neuropsychiatric symptoms, pain, nutritional status, and the incidence of falls and fractures.

Discussion: LEDEN will provide the preliminary evidence needed to inform the development of larger and more complex interventions using exercise or non-exercise social interventions.

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1. Introduction

Dementia is a common condition in late life [1–3]; the prevalence of dementia is expected to markedly rise in the coming decades [3,4]. Dementia burden has increased in the last two decades [5], including in terms of increased health costs [6]. Of particular importance is the fact that dementia increases the risk of developing functional limitations and disability [7–9]; therefore, the maintenance of optimal levels of functional ability is a crucial aspect of the healthcare of people with dementia (PWD) [10]. Although dementia cannot be reversed, evidence suggests that disability in activities of daily living (ADL) can be delayed [11] and quality of life enhanced by appropriated interventions.

Anti-dementia drugs in most RCT testing drug effectiveness against placebo proved to have modest [12–15] or no [16–20] effects on ADL function in PWD. Therefore, developing safe and effective non-pharmacological interventions aiming at delaying the progression of declines in functional ability, particularly among institutionalised, often disabled PWD, is an urgent need worldwide with important public health implications.

Among the potential interventions for PWD living in the institutional setting, physical exercise, ie, planned, structured, repetitive, and purposeful physical activity, constitutes a promising intervention that has received increased attention in the last years. Exercise has been found to improve functional ability, physical function, neuropsychiatric symptoms (particularly depression), and even cognitive function (although the clinical relevance of this latter benefit is questionable) in PWD. The recent Cochrane review and meta-analysis by Forbes et al. [11] on exercise for PWD found that people who exercised, compared to
controls, improved their ability to perform ADLs and their cognitive function; however, the heterogeneity across the studies entered into that meta-analysis was high, which preclude any solid conclusion to be drawn. Another Cochrane review and meta-analysis [21] on the benefits of physical therapy for long-term care residents showed that exercise improved ADL function and physical function (eg, walking speed). Although the target population was not composed only of PWD, this meta-analysis studied residents of long-term care facilities, institutions where the prevalence of dementia is very high. Our research team has conducted a systematic review and meta-analysis about exercise effects on neuropsychiatric symptoms in PWD (Unpublished data. Study protocol [22] was registered in PROSPERO database). Our main finding was that exercise significantly reduced depressive symptoms in PWD; while exercise tended to reduce global levels of neuropsychiatric symptoms, the analysis did not reach statistical significance.

Although research in PWD using behavioural interventions and performed in nursing homes (NH) presents non-negligible methodological advantages (eg, interventions being developed in the life space of the study participants, research monitoring may be facilitated and adherence rates probably improved, easy access to a large number of PWD and disabled people), very few high, and even moderate, quality exercise RCTs were developed in institutionalised PWD [23]. Most RCTs in NH did not apply cluster-randomisation [21], which means that contamination between research’s arms may not be excluded; to avoid contamination [24], cluster-randomisation in RCTs using behavioural interventions is highly warranted. Furthermore, the benefits of group-based exercise (ie, the majority of exercise RCTs in NH are performed in group) may be partly dependent on the socialisation promoted through any group-based intervention. To date, exercise RCTs have used usual care as a comparator group or operationalised a socially active-control group through “light” and little structured interventions, such as social visits [25,26] or causal conversations [27,28]. To the best of our knowledge, no exercise RCTs in institutionalised PWD used structured social/recreational activities as comparators (see the review by Forbes and colleagues for further details on comparators) [10]. Therefore, we designed the LEDEN study to fill in the above mentioned gaps. LEDEN is a cluster-randomised pilot study with the main objective of examining the effects of a 6-month exercise training, compared with a 6-month structured social/recreational activity, on the ability to perform ADLs in PWD living in NHs. Secondary objectives are to investigate if changes on ADL performance remain in 3- and 6-month postintervention follow-ups, and the effects of the interventions on participants’ physical function, incident falls and fractures, neuropsychiatric symptoms, pain, nutritional status and use of psychotropic drugs. We will also investigate the cost-effectiveness of the interventions. The main hypothesis of the LEDEN study is that exercise training delays the declines in functional ability (ADL performance) in PWD, such a positive effect being independent of the socialisation aspect related to group-based activities.

2. Methods and analysis

The reporting of this protocol is based on the guidance provided by the SPIRIT Statement [29].

2.1. Study design

LEDEN is a cluster-randomised controlled pilot trial composed of two research arms: exercise training group (experimental group) and a social/recreational activity group (control group). All participating NHs are located in France. The total duration of the study is 12 months, being six months of intervention plus six months of observational follow-up.

2.2. Eligibility criteria

The sole inclusion criterion for the selection of NHs is that the NH staff volunteers to participate in LEDEN. For patients, inclusion criteria are: confirmed diagnosis of Alzheimer's disease, vascular or mixed dementia according to the criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV); mini-mental state examination (MMSE) ≥20 (out of 30); age ≥65 years-old; living in one of the participating NHs for at least 3 months at the moment of baseline measurements; to be able of walking at least 4 m (with walking devices if needed but without human assistance); to be able to rise from a chair without help or with minimal human assistance. Exclusion criteria are: MMSE >20 (out of 30); terminal illness with life expectancy less than 6 months; diagnosis of Parkinson's disease; diagnosis of dementia with Lewy bodies; unstable cardiovascular condition or any other health condition that might be deteriorated by physical exercise; planned transfer from the NH to another NH or to home or to surgery during the 6-month period of intervention; already participating in physical exercise ≥2 times/week in the last 2 months prior to the date of baseline assessment.

Exercise interventionists will be professional exercise instructors with a 3-year university diploma (undergraduate studies) in Science and Techniques of Physical Activity and Sports (from the French term STAPS). All exercise instructors will already have experience in working with patients in the NH setting, particularly PWD patients. As for exercise interventionists, interventionists for the control group will already have experience in working with institutionalised older adults, particularly PWD patients.

2.3. Interventions

The interventions in the LEDEN study will be added to already existing activities in the NHs. Therefore, participants meeting study inclusion/exclusion criteria will not be asked to stop their usual activities. However, once enrolled in the LEDEN study, participants engage to not participate to another RCT during the whole duration of LEDEN, ie, 12 months. Participants can, however, participate in observational studies simultaneously to their participation in LEDEN if the observational study is supposed not to affect the outcome measures of LEDEN, particularly, functional ability.

2.4. Exercise programme (experimental group)

Exercise sessions will ideally be done in groups of three-to-eight persons to facilitate socialisation among participants and to allow the instructor to guide participants closely; although being a group-based exercise programme, participants will be guided and the exercises will be adapted in an individual basis, which may increase adherence and compliance rates [30]. The exercise training will take place in the NH, twice weekly, 60 min per session (session duration can be shorter in the first weeks of intervention according with participants’ physical capacity), during 6 months. Interval between two exercise sessions will be of at least 48 h. The exercise programme will be a multicomponent training, with exercises specifically developed to improve participants’ flexibility, coordination and balance, muscle toning, and cardiorespiratory capacity. All exercise sessions will be accompanied by music. Exercise intensity targeted is moderate; exercise progression will be set individually and according to participants’ physical and cognitive (ie, comprehension of the instructions) abilities. Although each exercise session may be modified by the exercise instructor according to participants’ capabilities and interests, an ideal exercise session would be as follow:

1) First, participants execute 10 min of range of motion and a few light calisthenic exercises (for improving flexibility and preparing participants for the next exercises). The exercise instructor will establish a
motivating atmosphere by helping participants to make the movements correctly and then providing positive feedback for each person individually; this interaction between instructors and participants is a key factor to increase exercise compliance and adherence, as well as to motivate participants to improve their engagement at each single session of exercise.

2) After that, participants do 10 min of coordination/balance exercises. Since sitting, standing, and initiating walks are commonly associated to falls [31], we will focus on activities that explore these physical actions such as rising from a chair safely and short walks with direction changes.

3) Then, participants perform 10 to 15 min of muscle strength training. For this, weight-bearing exercises (for the lower-body) and light hand-held materials (for the upper-body), including therabands, may be used. The number of repetitions will vary according to the physical outcome (ie, developing muscle strength, power or endurance) and participants’ physical capacity. For example, rising from a chair can constitute an extremely difficult task for some participants: 1 repetition for improving muscle strength would be a challenging goal for such a person, at least in the beginning of the exercise programme; as this person progresses, the instructor would introduce a muscle power component (emphasising speed of execution). We will focus on exercises to be executed in the upright position, but exercises in a sitting position may be done to reduce the magnitude of the effort and/or to safety issues for some exercises.

4) Participants execute from 20 to 25 min of aerobic exercises. They perform bouts of walking (preferably ≥3 min/bout), intercalated by light exercises (using all large muscle groups, such as the muscles of the thigh, back and pectoral) disposed in a circuit-training format. These light exercises will avoid that, between two bouts of walking, participants’ heart rate drops to the rest levels; it would warrant the maintenance of a sustained, moderate aerobic component.

5) Finally, the exercise session finishes with 5-minute calm down exercises (eg, very light walking followed by muscle stretching).

2.5. Social/recreational activity (control group)

The structured social/recreational intervention is an innovative approach introduced by the LEDEN study. The rationale for including an active comparator is to control for the additional positive effects of the exercise training on some outcomes (eg, neuropsychiatric symptoms) that would be related with the socialisation factor rather than promoted by the exercise itself. Participants in this group will participate in group-based activities (eg, painting), with no physical activity intervention or advice being provided to these participants. Interventionists will be professionals external to the NH. Although, for practical reasons, we did not define a single standard social activity intervention (the same intervention being not available in the geographical location of all participating NHzs), the selected interventions must represent a new activity for the patient. A non-exhaustive list of potential social activities are: plastic arts (ie, practice of different art techniques, such as, painting, collage, modelling/shaping), musical mediation and musical instrument classes (ie, using music and musical instruments to stimulate patients’ communication and sensorial skills; practice of musical instruments), and singing classes and choir. It is important to highlight that such interventions will have the same schedule than the exercise intervention, ie, they will take place in the NHs, twice weekly, 60 min per session, during 6 months.

3. Outcome measures

3.1. Primary endpoint

3.1.1. Functional ability

The effects of the 6-month interventions on the ability to perform ADLs will be evaluated using the Alzheimer Disease Cooperative Study (ADCS) ADL-sev [32]. This is a 19-item scale measuring the ability to perform basic (eg, bathing, toileting) and instrumental (eg, turning faucet/lights on/off) ADLs in the last four weeks. The ADCS-ADL-sev was specifically validated for people with moderate or severe Alzheimer’s disease (AD), ie, the large majority of PWD in NHzs. Scores in this scale vary from 0 to 54, with higher scores indicating better functional ability. The ADCS-ADL-sev has already been used successfully in the NH setting [33].

3.2. Secondary endpoints

3.2.1. Overtime stability of ADL changes

We will investigate the 3- and 6-month postintervention stability of changes in functional ability (ADCS-ADL-sev).

3.2.2. Cost-effectiveness

The costs of implementing the interventions involve both initial fixed (ie start-up) costs of the exercise and social activity interventions as well as the costs of running the interventions’ sessions. Start-up costs will be captured from the study budget: investment in exercise material, etc. The total costs of implementing the LEDEN intervention will be calculated from a societal perspective. Total costs will include: start-up costs, potential on-going costs (for instance: material renting), potential clinical costs (care that could be given after the physical sessions for patients experiencing pain), and intervention costs (salaries of interventionists). Note that our analyses will focus on the operating costs rather than the costs of research.

Therefore, economic analyses will be performed to explore whether the exercise programme is cost-effective compared with the social activity programme. The results of these analyses are useful from a health policy perspective as they will provide crucial information about the affordability of widespread implementation of the LEDEN interventions. Incremental cost-effectiveness ratio (ICER) calculations of the exercise training, compared to the social activity intervention, will be done. The primary effectiveness measure for the cost-effectiveness analysis will be the ADSC-ADL-sev measure. The ADCS-ADL-sev measured among compliant patients compared with the social activity group will provide the incremental functional benefit resulting from the intervention at 3 months and at 6 months. To calculate the ICER, the additional cost attributable to the exercise compared with the social intervention will be divided by the differences in the ADCS-ADL-sev measures between the two groups: ICER (exercise session) = increase in cost due to exercise sessions/increase in the functional status. This ratio indicates the additional cost generated by the exercise programme for increasing patients’ ADSC-ADL-sev score of one unit. In addition, ICER for subgroups of NH residents will be computed. Heterogeneity in cost-effectiveness results among subgroups can indeed provide useful information for policy decision-maker in a context of limited available resources. Hence, ICER according to dementia severity and gender will be provided.

Furthermore, we will examine the effects of the 6-month interventions on:

3.2.3. Physical function

Physical function will be evaluated by the short physical performance battery (SPPB) (score from 0 to 12). The SPPB is a validated [34] performance battery composed of: timed short distance walk (4 m at usual pace), timed repeated chair stands (5-repetition chair rise), and timed balance tests (standing balance). Each of these tests is assigned a score ranging from 0 to 4, with 4 indicating the highest level of performance and 0 the inability to complete the test. A summary score ranging from 0 (worst performers) to 12 (best performers) is calculated by adding walking speed, chair stands and balance scores.
3.2.4. Neuropsychiatric symptoms
The frequency and severity of neuropsychiatric symptoms will be assessed using the neuropsychiatric inventory-nursing home version (NPI-NH). The NPI is a validated [35] questionnaire investigating 10 behavioural and two neurovegetative areas; scores vary from 0 to 12 for each item, with higher scores indicating higher behavioural disturbances. The total NPI score is obtained by adding the scores of the 10 behavioural areas.

3.2.5. Pain
Pain will be evaluated by the Algoplus scale, which measures pain in older people unable to communicate verbally [36], including PWD. This scale contains 5 items, each of them scored as 0 (absence of pain) or 1 (presence of pain); the total score varies therefore from 0 to 5, with higher scores indicating higher pain.

3.2.6. Nutritional status
This will be assessed using the Mini Nutritional Assessment (MNA), an instrument largely used in NHs [37,38]. Scores on the MNA vary from 0 to 30, with higher scores indicating better nutritional status.

3.2.7. Falls and fractures
The dates of falls and fractures (body region involved: wrist, hip, femur) will be recorded by the NH staff for each participant throughout the study. This information will be sent to the research team regularly.

3.2.8. Cognitive function
This will be assessed by the MMSE [39], in its French version (French Health Authority (Haute Autorité de Santé — HAS) website: http://www.has-sante.fr/portail/plugins/ModuleXitiKLEE/types/FileDocument/doXiti.jsp?id=r_1497235 Accessed on June 15th 2015). Scores in this questionnaire vary from 0 to 30, with higher scores indicating higher cognitive function.

3.3. Time schedule
The overall duration of the study is two years. The interventions are preset to start between June and September 2015. Provisory calendar is: up to one year for setting up the study (from July 2014 to July 2015); one-to-two months for participants’ recruitment (June/July 2015); six months for the intervention (from June/July 2015 to December/January 2016); six months for follow-up (from December/January 2016 to June/July 2016). Table 1 shows the calendar for the LEDEN study. Baseline assessments will occur only after obtaining the informed consent from patient’s next of kin and legal representative, and from the patient him/herself if appropriate (according to understanding and communication skills). Table 2 shows patients’ follow-up of data collection and outcome measures assessment.

3.4. Blinding
All assessments in the LEDEN study will be performed by the NH staff through a collaborative work of the NH coordinating physician with other NH staff members, particularly, nurses, nurses’ aide, psychologists, and physiotherapists/ergo-therapists. Therefore, outcome assessors are the patient’s healthcare providers and they will not be blinded to participants’ group allocation. Blinding of patients is very difficult to make and maintain throughout the study in RCTs using behavioural interventions; in the LEDEN study, patients will not be blinded to group allocation. In an effort to reduce inter-rater assessment bias, the same assessors will evaluate participants throughout the study; however, this procedure will be dependent on staff turn-over. Moreover, the statistical analyst will be blinded to group allocation.

3.5. Sample size and recruitment
Because LEDEN is a pilot study designed to inform the development of a larger, multi-country controlled exercise trial among PWD living in NHs, feasibility is an important aspect to take into account. Thus, to facilitate the recruitment of NHs and the engagement of their staff in the success of LEDEN, we selected a convenience sample of for-profit NHs belonging to the Korian group. The partnership with a private company in the healthcare and medico-social sector provided us with an easy access to a large number of NHs dealing with PWD patients, increasing the feasibility of LEDEN. Moreover, the fact that all NHs belong to the same private group may represent a methodological advantage for this small-size, pilot study since it may mean that the routine healthcare provided to patients are comparable across NHs (e.g. similar ratios of coordinating physician, nurses, nurses’ aide per bed, the use of the same protocols of care). Although we are aware that such a procedure will reduce the generalisability of our findings, we made a clear methodological choice by privileging study feasibility instead of results’ generalisability.

To recruit NHs, the Korian group launched a call for volunteer participation in the LEDEN study across its NHs located in France; 37 NHs indicated to be interested in participating. After a thorough explanation about the LEDEN study and the practical implication of the NH staff in data collection through the whole duration of the study, only eight NHs remained interested in participating in LEDEN. All the eight NHs were therefore selected. Based on our previous experience in performing exercise RCTs in NHs [40], we estimated that recruiting 140 PWD (ie, in average 18 PWD per NH) is feasible and will allow us to reasonably calculate accurate estimates of changes in our main outcome measure, ie, functional ability.

3.6. Randomisation
Due to organisation issues related to LEDEN interventions, the cluster randomisation had to be performed before patients’ recruitment and

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Table 1
Calendar for the LEDEN study.

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<td>Funding year — quarter</td>
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<tr>
<td>Funding year</td>
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<td>Study setting up</td>
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<td>Participants’ enrolment</td>
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<td>Eligibility screen</td>
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<td>Informed consent: patient, next of kin, and legal representative</td>
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<td>Randomisation/group allocation</td>
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<td>Baseline assessments</td>
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<td>Interventions</td>
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<td>Follow-up (post-intervention)</td>
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<td>Close-out assessments</td>
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<td>Data analyses</td>
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Baseline assessments. Indeed, LEDEN is a pilot study that partly relies on the NH staff engagement for its set-up and implementation. NHs participating in LEDEN were geographically spread in the French territory (see Fig. 1) and will have, thus, different interventionists; therefore, NH staff needs time to identify, contact, and recruit potential interventionists, particularly for the social activity intervention.

LEDEN is a cluster RCT with NHs as the unit of randomisation. Allocation ratio for exercise or control group is 1:1. Randomisation was performed by a statistician blinded to the identity of the NHs and not involved in the recruitment of facilities and patients or in data collection. The allocation sequence was stratified by the median value of the prevalence of dementia in the NH and was performed using random permuted block sizes of two within each of the two strata using the RALLOC command of Stata (StataCorp, College Station, TX). Sequentially numbered, opaque, sealed envelopes were used to warrant concealment of group allocation until the moment group assignment was revealed to participating NHs.

### 3.7. Data collection and quality control

All data will be collected by the NH staff, except data related to the interventions that will be collected by the interventionists (for example, data on intervention compliance, participants’ engagement in the intervention, or adverse events occurring during the intervention). The data will be collected in an electronic case report form. An internet-based, web browser application will be used to manage all the data regarding

<table>
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<th>Measurements</th>
<th>Assessment timeline</th>
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<tr>
<td>Eligibility screen</td>
<td>Baseline (t0)</td>
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<td>3-Month intervention (t1)</td>
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<td>Post-intervention (t6)</td>
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<td>3-Month post-intervention (t9)</td>
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<td>6-Month post-intervention (t12)</td>
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| Dementia                                  | X                   |
| Social/health-related variables           | X                   |
| Drugs                                     | X                   |
| ADCS-ADL-sev                               | X                   |
| SPPB                                      | X                   |
| MMSE                                      | X                   |
| NPI-NH                                    | X                   |
| Algotplus                                 | X                   |
| MNA                                       | X                   |

Note. ADCS-ADL-sev, Alzheimer Disease Cooperative Study-activities of daily living-severe; MMSE, mini-mental state examination; MNA, mini-nutritional assessment; NPI-NH, neuropsychiatric inventory-nursing home; SPPB, short physical performance battery.

* The primary endpoint of this study is assessed using the ADCS-ADL-sev at t6, ie, at post-intervention.

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**Fig. 1.** Geographical distribution of nursing homes participating in the LEDEN study. Map of France with the delimitations of the French Departments. Nursing homes participating in the LEDEN study are located in the areas highlighted with a black point. This map was obtained from Pacha Cartographie at [http://www.pacha-cartographie.com/fonds-de-carte/](http://www.pacha-cartographie.com/fonds-de-carte/).
the assessment of the outcome measures. Entry into this area is password protected and encrypted; only the NH local coordinator (overall the NH coordinating physician) and his/her delegates (all of them NH staff members) have access to this area. NH local coordinators will have access only to the data regarding his/her own participants (ie, participants living in the NH where he/she is responsible for). Upon study completion, after all waves of data collection of the outcomes measures are finished and after the completion of the appropriate quality control procedures, the database is certified. The database is taken off-line and archived. The final datasets are then ready to be used; all data are stored in an anonymised format according to the current good clinical practice guidelines.

Most assessment tools are already used in clinical routine in NHs. Nevertheless, the staff of each participating NH received an in-person 2-hour training (provided by the researchers Yves Rolland and Philippe de Souto Barreto) on how to perform the assessments plus a 45-minute training (provided by the researcher Philippe de Souto Barreto) made by telephone on how to use the LEDEN website for data entry. Roughly, at least three staff members of each NH participated in the training sessions. Most of the time they were the NH coordinating physician, the referent nurse, and the psychologist, but also the NH director, physiotherapist, and ergo-therapist.

A clinical research associate appointed by the sponsor will regularly visit each study centre during the process of setting up the study, during the study depending on the frequency of inclusions, and at the end of the study. During these visits, the following aspects will be reviewed: informed consent; compliance with the study protocol and the procedures set out in it; and the quality of the data collected in the case report form: its accuracy, missing data, consistency of the data with the source documents (medical records, appointment diaries, etc.).

3.8. Statistical analysis

Data will be analysed using a modified intention-to-treat approach in which all participants with at least one postintervention assessment will be analysed. Multilevel analysis will be first performed separately on the primary outcome measure (ADCS-ADL-sev) using a three-level (with a random effect at the level of the NH and a random effect at the level of participants, ie, a model in which participants are nested within NHs) regression model adjusted for the variable used to stratify the randomisation (ie, prevalence of PWD in the NH). Analysis for the secondary outcome measures will use similar three-level regression models. Statistical significance is determined by a \( p < 0.05 \). Secondary outcomes will be adjusted for multiple comparisons using the False Discovery Rate [41], ie, the proportion of true null hypotheses rejected among the rejected. For example, in the Hochberg procedure [41], we order the observed \( p \)-values from largest to smallest; if the largest observed \( p \)-value is \( >0.05 \), then all the tests performed are significant. If not, we compare the second largest observed \( p \)-value to the next threshold of 0.05/2, ie, 0.025, and so on. Analyses will be performed using Stata (v.14.0, Texas, USA) and SAS (v. 9.3, SAS Institute Inc, Cary, NC) statistical software.

3.9. Ethics

The LEDEN study follows the principles of the Declaration of Helsinki and complies with ethics standards for research in France. The NH coordinating physician firstly obtained the signed informed consent from the next of kin and the legal representative (if appropriate) of all potentially eligible participants. Then, a member of NH medical staff informed all potentially eligible participants about the study and its objectives, and tried to collect a signed consent as appropriate (due to the very low cognitive function and communication skills of PWD in NHs, we expected that the majority of potentially eligible participants would be unable to provide a signed informed consent). Next of kin, legal representatives, and patients were informed verbally and by written that study participants may withdraw from the study at any time during the study.

The study protocol has already been approved by the Advisory Committee for the Protection of Persons participating in Biomedical Research (CPP SOOM III. Registration number: 2014-A01713-44), the Consultant Committee for the Treatment of Information in Research on Health (CCTIRS. Registration number: 15.159) and the National Agency for the Security of Drugs and Health products (ANSM. Registration number: 141502B-31). The LEDEN protocol was registered in a clinical trial registry under the following identifier: NCT02444078.

4. Discussion

The most innovative aspect of LEDEN is the operationalisation of a well-structured socially-active control group. Since developing an exercise intervention in PWD who live in NHs is more difficult to organise and comprises more health risks than doing other social/recreational activities, it is indispensable to know whether the health benefits associated with exercise outweigh its risks in this vulnerable population and whether the exercise intervention is viable in terms of cost-effectiveness.

Most RCTs of exercise for institutionalised PWD performed to date have had a short length. According to a recent review [23], only two studies had an intervention length of 6 months or over, and only one (a RCT performed by our team [40]) was rated as having a high-quality design. Short-term interventions may constitute a shortcoming because very old, institutionalised PWD with moderate to severe dementia probably needs more time to adapt to and to progress on exercise, compared with healthier older adults. Although one could argue that exercise may be associated to health risks, such as cardiovascular events, falls and fractures, the most recent and updated Cochrane review and meta-analysis about exercise for PWD stated that none of the reviewed studies reported serious adverse events attributable to the exercise intervention [11]. Moreover, although the exercise training in the LEDEN study will be designed to be challenging for participants, it will be led by professional exercise instructors with experience in exercise for PWD as well as exercise in the NH setting.

The importance of exercise for health promotion has already been demonstrated in different populations. Regarding PWD living in NHs, LEDEN will provide the preliminary evidence needed to inform the development of larger and more complex (eg, involving several countries with different health systems) interventions using exercise or non-exercise social interventions.

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Sponsor’s role

Both the sponsor and funding agencies of the LEDEN study had no role in the design of this study and will not have any role in the execution of the interventions, in the analyses and interpretation of the data, or in the decision to submit results.

Competing interests

Philippe Denormandie and Didier Armaingaud are employees of the Korian group.
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