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## Original Article

## Precision nutrition impact on metabolic health and quality of life in aging population after a 3-month intervention: A randomized intervention



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## ABSTRACT

**Objectives:** Innovative precision dietary procedures are required to promote healthy aging. This study aimed to evaluate the effects of a personalised strategy based on the inclusion of individualised foods and digital tools on overall health status and quality of life within a follow-up of 3 months in older adults with overweight or obesity. **Methods:** 127 men and women aged between 50 and 80 years with overweight/obesity participated in the study—between January 2020 and September 2020 at the Center for Nutrition Research-University of Navarra and IMDEA-ALIMENTACIÓN—and were randomly assigned to a usual-care group (standard recommendations) or precision group (precision nutrition strategy based on the inclusion of individualised foods and a mobile application). Anthropometry, body fat percentage, biochemical parameters, diet, and quality of life (SF-36 Health Survey) were assessed at baseline and after 3 months.

**Results:** Both strategies were found to improve overall metabolic health; however, the precision approach demonstrated significantly better outcomes. The precision strategy reduced body weight at 3 months (−4.3 kg;  $p < 0.001$ ) with significant improvements in body fat percentage, blood pressure and general metabolic health (glycated haemoglobin; alanine aminotransferase; aspartate aminotransferase; hepatic steatosis index) in comparison with the standard recommendations. The precision approach significantly enhanced the quality of life (SF-36) of individuals, with additional improvements in emotional well-being ( $p = 0.024$ ) and vitality ( $p = 0.008$ ). Adherence to the Mediterranean diet was significantly associated with a higher quality of life and vitality.

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**Conclusion:** These results support the benefit of precision nutrition approaches for promoting healthy aging and emotional well-being, enhancing the quality of life in aging populations, during the COVID-19 pandemic.

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## 1. Introduction

Population aging is the 21st century's major demographic phenomenon [1]. The global population aged 60 years and over numbered 1 billion in 2020, more than twice as large as in 1980, and it is expected to reach nearly 2.1 billion by 2050. This increase is occurring at an unprecedented pace and will accelerate in the coming decades, particularly in developing countries [2].

In 2022, 19.09% of the Spanish population was aged 65+. Furthermore, it is projected that adults aged 65+ will constitute 26% of the Spanish population by 2037 [3].

With increasing age, numerous underlying physiological, psychosocial and emotional changes occur [4]. The incidence of chronic disease also rises [5], after long exposure to unhealthful lifestyles (unhealthy diets, physical inactivity, tobacco consumption, alcohol use, and stress) [6], leading to a decline in overall quality of life.

Consequently, integrated dietary strategies and actions are required to promote healthy aging and reduce the burden of disability and mortality in older populations [7]. Nutritional research and guidelines focus on population averages. However, the high inter-person variability in response to foods and diets demands the development of group-based nutrition and more personalised approaches to optimise the quality of diet and food intake in adults [8].

The promising field of precision nutrition is rising as a therapeutic approach that aims to design tailored dietary interventions to prevent and manage chronic diseases. Indeed, precision nutrition approaches contemplate the interindividual heterogeneity caused by genetic/epigenetic dissimilarities, individual facets (age, gender), the lifestyle and environmental exposome diversity, microbiome variations, and singular behavioural/psychological features [9,10]. Bioactive compounds and functional foods may also play an important role on active aging avoiding the risk of diseases [10]. Indeed, dietary fibre, omega-3 PUFA acids and phytosterols, phytoestrogens and polyphenols have been identified as promoters of healthy aging [10,11]. In fact, functional food-based strategies hold a great promise for providing health benefits for the elderly [12].

However, one of the main limitations of a dietary prescription is the lack of compliance. This is usually due to the complexity of the prescription itself and/or the lack of commitment of the individual. The inclusion of digital tools to empower and motivate individuals and support them in managing the dietary strategy could overcome this limitation [13].

With this background, the general objective of this investigation was to assess the effects of a precision dietary intervention based on the inclusion of individualised foods and digital tools on general health status including, anthropometry, body composition, general metabolic determinations, dietary intake, gastrointestinal health, and quality of life within a follow-up of 3 months in adults with overweight or obesity.

## 2. Materials and methods

### 2.1. Study population

The study's primary outcome was the improvement of the global health status of the participants, measured by means of an *a priori* metabolic health score (Supplementary Table 1). This novel score encompassed twelve items: (a) body mass index (BMI); (b) waist circumference; (c) glycated haemoglobin (HbA1c); (d) total cholesterol (TC); (e) high-density lipoprotein cholesterol (HDL-c); (f) low-density lipoprotein cholesterol (LDL-c); (g) triglycerides (TG); (h) uric acid; (i) systolic blood pressure | diastolic blood pressure; (j) gastrointestinal

health (gastrointestinal symptoms rating scale (GSRS)); (k) cognitive function (mini mental state examination (MMSE)) and (l) extra negative point if reducing medication. For each variable, cut-off points were established according to the reference ranges. These items received a minimum of 0 point for normal values, 1 point for borderline and at-risk values and a maximum of 2 points for pathological values, except for HDL-c, whose values were stratified into two groups according to AHA recommendations, assigning 0 points to optimal levels and 1 point to altered values. Additionally, 1 point was subtracted from the overall score in those participants who reduced the dose or stopped a certain pharmacological treatment (oral antidiabetics, antihypertensive and/or lipid-lowering agents) due to the dietary strategy. Finally, we constructed the score by summing all the values, ranging from 0 to 21, where higher scores indicate a worse metabolic health.

A total of 569 candidates were assessed for eligibility, of which 422 were excluded (366 did not meet the inclusion criteria and 56 declined to participate). Thus, 147 participants were recruited between January 2020 and September 2020 at the Center for Nutrition Research-University of Navarra- (n = 88; 87.5% of participants finished the intervention) and IMDEA-ALIMENTACIÓN (n = 59; 84.7% of participants completed the 3-month program) and were randomly assigned to a usual-care group (standard recommendations; n = 72) or precision group (precision nutrition strategy; n = 75). After 3 months of intervention (December 2020), 127 participants completed the evaluation (usual-care group: n = 63; precision group: n = 64) (Fig. 1). The eligible participants were adult men and women aged 50–80 years old with BMI > 27 kg/m<sup>2</sup> (overweight grade 2/obesity class 1), who met at least one of the following risk factors: fasting glucose ≥100–≤125 mg/dL or type 2 diabetes (independently of antidiabetic medication) [14], hypertension (systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg or under antihypertensive medication) [15], LDL-cholesterol ≥160 mg/dL independently of lipid-lowering therapy [16], HDL-cholesterol ≤40 mg/dL (men)/≤50 mg/dL (women), independently of lipid-lowering therapy [20], triglycerides ≥150 mg/dL independently of lipid-lowering therapy [16], waist circumference >95 cm (men)/>82 cm (women) [17] or sedentary behaviour (AHA) [18]. Exclusion criteria included BMI ≤ 27 kg/m<sup>2</sup> and BMI ≥ 35 kg/m<sup>2</sup>, relevant functional or structural digestive abnormalities (malformations, angiodysplasia, active peptic ulcers, chronic inflammatory diseases, or malabsorption), endocrine disorders (hyperthyroidism or uncontrolled hypothyroidism), undergone surgical interventions with permanent sequelae (gastro-duodenostomy, bariatric surgery), active cancer in the last five years or under therapy, weight loss ≥3 kg and unstable drug therapy in the last three months before the start of the study. Other exclusion criteria included any severe psychiatric disorders, no autonomy, inability to follow the diet (food allergy, intolerances) as well as difficulties following scheduled visits.

AHA Recommendations for Physical Activity in Adults: at least 150 min per week of moderate-intensity aerobic activity or 75 min per week of vigorous aerobic activity, or a combination of both, preferably spread throughout the week.

### 2.2. Study design

The current research was a parallel-group, multicentre, randomized trial conducted in Spain to assess the effects of a personalised dietary intervention based on the inclusion of individualised foods and digital tools on general health status including anthropometry, body composition, general metabolic determinations, dietary intake, quality of life and gastrointestinal health, for preventing age-related chronic diseases in

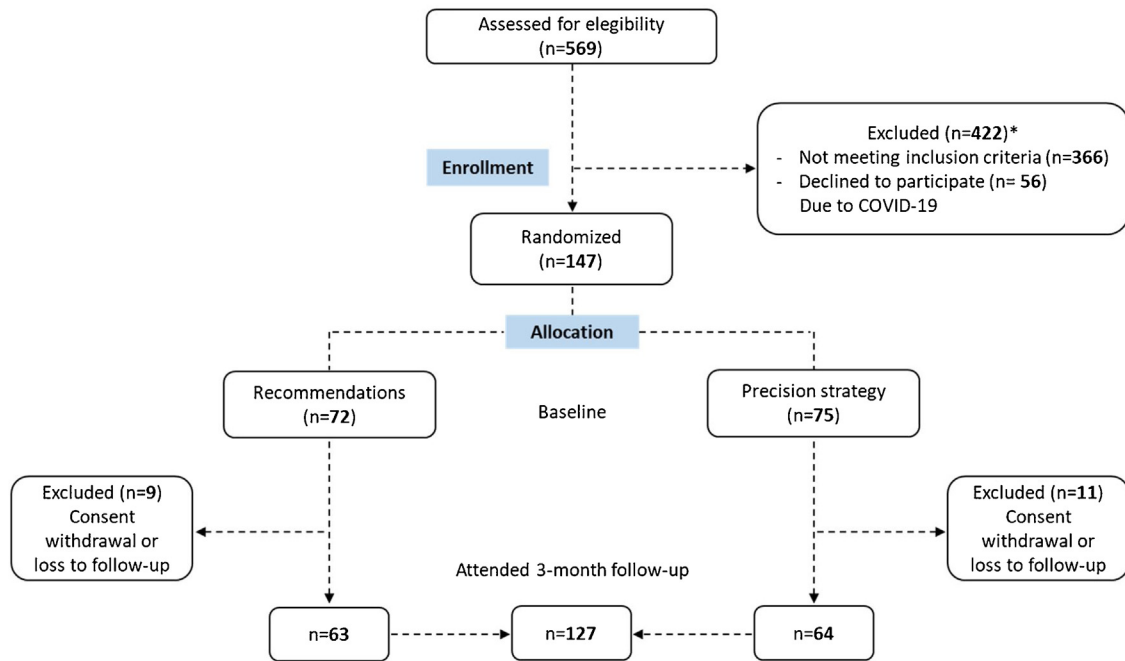


Fig. 1. Flowchart of the participants in the intervention study.

adults with overweight or obesity within a follow-up of 3 months. A total of five visits were established along with the 12-weeks trial. At the beginning and the end of the study, participants attended the Nutrition Intervention Unit or the Clinical Trials Unit in a fasting state. Blood samples were drawn by venipuncture after an 8–10 h overnight fast in a clinical setting. After 10 min of rest, blood pressure was measured. Later, anthropometric measurements and body fat analysis were performed. Volunteers were also informed of a mobile application designed and developed with the objective of empowering, motivating and supporting them in the management of the dietary strategy (Supplementary material 1). The dietitians gave the volunteers the information sheet and instructions of the app (content, different sections, etc.), and explained to them how it works, solving any doubts that volunteers might have (available only for the precision group).

Participants were also asked to fill different questionnaires about health status (SF-36 Health Survey), gastrointestinal symptoms (GSRs), dietary assessment (7-day recall), Mediterranean diet adherence (14-Item Mediterranean Diet Assessment Tool), physical activity (International Physical Activity Questionnaire, IPAQ) and drug therapy modifications. Moreover, the precision group were asked to collect a sensory perception questionnaire and a food consumption record of the individualised foods for the assessment of compliance at the beginning and after 3 months of study.

In the sensory perception questionnaire, five variables were evaluated: desire to eat the product, taste, smell, consistency, and effectiveness, on a scale from 0 to 100, where 0 corresponds to “no sensation” and 100 “maximum sensation”. Attending the food consumption record, participants were instructed to report the number of servings consumed per each test food. The degree of compliance (%) was calculated as number of servings consumed divided by the total number of recommended servings per 12 weeks. All precision products showed acceptable intake compliance, greater than 67%.

Study data were collected and managed using REDCap electronic data capture tools hosted at (UPM) [19,20].

Apart from the baseline and the endpoint visits, participants in the usual-care group attended online group sessions, conducted by a pharmacist and nutritionist, due to the COVID-19 pandemic. Sessions consisted of informative talks about the prescribed dietary pattern, food label use, seasonal shopping lists, meal plans and recipes, and sleep

habits; encouraging them to follow the dietary strategy. Contrary, participants allocated to the precision group attended face-to-face visits with the dietitians to supervise the adherence to the diet, as well as to pick up the food products. Additionally, anthropometric, body fat percentage, and blood pressure measurements were assessed.

### 2.3. Dietary intervention

The study compared the effects of two dietary strategies: a diet based on the Spanish Society of Community Nutrition (SENC) dietary guidelines [21] and the precision diet, designed by the Centre for Nutrition Research and based on the inclusion of individualised foods and digital tools.

On the one hand, usual-care group follow a strategy based on the SENC dietary guidelines and its Pyramid of Healthy Eating, that included recommendations about food groups -whole grains, fruits, vegetables, healthy fats (olive oil), legumes, dairy products, fish, eggs, and lean meats-, serving sizes, frequency of consumption and practical tips for designing menus, among others. Participants were also strongly advised to use the Healthy Eating Plate (Harvard) [22] to structure and prepare the main meals (lunch and dinner). In this way, at least  $\frac{1}{2}$  of the plate should be composed of vegetables,  $\frac{1}{4}$  of lean protein, and  $\frac{1}{4}$  of low glycaemic index carbohydrates. The diet encouraged participants to eat 5 times/day (breakfast, lunch, dinner, and two snacks).

On the other hand, the precision group was instructed to follow a Mediterranean and mixed diet based on the inclusion of digital tools and individualised foods designed according to the particularities of the participants. This defined diet included specific guidelines to participants -specific foods, quantities, advise on the use of healthy culinary techniques (steamed, safe raw preparations or less processed foods), etc.- and has a conventionally balanced distribution of macronutrients: 50% of the total caloric value from carbohydrates, 20% from proteins, and 30% from lipids. The diet included whole grains, legumes, fruits, vegetables, and unsaturated fatty acids- extra virgin olive oil and omega-3 fatty acids (fatty fishes and nuts). individualised foods consisted of a variety of main meals, snacks and desserts, and were a) smoothie, b) fruit compote, c) extruded meat product, d) wholemeal bread, e) wholemeal biscuit, and f) microwavable deep-frozen vegetable products (Table 1). Meal plan involved eating 5 times/day (breakfast, lunch, dinner, and two snacks — (Supplementary Table 1).

**Table 1**  
Composition of the functional foods.

| Composition          | Smoothie | Fruit compote | Extruded meat | Wholemeal bread | Wholemeal biscuit | Microwaveable deep-frozen vegetable dishes* |      |      |       |       |
|----------------------|----------|---------------|---------------|-----------------|-------------------|---------------------------------------------|------|------|-------|-------|
|                      |          |               |               |                 |                   | HTA                                         | GH   | BH   | VH    | OB/DM |
| Energy intake (kcal) | 21       | 63.5          | 188           | 225             | 435               | 111                                         | 128  | 117  | 105.5 | 85    |
| CHO (g)              | 4.9      | 13            | 7.6           | 41.3            | 66                | 11.8                                        | 16.2 | 12.3 | 14.9  | 10    |
| Fiber (g)            | 1.6      | 4.7           | 9.3           | 3.7             | 7.9               | 5.8                                         | 5    | 8.5  | 2.9   | 5.7   |
| Sugars (g)           | 4.9      | 6.4           | 4.5           | 2.6             | 21                | 2.4                                         | 1.4  | 2    | 5.2   | 1.6   |
| Protein (g)          | 4.0      | 0.2           | 18.4          | 9.2             | 7.3               | 7.1                                         | 6.8  | 6.5  | 4.4   | 3.9   |
| Lipids (g)           | 0.0      | 0.2           | 9.4           | 1.7             | 14.0              | 2.7                                         | 3.4  | 3.2  | 3.1   | 2.5   |
| SFA (g)              | 0.0      | <0.1          | 3.6           | 0.3             | 1.6               | 0.4                                         | 0.6  | 0.5  | 0.5   | 0.4   |
| MUFA (g)             | 0.0      | <0.1          | 4.2           | 0.7             | 10.0              | 1.9                                         | 2.1  | 1.8  | 1.7   | 1.7   |
| PUFA (g)             | 0.0      | <0.1          | 1.5           | 0.7             | 2.4               | 0.6                                         | 0.7  | 0.9  | 0.9   | 0.4   |
| Na (mg)              | 0.0      | 62.5          | 500           | 526             | 160               | 61                                          | 210  | 161  | 126   | 58    |

The nutritional information is reported per 100 g. Abbreviations: CHO: Carbohydrates; MUFA: Monounsaturated Fatty Acids; Na: Sodium; PUFA: Polyunsaturated Fatty Acids; SFA: Saturated fatty acids. \*Microwaveable deep-frozen vegetable products designed for the management of BH: Bone Health; GH: Gastrointestinal Health; HTA: hypertension; OB/DM: Obesity/Diabetes; VH: Visual Health.

Caloric needs were not established in participants allocated to the usual-care group. While energy requirements of participants allocated in the precision group were calculated using the Harris Benedict formula. To avoid an overestimate of caloric intake (all participants with overweight or obesity class 1), caloric needs were adjusted considering a BMI of 25 kg/m<sup>2</sup>/corrected weight, instead of their real weight. The physical activity factor considered was 1.2, as the studied population was quite sedentary. In exceptional cases where individuals engaged in a high level of physical activity, this value was adjusted.

Regarding physical activity, both usual-care and precision groups were instructed to continue with their usual physical activity during the intervention.

The individualised products were designed and developed specifically for this study, aimed at effective prevention of age-related diseases, improving the quality of life of aging population, channeling the recent high-level scientific advances to society, and helping to reduce health costs associated with aging. Different food industries designed and developed the individualised foods tested in the present project. AMC Innova Juice and Drinks S.L. supplied the smoothie evaluated in the study; Iberfruta Muerza, S.A provided the fruit compote; the extruded meat product was supplied by Hijo de José Martínez Somalo, S.L; Europastry, S. A. developed the wholemeal bread; Galletas Gullón, S.A. provided the wholemeal biscuit, and finally Congelados de Navarra, S.A designed and supplied the microwaveable deep-frozen vegetable dishes. The analytical characterization of the test foods was determined by CNTA (Spain) or Eolisa Laboratorios (Zaragoza, Spain), when corresponding.

#### 2.4. Anthropometrics, body composition and blood pressure measurements

Body weight (kg) and height (cm) were measured in light clothing and without shoes using a calibrated scale and a wall-mounted stadiometer, respectively [23]. Waist circumference (cm) was measured midway between the lowest rib and the iliac crest using a measuring tape. Waist-hip ratio (WHR) was calculated by dividing the waist circumference by the hip circumference. BMI was calculated as weight (kg) divided by the square of height (m) [24]. Body fat percentage was assessed by bioimpedance analysis (BIA) (UNAV: SC-330, Tanita, Tokyo, Japan; IMDEA: BF511-OMRON HEALTHCARE UK, LT, Kyoto, Japan). Blood pressure was measured with the use of an automatic monitor device following WHO criteria [25] (UNAV: Intelli Sense. M6, OMRON Healthcare, Hoofddorp, The Netherlands; IMDEA: OMRON Healthcare UK, LT, Kyoto, Japan).

#### 2.5. Biochemical assessment

Blood samples were collected at baseline and after 3 months of intervention after 8–10 h overnight fast. The blood samples were

processed (15 min; 3500 rpm; 5 °C) at the Centre for Nutrition Research (University of Navarra) or at the laboratory Unilabs.

The biochemical analyses included glucose (mg/dL), HbA1c (%), TC (mg/dL), HDL-c (mg/dL), TG (mg/dL), uric acid (mg/dL), alanine aminotransferase (ALT, mg/dL) and aspartate aminotransferase (AST, mg/dL) levels, which were measured by specific calorimetric assays in an autoanalyser Pentra C200 (Horiba ABX Diagnostics, Montpellier, France). The LDL-c levels were calculated using the Friedewald formula [26]: LDL-c = TC – HDL-c – TG/5. The hepatic steatosis index (HSI) was also assessed using the following formula: HSI = 8 × ALT/AST ratio + BMI (+ 2, if diabetes; + 2, if female) [27].

#### 2.6. Lifestyle assessment: diet and physical activity variables

Dietary intake was assessed with a 7-day validated food-recall questionnaire at the end of the study period. These questionnaires were analysed using Nutrium<sup>®</sup> software (Braga, Portugal), with data from accepted Spanish food composition tables (CESNID, BEDCA). Additionally, the precision group had to record the consumption of the tested foods using a notebook to further evaluate the adherence to meal consumption as well as a sensory perception questionnaire.

The Mediterranean dietary pattern was calculated using a validated 14-point Mediterranean dietary score, considering the habitual frequency of consumption or amount consumed of 12 main components of the Mediterranean diet and two food habits related to the Mediterranean diet (cereals, fruits and nuts, vegetables, legumes, fish, meat, dairy products, ratio of monounsaturated to saturated fatty acids, and alcohol). Each of the 14 items is scored 1 or 0, depending on whether participants adhere to each Mediterranean diet component or not. The final score ranged from 0 to 14 and a higher score indicates a better adherence to the Mediterranean diet [28].

Physical activity was evaluated with the validated Spanish version of the International Physical Activity Questionnaire short form (IPAQ-SF). The short form records the activity of four intensity levels during the last 7 days: 1) vigorous-intensity activity such as aerobics, 2) moderate-intensity activity such as leisure cycling, 3) walking, and 4) sitting [29].

#### 2.7. Digital tools

Digital tools were included in the precision strategy to empower and motivate target population and to support them in the management of the dietary strategy.

The app was specifically designed and developed for this study, based on the particularities of older adults. For this reason, it was easily accessible, easy to learn and to use, representing a clear benefit to them and fit with their goals, expectations, and lifestyles.

Volunteers received the information sheet of the application in Spanish. Participants accessed the application using a specific link (bit.ly/

appnutriprecision) through a mobile device, a tablet, or a computer. The app contained different sections of interest: the assigned diet, agenda (follow-up visits, motivational messages and library (documents/recommendations).

Some examples of motivational messages: Consume more and a higher variety of vegetables. The diversity of colours and textures provides antioxidants and protective substances //Choose low-processed, fresh, and seasonal foods.// Our body is made up of over 70% water. Maintaining adequate hydration is necessary at all stages of life.

## 2.8. Health and cognitive assessment

Health status was evaluated using the Spanish version of the short form 36 health survey questionnaire (SF-36) [30]. The SF-36 questionnaire is a self-administered questionnaire containing 36 items, which measures health on eight multi-item dimensions: physical functioning, physical role limitations, bodily pain, general health perceptions, vitality, social functioning, emotional role limitations and mental health. A scoring algorithm is used to convert the raw scores into the eight dimensions. The scores are transformed to range from zero (worst possible health) to 100 (best possible health).

For assessing the cognitive function, we included the Mini mental state examination (MMSE) questionnaire, which is an 11-items questionnaire that measures five areas of cognitive function: orientation, registration, attention and calculation, recall, and language.

## 2.9. Gastrointestinal health assessment

Gastrointestinal health was assessed by the GSRS [31]. The GSRS is a self-reported questionnaire of 15 items combined into five symptom clusters depicting reflux, abdominal pain, indigestion, diarrhoea and constipation. The GSRS has a seven-point graded Likert-type scale where

1 represents the absence of troublesome symptoms and 7 represents very troublesome symptoms [32].

## 2.10. Statistical procedures

The sample size calculation was obtained considering the “a priori” metabolic health score as the primary outcome. The difference expected in the score between dietary groups was of 0.5 points  $\pm$ 0.75 with a 95% confidence interval ( $\alpha = 0.05$ ) and a statistical power of 80% ( $\beta = 0.8$ ). A total of 50 participants per study group were estimated with this approach, but 70 subjects were included in each arm of the study, considering an estimated drop-out rate of 20–30% according to the previous experience of the research group. Randomization was conducted by stratifying according to sex and age, and through Excel function RANDOM.BETWEEN.

Normality of variables was initially studied by using the Shapiro–Wilk test. Data were expressed as a mean  $\pm$  standard deviation for continuous traits and percentage for categorical variables. Comparisons between two independent groups were performed using Student’s *t*-test and Mann–Whitney *U* test for normal and non-normal distribution, respectively. Comparisons between two dependent groups were determined using Student’s *t*-test normal distribution and Wilcoxon signed-rank test for non-normal distribution. If the variables were qualitative, differences in the frequency distribution among groups were assessed by means of Chi-square test (Contingency  $R \times C$ , for independent samples) or Fisher’s exact test (Contingency  $2 \times 2$ , for independent samples). Correlations were assessed using Pearson for normal distribution or the nonparametric counterpart test (Spearman) for not normal distribution. Simple or multivariable linear regressions were performed for normally distributed data and quantile regression were employed for non-normal distribution.

The software used for statistical analysis was Stata versions 12.1 or 14.0 (StataCorp, College Station, TX, USA) and GraphPad Prism 6 (GraphPad Software, San Diego, CA, USA).

**Table 2**

Characteristics at baseline and after 3 months of dietary intervention in the study participants according to the group.

| Characteristics                         | Recommendations           |                           | <i>p</i> -Value <sup>a</sup> | Precision strategy        |                           | <i>p</i> -Value <sup>a</sup> | Baseline <i>p</i> -Value <sup>b</sup> | $\Delta$ <i>p</i> -Value <sup>c</sup> |
|-----------------------------------------|---------------------------|---------------------------|------------------------------|---------------------------|---------------------------|------------------------------|---------------------------------------|---------------------------------------|
|                                         | Baseline ( <i>n</i> = 72) | 3 months ( <i>n</i> = 63) |                              | Baseline ( <i>n</i> = 75) | 3 months ( <i>n</i> = 64) |                              |                                       |                                       |
| Age (years old)                         | 57 (54; 61)               |                           | –                            | 58 (54; 63)               |                           | –                            | 0.404                                 | –                                     |
| <65                                     | 62                        |                           |                              | 60                        |                           |                              |                                       |                                       |
| $\geq$ 65                               | 10                        |                           |                              | 15                        |                           |                              |                                       |                                       |
| Sex (men/women)                         | 31/41                     |                           | –                            | 31/44                     |                           | –                            | 0.743 <sup>c</sup>                    | –                                     |
| Total PA - IPAQ-SF score (MET-min/week) | 1785 (792; 2373)          | 1857 (1039; 2626)         | 0.408                        | 1114 (693; 2415)          | 1386 (693; 2383)          | 0.712                        | 0.329                                 | 0.637                                 |
| Anthropometry and body composition      |                           |                           |                              |                           |                           |                              |                                       |                                       |
| Weight (kg)                             | 87 (79; 95)               | 86.8 (77; 92)             | <0.001                       | 81.9 (76; 94)             | 77.7 (72; 89)             | <0.001                       | 0.168                                 | <0.001                                |
| BMI (kg/m <sup>2</sup> )                | 31.2 (29; 34)             | 30.6 (29; 33)             | <0.001                       | 31.1 (29; 33)             | 29.6 (28; 31)             | <0.001                       | 0.643                                 | <0.001                                |
| Waist circumference (cm)                | 102.8 (11)                | 102.2 (11)                | 0.160                        | 104.9 (9)                 | 99.4 (9)                  | <0.001                       | 0.287                                 | <0.001                                |
| WHR                                     | 0.97 (0.1)                | 0.98 (0.1)                | 0.208                        | 1.0 (0.07)                | 0.97 (0.08)               | <0.001                       | 0.103                                 | <0.001                                |
| Body fat percentage (%)                 | 37.2 (32; 45)             | 38.5 (33; 45)             | 0.417                        | 39.1 (31; 44)             | 38 (29; 42)               | <0.001                       | 0.868                                 | <0.001                                |
| SBP (mmHg)                              | 130 (118; 142)            | 130 (119; 145)            | 0.923                        | 132 (121; 144)            | 128 (119; 139)            | 0.006                        | 0.375                                 | 0.042                                 |
| DBP (mmHg)                              | 81 (77; 90)               | 82 (74; 87)               | 0.011                        | 85 (81; 90)               | 79 (73; 85)               | <0.001                       | 0.052                                 | <0.001                                |
| Biochemical parameters                  |                           |                           |                              |                           |                           |                              |                                       |                                       |
| Total cholesterol (mg/dL)               | 221.4 (49)                | 213.4 (44)                | 0.072                        | 223.5 (40)                | 211.6 (41)                | <0.001                       | 0.946                                 | 0.327                                 |
| LDL cholesterol (mg/dL)                 | 140.4 (43)                | 138.5 (42)                | 0.580                        | 142.7 (36)                | 140.4 (37)                | 0.384                        | 0.969                                 | 0.939                                 |
| HDL cholesterol (mg/dL)                 | 49.4 (42; 62)             | 50.4 (43; 59)             | 0.307                        | 52.5 (42; 62)             | 47.0 (42; 55)             | <0.001                       | 0.427                                 | 0.004                                 |
| Triglycerides (mg/dL)                   | 108.5 (86; 184)           | 102 (79; 154)             | 0.001                        | 111 (88; 147)             | 101 (78; 131)             | 0.005                        | 0.602                                 | 0.484                                 |
| HbA1c (%)                               | 5.7 (5.4; 6)              | 5.6 (5.4; 5.9)            | 0.169                        | 5.7 (5.4; 6)              | 5.5 (5.4; 5.7)            | <0.001                       | 0.988                                 | <0.001                                |
| Uric acid (mg/dL)                       | 5.5 (4.9; 6.4)            | 5.3 (4.7; 6.1)            | 0.001                        | 5.5 (4.6; 6.3)            | 5.2 (4.4; 6)              | <0.001                       | 0.630                                 | 0.272                                 |
| ALT (IU/L)                              | 23.6 (19; 29)             | 25 (19; 33)               | 0.043                        | 23.2 (19; 37)             | 22.9 (17; 28)             | 0.023                        | 0.356                                 | 0.002                                 |
| AST (IU/L)                              | 21.7 (19; 26)             | 22.7 (21; 26)             | 0.007                        | 23.9 (19; 30)             | 23 (19; 26)               | 0.065                        | 0.041                                 | 0.002                                 |
| HSI (arbitrary units)                   | 41.0 (38; 46)             | 40.7 (38; 45)             | 0.229                        | 41.0 (38; 45)             | 38.4 (36; 42)             | <0.001                       | 0.758                                 | <0.001                                |

Data are presented as the mean (SD) for normally distributed data or the median (interquartile range) for non-normal distribution. Abbreviations: ALT: alanine aminotransferase; AST: aspartate aminotransferase; BMI: body mass index; DBP: diastolic blood pressure; GGT: gamma-glutamyltransferase; HbA1c: glycosylated hemoglobin; HDL: high density lipoprotein; HOMA-IR: homeostasis model assessment-insulin resistance; IPAQ-SF: International Physical Activity Questionnaire; LDL: low density lipoprotein; MET: metabolic equivalent task; PA: physical activity; SBP: systolic blood pressure; WHR: waist-hip ratio. <sup>a</sup>Comparison within dietary groups (baseline and after 3 months). <sup>b</sup>Baseline differences between the recommendations and precision strategy. <sup>c</sup>Comparison of changes (baseline and 3 months) between the recommendations and precision strategy. <sup>e</sup>Chi-squared test for baseline differences between the recommendations and precision strategy.

### 3. Results

Participants were categorized according to the assigned group (standard recommendations vs precision strategy). Table 2 provides an overview of anthropometric data and body fat percentage. Both dietary strategies revealed a significant reduction in body weight, BMI, and diastolic blood pressure after 3 months of study ( $p < 0.001$  for all comparisons). The precision group also achieved lower waist circumference ( $p < 0.001$ ), WHR ( $p < 0.001$ ), and systolic blood pressure ( $p < 0.01$ ) after 3-months compared to the usual-care group. Furthermore, the changes in body weight ( $p < 0.001$ ), BMI ( $p < 0.001$ ), waist circumference ( $p < 0.001$ ), WHR ( $p < 0.001$ ), fat mass ( $p < 0.001$ ) and both systolic ( $p < 0.05$ ) and diastolic blood pressure ( $p < 0.001$ ) were significantly greater in the precision group compared with the usual-care group. No differences in age, sex, and physical activity were found between groups (Table 2).

Regarding the biochemical parameters (Table 2), both groups showed significant improvements in triglyceride and uric acid concentrations, with no significant differences detected between groups. Total cholesterol and HDL-c levels significantly decreased in the precision group after 3 months ( $p < 0.001$ ), however, HDL-c reduction was slight and not clinically relevant [33]. The precision strategy achieved a significant reduction in HbA1c ( $p < 0.001$ ), ALT ( $p < 0.01$ ), AST ( $p < 0.001$ ) and HSI values ( $p < 0.001$ ). Moreover, the changes from baseline to 3 months of intervention for all these variables were significantly higher in the precision group compared to the usual-care group.

No significant differences were observed in total energy intake at 3-months between both groups. Percentages of carbohydrates and proteins, as well as fibre content, were significantly greater in the precision group, while the percentage of lipids was significantly lower. The precision group exhibited significantly lower sodium consumption while sugar intake was significantly higher than the usual-care group ( $p < 0.001$ ).

Notably, the adherence to the Mediterranean diet significantly increased in both groups after 3 months of intervention, but no significant differences were observed between them. No differences at baseline in the adherence to the Mediterranean diet were also observed.

Regarding the results obtained from the *a priori* metabolic health score, both usual-care and precision groups significantly reduced the whole punctuation of the score after 3 months of intervention, achieving a better metabolic health, although no significant differences were found between groups.

The quality of life of the precision group (SF-36) significantly increased after the 3-month study, with significant differences between strategies (Table 3). Regarding specific dimensions of SF-36, both groups significantly increased general health and physical function. In addition,

**Table 3**

Quality of life at baseline and after 3 months of dietary intervention in the study participants according to the group.

| Characteristics            | Recommendations           |                           |                              | Precision strategy        |                           |                              | Baseline <i>p</i> -Value <sup>b</sup> | $\Delta$ <i>p</i> -Value <sup>c</sup> |
|----------------------------|---------------------------|---------------------------|------------------------------|---------------------------|---------------------------|------------------------------|---------------------------------------|---------------------------------------|
|                            | Baseline ( <i>n</i> = 72) | 3 months ( <i>n</i> = 63) | <i>p</i> -Value <sup>a</sup> | Baseline ( <i>n</i> = 75) | 3 months ( <i>n</i> = 64) | <i>p</i> -Value <sup>a</sup> |                                       |                                       |
| Quality of life            |                           |                           |                              |                           |                           |                              |                                       |                                       |
| Total SF-36 score (points) | 83.2 (74; 88)             | 83.9 (73; 89)             | 0.656                        | 81 (69; 88)               | 83.8 (78; 88)             | <0.001                       | 0.323                                 | 0.041                                 |
| SF-36 domains              |                           |                           |                              |                           |                           |                              |                                       |                                       |
| General health             | 65 (50; 75)               | 65 (55; 75)               | <0.001                       | 70 (50; 80)               | 72.5 (60; 85)             | <0.001                       | 0.367                                 | 0.300                                 |
| Physical functioning       | 90 (80; 95)               | 90 (85; 100)              | 0.009                        | 90 (80; 95)               | 90 (85; 100)              | 0.005                        | 0.414                                 | 0.870                                 |
| Role physical              | 89.9 (28)                 | 89.1 (28)                 | 0.816                        | 87.9 (29)                 | 93 (21)                   | 0.216                        | 0.288                                 | 0.398                                 |
| Role emotional             | 87.6 (28)                 | 86.6 (30)                 | 0.614                        | 82.3 (33)                 | 91.7 (20)                 | 0.024                        | 0.072                                 | 0.041                                 |
| Social functioning         | 89.1 (15)                 | 86.1 (22)                 | 0.217                        | 89.4 (16)                 | 91.0 (16)                 | 0.251                        | 0.588                                 | 0.092                                 |
| Bodily pain                | 80 (60; 100)              | 80 (67; 100)              | 0.465                        | 80 (57; 100)              | 80 (70; 100)              | 0.031                        | 0.707                                 | 0.344                                 |
| Vitality                   | 65 (50; 75)               | 65 (55; 80)               | 0.441                        | 60 (45; 65)               | 70 (57; 77)               | 0.008                        | 0.280                                 | 0.206                                 |
| Mental health              | 76 (68; 84)               | 76 (68; 84)               | 0.890                        | 76 (60; 88)               | 76 (68; 84)               | 0.809                        | 0.726                                 | 0.949                                 |

Data are presented as the mean (SD) for normally distributed data or the median (interquartile range) for non-normal distribution. Abbreviations: SF-36: Short-Form 36 Health Survey. <sup>a</sup>Comparison within dietary groups (baseline and after 3 months). <sup>b</sup>Baseline differences between the recommendations and precision strategy. <sup>c</sup>Comparison of changes (baseline and 3 months) between the recommendations and precision strategy. <sup>e</sup>Chi-squared test for baseline differences between the recommendations and precision strategy.

**Table 4**

Correlation analysis between the change in SF-36 — emotional role, vitality — and health variables.

| $\Delta$ SF-36 – Dimensions                       |          |          |
|---------------------------------------------------|----------|----------|
|                                                   | <i>r</i> | <i>p</i> |
| <b><math>\Delta</math> SF-36 – Emotional Role</b> |          |          |
| $\Delta$ BMI (kg/m <sup>2</sup> )                 | -0.148   | 0.097    |
| $\Delta$ Waist circumference (cm)                 | -0.191   | 0.032    |
| $\Delta$ WHR                                      | -0.183   | 0.040    |
| <b><math>\Delta</math> SF-36 – Vitality</b>       |          |          |
| $\Delta$ Waist circumference (cm)                 | -0.225   | 0.011    |
| $\Delta$ WHR                                      | -0.278   | 0.002    |
| $\Delta$ Body fat percentage (%)                  | -0.195   | 0.031    |
| $\Delta$ Mediterranean diet score (points)        | 0.227    | 0.011    |
| 3-month CHO (%)                                   | 0.165    | 0.082    |
| 3-month Sugars (%)                                | 0.203    | 0.031    |
| 3-month Fats (%)                                  | -0.194   | 0.040    |
| 3-month SFA (%)                                   | -0.254   | 0.007    |

Abbreviations: BMI: body mass index; CHO: carbohydrates; SFA: saturated fatty acids; WHR; waist-hip ratio.

the precision group showed significant improvements in vitality, body pain and emotional role. The change from baseline to 3 months of intervention for the emotional role was significantly greater in the precision group. In the correlation analysis, significant associations were found between the change observed in the whole SF-36 punctuation and changes registered in the Mediterranean diet adherence score and body fat percentage. Thus, to further explore the relationships between the changes in SF-36 score and health variables, regression analysis was performed. Variables that individually were significantly associated with the change in the SF-36 were the adherence to the Mediterranean diet and the WHR. After adjusting for potential confounders (group of intervention, centre, age, and sex), Mediterranean diet adherence and WHR explained up to 10.9% of the variation in the change of SF-36 (Adjusted R<sup>2</sup> = 0.109; *p*-model = 0.003).

When specific dimensions of SF-36 were assessed, potential associations of emotional well-being and vitality with metabolic health variables were found (Table 4). Improvements in emotional status were significantly correlated with reductions in waist circumference and WHR (Table 4). When analysing vitality, significant negative associations with the changes in waist circumference, WHR and body fat percentage were found. Concerning dietary factors, improvements in vitality were significantly correlated with lower fat and saturated fatty acids and increased Mediterranean diet score and sugar intake (Table 4).

The acceptability and compliance of the food intake were positive after 3-months of intervention: a) smoothie: 76.9%; b) fruit compote:

68.6%; c) extruded meat product: 76.7% d) wholemeal bread: 73.2%; e) wholemeal biscuit: 81.6% and f) microwaveable deep-frozen vegetable products, designed for hypertension management: 98.3%; gastrointestinal health: 93.3%; bone health: 90%; visual health: 100%; obesity/diabetes: 67.5%.

Regarding the gastrointestinal health, the precision group reported a significant reduction in hunger pangs at 3 months of intervention, without notable differences between groups. The precision group also showed a greater reduction in belching, with significant differences compared with the usual-care group.

It is important to mention that all analyses were also stratified according to intervention site in order to explore possible differences between them. No differences were observed in the studied variables and analyses were conducted considering all data without stratification.

#### 4. Discussion/conclusion

The major findings of this investigation were that the precision strategy, a mixed, balanced, and moderated diet designed in combination with individualised foods and digital tools, showed an improvement in quality of life, mainly based on better emotional well-being and vitality, which were associated to improvements in anthropometry and metabolic health as well as to higher adherence to the Mediterranean diet score during a period of 3 months.

##### 4.1. Impact of the intervention on metabolic health

The present research proposes a personalised dietary strategy based on the inclusion of novel individualised foods and digital tools, designed considering the specific requirements of older populations, enhancing the quality of life and general well-being. The precision group exhibited key metabolic improvements in weight loss, blood pressure, glycemic control, hepatic health and other cardiometabolic risk factors, compared with the recommendations based on the SENC dietary guidelines. Overweight/obesity, elevated blood pressure or raised HbA1c and transaminase levels are metabolic risk factors that can potentially lead to cardiovascular disease, diabetes, NAFLD condition or other age-related chronic diseases [34]. In addition, aging remains the single largest risk factor for heart attacks, stroke, diabetes, and most chronic diseases [35]. The proposed strategy contributes to improvements or reduced risk of metabolic disturbances.

Age-related changes in body fat distribution and metabolism lead to a low grade, chronic inflammatory state, called inflammaging, which contributes to the pathogenesis of chronic diseases [36]. Although the metabolic health score was designed *a priori* for the study, and needs to be validated, it helps to understand how the changes occur and a global vision of the nutritional status of the studied population. In the present study, uric acid was determined to evaluate the possible anti-inflammatory effects of the nutritional strategies. In both groups, lower uric acid concentrations were detected after 3 months of intervention. Both strategies may therefore lead to modulate the pro-inflammatory environment in aging. Although the precision strategy achieved a greater reduction in body weight, which does improve inflammation [37], no significant differences in uric acid levels were found between groups. The analyses of other inflammatory biomarkers could be done to better understand the possible anti-inflammatory mechanisms of these diets.

##### 4.2. Characteristics of the intervention: dietary traits and digital tools

The precision diet is characterized by an adequate macronutrient distribution. It is also a high-fibre approach (most individualised foods are rich in this macronutrient), and lipids come mainly from olive oil and omega-3 fatty acids. However, sugar intake was significantly higher in comparison with the usual-care group. The precision group is found to consume 20.5% of total calories from total sugars (sum of free sugars,

intrinsic sugars from fruit and vegetables and milk sugars). We do not have the data of free sugars, but most of the sugars found in the diet come from fruit, vegetables, and dairy products. WHO recommends reducing free sugar intake at all stages of life to under 10 percentage of total energy [38]. No recommendations have been stated for total sugars as there is no reported evidence of adverse effects of consumption of intrinsic sugars and sugars naturally present in milk. Our results did not show negative effects of total sugar intake in glucose metabolism of participants allocated to the precision group. Indeed, those participants significantly decreased HbA1c concentrations after 3 months of intervention. Fibre and interactions with other nutrients could positively influence the regulation of glucose homeostasis and metabolism [39].

As a novelty, our study was focused on innovative individualised foods with specific bioactive compounds, particularly designed for older adults to cover their specific nutrient requirements. Interestingly, promising strategies dealing with the incorporation of enriched foods in the diet were successfully initiated. In this context, Berasategi et al., demonstrated improvements in the nutrient profile after incorporating selected functional foods enriched in fibre, calcium, iodine, fat-soluble vitamins, and omega-3 fatty acids in the diet [40].

The implementation of a mobile health application also encouraged an active and healthy lifestyle and helped to follow the dietary strategy assigned [13]. The app was specifically designed based on the particularities of older adults. It was easily accessible, easy to learn and to use. During the study, volunteers did not have any problem using the app. Thus, the use of the app allowed a better personalization, monitoring and even enhance motivation in the subjects. These strategies enable to create new precision nutritional approaches and maximize the degree of individualization.

##### 4.3. Impact of the intervention on quality of life

Maintaining or improving quality of life and well-being is a global goal across the lifespan. Despite the complex health conditions and needs associated with aging, very little was found in the literature on the association between dietary patterns and quality of life in older adults [41,42]. This study confirms that participants allocated to the precision group showed improved quality of life after a 3-month intervention, with significant differences between both strategies. Particularly, the precision group showed significant improvements in vitality and emotional role. Our study population presented a good quality of life (whole SF-36 punctuation >80 points). When comparing our results with normative data for adults aged 55–64 years provided by Jenkinson et al., we reported slightly higher punctuations on all variables of the SF-36 [43]. Similar results were found in our study in comparison to normative data reported by López-García et al. in Spanish adults aged over 60 years [44]. These results are of great importance and have more relevance since the COVID-19 pandemic has a severe impact on emotional status and mental health among the older population [45]. Integrative and personalised strategies as the one proposed in the present study could be effective for enhancing physical, mental, emotional, and immune resilience, well-being and general health status of the older population.

##### 4.4. Association between quality of life and Mediterranean diet

Notably, the results of this study indicate that Mediterranean diet adherence significantly correlated with the adults' quality of life, with additional associations with emotional well-being and vitality. These results were in line with previous studies that found associations of the Mediterranean diet with improved health, longevity, vitality, and reductions in all-cause mortality risk, obesity, diabetes, NAFLD and cardiovascular events [46]. Interestingly, Milte et al. showed improved emotional well-being in women with high-quality diets (dietary guideline index, recommended food score) [42]. The underlying mechanisms for these beneficial effects are likely to be various, including its antioxidant

and anti-inflammatory properties due to omega-3 fatty acids, B vitamins and polyphenols, among others [47,48].

Promoting healthy aging by tailoring nutritional guidance based on the specific person's characteristics is an emerging science that has great promise. Functional-food-based strategies hold significant potential for providing health benefits for the elderly, but additional research is needed to know the potential of precision foods on healthy and active aging avoiding the risk of diseases. Although precision nutrition is still at the preliminary validation stage, by integrating the omics technologies with big data techniques, it will have the potential to provide personalised nutrition guidance for more effective prevention and management of chronic diseases [49].

#### 4.5. Limitations and strengths

Some limitations should be acknowledged concerning this investigation. First, dietary intake of participants was not assessed at baseline, although adherence to the Mediterranean diet was evaluated. Second, nutritional information and other data come from self-reported questionnaires and thus, the results are susceptible to possible bias. Third, the sample size is relatively low, but the results are plausible. Fourth, the isolated effect of the mobile application could not be evaluated in this study. Instead, the combined effects of the mobile application and the diet based on function foods have been investigated. Fifth, the precision diet was adjusted to a BMI of 25 kg/m<sup>2</sup> to avoid an overestimation of the caloric intake. No total caloric restriction was advised in the usual-care group, although participants were strongly advised to use the Healthy Eating Plate, to control the portion size. Sixth, a double-blind design was not possible to conduct due to type of intervention. Instead, we employed alternative strategies to control for biases and strengthen the validity of our findings including the random assignment, control for confounding variables, the use of the control group and standardized protocols. Seventh, face-to-face group sessions were proposed in the usual-care group. However, due to the COVID-19 breakout, additional measures have to be taken. We had to shift the in-person visits to online meetings as much as possible. In this context, different studies were conducted to test the effectiveness and/or possibilities of telemedicine during the COVID-19 pandemic, suggesting that remote consultation in the nutrition practice is feasible and may result in better clinical care, complementing the traditional model [50,51].

On the other hand, some strengths should be mentioned. First, all questionnaires were revised by qualified dietitians in order to diminish possible fill-in errors. Second, it is a randomized parallel controlled trial, considered to be the gold standard for evaluating the efficacy and safety of dietary interventions. Additionally, the effectiveness of our intervention, consisted of a personalised diet including individualised foods, a mobile application and individual follow-ups that tended to promote long term behavioural changes and a healthy lifestyle.

#### 4.6. Conclusion

In conclusion, the precision strategy, a personalised diet based on the inclusion of individualised foods and specific digital tools, was able to enhance the quality of life and emotional well-being, with additional improvements in body composition and general metabolic health in older adults with overweight/obesity, compared to standard recommendations. These results support the benefit of precision nutrition approaches for promoting healthy aging, enhancing the quality of life of adults during a specific period of time such as the COVID-19 pandemic.

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#### Statement of ethics

This study was properly registered at the Clinicaltrials.gov with identifier NCT04786925 (registration date 5 March 2021). The trial was approved by the Research Ethics Committee of the University of Navarra (ref. 2019.183) and IMDEA-ALIMENTACIÓN (ref. IMD PI-039). Procedures were performed in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki). All participants gave written informed consent prior to the inclusion in the trial.

#### Conflict of interest statement

Navas-Carretero, Santiago reports financial support was provided by Centre for the Development of Industrial Technology. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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#### Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.jnha.2024.100289>.

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