Intelligent Medicine 2 (2022) 181–192

Contents lists available at ScienceDirect

Intelligent Medicine

journal homepage: www.elsevier.com/locate/imed

Research Article

Nutritional and physical improvements in older adults through the DOREMI remote coaching approach: a real-world study

Federico Vozzi[1,*], Filippo Palumbo[2], Erina Ferro[2], Karl Kreiner[3], Franca Giugni[1], Rachel Dutton[4], Shirley Hall[5], Daniele Musian[6], Marina Parolini[7], Patrizia Riso[8], Oberdan Parodi[9]

[1] *Institute of Clinical Physiology IFC-CNR, Via Giuseppe Moruzzi 1, Pisa, Italy*
[2] *Institute of Science and Information Technology ISTI-CNR, Via Giuseppe Moruzzi 1, Pisa, Italy*
[3] *Austrian Institute of Technology AIT, Giefinggasse 4, Wien, Austria*
[4] *Fry Accord, 178 Birmingham Road, West Bromwich, West Midlands, United Kingdom*
[5] *The ExtraCare Charitable Trust, 7 Harry Weston Road, Binley, Coventry, United Kingdom*
[6] *SI4Life Scrl, Corso Podestà 1/21-22-23, Genoa, Italy*
[7] *Institute of Clinical Physiology IFC-CNR, ASST Grande Ospedale Metropolitano Niguarda, Piazzale Ospedale Maggiore 3, Milan, Italy*
[8] *Department of Food, Environmental and Nutritional Sciences DEFENS, University of Milan, Via Luigi Mangiagalli, 25, Milan, Italy*
[9] *Fondazione Toscana Gabriele Monasterio FTGM, Via Giuseppe Moruzzi 1, Pisa, Italy*

ARTICLE INFO

Keywords:
Nutrition
Physical activity
Elderly
Healthy aging
Information and communication technologies

ABSTRACT

Background Malnutrition (excess or defect) and sedentariness act as an accelerator in the older people frailty process. A systemic solution has been developed to engage older people in a healthier lifestyle using serious games and food monitoring. The study aimed to evaluate protocol influence on variables related to unhealthy behaviors improving dietary habits through a remote nutritional coaching approach and stimulating the population to increase physical activity through Exergames.

Methods Thirty-two subjects (25 Treatments and 7 Controls, aging 65–80 years), of which 15 (11 Treatments and 4 Controls) living in the UK (ACCORD and ExtraCare Villages placed in Shenley Wood (Milton Keynes), St. Crispin (Northampton), and Showell Court (Wolverhampton)) and 17 (14 Treatments and 3 Controls) in Italy (Genoa, Liguria), were recruited and characterized in terms of nutritional status, physical, somatometric, hemodynamic and biochemical measurements, and body composition. Participants were stimulated to adopt the Mediterranean dietary pattern, by a food diary diet-app, and perform regular physical activity, by the Exergame app, for three months. At the end of the trial, users underwent the same test battery. Data were tested for normality of distribution by the Shapiro-Wilk test. Comparisons between groups were performed at baseline by unpaired Student's *t*-test for continuous variables, chi-square test, or Fisher's exact test for categorical variables. Analysis of Variance (ANOVA) for repeated measures was used to analyze the significance of changes over time between groups.

Results At the end of the trial, significant reductions of systolic (15 mmHg, $P = 0.001$), diastolic (5 mmHg, $P = 0.025$), mean (10 mmHg, $P = 0.001$) blood pressure, and rate-pressure product (RPP) (1,105 mmHg*bpm, $P = 0.017$) values were observed in DOREMI users. A trend of improvement of physical performance by the short physical performance battery (SPPB) was observed for balance and walk subtests. A significant decrease (0.91 kg, $P = 0.043$) in Body Mass Index (BMI) was observed in overweight subjects (BMI >25 kg/m^2) after DOREMI intervention in the entire population. The Mini Nutritional Assessment (MNA) score (1, $P = 0.004$) significantly increased after intervention, while waist measure (3 cm, $P < 0.001$) significantly decreased in the DOREMI users. A reduction in glycated hemoglobin (Hb) was registered (0.20%, $P = 0.018$) in the DOREMI UK users.

Conclusions Improvement of healthy behavior by technological tools, providing feedback between user and remote coach and increasing user's motivation, appears potentially effective. This information and communication technologies (ICT) approach offers an innovative solution to stimulate healthy eating and lifestyle behaviors, supporting clinicians in patient management.

* Corresponding author: Federico Vozzi, Institute of Clinical Physiology IFC-CNR, Via Giuseppe Moruzzi 1, Pisa, Italy (Email: vozzi@ifc.cnr.it).

https://doi.org/10.1016/j.imed.2022.04.001
Received 21 June 2021; Received in revised form 17 February 2022; Accepted 1 April 2022

1. Introduction

All countries in Europe are experiencing an aging of their populations, with a decrease in the number of working-age people per retiree. By 2050, an estimated 35% of the European population will be over 60, compared to 20% in 2005, especially among those above 80 years [1]. A direct consequence of this trend is the increase in care costs in the long-term at the increase of population aging: this trend could be counteracted if specific measures are implemented in these years [2]. A fundamental role in the preservation of a healthy state is represented by the promotion of an active lifestyle in older people, focusing on physical activity, balanced nutrition and cognitive exercise: this approach, aging on well-being, can reduce frailty and postpone the natural psychological decline in older people [3–5].

Prospects for healthy aging are characterized at first by "proper nutrition"; to improve the quality of dietary habits evidence-based strategies have been proposed, through appropriate protocols that consider needs linked to specific cultures, environmental and lifestyle habits [6–7]. This approach must be considered not only in promoting a daily food-based guideline but also in empowering knowledge on components of foods, about which little is known. A correct understanding of food components, rather than prescriptions of multivitamin and mineral supplementation, can lower major health diseases affecting older people, either in primary or secondary prevention [6,8].

Furthermore, regular exercise can provide benefits to older people from fighting sedentariness.

Research and trials provide specific recommendations on living an active daily life, physically correct, including exercises that empower endurance and flexibility, strengthen muscles, and improve balance [9–10]. These long-term recommendations prevent all typically age-associated diseases, including hypertension, cardiovascular diseases, diabetes (NIDDM), mainly if joined to healthy nutrition.

Increasing interest in problems regarding sedentariness and malnutrition as risk factors for chronic diseases has been seen, and the two impairments are strictly linked to cognitive decline [3,11]. Unhealthy dietary and sedentary habits influence cognitive decline, which has a relevant impact on the independence and the autonomy of older people, playing a primary role in the further progressive removal of a well-balanced diet and regular physical activity. On the other side, cognitive impairment in non-supported /assisted subjects can favor the sedentariness and/or malnutrition creating a vicious loop with a self-sustained condition. Measures and lifestyle protocols that synergistically act against these three impairments can prevent or delay a systemic deterioration of health and quality of life, restoring the previously lost well-being [3]. Lifestyle interventions addressing the three impairments may become effective therapies in elderly people, leading to increase participation and engagement in everyday life, with the vision of reducing contemporary physical, nutritional and cognitive decline [12]. To prevent frailty older people, a quite continuous assistance is mandatory, although this approach require specialized personnel not even available. A potential solution can be the remote control offered by Information and Communication Technologies (ICT) systems and apps, which were developed in the last years. Still, these were mainly focused on Ambient Assisted Living (AAL) and remote real-time telemonitoring [13–17] or for a general audience used to new technologies and self-monitoring (RunKeeper®, Vivago®, LoseIt®).

The DOREMI project aimed at developing a systemic solution for healthy aging able to prolong the functional and cognitive capacity of the older people by empowering, stimulating and unobtrusively monitoring the daily activities according to "DOREMI Active Ageing" lifestyle protocols trough the support of a remote coaching [18]. The integrated control of psychologically related socio-physical disabilities, vital signs combined with nutritional behavior, physical activity and social interaction may represent a preventive approach towards the further deterioration of the cognitive decline and onset of new clinical manifestations [18]. This work aims to present the impact of DOREMI protocols, based on ICT remote empowerments and solutions, as an effective interventional method related to healthy aging contrasting unhealthy dietary and physical habits in a selected target of the older people population. In particular, the study presents the results of the DOREMI experimentation involving older people, located in the UK and Italy, which were supported for three months by the DOREMI system in pursuing a healthy lifestyle in terms of physical activity and dietary habits. Before and after the experimental protocol a set of tests, clinical, physical and biological parameters were collected and analyzed.

2. Methods

2.1. Ethics approval and informed consent

This study was conducted according to the guidelines laid down in the Declaration of Helsinki. All procedures involving research study participants were approved by the Faculty Research Ethics Committee of De Montfort University and by Comitato Etico Centrale IRCCS Regione Lombardia (section IRCSS Fondazione Don Carlo Gnocchi). Written informed consent was obtained from all subjects/patients.

2.2. Users' selection and study design

DOREMI trial was performed in the UK and Italy. A preliminary screening assessment was conducted to establish the essential inclusion and exclusion (Table 1) criteria relevant for the evaluation of the DOREMI system.

After this first screening, a preliminary group of individuals that potentially have the requirements for participating in the validation process was identified.

However, as the first step to achieve the final group of participants, people with mild to moderate cognitive impairment were selected on the basis of cognitive ability through administration of the Montreal Cognitive Assessment (MoCA) test [19]. MoCA is a short, validated test designed to detect mild to moderate cognitive impairment. The MoCA can provide a global cognitive function score and was used to identify individuals with an estimate of mild cognitive impairment, as indicated by a score of 19–26.

The second step of DOREMI population selection was based on the identification of nutritional and/or physical impairment through the support of Mini Nutritional Assessment (MNA) and Physical Activity Scale for the Elderly (PASE) tests, respectively. As a matter of fact, according to the patient's selection study protocol, at least one of the following two points relating to sedentariness and nutrition was fulfilled:

- Nutritional screening and assessment. The MNA® test was used to identify malnourished users or at risk of malnutrition [20]. The cut-off for malnutrition was an MNA score between 17 and 23.5 points.
- Physical Activity assessment. The PASE [21–22] is a brief instrument for assessing physical activity. The cut-off for sedentariness was a score lower than 105 points.

Furthermore, to better characterize the DOREMI population and support the selection process, a third step was based on:

- Degree of Balance assessment. The Berg Balance Scale (BBS) [23] aims at measuring the degree of balance of an older person by assessing the performance of functional tasks. A score of 56 indicates functional balance. A score of < 45 indicates individuals may be at greater risk of falling.
- Medical evaluation. This aims to prevent the selection of individuals whose clinical conditions could hinder the effectiveness of the treatment activity and/or produce side effects that could affect the data collected during the trial activity.

In total, 32 subjects (25 Treatments and 7 Controls), of which 15 (11 Treatments and 4 Controls) in the United Kingdom and 17 in Italy (14 Treatments and 3 Controls), were recruited.

Table 1 DOREMI inclusion and exclusion criteria

Inclusion criteria
1. Age between 65 and 80 years
2. Balanced rate of male and female based on the average population composition of the selected countries (UK: 44% male; 56% female; Italy: 42% male; 58% female; EU28: 41% male, 59% female)
3. Living alone in the identified residential retirement communities/apartments
4. Possessing basic computer skills (using computers and the internet at least occasionally, any experience of having used a touchscreen device)
5. Opportunity to actively choose their diet
Exclusion criteria
1. Advanced cancer (people with cancer in clinical remission or stability can be included)
2. Dementia
3. Speech, hearing and vision problems which may interfere with DOREMI intervention activities
4. Severe neurological disorders (including, but not limited to epilepsy, multiple sclerosis, Parkinson disease, Alzheimer disease, previous major stroke)
5. History of severe head injury
6. History of substance abuse or alcohol abuse in the previous 5 years
7. Moderate to severe aortic stenosis
8. Hypertrophic cardiomyopathy
9. Advanced heart failure (NYHA III/IV) based on the New York Heart Association Functional Classification score (The Criteria Committee of the New York Heart Association, 1994)
10. Patient with an implantable cardioverter-defibrillator (ICD) or implanted cardiac resynchronization device (CRT-D)
11. Severe chronic renal failure (Glomerular filtration rate between 15 and 29 ml/min)
12. Severe hepatic failure (Child's Classes B and C)
13. Chronic obstructive pulmonary disease
14. Uncompensated diabetes mellitus (HbA1c > 8.5%)
15. Chronic hematologic disorders
16. Peripheral arteriopathy (Leriche-Fontaine Class III and IV)
17. Severe disabilities due to osteoarticular pathologies

2.3. Informed consent and randomization

The selected subjects were requested to sign the Informed Consent approved by the UK and IT Ethical Committee. The work described has been carried out by The Declaration of Helsinki for experiments involving humans. The stratified randomization method was adopted to balance the allocation to intervention or control groups in two strata (male/female) and two conditions (intervention/control) to prevent an unbalanced selection by gender. The allocation has been set to account for about a 3:1 ratio of intervention and control participants. The individuals of the two strata have been randomly assigned to the two groups with a sealed envelope method with an individual random assignment performed by a computer random-number generator.

2.4. System architecture, apartment requirements, equipment installation

To monitor subjects' conditions and provide serious games supporting the DOREMI lifestyle, the subjects were equipped with technological kits, including wearable and environmental sensors and devices installed in the subjects' apartments (Supplementary material).

The data produced by the sensors and from the games is thus collected in the remote server, stored and processed.

The analysis of the data from the sensors happens offline (at midnight every day) and proceeds through three phases: data pre-processing, activity recognition (based on machine learning models), and reasoning (based on decision trees). The activity recognition phase produces high-level information (for example, it produces the Berg-scale assessment of the subject balance [24] or the calorie expenditure from the heartbeat data) that can be given in input to the reasoning stage. In turn, the reasoner takes in input all the refined sensor data plus the data on the use of the exergames and on the performance achieved at the cognitive games to verify the adherence of the user with the protocol and to assess the subject's progress in the games and the physical conditions. The results of the reasoner are in turn, stored in a database in the server and provided to the specialists through a web-based dashboard. Furthermore, the reasoning results also provide feedback to the games, to increase the level of difficulty of the cognitive games and increase the intensity of the exergames.

A detailed description of the technological kits and the DOREMI architecture can be found [25], and the analysis of its reliability and its acceptance by the users is presented [26].

2.5. Baseline data collection

2.5.1. Physical activity

In addition to the PASE and BBS tests performed, the following evaluation was conducted:

- Six Minute Walking Test (6MWT). The 6MWT is helpful to assess aerobic functionality and effectiveness of interventions on lifestyles [20].
- Hemodynamic parameters: analysis of blood pressure, heart rate and Rate Pressure Product (RPP), before and after 6MWT, were collected to obtain information about the ability of the subjects to perform daily living activities.
- Physical activity capabilities through Short Performance Physical Battery (SPPB) administration, composed by a set of gait speed, chair stand, and balance tests [27]. This test can be predictive for possible disability and help to monitor older people.

2.5.2. Nutritional status and dietary habits

Besides the MNA test to evaluate nutritional status, both treated and control groups underwent to the following evaluations:

- Interview on: number of meals, daily fluid intake, quality of food intake, cooking methods and capacity of making healthy dietary choices; in addition, a 24 h dietary recall was registered with the support of a nutritionist and transferred to the METADIETA® app for the definition of correcting measures and development of personalized plans (see dedicated paragraph)
- Somatometric parameters: weight, height, measures of fat and muscle area of the arm circumference, fat and muscle area of the thigh, circumference of the waist and hip and their ratio
- Blood and urine tests: white and red blood cells count, glycemia, HGT, total cholesterol, HDL, LDL, triglyceride levels, target vitamins, and minerals
- Body composition analysis using Bioelectrical Impedance Vector Analysis BIVA® (Akern S.r.l., Pontassieve, Italy), collecting data on:

Phase Angle (PA), Resistance (Rz), Reactance (Xc), Total Body Water (TBW), Extra Cellular Water (ECW), Intra Cellular Water (ICW), Fat-Free Mass (FFM), Body Cell Mass (BCM), Fat Mass (FM), Muscle Mass (MM), Basal Metabolic Rate (BMR)

2.6. Training

The training implementation was carried out in the two pilot sites in the UK and Italy, sharing the same learning methodologies, modules and materials.

2.6.1. Hardware training

This session included a description of the DOREMI system (how it works, how to use it, how to charge devices), composed of accessible and user-friendly language. The contents included: DOREMI box/operations center, wristband, smartphone, balance board and tablet

2.6.2. General information on healthy active lifestyles

All participants received information on Nutrition and Physical Activity for a healthy, active lifestyle. In particular, for nutritional aspects, the knowledge/material provided to volunteers included: information on the Mediterranean diet, impact on physical health, suggestions for healthy diet adapted to older adults, essential elements of nutrition, personalized nutrition plan (for the intervention group only), nutrition glossary. The material proposed was designed with a user-friendly approach, describing the benefit of the Mediterranean diet, tips to adopt a Mediterranean lifestyle, guidelines with dietary recommendations for healthy eating in the over 65 (based on NU-AGE European project Guidelines), concepts used in nutrition (supported by a glossary), explanation of DOREMI ICT solution for the recording of food intake and the use of dietary advices and, finally, information about training and treatment activities.

Regarding physical activity, this section included the following items: benefits of physical activity, activities to be performed, global recommendations from WHO, the physical activity pyramid, the physical activity impact on health. Specific guidelines for physical activity were prepared to support a healthy and active lifestyle in DOREMI users. Material proposed a user-friendly approach, described benefits of physical activity, illustrated Global Recommendations on Physical Activity for Health [28], defined concepts used in physical activity, showed how to perform indoor and outdoor PA protocol by use of simple text and images.

2.6.3. Gamified environment

This session included the following contents: Game environment (How to start; Settings; Statistics; 10 European Cities); Physical activity training (DOREMI protocol, Indoor activities, DOREMI exergames, practice with the exercises, outdoor activities, the walking health program, guidelines for outdoor physical activities, physical activity monitoring tables, glossary). During the session, tablets were distributed to participants to experiment with the DOREMI game environment. At the end of the session, all the subjects received the DOREMI user manual related to the DOREMI game environment.

The subjects in the control group received only written instruction on general physical activity routine appropriate for the older subjects without any personalization. The DOREMI group was also instructed to follow instructions of the Exergames app with a personalized activity plan.

2.6.4. METADIETA® training

A specialist trained participants to use the METADIETA® module, providing volunteers with simple instructions and training them on using the smart touch photo diary. During the training, the user learned how to: choose the referral meals; visualize foods' categories; choose foods' groups; visualize foods in three different portions each; and choose a photo with the selected amount of food. The METADIETA® manual was prepared and distributed to participants: this described with a friendly approach, the use of the app, how to interact with it and send data to the specialists. Volunteers were asked to send their food diaries at least three times per week in the treatment period.

Through the system, the Nutritionists received feedback on: 1) the ability to use the tool (i.e., adequate insertion of daily food intake) and 2) the actual utilization (i.e., frequency of use).

2.6.5. Development of personalized dietary plans

During the last five days of the training phase, based on the dietary data received through the METADIETA® app, Nutritionists defined for each user a personalized nutritional plan adapted to take into consideration anthropometric characteristics, general physical condition, specific nutritional requirements and, when possible, individual eating pattern and food preference. The personalized intervention was distributed to each subject of the intervention group. The personalized dietary plan was available for the subjects in the METADIETA® software. The subjects in the control group received only general written instruction on the Mediterranean-based dietary pattern appropriate for the older subjects without any personalization. They were also instructed to send their food intake records through the METADIETA® app.

2.7. Intervention

2.7.1. Physical activity

Participants registered their weight and balance using the balance board. At least 3 times/week, the participants consulted the gamified environment to receive their exercise suggestions by the DOREMI exergame, together with feedback and recommendations based on the previous day's activity. Participants selected a physical activity from a set of videos pre-selected by the system by the characteristics of their personalized plan.

The DOREMI wristband registered the movements of the participants. The system registered outdoor physical activities through the wristband and Smartphone. The following information was collected:

- The balance board noted weight and balance.
- The wristband registered the number of steps, heart rate, exercise intensity.
- The step counter and the GPS in the mobile phone sensor registered outdoor covered distance.
- The data were transmitted to the server and several parameters (caloric consumption, max-min-average heart rate, balance level and steps/covered distance) were calculated.

The medical DOREMI team had access to the data of each participant to check the achieved progress. This also checked the suggestions provided by the system about the physical activity protocols for the following weeks and related recommendations pre-selected by the system. It could accept, refuse or modify the proposal of the system (this ensured that a technical error does not cause participants to be given unsuitable exercise guidelines). The system registered the final choice and prepared the new physical activity protocol.

2.7.2. Monitoring of dietary behavior

Monitoring of food intake and delivery of personal dietary plans have been conducted remotely by the nutritionists. The participants had to register their food intake three times each week by selecting appropriate items from the database within the METADIETA® software. They indicated the size of the portion they had consumed using the simple interface. Once they selected the foods, data were transferred to the DOREMI server by sync system.

The DOREMI system registered the bodyweight of participants to calculate BMI and used the accelerometer data and heart rate of the wristbands of participants to calculate the mean energy expenditure. The recorded logs were sent to METADIETA® to produce the following information per each participant: the number of meals per day; consumption of fruit and vegetables; energy intake; nutrient composition of the diet (fat, protein, fiber, etc.); suggestions and recommendations

depending on individual food intake registered and revised personal dietary plan if needed.

The Nutritionists who acted premises remotely to access participant data to check the progress achieved by each participant about eating behavior; access the suggestions and recommendations automatically provided by the system about the personal dietary plan for the following days; accept, refuse or directly modify the suggestions and recommendation proposed by the system about the personal dietary plan; provide nutritional coaching on demand to participants (the nutritionist was available by telephone, email, Skype, via the METADIETA® software).

2.8. Final evaluation

The post-intervention assessment was conducted in the last five days of the DOREMI trial, administering the same tests used for the sample selection and the baseline assessment phases. During the trial, one UK participant decided to stop with the intervention.

2.9. Statistical analysis and dataset

Continuous variables are presented as mean ± standard deviation or median (25th; 75th percentile), and categorical variables are as frequencies (percentages). Data were first tested for normality of distribution by the Shapiro-Wilk test; logarithmic conversion was performed for non-normally distributed variables.

Comparisons between groups were performed at baseline by unpaired Student's *t*-test for continuous variables, chi-square test or Fisher's exact test for categorical variables.

Analysis of Variance (ANOVA) for repeated measures was used to analyze the significance of changes over time between groups. There was one within-subjects' factor, i.e., Time, with two levels (basal and follow-up), one between-subjects factor, i.e., Group with two levels (cases and controls) and one Within-Between interaction factor, i.e. time*group interaction. A two-tailed $P < 0.05$ was considered to be statistically significant. Statistical analysis was performed using SPSS for Windows, release 17.0 (SPSS, Chicago, IL). The DOREMI dataset is available on Zenodo (10.5281/zenodo.6024747)

3. Results

3.1. Physical activity: total population

Significant results for physical activity in the entire population were observed for hemodynamic parameters pre- and post-6MWT and BERG score (Table 2).

For 6MWT, the values for Systolic (pre-, $P = 0.001$; post-, $P = 0.021$), Diastolic (pre-, $P = 0.025$; post-, $P = 0.004$) and Mean (pre-, $P = 0.001$; post-, $P = 0.001$) blood pressure and RPP (pre-, $P = 0.017$; post-, $P = 0.016$) showed a significant and considerable reduction in the two groups at the end of trial, often more marked in DOREMI users. The analysis pointed out a significant increase in its value in the two populations ($P = 0.006$) for the BERG score at the end of the trial. For SPPB, data aggregation highlighted an increasing trend for Balance and Walk subtests ($P = 0.083$ and $P = 0.090$, respectively).

3.2. Physical activity: UK trial

SPPB total score showed a significant increase in both control and DOREMI users ($P = 0.036$), also highlighting a trend to significant values both in gate speed ($P = 0.055$) and in chair stand ($P = 0.081$) subtests (Table 3).

Significant results were observed for parameters collected during 6MWT. In particular, the analysis showed:

- A significant increase ($P = 0.014$) of covered meters in DOREMI Users (+33 m) and Controls (+42 m).

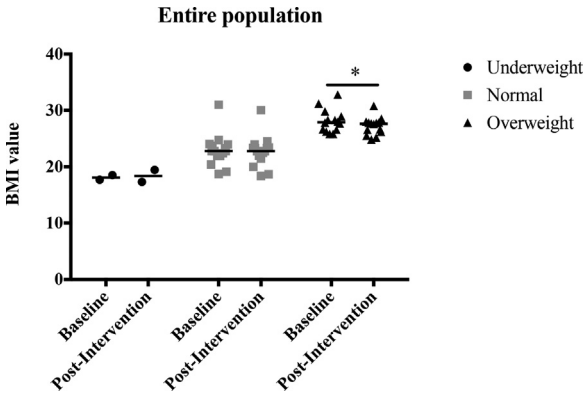

Figure 1. Clusterization of subjects using BMI value (kg/m^2). $P = 0.043$. Modulation of BMI entire population (control and DOREMI users) at baseline and post-intervention.

- A significant reduction of baseline Systolic Blood Pressure ($P = 0.001$);
- A significant reduction of Mean Blood Pressure values in the two groups after two months of trial (*P* values of 0.007 and 0.028, respectively)
- A significant reduction of Rate Pressure Product in the two groups (*P* values of 0.003 and 0.011, respectively)

An interesting result was observed for the BERG test, with a significant increase of its value in the two populations ($P = 0.011$) at the end of the trial, particularly for the marked increase of score in the Control group (+5 points respect to baseline).

3.3. Physical activity: Italy trial

Italian trial results, for physical activity, are fairly superimposable with those of the UK. SPPB test showed a significant increase of DOREMI Users score respect to Control ($P = 0.027$) at the end of the trial (Table 4).

Significant results were observed for hemodynamic parameters collected during 6MWT. Statistical analysis showed, in particular, a significant reduction, in Control and DOREMI Users of Systolic Blood Pressure ($P = 0.027$) (decrease of 8 and 7 mmHg, respectively), Diastolic Blood Pressure ($P = 0.025$) and Mean Blood Pressure in the 2 groups after 2 months of trial, (*P* values of 0.019 and 0.014, respectively); a significant increase of baseline Heart Rate in the two groups, at the end of the trial, ($P = 0.049$), likely caused by baroreflex modulation consequent to the decrease of systemic blood pressure.

3.4. Nutritional status and somatometric parameters: total population

Analysis of the entire DOREMI population showed a modulation in MNA tests and somatometric assessment parameters (Table 2).

The post-intervention MNA test showed an increase of score in both groups (control and treatment) in a significant manner ($P = 0.003$), with a 1-point average increase in DOREMI users. Data analysis of somatometric parameters highlighted a significant decrease of BMI (baseline 25 kg/m^2 (22 kg/m^2;28 kg/m^2), Post-Intervention 24 (22 kg/m^2;28 kg/m^2), $P = 0.026$) in the entire population.

Furthermore, clustering subjects for BMI values - underweight (<18.5 kg/m^2), normal (18.5–24.9 kg/m^2), overweight (>25.0 kg/m^2) - a significant decrease ($P = 0.043$) in the overweight groups was observed (Figure 1).

Further analysis showed a trend towards a decrease ($P = 0.062$) for overweight DOREMI-treated users (Figure 2). Although trial duration was short, this modulation of BMI value could be related to small changes in dietary habits during the trial, as reported below.

Table 2 Statistical analysis of DOREMI entire population (UK & Itay) trial data (median (IQR))

Parameters	Baseline		Follow-up		*P* values for time	*P* values for time*group interaction	*P* values for group
	Controls	Cases	Controls	Cases			
Metabolic parameters	*n* = 7	*n* = 24	*n* = 7	*n* = 24			
BMI (kg/m^2)	26 (22; 28)	24 (22; 28)	27 (22; 28)	24 (23; 27)	0.023	0.419	0.319
Weight (kg)	72 (59; 73)	65 (55; 76)	73 (59; 74)	65 (55; 74)	0.053	0.459	0.355
Circumference waist (cm)	96 (92; 106)	93 (84; 96)	96 (86; 102)	90 (78; 95)	<0.001	0.343	0.071
Circumference hip (cm)	108 (98; 110)	105 (95; 114)	104 (98; 108)	104 (95; 112)	0.007	0.234	0.907
Waist-to-hip ratio	0.90 (0.87; 0.99)	0.85 (0.82; 0.89)	0.88 (0.88; 0.99)	0.85 (0.82; 0.88)	0.137	0.880	0.006
Phase angle	4.55 (4.18; 4.83)	4.50 (4.18; 4.93)	4.60 (4.28; 4.95)	4.70 (4.08; 5.15)	0.279	0.866	0.896
Resistance (Ω)	556 (507; 589)	625 (568; 678)	539 (485; 556)	609 (563; 683)	0.165	0.299	0.027
Reactance (Ω)	45 (42; 46)	48 (44; 54)	42 (40; 46)	50 (41; 57)	0.780	0.340	0.090
Total body water (L)	34 (31; 39)	32 (28; 36)	35 (32; 40)	31 (28; 35)	0.992	0.202	0.149
Extra cellular water (%)	53 (52; 55)	54 (52; 56)	54 (52; 55)	53 (50; 57)	0.508	0.741	0.837
Intra cellular water (%)	47 (45; 48)	46 (44; 49)	46 (45; 48)	47 (43; 50)	0.515	0.732	0.833
Fat free mass (kg)	33 (27; 49)	36 (26; 43)	36 (28; 47)	35 (27; 42)	0.445	0.214	0.630
Body cell mass (kg)	14 (13; 22)	17 (12; 20)	17 (13; 22)	18 (12; 20)	0.196	0.614	0.704
Fat mass (kg)	14 (12; 16)	18 (11; 22)	15 (12; 28)	18 (11; 22)	0.408	0.902	0.978
Muscle mass (kg)	27 (25; 30)	24 (22; 26)	27 (25; 31)	25 (23; 26)	0.649	0.557	0.134
Basal metabolic rate (kcal)	1,379 (1,312; 1,419)	1,298 (1,255; 1,350)	1,371 (1,317; 1,450)	1,307 (1,281; 1,355)	0.614	0.635	0.144
Blood analysis	*n* = 6	*n* = 15	*n* = 6	*n* = 15			
Glucose (mg/dl)	90 (84; 97)	81 (77; 85)	86 (80; 108)	87 (83; 107)	0.164	0.443	0.682
Hb glycate (%)	5.9 (5.3; 6.6)	5.7 (5.6; 6.3)	5.6 (5.2; 6.3)	5.6 (5.4; 6.2)	0.064	0.214	0.738
Total cholesterol (mg/dl)	220 (180; 233)	193 (166; 211)	213 (171; 240)	193 (155; 206)	0.580	0.684	0.285
HDL cholesterol (mg/dl)	73 (56; 75)	66 (58; 85)	64 (58; 75)	62 (58; 81)	0.368	0.635	0.813
LDL cholesterol (mg/dl)	118 (73; 140)	91 (71; 136)	118 (76; 158)	81 (66; 122)	0.793	0.202	0.348
Triglycerides (mg/dl)	108 (77; 163)	87 (69; 124)	106 (91; 163)	97 (83; 117)	0.489	0.843	0.304
Creatinine (mg/dl)	0.78 (0.70; 0.80)	0.86 (0.68; 0.97)	0.80 (0.66; 0.81)	0.80 (0.71; 0.99)	0.619	0.950	0.233
WBC (× 10^3/ul)	6.05 (5.05; 7.28)	6.00 (5.38; 7.65)	5.55 (4.55; 6.58)	6.10 (4.63; 7.23)	0.127	0.669	0.657
RBC (× 10^6/ul)	4.63 (4.34; 4.90)	4.45 (4.07; 4.72)	4.65 (4.18; 4.95)	4.58 (3.99; 4.81)	0.892	0.658	0.407
Hemoglobin (g/dl)	13.7 (12.9; 14.3)	12.8 (12.3; 13.5)	14.1 (12.3; 14.5)	13.3 (11.6; 14.2)	0.142	0.524	0.350
Hematocrit (%)	43 (39; 44)	40 (38; 42)	43 (37; 45)	40 (36; 43)	0.667	0.973	0.331
MCV (fl)	90 (87; 95)	93 (88; 95)	91 (86; 96)	91 (88; 95)	0.611	0.249	0.892
MCH (pg)	30 (28; 30)	30 (28; 30)	30 (29; 31)	31 (29; 31)	0.046	0.813	0.924
Platelets (× 10^3/ul)	256 (241; 270)	268 (192; 310)	251 (183; 283)	269 (221; 327)	0.450	0.273	0.555
Neutrophil (× 10^3/ul)	3.32 (3.01; 4.99)	3.69(2.68; 4.19)	2.80 (2.33; 4.38)	3.28 (2.40; 4.23)	0.198	0.521	0.925
Lymphocytes (× 10^3/ul)	1.91 (1.63; 2.17)	1.86 (1.51; 2.40)	1.88 (1.52; 2.15)	1.85 (1.49; 2.58)	0.480	0.771	0.556
Monocytes (× 10^3/ul)	0.41 (0.39; 0.49)	0.40 (0.32; 0.48)	0.36 (0.31; 0.40)	0.40 (0.25; 0.42)	0.013	0.300	0.996
Eosinophil (× 10^3/ul)	0.18 (0.09; 0.26)	0.20 (0.15; 0.28)	0.15 (0.08; 0.28)	0.19 (0.16; 0.26)	0.707	0.590	0.355
Basophil (× 10^3/ul)	0.03 (0.02; 0.05)	0.04 (003; 0.08)	0.03 (0.03; 0.05)	0.04 (0.02; 0.05)	0.305	0.305	0.424
Urine analysis	*n* = 3	*n* = 15	*n* = 3	*n* = 15			
pH	6.0 (5.0; 7.5)	6.0 (5.5; 6.0)	5.0 (5.0; 7.5)	6.0 (5.0; 6.5)	0.672	0.606	0.725
Specific gravity	1,020 (1,010; 1,030)	1,024 (1,014; 1,030)	1,010 (1,010; 1,030)	1,015 (1,010; 1,020)	0.156	0.693	0.994
Six minutes walking test (6MWT)	*n* = 7	*n* = 22	*n* = 7	*n* = 22			
Systolic blood pressure pre 6MWT (mmHg)	150 (130; 158)	143 (139; 160)	140 (125; 150)	128 (120; 131)	0.001	0.507	0.333
Systolic blood pressure post 6MWT (mmHg)	165 (145; 182)	160 (153; 173)	165 (136; 170)	150 (138; 155)	0.021	0.543	0.428
Diastolic blood pressure pre 6MWT (mmHg)	85 (75; 87)	80 (75; 85)	80 (70; 80)	75 (70; 80)	0.025	0.966	0.773
Diastolic blood pressure post 6MWT (mmHg)	85 (72; 103)	90 (83; 98)	80 (67; 90)	85 (78; 90)	0.004	0.706	0.432
Mean blood pressure pre 6MWT (mmHg)	103 (97; 111)	103 (96; 109)	100 (93; 102)	93 (89; 95)	0.001	0.671	0.525
Mean blood pressure post 6MWT (mmHg)	111 (101; 128)	113 (108; 123)	107 (97; 112)	105 (97; 110)	0.001	0.870	0.859
Heart rate pre 6MWT (bpm)	58 (53; 73)	69 (63; 73)	58 (57; 68)	69 (64; 74)	0.925	0.493	0.046
Heart rate post 6MWT (bpm)	83 (68; 100)	90 (81; 101)	83 (70; 94)	86 (80; 92)	0.291	0.462	0.230
RPP pre 6MWT (mmHg*bpm)	8,580 (7,800; 11,571)	9,975 (8,517; 11,795)	8,120 (6,270; 9,610)	8,870 (7,739; 9,908)	0.017	0.710	0.320
RPP post 6MWT (mmHg*bpm)	13,836 (11,455; 16,070)	14,976 (12,620; 16,833)	13,270 (11,149; 14,910)	12,800 (11,035; 14,330)	0.016	0.279	0.648
Blood oxygen saturation pre 6MWT (%)	98 (97; 98)	98 (97; 98)	98 (95; 99)	98 (96; 98)	0.472	0.472	0.504
Blood oxygen saturation post 6MWT (%)	97 (95; 97)	97 (96; 98)	96 (94; 97)	97 (96; 98)	0.818	0.436	0.119
Δ post-pre 6MWT systolic blood pressure (mmHg)	9.50 (0.25; 19.50)	14.00 (−0.50; 22.50)	22.50 (10.00; 33.75)	20.00 (12.50; 25.00)	0.038	0.449	0.843
Δ post-pre 6MWT diastolic blood pressure (mmHg)	5.00 (−4.00; 13.75)	11.00 (3.50; 15.00)	5.00 (−3.50; 10.00)	10.00 (0.00; 15.00)	0.317	0.783	0.238
Δ post-pre 6MWT mean blood pressure (mmHg)	5.00 (0.17; 18.08)	13.00 (2.00; 19.50)	8.33 (5.17; 14.17)	13.33 (7.67; 16.67)	0.533	0.801	0.324
Δ post-pre 6MWT heart rate (bpm)	23 (16; 29)	24 (15; 31)	23 (12; 30)	16 (14; 22)	0.187	0.252	0.727
Δ post-pre 6MWT RPP (mmHg*bpm)	4,091 (3,164; 5,289)	5,526 (3,859; 5,919)	4,685 (3,221; 6,404)	3,820 (3,200; 4,645)	0.797	0.183	0.855
Δ post-pre 6MWT blood oxygen saturation (%)	−0.50 (−3.25; 1.50)	0.00 (−1.00; 0.00)	−2.00 (−4.50; 1.25)	0.00 (−2.00; 0.00)	0.652	0.184	0.467
Covered meters after 6MWT (m)	479 (286; 506)	490 (382; 520)	490 (338; 524)	450 (405; 490)	0.157	0.195	0.717
Short physical performance battery (SPPB)							
Balance	4 (3; 4)	4 (4; 4)	4 (4; 4)	4 (4; 4)	0.083	0.935	0.436
Walk	3 (2; 4)	4 (3; 4)	3 (3; 4)	4 (4; 4)	0.090	0.531	0.244
Chair stand	2 (2; 3)	3 (2; 4)	2 (2; 3)	3 (3; 4)	0.694	0.350	0.167
SPPB total score	9 (7; 11)	11 (9; 12)	9 (9; 11)	11 (9; 12)	0.139	0.433	0.484
Screening tests							
MNA total score	27 (22; 28)	26 (25; 27)	27 (26; 29)	27 (26; 28)	0.004	0.370	0.837
PASE total score	62 (19; 97)	25 (20; 70)	61 (19; 97)	23 (19; 81)	0.243	0.897	0.559
Berg total score	49 (47; 52)	53 (50; 55)	52 (47; 56)	53 (50; 55)	0.006	0.006	0.141

BMI: body mass index; WBC: white blood cells; RBC: red blood cells; MCV: mean cell volume; MCH: mean cell hemoglobin; RPP: rate pressure product; MNA: mini nutritional assessment; PASE: physical activity scale for the elderly.

Table 3 Statistical analysis of UK trial data (median (IQR))

Parameters	Baseline		Follow-up		*P* values for time	*P* values for time*group interaction	*P* values for group
	Controls ($n = 4$)	Cases ($n = 10$)	Controls ($n = 4$)	Cases ($n = 10$)			
Metabolic Parameters							
BMI (kg/m^2)	27 (23; 28)	24 (23; 28)	27 (22; 28)	24 (23; 28)	0.074	0.512	0.622
Weight (kg)	68 (59; 73)	68 (59; 72)	67 (57; 73)	67 (58; 75)	0.096	0.447	0.974
Height (cm)	162 (157; 162)	165 (159; 166)	162 (157; 162)	165 (15; 166)	0.119	0.404	0.254
Fat muscle arm circumference (m^2)	30 (27; 31)	31 (30; 32)	29 (26; 30)	31 (30; 31)	0.025	0.625	0.284
Fat muscle thigh (m^2)	55 (45; 59)	56 (52; 57)	56 (46; 57)	54 (52; 55)	0.210	0.122	0.696
Circumference waist (cm)	96 (91; 104)	95 (90; 97)	91 (85; 101)	91 (87; 97)	0.001	0.295	0.722
Circumference hip (cm)	109 (104; 116)	108 (103; 117)	106 (97; 109)	107 (100; 113)	0.001	0.193	0.935
Waist-to-hip ratio	0.88 (0.87; 0.90)	0.82 (0.82; 0.89)	0.88 (0.84; 0.93)	0.86 (0.84; 0.88)	0.832	0.751	0.509
Phase angle	4.30 (3.80; 4.70)	4.15 (3.88; 4.70)	4.40 (3.90; 4.48)	4.05 (3.65; 4.58)	0.518	0.518	0.772
Resistance ohms	573 (519; 625)	626 (526; 690)	533 (494; 598)	596 (553; 637)	0.058	0.687	0.242
Reactance ohms	44 (39; 48)	45 (40; 50)	41 (38; 42)	42 (37; 51)	0.016	0.722	0.553
Total body water (L)	33 (30; 38)	33 (29; 36)	34 (31; 39)	34 (30; 36)	0.036	0.219	0.652
Extra cellular water (%)	54 (53; 58)	56 (52; 58)	55 (54; 57)	57 (53; 60)	0.261	0.708	0.566
Intra cellular water (%)	46 (42; 48)	44 (42; 48)	45 (43; 46)	43 (40; 47)	0.253	0.721	0.562
Fat free mass (kg)	28 (26; 32)	26 (25; 29)	29 (26; 33)	27 (25; 29)	0.341	0.234	0.339
Body cell mass (kg)	12.9 (10.7; 14.0)	11.9 (10.7; 15.8)	14.0 (12.7; 16.5)	12.2 (10.6; 17.9)	0.335	0.643	0.902
Fat mass (kg)	13.2 (10.6; 15.6)	12.7 (9.7; 20.1)	13.4 (9.7; 24.6)	15.0 (9.8; 19.2)	0.442	0.909	0.717
Muscle mass (kg)	26 (22; 30)	23 (22; 27)	26 (23; 30)	25 (22; 25)	0.978	0.403	0.483
Basal metabolic rate (kcal)	1,346 (1,245; 1,409)	1,286 (1,235; 1,347)	1,341 (1,259; 1,429)	1,303 (1,227; 1,316)	0.863	0.407	0.475
Blood analysis							
Glucose (mg/dl)	89 (78; 104)	81 (70; 136)	85 (77; 126)	86 (80; 143)	0.193	0.504	0.755
Hb glycate (%)	5.90 (5.33; 6.55)	5.65 (5.60; 6.80)	5.60 (5.15; 6.28)	5.45 (5.40; 6.58)	0.018	0.310	0.656
Total cholesterol (mg/dl)	217 (158; 232)	172 (155; 201)	217 (161; 249)	165 (154; 201)	0.846	0.323	0.191
HDL cholesterol (mg/dl)	66 (55; 76)	73 (58; 90)	68 (56; 76)	64 (58; 86)	0.292	0.160	0.476
LDL cholesterol (mg/dl)	118 (73; 140)	85 (69; 107)	118 (76; 158)	77 (66; 101)	0.993	0.323	0.117
Triglycerides (mg/dl)	126 (101; 173)	82 (68; 116)	125 (101; 172)	93 (83; 129)	0.745	0.656	0.160
Creatinine (mg/dl)	0.75 (0.65; 0.79)	0.86 (0.68; 1.02)	0.74 (0.63; 0.84)	0.82 (0.72; 1.06)	0.317	0.651	0.178
WBC ($\times 10^3$/ul)	6.05 (5.23; 7.70)	6.00 (5.35; 7.80)	5.25 (4.45; 7.03)	6.55 (4.63; 7.35)	0.225	0.436	0.664
RBC ($\times 10^6$/ul)	4.60 (4.13; 4.87)	4.48 (3.91; 4.74)	4.70 (4.3; 5.02)	4.71 (3.64; 4.82)	0.078	0.348	0.459
Hemoglobin (g/dl)	13.9 (12.5; 14.5)	12.8 (11.7; 13.9)	14.3 (12.2; 14.7)	13.7 (11.5; 14.5)	0.008	0.930	0.544
Hematocrit (%)	44 (37; 44)	40 (37; 44)	45 (39; 45)	43 (35; 44)	0.234	0.415	0.443
MCV (fl)	92 (88; 97)	93 (90; 95)	91 (87; 97)	92 (90; 97)	0.316	0.909	0.710
MCH (pg)	30 (28; 31)	30 (28; 30)	30 (28; 31)	31 (29; 31)	0.125	0.065	0.597
Platelets ($\times 10^3$/ul)	264 (254; 271)	279 (184; 323)	251 (198; 277)	260 (208; 332)	0.238	0.325	0.745
Neutrophil ($\times 10^3$/ul)	3.32 (3.01; 4.99)	3.63 (2.64; 4.29)	2.80 (2.34; 4.38)	3.55 (2.56; 4.26)	0.265	0.417	0.989
Lymphocytes ($\times 10^3$/ul)	1.91 (1.63; 2.17)	1.80 (1.50; 2.68)	1.88 (1.52; 2.15)	1.94 (1.47; 2.62)	0.560	0.856	0.561
Monocytes ($\times 10^3$/ul)	0.41 (0.39; 0.49)	0.40 (0.30; 0.51)	0.36 (0.31; 0.40)	0.41 (0.25; 0.43)	0.020	0.232	0.960
Eosinophil ($\times 10^3$/ul)	0.18 (0.09; 0.26)	0.21 (0.15; 0.29)	0.15 (0.08; 0.28)	0.18 (0.16; 0.29)	0.689	0.579	0.352
Basophil ($\times 10^3$/ul)	0.03 (0.02; 0.05)	0.04 (0.03; 0.07)	0.03 (0.03; 0.05)	0.04 (0.02; 0.06)	0.535	0.284	0.506
Urine analysis							
pH	6 (5; 7)	6 (6; 6)	5 (5; 8)	6 (5; 6)	0.420	0.987	0.684
Specific gravity	1.02 (1.01; 1.03)	1.03 (1.03; 1.03)	1.01 (1.01; 1.03)	1.01 (1.01; 1.02)	0.066	0.285	0.709
Six minutes Walking Test (6MWT)							
Systolic blood pressure pre 6MWT (mmHg)	155 (135; 192)	161 (136; 189)	133 (114; 148)	123 (119; 126)	0.001	0.589	0.645
Systolic blood pressure post 6MWT (mmHg)	165 (148; 185)	165 (144; 187)	165 (134; 70)	140 (133; 153)	0.072	0.408	0.442
Diastolic blood pressure pre 6MWT (mmHg)	81 (63; 87)	52 (75; 93)	75 (59; 88)	78 (70; 80)	0.166	0.599	0.486
Diastolic blood pressure post 6MWT (mmHg)	79 (62; 104)	90 (75; 98)	73 (60; 83)	80 (73; 85)	0.051	0.638	0.451
Mean blood pressure pre 6MWT (mmHg)	106 (87; 122)	110 (95; 121)	98 (78; 103)	93 (86; 94)	0.007	0.550	0.855
Mean blood pressure post 6MWT (mmHg)	110 (91; 128)	114 (98; 124)	105 (86; 109)	97 (96; 105)	0.028	0.779	0.864
Heart rate pre 6MWT (bpm)	65 (54; 76)	71 (63; 78)	58 (51; 72)	67 (64; 75)	0.242	0.553	0.204
Heart rate post 6MWT (bpm)	88 (66; 107)	99 (78; 107)	78 (65; 100)	85 (81; 94)	0.143	0.920	0.409
RPP pre 6MWT (mmHg*bpm)	11,334 (7,902; 12,017)	11,047 (8,615; 13,424)	7,195 (6,161; 10,693)	8,120 (7,676; 9,395)	0.003	0.719	0.510
RPP post 6MWT (mmHg*bpm)	15,096 (10,401; 17,970)	15,939 (13,208; 17,759)	13,260 (8,966; 16,170)	11,070 (10,860; 13,780)	0.011	0.389	0.855
Blood oxygen saturation pre 6MWT (%)	98 (95; 98)	98 (97; 98)	97 (93; 99)	97 (95; 98)	0.055	0.756	0.697
Blood oxygen saturation post 6MWT (%)	96 (94; 98)	97 (95; 98)	95 (94; 95)	97 (97; 98)	0.960	0.405	0.102
Δ post-pre 6MWT systolic blood pressure (mmHg)	9.50 (−9.25; 15.50)	−2.00 (5.00; 19.00)	22.50 (11.25; 41.25)	15.00 (10.00; 30.00)	0.890	0.657	0.747
Δ post-pre 6MWT diastolic blood pressure (mmHg)	−1.50 (−8.00; 20.00)	2.00 (−2.50; 12.50)	3.50 (−14.50; 5.00)	5.00 (−2.50; 10.00)	0.525	0.421	0.703
Δ post-pre 6MWT mean blood pressure (mmHg)	4.50 (−7.50; 17.25)	−1.00 (−3.17; 14.00)	6.50(2.83; 11.67)	10.00 (5.00; 10.83)	0.465	0.804	0.861
Δ post-pre 6MWT heart rate (bpm)	23 (12; 31)	24 (10; 32)	21 (8; 33)	20 (14; 24)	0.483	0.645	0.987
Δ post-pre 6MWT RPP (mmHg*bpm)	3,762 (2,393; 6,060)	5,189 (2,287; 5,840)	4,685 (2,234; 7,429)	3,700 (2,900; 5,285)	0.805	0.551	0.807
Δ post-pre 6MWT blood oxygen saturation (%)	−1.0 (−4.0; 2.0)	0 (−3.5; 1.0)	−1.5 (−5.0; 2.0)	0 (−5.0; 2.0)	0.650	0.385	0.631
Covered meters after 6MWT (m)	388 (262; 494)	384 (311; 513)	421 (332; 517)	407 (387; 505)	0.014	0.730	0.858
Short physical performance battery (SPPB)							
Balance	4 (3; 4)	4 (1; 4)	4 (4; 4)	4 (2; 4)	0.081	0.865	0.275
Walk	3 (2; 4)	3 (2; 4)	4 (2; 4)	4 (3; 4)	0.055	0.334	0.885

(*continued*)

Table 3 (*continued*)

Parameters	Baseline		Follow-up		*P* values for time	*P* values for time*group interaction	*P* values for group
	Controls (n = 4)	Cases (n = 10)	Controls (n = 4)	Cases (n = 10)			
Chair stand	3 (1; 3)	2 (1; 3)	2 (1; 3)	3 (2; 4)	0.355	0.114	0.607
Total score	9 (6; 11)	8 (4; 11)	9 (7; 11)	10 (7; 12)	0.036	0.162	0.793
Screening tests							
MNA Total score	23 (21; 27)	25 (22; 27)	27 (25; 29)	27 (25; 28)	0.003	0.606	0.746
PASE Total score	83 (64; 100)	76 (59; 90)	93 (68; 120)	86 (66; 107)	0.227	0.705	0.991
Berg Total score	48 (47; 51)	51 (49; 55)	53 (48; 56)	52 (49; 55)	0.011	0.011	0.392

BMI: body mass index; WBC: white blood cells; RBC: red blood cells; MCV: mean cell volume; MCH: mean cell hemoglobin; RPP: rate pressure product; MNA: mini nutritional assessment; PASE: physical activity scale for the elderly.

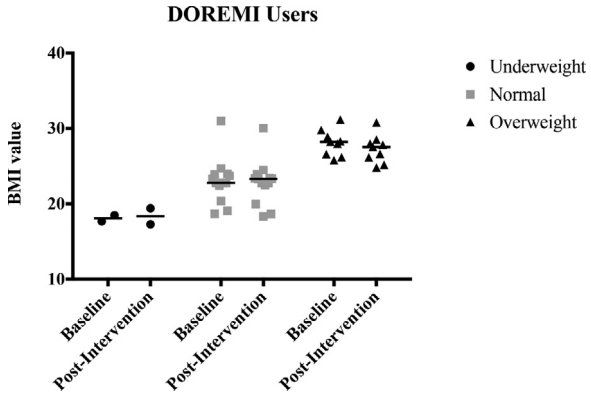

Figure 2. Clusterization of entire DOREMI user's population using BMI value (kg/m^2). Modulation of BMI DOREMI users at baseline and post-intervention.

In addition, a significant reduction in the waist ($P \leq 0.001$) and arm ($P = 0.007$) circumference and waist-to-hip ratio ($P = 0.006$) was highlighted in the whole group of subjects at the end of the trial. Finally, also glycated hemoglobin showed a trend towards a reduction ($P = 0.064$).

3.5. Nutritional status and somatometric parameters: UK trial

The post-intervention MNA test, selected as primary KPI, showed an increase of score in both groups in a significant manner ($P = 0.003$) (Table 3).

Data analysis of somatometric parameters highlighted a significant reduction, in the two groups at the end of DOREMI trial, of the waist ($P = 0.001$) and hip ($P = 0.001$) circumference and of upper-arm fat area ($P = 0.025$) as also a decrease trend for BMI and weight (P values of 0.074 and 0.096, respectively).

Among blood biomarkers, most relevant variations were observed for glycated hemoglobin (decrease, $P = 0.008$) and hemoglobin (increase, $P = 0.008$). An interesting trend was observed for LDL values, with a decrease in DOREMI Users respect to Control, (83±23) *vs*. (117±44) mg/dl, respectively.

BIVA analysis showed a significant increase of TBW ($P = 0.016$) in Control and Treated subjects at the end of the trial.

3.6. Nutritional status and somatometric parameters: Italy trial

Data analysis of the Italian trial produced similar results compared to the UK one even if the MNA score did not increase in the IT population, conversely to the observed changes for the UK population (Table 4).

Data analysis of somatometric parameters highlighted a significant reduction of waist-to-hip ratio in DOREMI users respect to Control group ($P = 0.002$) as also a trend to decrease, in the two groups, for the weight ($P = 0.053$)

BIVA analysis showed a significant decrease in Total Body Water ($P = 0.021$) in Control and Treated participants at the end of the trial.

4. Discussion

DOREMI solution was mainly focused on stimulation and involvement of older people in modifying the lifestyle towards the active aging paradigm through creative, personalized and engaging solutions addressing the impacting factors related to sedentariness, malnutrition and cognitive decline. This approach was supported by an unobtrusively monitoring system able to collect daily life parameters and to support the specialist (either a general practitioner or a geriatric) in the periodic verification of lifestyle protocols compliance: this system was constituted by a gamified environment for diet and physical activity; a wireless sensor network (WSN) for context-awareness; behavioral pattern recognition on activity and location information based on machine learning; innovative and auto configurable wireless sensors; customized devices and sensors, sensor fusion and integration and networking technologies; serious games for physical activity stimulation.

During the DOREMI trial, the Exergame app has stimulated participants to perform physical activity favoring a slight but significant increase in several parameters related to physical evaluation tests. In particular, significant modulation of 6MWT-related hemodynamic parameters was observed. Pooled data highlighted a significant decrease in the entire population of arterial blood (systolic, diastolic, mean) pressure and RPP product, often more pronounced in DOREMI users. The DOREMI protocol determined an increase of physical exercise tolerance favoring the arterial blood pressure-lowering (in the entire population) and the increase of covered meters (as in UK users), as previously reported [29–30]. These changes further confirm the beneficial effects of physical activity [31–34] obtained by the DOREMI protocol, either administered by the Exergame or by coaching through experts during the training phase of the trial.

A significant increase in BERG score in the pooled population was highlighted about balance assessment. BERG is useful to measure the degree of balance among older people by assessing the performance of functional tasks [35]: literature has shown how balance loss could predict of risk of falling, increased dependency, illness, and sometimes-early death [36–37]. Exercise interventions designed for improving balance are typically those in which participants exercise in standing and moving positions of increasing difficulty to challenge the body's ability to anticipate and respond to the demands of different tasks or environments [38]. Our finding on the positive correlation between the BERG score and the increase of physical activity is confirmed by the work of Howe et al. [39–40].

In the DOREMI trial, a positive trend in physical activity assessment, both in Treated and Control users, was observed, particularly for Balance and Walk subtests. SPPB has been used as a predictive tool for possible disability, to monitor pre-frailty risk and can aid in the monitoring of function in older people. Randomized controlled trials in older people have shown that structured physical activity interventions, including resistance and endurance exercises, substantially impact a series of physical performance activities, such as walking speed, stair-

Table 4 Statistical analysis of IT trial data (median (IQR))

Parameters	Baseline		Follow-up		*P* values for time	*P* values for time*group interaction	*P* values for group
	Controls	Cases	Controls	Cases			
Metabolic parameters	*n* = 3	*n* = 14	*n* = 3	*n* = 14			
BMI (kg/m^2)	26 (22; 33)	24 (20; 27)	27 (22; 28)	24 (20; 27)	0.076	0.158	0.429
Weight (kg)	72 (59; 83)	63 (49; 74)	74 (59; 80)	63 (48; 73)	0.336	0.694	0.259
Circumference waist (cm)	100 (92; 107)	88 (75; 94)	100 (86; 107)	84 (75; 94)	0.103	0.909	0.058
Circumference hip (cm)	98 (97; 108)	102 (91; 110)	98 (98; 108)	102 (91; 110)	0.590	0.823	0.997
Waist-to-hip ratio	0.99 (0.95; 1.02)	0.84 (0.82; 0.88)	0.99 (0.88; 1.02)	0.82 (0.79; 0.87)	0.094	0.803	0.002
Phase angle	4.60 (4.50; 5.2)	4.60 (4.43; 4.98)	4.80 (4.70; 5.4)	5.05 (4.70; 5.30)	0.109	0.634	0.945
Resistance (ohms)	549 (485; 562)	616 (571; 681)	549 (485; 556)	644 (571; 690)	0.360	0.209	0.059
Reactance (ohms)	45 (45; 46)	54 (46; 58)	46 (45; 47)	54 (48; 63)	0.308	0.476	0.082
Total body water (liters)	36 (33; 42)	31 (27; 34)	35 (33; 41)	30 (27; 34)	0.021	0.765	0.155
Extra cellular water (%)	53 (50; 54)	53 (51; 54)	52 (49; 53)	50 (49; 53)	0.099	0.659	0.858
Intra cellular water (%)	47 (47; 50)	47 (46; 49)	48 (47; 52)	50 (47; 51)	0.099	0.659	0.858
Fat free mass (kg)	49 (45; 57)	42 (38; 47)	47 (45; 56)	41 (37; 46)	0.055	0.738	0.145
Body cell mass (kg)	22 (21; 28)	20 (18; 21)	22 (21; 28)	20 (18; 21)	0.389	0.887	0.111
Fat mass (kg)	15 (14; 34)	19 (10; 25)	16 (14; 33)	19 (13; 25)	0.843	0.537	0.683
Muscle mass (kg)	28 (26; 35)	25 (22; 27)	28 (27; 35)	25 (23; 26)	0.572	0.905	0.103
Basal metabolic rate (kcal)	1,394 (1,346; 1,562)	1,316 (1,261; 1,358)	1,381 (1,371; 1,574)	1,334 (1,283; 1,361)	0.413	0.852	0.105
Blood analysis	*n* = 2	*n* = 5	*n* = 2	*n* = 5			
Glucose (mg/dl)	91 (88; 93)	82 (80; 85)	91 (84; 98)	91 (87; 102)	0.173	0.204	0.475
Hb glycated (%)	–	5.7 (5.4; 5.8)	–	5.7 (5.6; 6.0)	NA	NA	NA
Total cholesterol (mg/dl)	231	211 (192; 232)	199	206 (196; 229)	NA	NA	NA
HDL cholesterol (mg/dl)	73	58 (49; 72)	64	58 (50; 68)	NA	NA	NA
LDL cholesterol (mg/dl)	–	156 (155; 157)	–	130 (125; 134)	NA	NA	NA
Triglycerides (mg/dl)	55	107 (75; 128)	83	103 (86; 113)	NA	NA	NA
Creatinine (mg/dl)	0.80 (0.80; 0.80)	0.70 (0.67; 0.90)	0.80 (0.80; 0.80)	0.70 (0.70; 0.80)	0.602	0.602	0.516
WBC (× 10^3/ul)	5.95 (4.90; 7.00)	6.06 (5.33; 7.38)	5.75 (5.20; 6.30)	5.44 (4.42; 6.78)	0.376	0.607	0.959
RBC (× 10^6/ul)	4.70 (4.50; 4.90)	4.45 (4.18; 4.73)	4.35 (3.90; 4.80)	4.50 (4.19; 4.62)	0.100	0.118	0.786
Hemoglobin (g/dl)	13. 8 (13.6; 13.9)	12.9 (12.7; 13.1)	13.3 (12.6; 14.0)	13.1 (11.9; 13.7)	0.579	0.538	0.264
Hematocrit (%)	42 (41; 42)	40 (38; 41)	39 (37; 41)	38 (37; 40)	0.102	0.520	0.265
MCV (fl)	88 (86; 90)	88 (84; 94)	91 (87; 95)	87 (81; 90)	0.915	0.157	0.651
MCH (pg)	29 (29; 30)	29 (27; 31)	31 (29; 32)	30 (26; 32)	0.213	0.227	0.654
Platelets (× 10^3/ul)	237 (227; 246)	243 (216; 269)	231 (177; 285)	271 (248; 293)	0.665	0.532	0.628
Neutrophil (× 10^3/ul)	–	3.70	–	2.40	NA	NA	NA
Lymphocytes (× 10^3/ul)	–	2.20	–	1.80	NA	NA	NA
Monocytes (× 10^3/ul)	–	0.40	–	0.30	NA	NA	NA
Eosinophil (× 10^3/ul)	–	0.20	–	0.20	NA	NA	NA
Basophil (× 10^3/ul)	–	0.10	–	0	NA	NA	NA
Urine analysis							
pH	–	5.5 (5.5; 6.6)	–	6.0 (5.5; 7.0)	NA	NA	NA
Specific gravity	–	1015 (1010; 1024)	–	1017 (1014; 1022)	NA	NA	NA
Six minutes Walking Test (6MWT)	*n* = 3	*n* = 12	*n* = 3	*n* = 12			
Systolic blood pressure pre 6MWT (mmHg)	140 (130; 150)	140 (140; 145)	140 (130; 155)	130 (123; 139)	0.203	0.089	0.327
Systolic blood pressure post 6MWT (mmHg)	163 (145; 180)	157 (153; 170)	155 (140; 170)	150 (150; 160)	0.027	0.957	0.813
Diastolic blood pressure pre 6MWT (mmHg)	85 (80; 90)	77 (75; 84)	80 (75; 80)	75 (71; 75)	0.025	0.269	0.090
Diastolic blood pressure post 6MWT (mmHg)	95 (90; 100)	90 (87; 99)	90 (90; 90)	90 (81; 90)	0.083	0.800	0.431
Mean blood pressure pre 6MWT (mmHg)	103 (97; 110)	98 (96; 104)	100 (97; 102)	94 (90; 97)	0.019	0.705	0.118
Mean blood pressure post 6MWT (mmHg)	118 (108; 127)	112 (109; 123)	112 (107; 117)	110 (103; 113)	0.014	0.798	0.544
Heart rate pre 6MWT (bpm)	58 (52; 66)	66 (61; 70)	62 (58; 68)	70 (65; 74)	0.049	0.945	0.104
Heart rate post 6MWT (bpm)	78 (70; 85)	88 (83; 96)	86 (82; 90)	87 (77; 92)	0.708	0.212	0.322
RPP pre 6MWT (mmHg*bpm)	8,120 (7,800; 8,580)	9,205 (8,340; 10,188)	8,840 (8,120; 9,610)	9,310 (8,445; 10,058)	0.457	0.174	0.323
RPP post 6MWT (mmHg*bpm)	12,463 (12,325; 12,600)	14,520 (12,610; 16,090)	13,270 (12,600; 13,940)	13,000 (11,425; 14,400)	0.722	0.225	0.476
Blood oxygen saturation pre 6MWT (%)	97 (97; 98)	98 (97; 99)	98 (96; 100)	98 (98; 99)	0.137	0.232	0.662
Blood oxygen saturation post 6MWT (%)	97 (97; 97)	97 (96; 98)	97 (97; 97)	97 (96; 98)	0.584	0.584	0.838
Δ post-pre 6MWT systolic blood pressure (mmHg)	18 (5; 30)	16 (12; 24)	20 (10; 30)	20 (20; 25)	0.429	0.970	0.858
Δ post-pre 6MWT diastolic blood pressure (mmHg)	8 (5; 10)	15 (11; 19)	10 (10; 10)	15 (6; 19)	0.808	0.323	0.474
Δ post-pre 6MWT mean blood pressure (mmHg)	11 (5; 17)	17 (12; 21)	13 (10; 17)	17 (13; 18)	0.894	0.406	0.526
Δ post-pre 6MWT heart rate (bpm)	23 (18; 27)	25 (19; 30)	23 (22; 24)	16 (14; 21)	0.361	0.306	0.500
Δ post-pre 6MWT RPP (mmHg*bpm)	4,502 (4,205; 4,800)	5,563 (4,154; 6,075)	4,790 (3,760; 5,820)	3,990 (3,150; 4,658)	0.486	0.272	0.893
Δ post-pre 6MWT blood oxygen saturation (%)	−0.5 (−1.0; 0.0)	−1.0 (−1.0; 0.0)	−2.0 (−3.0; −1.0)	−1.0 (−2.0; 0.0)	*0.002*	*0.017*	*0.494*
	n = 2	*n* = 13	*n* = 2	*n* = 13			
Covered meters after 6MWT (m)	503 (480; 525)	500 (470; 520)	503 (480; 525)	450 (443; 495)	0.300	0.300	0.448
Short physical performance battery (SPPB)	*n* = 3	*n* = 13	*n* = 3	*n* = 13			
Balance	4 (4; 4)	4 (4; 4)	4 (4; 4)	4 (4; 4)	NA	NA	NA
Walk	3 (3; 4)	4 (4; 4)	3 (3; 4)	4 (4; 4)	NA	NA	NA

(*continued*)

Table 4 (*continued*)

Parameters	Baseline		Follow-up		*P* values for time	*P* values for time*group interaction	*P* values for group
	Controls	Cases	Controls	Cases			
Chair stand	2 (2; 4)	3 (3; 4)	2 (2; 4)	4 (3; 4)	0.919	0.919	0.152
SPPB total score	9 (9; 12)	11 (11; 12)	9 (9; 12)	12 (11; 12)	0.919	0.919	0.027
Screening tests	*n* = 3	*n* = 14	*n* = 3	*n* = 14			
MNA total score	28 (27; 29)	27 (26; 28)	28 (27; 29)	27 (26; 28)	1.000	1.000	0.154
PASE total score	19 (16; 23)	21 (19; 23)	19 (16; 25)	20 (19; 22)	0.901	0.145	0.645
Berg total score	52 (44; 56)	53 (51; 56)	52 (44; 56)	53 (51; 56)	NA	NA	NA

BMI: body mass index; WBC: white blood cells; RBC: red blood cells; MCV: mean cell volume; MCH: mean cell hemoglobin; RPP: rate pressure product; MNA: mini nutritional assessment; PASE: physical activity scale for the elderly; NA: not applicable.

climb speed, balance, and chair stands [41–43]. Several studies have shown that physical activity deeply impacts the SPPB score changes [44–45].

The importance of adequate nutritional status in the older people is critical for preventing age-related diseases such as atherosclerosis, type 2 diabetes, neurodegenerative disorders causing cognitive decline. It ends with reducing medical and social costs crossing through the main concept of the quality of life [46].

METADIETA® app has supported participants to manage a healthier diet during the DOREMI trial. As for physical activity, a positive trend in specific tests and parameters selected for Trial outcome evaluation was observed. One first result was a significant increase in the MNA score in the pooled population. MNA test is a validated nutritional screening and assessment tool that can identify geriatric users age 65+ who are malnourished or at risk of malnutrition (defect) [20,47-48]. A valuable result is a significant decrease in BMI value in the overweight population, with a decreasing trend in DOREMI users.

The significant modulation of the MNA and BMI scores confirmed the positive changes of overall dietary habits (i.e., more attention to selection and amounts of food consumed more than a change of individual dietary pattern) in our older population. In particular, the support of the e-food dairy (METADIETA® app) seems useful to be aware of food composition and suggested daily amount helping people select a more appropriate choice and portions of meals and foods.

Furthermore, a significant decrease in waist and hip circumference was observed, particularly with a significant reduction in waist-to-hip ratio. Waist and hip measures and their ratio are a simple evaluation of body fat excess. High waist circumference is associated with an increased risk for type-2 diabetes, dyslipidemia, hypertension, and CVD in patients with a BMI in a range between 25 and 34.9 kg/m^2 [49]. The monitoring of waist circumference and BMI could estimate abdominal tissue fat in the absence of a BMI change. Furthermore, in obese patients with metabolic complications, changes in waist circumference are useful predictors of changes in CVD risk factors [50].

From a biochemical point of view, DOREMI produced a significant decrease in glycated hemoglobin in the entire population and an increase of hemoglobin (UK trial). During the training of Control and Treated users, the suggestions on the Mediterranean diet produced a change in users' dietary habits with a double effect: a) a healthy and well-balanced caloric diet, with a reduction of glucose and fatty acid intake. This dietary approach resulted in a significant reduction of glycated hemoglobin and a trend reduction of LDL cholesterol; b) an increase of fresh green leafy vegetables, legumes and fruits consumption that, producing micronutrient intake as iron, folic acid and Vitamin B12, can significantly increase hemoglobin [51] and producing and effect also on RBC release from bone marrow.

Two are the most notable health promotion and disease prevention programs that target the leading causes of morbidity and premature mortality, among them obesity, hypertension, and mental disorders: Malnutrition (obesity/abnormal diet lifestyle) and Sedentariness.

Malnutrition, due to the discrepancy between needs, intake and utilization of nutrients, represents the primary cause responsible for a deterioration of the health of the older user and constitutes a major risk factor for many chronic-degenerative diseases [52].

Sedentariness is responsible for the high incidence of household falls and injuries, which happen to one-third of the > 60′s, with a consequent disability and physical and psychological repercussions that accelerate a physiological and functional decline [53]. This loop can induce a state of depression or social isolation, so it's essential to the older people, living in a safe home environment and performing the daily physical activity by following specific programs selected by the primary care specialist.

4.1. Study limitations

The results of the DOREMI trial have produced interesting and promising effects on physical activity and the dietary habits of involved older people. Changes in diet and physical activity parameters show the efficacy of the DOREMI approach, although these changes occurred in both groups of participants. Treated and control cases modulated in a positive direction their parameters. A possible explanation of this behavior could be mainly related to three main aspects: (1) the training phase: the peculiar aspects of guidelines were carefully presented to both cases and controls by the trainees. Several information on changing their lifestyle habits was furnished and were strongly highlighted how following these "tips" could have produced significant results in terms of quality-of-life improvements. These suggestions could have stimulated Controls to significantly change their daily habits, generating an unintentional "competition" with DOREMI Users [26]; (2) the ethical issue: the study protocol design, with the use of specific hardware and software systems, have forced to aware Control participants to DOREMI peculiar aspects stimulating this group to change their habits; (3) duration of the trial: trial duration of 60 days (plus 15 days of training) was probably too short to observe a clear difference between Control and DOREMI Users.

DOREMI study presents peculiar characteristics linked with two different populations with a different lifestyle. In the UK trial, interesting and promising findings have been observed. Changes in diet and physical activity parameters show the efficacy of the DOREMI approach, although these changes occurred in both groups of participants. Possible explanations of this behavior could be related to: (1) the model of the UK trial: namely, Control and Treated users lived together in the same villages. This "spontaneous" social inclusion may have favored the exchange of information between the two groups, as well as the sharing of specific activities (outdoor walking, physical exercises, diet suggestions). This behavior undoubtedly increases in Control group motivation and "healthy" competition with the DOREMI User group; (2) the daily presence of trainers at villages during the 15-days training played a role towards healthy dietary and physical activity habits, further supported by simple and clear guidelines.

On the other hand, IT trial participants showed a minor number of progress parameters with respect to UK "colleagues". Possible explanations of this trend could be related to the season: IT trial was carried out during summer (respect to the UK one performed during the winter season), influencing several metabolic parameters as well as dietary and

lifestyle habits, producing as a consequence a decrease of TBW at BIVA for perspiration not compensated by proportionate water intake and effect on diet composition and food intake, with a not relevant increase of MNA score.

5. Conclusions

Supporting a healthy and active lifestyle in the older people represents the primary defense frontline for active aging. The overall quality of life could be improved by ICT systems, which represent a novel tool to treat and manage the older people, helping them in relevant behavioral changes related to unhealthy habits. In particular, in our study, the first significant evidence of changes in terms of improvement of dietary-related, somatometric, physical and biochemical parameters was observed by the use of the DOREMI approach. These results suggest how the “translation” of best practice application in habits changes, mediated by new technological tools available, can furnish real support to prevent frailty in older people. The technological and integrated approach of physical activity and diet, presented by the DOREMI platform, represents an innovative solution to stimulate healthy and active aging of the population, with a potential cost reduction for European health care systems in the middle-long period.

Conflicts of interest statement

No competing financial interests exist.

Funding

This work was supported by the European Commission in the Framework of the FP7 DOREMI "Decrease of cOgnitive decline, malnutRition, and sedEntariness by older people empowerment in lifestyle Management and social Inclusion (DOREMI)" Project (Grant No. 611650).

Author contributions

All authors have read and approved the manuscript. Federico Vozzi: study concept and design,data analysis, manuscript drafting, critical revision; Filippo Palumbo: data analysis, critical revision; Erina Ferro: data analysis, critical revision; Karl Kreiner: data analysis, critical revision; Franca Giugni: study concept and design, critical revision; Rachel Dutton: study concept and design; Shirley Hall: study concept and design; Daniele Musian: study concept and design; Marina Parolini: data analysis, critical revision; Patrizia Riso: data analysis, critical revision, manuscript drafting; Oberdan Parodi: study concept and design, data analysis, manuscript drafting, critical revision.

Acknowledgements

We would like to show our gratitude to Prof. Stefano Chessa, Prof. Alessio Micheli, Dr. Davide Bacciu, and Dr. Claudio Gallicchio (Department of Computer Science, University of Pisa) for support in the realization of the DOREMI project and their comments on the manuscript.

We want to thank METEDA Srl for their support in the Nutrition task through the use of the METADIETA® App. Dr. Gioia Melloni is also acknowledged for her valuable contribution to the nutritional coaching group.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.imed.2022.04.001.

References

[1] United Nations World population ageing 2017 - highlights; 2017. Available from https://www.un.org/development/desa/pd/node/3335 .
[2] Rechel B, Doyle Y, Grundy E, et al. How can health systems respond to population ageing. Expert Opin Pharmaco 2009. doi:10.1517/14656566.2011.585637.
[3] Booth FW, Roberts CK, Laye MJ. Lack of exercise is a major cause of chronic diseases. Compr Physiol 2012;2(2):1143–211. doi:10.1002/cphy.c110025.
[4] Carmeli E, Imam B. Health promotion and disease prevention strategies in older adults with intellectual and developmental disabilities. Front Public Health 2014;2(5):31. doi:10.3389/fpubh.2014.00031.
[5] Tosato M, Zamboni V, Ferrini A, et al. The aging process and potential interventions to extend life expectancy. Clin Interv Aging 2007;2(3):401–12.
[6] Wells JL, Dumbrell AC. Nutrition and aging: assessment and treatment of compromised nutritional status in frail elderly patients. Clin Interv Aging 2006;1(1):67–79. doi:10.2147/ciia.2006.1.1.67.
[7] Baeyens JP, Elia M, Greengross SB, et al. Malnutrition among older people in the community: policy recommendation for change. European Nutrition for Health Alliance 2006.
[8] Marra MV, Wellman NS. Multivitamin-mineral supplements in the older americans act nutrition program: not a one-size-fits-all quick fix. Am J Public Health 2008;98(7):1171–6. doi:10.2105/AJPH.2007.122762.
[9] Svantesson U, Jones J, Wolbert K, et al. Impact of physical activity on the self-perceived quality of life in non-frail older adults. J Clin Med Res 2015;7(8):585–93. doi:10.14740/jocmr2021w.
[10] Garber CE, Blissmer B, Deschenes MR, et al. American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. Med Sci Sports Exerc 2011;43(7):1334–59. doi:10.1249/MSS.0b013e318213fefb.
[11] Amarya S, Singh K, Sabharwal M. Changes during aging and their association with malnutrition. J Clin Gerontol Geriatr 2015;6(3):78–84. doi:10.1016/j.jcgg.2015.05.003.
[12] Williams KN, Kemper S. Interventions to reduce cognitive decline in aging. J Psychosoc Nurs Ment Health Serv 2010;48(5):42–51. doi:10.3928/02793695-20100331-03.
[13] Brox E, Luque LF. 5th international conference on pervasive computing technologies for healthcare and workshops. PervasiveHealth 2011 2011. doi:10.4108/icst.pervasivehealth.2011.246049.
[14] Norgall T, Wichert R. Personalized use of ICT–from telemonitoring to ambient assisted living. Stud Health Technol Inform 2013;187:145–51.
[15] Cruz-Cunha MM. Handbook of research on ICTs and management systems for improving efficiency in healthcare and social care. IGI Global; 2013.
[16] Venkatasubramanian K, Deng G, Mukherjee T, et al. Ayushman: a wireless sensor network based health monitoring infrastructure and testbed. Lecture Notes in Computer Science 2005;3560:406–7. doi:10.1007/11502593_39.
[17] Varshney U. Pervasive healthcare and wireless health monitoring. Mobile Netw Appl 2007;12(2–3):113–27. doi:10.1007/s11036-007-0017-1.
[18] Palumbo F, La Rosa D, Ferro E. Stigmergy-based long-term monitoring of indoor users mobility in ambient assisted living environments: the DOREMI project approach. CEUR Workshop Proc 2016;1803:18–32 2017.
[19] Nasreddine ZS, Phillips NA, Bédirian V, et al. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. J Am Geriatr Soc 2005;53(4):695–9. doi:10.1111/j.1532-5415.2005.53221.x.
[20] Guigoz Y, Vellas B, Garry PJ. Mini nutritional assessment: a practical assessment tool for grading the nutritional state of elderly patients. Facts, Res Intervent Geriatr 1997:15–32 SUPPL.
[21] Washburn RA, Smith KW, Jette AM, et al. The Physical Activity Scale for the Elderly (PASE): development and evaluation. J Clin Epidemiol 1993;46(2):153–62. doi:10.1016/0895-4356(93)90053-4.
[22] Chad KE, Reeder BA, Harrison EL, et al. Profile of physical activity levels in community-dwelling older adults. Med Sci Sports Exerc 2005;37(10):1774–84. doi:10.1249/01.mss.0000181303.51937.9c.
[23] Berg KO, Wood-Dauphinee SL, Williams JI, et al. Measuring balance in the elderly: validation of an instrument. Can J Public Health 1992;83(2):S7–S11 Suppl.
[24] Bacciu D, Chessa S, Gallicchio C, et al. A learning system for automatic Berg Balance Scale score estimation. Eng Appl Artif Intell 2017;66:60–74. doi:10.1016/j.engappai.2017.08.018.
[25] Bacciu D, Chessa S, Gallicchio C, et al.. Smart environments and context-awareness for lifestyle management in a healthy active ageing framework, 9273. Cham: Springer International Publishing; 2015. p. 54–66.
[26] Palumbo F, La Rosa D, Ferro E, et al. Reliability and human factors in ambient assisted living environments. J Reliable Intell Environ 2017;3(3):139–57. doi:10.1007/s40860-017-0042-1.
[27] Guralnik JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. J Gerontol 1994;49(2):M85–94. doi:10.1093/geronj/49.2.M85.
[28] WHO Global recommendations on physical activity for health; 2010.
[29] Troosters T, Gosselink R, Decramer M. Six minute walking distance in healthy elderly subjects. Eur Respir J 1999;14(2):270–4. doi:10.1034/j.1399-3003.1999.14b06.x.
[30] Harada ND, Chiu V, Stewart AL. Mobility-related function in older adults: assessment with a 6-minute walk test. Arch Phys Med Rehabil 1999;80(7):837–41. doi:10.1016/s0003-9993(99)90236-8.
[31] Boyer JL, Kasch FW. Exercise therapy in hypertensive men. JAMA 1970;211(10):1668–71. doi:10.1001/jama.1970.03170100030006.
[32] Huang G, Shi X, Gibson CA, et al. Controlled aerobic exercise training reduces resting blood pressure in sedentary older adults. Blood Press 2013;22(6):386–94. doi:10.3109/08037051.2013.778003.

[33] Cornelissen VA, Buys R, Smart NA. Endurance exercise beneficially affects ambulatory blood pressure: a systematic review and meta-analysis. J Hypertens 2013;31(4):639–48. doi:10.1097/HJH.0b013e32835ca964.
[34] Rossi A, Moullec G, Lavoie KL, et al. Resistance training, blood pressure, and meta-analyses. Hypertension 2012;59(3):e22–3. doi:10.1161/HYPERTENSIONAHA.111.188805.
[35] Berg K. Balance and its measure in the elderly: a review. Physiother Can 2009;41(5):240–6. doi:10.3138/ptc.41.5.240.
[36] Baker SP, Harvey AH. Fall injuries in the elderly. Clin Geriatr Med 1985;1(3):501–12.
[37] Tinetti ME, Speechley M, Ginter SF. Risk factors for falls among elderly persons living in the community. N Engl J Med 1988;319(26):1701–7. doi:10.1056/NEJM198812293192604.
[38] Winter WD. Anatomy, Biomechanics and control of balance during standing and walking. 1995.
[39] Howe TE, Rochester L, Jackson A, et al. Exercise for improving balance in older people. Cochrane Database Syst Rev 2007;13(4):CD004963. doi:10.1002/14651858.CD004963.pub2.
[40] Howe TE, Rochester L, Neil F, et al. Exercise for improving balance in older people. Cochrane Database Syst Rev 2011;86(11):CD004963. doi:10.1002/14651858.CD004963.pub3.
[41] Miszko TA, Cress ME, Slade JM, et al. Effect of strength and power training on physical function in community-dwelling older adults. J Gerontol A Biol Sci Med Sci 2003;58(2):171–5. doi:10.1093/gerona/58.2.m171.
[42] Cress ME, Buchner DM, Questad KA, et al. Exercise: effects on physical functional performance in independent older adults. J Gerontol A Biol Sci Med Sci 1999;54(5):M242–8. doi:10.1093/gerona/54.5.m242.
[43] Buchner DM, Cress ME, de Lateur BJ, et al. The effect of strength and endurance training on gait, balance, fall risk, and health services use in community-living older adults. J Gerontol A Biol Sci Med Sci 1997;52(4):M218–24. doi:10.1093/gerona/52a.4.m218.
[44] Nelson ME, Layne JE, Bernstein MJ, et al. The effects of multidimensional home-based exercise on functional performance in elderly people. J Gerontol A Biol Sci Med Sci 2004;59(2):154–60. doi:10.1093/gerona/59.2.m154.
[45] Bean JF, Herman S, Kiely DK, et al. Increased velocity exercise specific to task (Invest) training: a pilot study exploring effects on leg power, balance, and mobility in community-dwelling older women. J Am Geriatr Soc 2004;52(5):799–804. doi:10.1111/j.1532-5415.2004.52222.x.
[46] World Health Organization. Guidelines on food fortification with micronutrients; 2006.
[47] Vellas B, Villars H, Abellan G, et al. Overview of the MNA–its history and challenges. J Nutr Health Aging 2006;10(6):456–65.
[48] Rubenstein LZ, Harker JO, Salva A, et al. Screening for undernutrition in geriatric practice: developing the short-form mini-nutritional assessment (MNA-SF). J Gerontol A Biol Sci Med Sci 2001;56(6):M366–72. doi:10.1093/gerona/56.6.m366.
[49] Chan JM, Rimm EB, Colditz GA, et al. Obesity, fat distribution, and weight gain as risk factors for clinical diabetes in men. Diabetes Care 1994;17(9):961–9. doi:10.2337/diacare.17.9.961.
[50] Lemieux S, Prud'homme D, Bouchard C, et al. A single threshold value of waist girth identifies normal-weight and overweight subjects with excess visceral adipose tissue. Am J Clin Nutr 1996;64(5):685–93. doi:10.1093/ajcn/64.5.685.
[51] Fishman SM, Christian P, West KP. The role of vitamins in the prevention and control of anaemia. Public Health Nutr 2000;3(2):125–50. doi:10.1017/s1368980000000173.
[52] Ahmed T, Haboubi N. Assessment and management of nutrition in older people and its importance to health. Clin Interv Aging 2010;5:207–16. doi:10.2147/cia.s9664.
[53] Paterson DH, Jones GR, Rice CL. Ageing and physical activity: evidence to develop exercise recommendations for older adults. Can J Public Health 2007;98(2):S69–S108 SupplS2E. doi:10.1139/H07-111.