Date to submit: 08-07-2025

Functional Epigenetic Optimization through Biofrequency-Guided Nutrition: Protocol for a Randomized Controlled Trial

Abstract

Background: Biomarker-based nutrition has demonstrated superior efficacy compared to population-level approaches in improving health outcomes. Biofrequency analysis, a non-invasive technique based on the detection of electromagnetic vibrational patterns in hair follicles, offers a promising avenue for rapid functional assessment of nutritional status and epigenetic signals without reliance on blood or urine sampling. **Objective:** First, to evaluate the effect of a 90-day biofrequency-guided nutritional intervention on functional epigenetic status, as reflected in changes in the optimization report generated by the S-Drive system; second, to assess changes in adherence to the Mediterranean diet, anthropometric indicators, movement behaviors, and psychological well-being. **Methods:** In this randomized controlled trial, 154 adults from the *Grupo Alcaraz Sport Association* (Region of Murcia, Spain) will be allocated to an experimental group receiving individualized lifestyle recommendations based on S-Drive biofrequency analysis and to a control group with no intervention. Participants in the experimental arm will apply tailored dietary guidance over 90 days. **Conclusion:** This study will generate foundational evidence on the utility of biofrequency technology for precision nutrition. If positive, the findings may inform scalable, low-risk strategies for personalized dietary interventions in preventive and community health settings.

Keywords: Biofrequency analysis, biomarker-based nutrition, dietary habits, mediterranean diet, nutritional biomarkers, nutritional intervention, young athletes

1. Introduction

Biomarker-based nutrition has emerged as a key strategy in the preventive and therapeutic management of non-communicable chronic diseases (NCDs), as it enables interventions guided by measurable indicators of nutritional, metabolic, and epigenetic status [1–4]. In contrast to population-level approaches, nutritional interventions informed by pathophysiological, behavioral, and molecular parameters have demonstrated greater efficacy in modulating risk biomarkers and improving clinical outcomes [5–8]. In a global context marked by high prevalence of obesity, type 2 diabetes, and hypertension, diseases with strong dietary and environmental components, it is imperative to develop tools that enable efficient collection of nutritional and metabolic data through a lens of precision and accessibility [9–12].

From a biochemical and functional perspective, nutritional status can be understood as the dynamic equilibrium between nutrient bioavailability and tissue requirements, shaped by multiple factors including dietary intake, intestinal absorption capacity, endocrine-metabolic regulation, and the epigenetic environment [4,13]. Characterizing this status, essential for clinical intervention, has historically relied on invasive analyses (blood, urine, or stool samples) and self-reported dietary records, both of which present significant limitations in terms of cost, acceptability, accuracy, and longitudinal traceability [2,3,14]. In this context, the integration of non-invasive technologies capable of indirectly capturing biophysical data offers a complementary alternative for preliminary nutritional profiling.

Among these emerging technologies, biofrequency stands out. It is based on the detection of electromagnetic frequencies emitted by cellular and tissue structures according to their molecular composition and functional state [15–18]. The underlying biological premise holds that molecular structures exhibit specific vibrational patterns that can be amplified, digitized, and interpreted through bioinformatic modeling algorithms [19,20]. In the nutritional field, these signals allow for inferences regarding functional imbalances related to micronutrient metabolism, enzymatic activity, oxidative stress, xenobiotic load, and other determinants of baseline physiological status [21,22]. Although its clinical validation remains in early stages, its applicability in primary, community, or preventive care contexts is promising due to its portability, speed, and low invasiveness [23,24].

The S Drive device uses hair strands with the follicular bulb intact, collected from the occipital region of the scalp, as the biological matrix. This structure contains a representative set of accumulated epigenetic and metabolic data from follicular growth [25]. Spectral digitization is carried out using an electromagnetic wave emitter-receiver coil, which captures the vibrational spectrum of the sample in a short timeframe (~3 minutes) [25]. The signal is then processed through a computational algorithm, generating a report with indirect biomarker estimates of essential micronutrient status, fatty acid profile, oxidative load, electromagnetic field (EMF/ELF) exposure, and putative food sensitivity [25]. The use of the follicular bulb is justified by its high mitotic rate and its functional integration into the cutaneous neuroendocrine axis, acting as a dynamic sensor of both internal and external environments [26].

From an epigenetic perspective, hair strand analysis enables the identification of post-translational DNA modifications and alterations in histone methylation or acetylation patterns associated with nutritional or environmental exposures [27–29]. Although indirect, this level of resolution allows for functional inferences regarding gene expression regulated by diet and its influence on physiological homeostasis [30]. In this regard, epigenetics provides a robust conceptual framework for understanding the bidirectional relationship between dietary factors

and phenotypic regulation, independent of genotypic change [31–33]. The combined approach of biofrequency and hair epigenetics represents a preliminary tool for metabolic risk stratification, identification of specific nutritional needs, and the design of more effective dietary interventions [34].

The implementation of emerging technologies in nutrition should not be assessed solely from a biomedical standpoint but must also take into account their psychosocial impact. Factors such as perceived autonomy, comprehension of the information received, and trust in the technological tool directly affect therapeutic adherence, especially among individuals without a diagnosed chronic condition [35,36]. In this sense, the delivery of personalized reports generated from biofrequency analysis may enhance motivation for change, improve self-efficacy, and boost perceived subjective well-being. Evaluating these aspects is crucial to determine the feasibility of implementing such technologies in public health programs and population-level clinical interventions. Exploring user experience with tools like this can provide valuable insights into their acceptability, perceived usefulness, and transformative potential for lifestyle habits.

Within this framework, the present study will have a twofold aim: (1) to evaluate the effect of a 90-day biofrequency-guided nutritional intervention on functional epigenetic status, as reflected in changes in the optimization report generated by the S-Drive system; (2) to assess changes in adherence to the Mediterranean diet, anthropometric indicators, movement behaviors, and psychological well-being. In a clinical environment where speed, operational efficiency, and technological accessibility are key factors, this technology may facilitate nutritional decision-making and enhance the therapeutic relationship. Accordingly, this study situates itself at the intersection of biomedical innovation and biomarker-based nutrition, with potential implications for the development of more effective public health strategies.

2. Materials and Methods

2.1 Study Design and Population

2.1.1 Study Type

This study will follow a randomized controlled trial design aimed at evaluating the impact of nutritional intervention on personal satisfaction and perceived quality of life. It will be registered in ClinicalTrials.gov. The protocol includes two assessment points: a baseline measurement at the start of the intervention (Day 0) and a second measurement after a follow-up period (Day 90), allowing for the analysis of within-subject changes associated with the intervention.

2.1.2 Study Population and Sampling Design

The research will be conducted with Spanish adults who are members of the *Grupo Alcaraz Sport Association* in the Region of Murcia, Spain. The target population consists of adults aged ≥ 18 residing in the Region of Murcia, Spain, who meet the predefined inclusion criteria: (1) no diagnosed chronic illnesses and (2) provision of written informed consent. These criteria are essential to ensure both the ethical validity of the procedure and the clinical homogeneity of the sample. To control for potential confounding effects related to sex and to ensure group equivalence, stratified random sampling by sex will be employed. This approach reduces within-group variance and increases the statistical power of the analysis [37].

The sample size was calculated based on a parallel group randomized experimental design with two evaluation points (pre-intervention: Day 0; post-intervention: Day 90). The formula used compares means between two independent groups using a two-tailed Student's t-

test, assuming a moderate effect size ($d = 0.5$), a significance level of $\alpha = 0.05$, and statistical power ($1–\beta$) of 80%, according to Cohen's criteria [38]. Under these assumptions, a minimum of 64 participants per group (n = 128 in total) was estimated. Considering the longitudinal nature of the study and the risk of attrition due to dropout, withdrawal, or incomplete data, a 20% adjustment was applied to the initial sample size, in line with recommendations for studies with follow-ups ≥30 days [39]. Consequently, the final sample size was set at 77 participants per group (n = 154), ensuring the required statistical power and maintaining the inferential robustness of the analyses, even in the presence of non-differential attrition [40].

2.1.3 Ethical Approval

The study protocol has been reviewed and approved by the Human Research Ethics Committee (CIH) of the University of Almería (Approval Code: UALBIO2025/010). All procedures will be conducted in accordance with the ethical principles set forth in the Declaration of Helsinki and in compliance with current Spanish legislation on biomedical research. Prior to enrollment, all participants will provide written informed consent, which will outline the study objectives, procedures, and associated rights. Participation will be voluntary and may be withdrawn at any time without any consequence. Personal data will be treated confidentially and anonymized in accordance with the General Data Protection Regulation (GDPR). No significant risks are anticipated, as the interventions are non-invasive.

2.2 Recruitment, Allocation and Baseline Assessment

Participants will be recruited through informational campaigns conducted at the *Grupo Alcaraz Sport Association*. Each potential participant will undergo an individual interview to provide detailed information about the study's objectives and procedures, assess eligibility based on predefined inclusion criteria, and confirm their availability for full participation. Written informed consent, either in physical or electronic format, will be obtained from all participants prior to initiating any study-related activity.

Upon enrollment, each participant will be assigned a unique identification code to ensure the confidentiality of personal data. Only the principal investigator will have access to participants' contact information, which will be used exclusively for follow-up, communication of study instructions, and delivery of individual results. During this initial meeting, the biological sample collection (comprising four strands of hair) will be scheduled to take place at designated time slots on the DZ Procenter clinic. Participants will then be randomly assigned to one of two study groups (control or experimental) using a computerized randomization process.

Each participant will complete a comprehensive assessment at two points: at baseline (pre-intervention) and at the conclusion of the study (post-intervention). These assessments will involve a structured questionnaire incorporating validated batteries and measurement tools designed to collect data on sociodemographic characteristics, anthropometric parameters, lifestyle habits, and psychological variables. Detailed descriptions of the instruments and outcome measures used are provided in the section "Instruments and Outcome Measures."

2.3 Collection and Analysis of Biological Samples

This study will employ a longitudinal experimental design with two time points for data collection: baseline (Day 0) and post-intervention (Day 90). The collection of biological samples will take place in a multidisciplinary room. Biological data will be obtained through the collection

and in situ analysis of hair samples, specifically from the occipital region of each participant's scalp. The sampling procedure will be conducted using sterile tweezers and will not require any invasive technique. Immediately after extraction, the samples will be analyzed on-site using a non-destructive method and subsequently discarded, thereby eliminating the need for storage or transportation.

The analytical process will be conducted using the S-Drive device (Cell Wellbeing, Hamburg, Germany). This technology incorporates a central spectral coil that functions via resonance frequency analysis. The device will capture the vibrational signature of the hair sample, which will then be digitized and transmitted to proprietary software. The system will process this information using a set of algorithms designed to identify frequency-based patterns related to various physiological systems. The analysis will generate a reading of biological markers associated with epigenetic processes, reflecting the resonance intensity of elements such as vitamins, amino acids, fatty acids, and other micronutrients. It is important to note that the system does not extract genetic information or quantify the presence of these compounds; instead, it interprets the intensity values of their frequency patterns based on resonance.

The generation of the epigenetic profile will consist of two main components: (1) a computational model responsible for interpreting the biofrequency data and (2) an integrated reference database derived from biological, nutritional, and botanical samples. The digitized data will be transmitted to secure servers located in Germany, where the algorithm will generate a comprehensive optimization map. This map will reflect systemic interactions and challenges within the body, based on the frequency intensity values of the analyzed biomarkers. The resulting information will be synthesized into individualized reports that provide lifestyle optimization strategies focused on dietary, environmental, and nutritional factors.

Both the S-Drive device and its associated analytical algorithm are proprietary technologies owned by Cell Wellbeing and are subject to confidentiality agreements. At the time of this study, technology has not yet been scientifically validated. Therefore, the aim of the present research will be to evaluate the potential impact of the personalized feedback provided by the system on health-related behavior modification. Additionally, the study will explore the feasibility of integrating this tool into professional health and wellness practice, with the long-term objective of contributing to its empirical validation.

The S-Drive is certified by multiple regulatory agencies, ensuring compliance with international safety and performance standards. These include recognition by the U.S. Food and Drug Administration (FDA) under the guidance document General Wellness: Policy for Low Risk Devices (FDA 1300013, UCM429674); CE certification under Directive 2014/30/EU and RoHS Directive 2011/65/EU, in compliance with standards EN 61326-1:2006 (EMC Requirements), EN 60950-1:2006+A12:2011, and EN 5502/55011/55024; ETL certification by Intertek, confirming compliance with UL standard 60950-1 and CSA standard c22.2 No. 60950-1 (ETL Component Recognition No. 5000055); and China Compulsory Certification (CCC) for electrical conformity. These certifications support the safety profile of the device within its intended scope of application.

2.4 Nutritional Intervention

Participants assigned to the experimental group will receive a standardized 90-day nutritional intervention based on the individualized S-Drive optimization report. This report is derived from biofrequency analysis of hair follicle samples and synthesizes potential

physiological imbalances into tailored lifestyle and dietary recommendations. The same report will also serve as the study's primary outcome, enabling assessment of functional changes from baseline to follow-up (see Section 2.5).

The intervention comprises two main components: a personalized dietary plan and a health education module. Participants will receive structured materials including: (1) detailed dietary guidelines; (2) a monthly sample meal plan; (3) a shopping list; (4) selected recipes, and (5) visual preparation aids.

To support adherence, a daily food intake log will be provided. The educational module will address key health concepts such as stress physiology, epigenetic mechanisms, chronic disease prevention, and mindful eating. Content will be delivered through printed materials and two initial group video sessions. Periodic email check-ins will be conducted to monitor adherence, reinforce key messages, and provide tailored feedback.

Participants in the control group will be instructed to maintain their habitual dietary habits and will not receive any intervention materials or follow-up support. This design ensures that all participants in the experimental group receive a consistent and evidence-informed intervention, while allowing valid comparisons with the control group.

2.4.1 Specific Dietary Guidelines

Participants will be instructed to prioritize hydration, consuming at least 2 liters of water daily, supplemented with herbal infusions (e.g., green tea) or homemade vegetable juices (e.g., celery and apple) [41]. Fruit intake will be limited to 1–4 pieces per day, consumed outside main meals and avoided in the evening, with an emphasis on single-variety servings [42]. Vegetables will be consumed abundantly, preferably raw or steamed, with the goal of achieving a diet composed of 60% raw and natural foods [43].

Dairy consumption will be restricted to organic goat or sheep yogurt and kefir, 2–3 times per week [44,45]. Whole grains such as buckwheat, brown rice, millet, amaranth, and quinoa will be encouraged, while gluten-containing grains like spelt, rye, and oats will be limited [46]. Legumes, including lentils, chickpeas, and adzuki beans, will be recommended as primary plant-based protein sources [47].

Animal proteins will be carefully selected: turkey, chicken, and rabbit will be permitted up to twice weekly, while fish will be included 2–3 times per week, avoiding large species and prioritizing wild-caught varieties [48,49]. Organic eggs will be recommended up to four times weekly, prepared scrambled, soft-boiled, or poached to preserve nutritional integrity [50].

Healthy fats will be sourced from avocado, raw nuts, and seeds, while extra virgin olive oil will be recommended for raw use [51]. Meals will be seasoned with spices such as turmeric, ginger, and rosemary, added after cooking to maximize bioactive properties [52]. Specialized foods like sprouts, seaweed, and mushrooms will be incorporated for their micronutrient density.

2.4.2 Meal Composition and Lifestyle

Meals will follow a 3:1 vegetable-to-protein or carbohydrate ratio, avoiding combinations of dense proteins with dense carbohydrates [42,43,49]. Participants will be encouraged to dine early and engage in light activity afterward [53]. Breakfasts will focus on vegetables and fruit smoothies, with no more than one fruit per serving [42]. Cooking methods will prioritize nutrient preservation, favoring steaming and low-temperature techniques over frying or high-heat roasting [54].

Lifestyle recommendations will include daily sun exposure (30 minutes in the morning) and physical activity emphasizing both muscular strengthening and mental well-being [53,55]. Strict avoidance of tobacco, alcohol, caffeine, processed foods, refined sugars, and artificial sweeteners will be mandated [56,57]. Red meat, processed meats (with the exception of high-quality Iberian ham), and large or farmed fish with high mercury content will be excluded [49].

This standardized approach will ensure that all participants receive the same optimized dietary framework, designed to improve most biomarkers under study while remaining feasible for a diverse group. The intervention will balance scientific rigor with practical applicability, eliminating the need for individualized adjustments and promoting measurable health outcomes.

2.4.3 Post-Intervention Assessment

At the conclusion of the 90-day period, biological sample collection (hair samples) and self-administered questionnaire procedures (see "Instruments and Outcome Measures" section) will be repeated for both groups following the same standardized protocol. The follow-up assessment will aim to determine observed changes in the experimental group compared to the control group.

2.5 Instruments and Measures

At baseline (Day 0) and at follow-up (Day 90), participants will complete a comprehensive self-administered questionnaire comprising multiple modules. These modules have been specifically designed to collect detailed data on sociodemographic characteristics, self-reported anthropometric measures, lifestyle-related behaviors (including physical activity, dietary patterns, and substance use), and psychological outcomes (encompassing depressive symptoms, anxiety, stress, and disordered eating behaviors). Validated instruments and structured items will be utilized within each module to ensure the methodological rigor and reliability of the data collection process across the two assessment time points.

Sociodemographic Data

Participants will provide self-reported information regarding their sex and age. Data will also be gathered on their current engagement in educational pursuits, employment status, participation in remunerated activities, and their specific occupation. Additionally, participants will be asked to indicate the primary reason for their most recent visit to primary care services. Educational attainment will be categorized as follows: (a) incomplete primary education (<6 years), (b) completed primary education (6 years), (c) incomplete secondary education (<4 years), (d) completed secondary education (4 years), (e) incomplete higher education (<2 years of baccalaureate studies), and (f) completed higher education (2 years of baccalaureate studies or a bachelor's degree).

Primary Outcome: Functional Epigenetic Optimization

unctional status will be assessed using the S-Drive optimization report, which analyzes resonance frequency patterns from hair follicle samples through proprietary algorithms. The report classifies each participant's physiological functioning into 12 core domains, grouped into four thematic categories:

- Micronutrient-related indicators: vitamins, minerals, amino acids, fatty acids, antioxidants.

- Systemic physiological indicators: immune system, gut health, circulatory function.
- Epigenetic and environmental stressors: exposure to electromagnetic fields (EMF), extremely low-frequency (ELF) radiation, toxins, food additives.
- Dietary guidance: food choices, hydration, and supplementation recommendations.

Each domain is classified into one of four qualitative levels: "not flagged" (no action required), "to be considered", "advisable", or "priority", indicating increasing levels of physiological imbalance or urgency for nutritional support.

For analytical purposes, these levels will be transformed into ordinal values (Not flagged = 0, To be considered = 1, Advisable = 2, Priority = 3). Two derived scores will be used: (1) the total number of "priority" domains per participant, and (2) a cumulative optimization score summing the ordinal values across all domains (range: 0–36). These variables will be analyzed to assess within-subject changes and between-group differences from baseline to follow-up.

Secondary Outcomes

Anthropometric Data

Anthropometric data, including current body weight (in kilograms) and height (in centimeters), will be self-reported by participants. These measurements will be used to compute body mass index (BMI), which is calculated by dividing weight in kilograms by the square of height in meters (kg/m^2). BMI categories will be defined in accordance with World Health Organization (WHO) standards: BMI < 18.5 ("underweight"), 18.5 ≤ BMI < 24.9 ("normal weight"), 25 ≤ BMI < 29.9 ("overweight"), 30 ≤ BMI < 34.9 ("obesity class I"), 35 ≤ BMI < 39.9 ("obesity class II"), and BMI ≥ 40 ("obesity class III") [58]. Although self-reported measurements may be susceptible to bias, previous research indicates that self-reported BMI estimates are generally valid in adult populations [59].

Lifestyle Data

24-Hour Movement Behaviors

Physical activity across work/school, transportation, and leisure domains will be assessed using the validated Spanish version of the Physical Activity Scale 2.1 (PAS-2.1S) [60]. This instrument comprises nine items: six items evaluate daily activities (sleep duration on weekdays and weekends, sedentary behavior, active physical activity, leisure time, and commuting time), and three items assess weekly physical activity. To assess sleep duration, participants will report average hours of sleep on weekdays and weekends. Sedentary behaviors will be captured through items spent commuting (by car or public transportation) and screen-based or reading activities during leisure time.

The weekly activity subscale will collect data on light (e.g., walking, light cleaning), moderate (e.g., gardening, moderate sports), and vigorous (e.g., running, football) leisure-time physical activities. Activity intensity levels will be expressed in Metabolic Equivalent of Task (METs), based on the Physical Activity Compendium [61]. MET values include sleep (0.9), sitting work (1.5), standing/walking work (2.0), heavy lifting or stair climbing (5.0), commuting while seated (1.5), leisure-time sitting (1.0), light activity (3.0), moderate activity (5.0), and vigorous activity (6.0). To compute total weekly METs, daily activities (work and transportation) will be multiplied by five (days) and sleep and leisure activities by seven (days). Missing daily activity

hours (if reported as <24 hours) will be multiplied by two to account for the discrepancy. METs from weekly activities will be summed up to obtain total energy expenditure.

Eating Patterns

Adherence to the Mediterranean diet

Adherence to the Mediterranean diet (MedDiet) will be measured using the PREvención con DIeta MEDiterránea (PREDIMED) questionnaire [62]. Participants will report the frequency or quantity of consumption of 12 core dietary components (e.g., fruits, vegetables, olive oil, nuts) and two related dietary habits. The 14-item tool assigns binary scores (0 or 1) to each component, with total scores ≥9 indicative of high adherence to the MedDiet.

Drug consumption

Tobacco smoking

Tobacco use will be assessed with two questions. First, participants will be asked: "Have you ever smoked tobacco in your lifetime?", with response options ranging from (a) never to (g) 30 times or more. Second, adolescents will be asked about current smoking frequency: (a) I do not smoke, (b) less than once a week, (c) more than once a week but not daily, and (d) every day.

Alcohol consumption

Alcohol consumption will be evaluated through the question: "Have you ever consumed alcohol in your lifetime?", with response options: (a) never, (b) once or twice, (c) 3 to 5 times, (d) 6 to 9 times, (e) 10 to 19 times, (f) 20 to 29 times, and (g) 30 times or more. Further, participants will indicate the frequency of consumption of various alcoholic beverages, with responses converted into days per week: : (a) never (0 points), (b) almost never (0.10 points), (c) monthly (0.25 points), (d) weekly (1 point), and (e) daily (7 points). Mean weekly frequency will be computed. Participants will be categorized into: (a) non-drinkers (never consumed any alcoholic beverage), (b) regular drinkers (weekly or more frequently), and (c) irregular drinkers (monthly or less frequently). Binge drinking will be assessed with: "Have you ever consumed enough alcohol to become intoxicated?", with frequency options: (a) never, (b) once, (c) 2-3 times, (d) 4-10 times, and (e) more than 10 times. Excessive consumption will be defined as having become intoxicated once or more.

Cannabis use

Cannabis consumption will be assessed with the question: "Have you ever used cannabis in your lifetime?", using response options: (a) never, (b) once or twice, (c) 3 to 5 times, (d) 6 to 9 times, (e) 10 to 19 times, (f) 20 to 29 times, and (g) 30 times or more.

Psychological Outcomes

Depressive Symptoms

Depressive symptoms will be measured using the Spanish version of the Beck Depression Inventory-II (BDI-II) [63]. This self-administered instrument consists of 21 items, each with four response options representing increasing severity over the preceding two weeks. Item scores range from 0 to 3, yielding a total score between 0 and 63.

Anxiety Symptoms

Anxiety symptoms will be evaluated using the Generalized Anxiety Disorder-7 (GAD-7) questionnaire, validated for primary care [64]. This instrument contains seven items [65], assessing symptoms such as nervousness, worry, restlessness, and irritability over the previous 14 days. Items are rated on a four-point Likert scale: never (0 points), several days (1 point), half of the days (2 points), and almost every day (3 points). Total scores range from 0 to 21, with thresholds as follows: no anxiety (0-4 points), mild anxiety symptoms (5-9 points), moderate anxiety symptoms (10-14 points), and severe anxiety symptoms (15-21 points).

Perceived Stress

Perceived stress will be assessed using the Spanish version of the Perceived Stress Scale-14 (PSS-14) [66,67]. This 14-item instrument utilizes a five-point response scale: never (0 points), almost never (1 point), once in a while (2 points), often (3 points), and very often (4 points). The total score is calculated by reversing the responses for items 4, 5, 6, 7, 9, 10, and 13 using the conversion scale (0=4, 1=3, 2=2, 3=1, 4=0) and then summing the scores of all 14 items. Higher scores reflect greater perceived stress.

Disordered Eating

Disordered eating behaviors will be evaluated using the Sick, Control, One, Fat, Food (SCOFF) questionnaire, a concise and validated screening instrument designed to identify individuals at risk for eating disorders [68]. The SCOFF consists of five items that capture core dimensions of disordered eating, including restrictive intake, preoccupation with weight and shape, and compensatory behaviors. Each item requires a binary (yes/no) response, and a score of ≥2 affirmative answers indicate an increased risk for an eating disorder.

2.6 Data Analysis

All statistical analyses will be performed using R software (version 4.4.1; R Foundation for Statistical Computing, Vienna, Austria) within the RStudio environment (version 2024.9.0.375; Posit PBC, Boston, MA, USA). A two-tailed p-value < 0.05 will be considered statistically significant.

2.6.1. Descriptive Analysis

Descriptive statistics will be computed to characterize the sample in terms of sociodemographic, anthropometric, lifestyle, and psychological variables, stratified by sex and group assignment (intervention vs. control). Continuous variables will be summarized using means and standard deviations (or medians and interquartile ranges, when non-normally distributed). Categorical variables will be presented as absolute and relative frequencies.

2.6.2. Inferential Analysis

Baseline comparisons between groups will be conducted to assess initial comparability. Categorical variables will be analyzed using chi-square or Fisher's exact tests; continuous variables using t-tests or ANOVA (or non-parametric equivalents such as Mann–Whitney U or Kruskal–Wallis tests, as appropriate).

Longitudinal changes in outcomes from baseline (Day 0) to follow-up (Day 90) will be analyzed using repeated-measures models. Specifically:

- For continuous outcomes: linear mixed-effects models will be applied.

- For categorical outcomes: generalized linear mixed-effects models (GLMMs) will be used.

All models will include subject-specific random effects and fixed effects for group, time, sex, and relevant interactions. These models will account for intra-individual correlation and allow estimation of time-by-group effects.

2.6.3. Analysis of the Primary Outcome (S-Drive Report)

The primary outcome (functional epigenetic optimization) will be operationalized using two metrics derived from the S-Drive report:

1. Priority count: the number of physiological domains marked as "Priority" (range: 0–12).
2. Optimization score: the sum of ordinal values assigned to each domain (Not flagged = 0, To be considered = 1, Advisable = 2, Priority = 3; total range: 0–36).

These outcomes will be analyzed as follows:

- Within-group changes (pre–post) will be assessed using the Wilcoxon signed-rank test (for paired data).
- Between-group comparisons of change scores will be analyzed using the Mann–Whitney U test.
- Additionally, ordinal or linear mixed-effects models will be employed to model longitudinal changes, adjusting for baseline values, sociodemographic characteristics, and relevant behavioral covariates.

  This analytical strategy accommodates the ordinal nature of the data and enables robust estimation of the intervention's effect on the functional profile.

2.6.4. Analysis of Secondary Outcomes

Secondary continuous outcomes will be analyzed using linear mixed-effects models, while binary or ordinal outcomes (e.g., alcohol use, disordered eating risk, anxiety levels) will be modeled using GLMMs or ordinal logistic models, as appropriate. Covariates will be included to adjust for potential confounding.

2.6.5. Missing Data

The extent and patterns of missing data will be explored by group and sex. If missingness is <5%, complete-case analysis will be used. If >5% and data are assumed to be missing at random (MAR), multiple imputation techniques (e.g., via chained equations) will be applied to minimize potential bias and preserve statistical power.

3. Discussion

This protocol outlines the methodological design of a randomized controlled trial aimed at evaluating the functional utility, preliminary clinical efficacy, and acceptability of a biofrequency-guided nutritional intervention in Spanish adults. In a context marked by the high prevalence of NCDs [69] and the limited capacity of healthcare systems to provide personalized preventive strategies [9], the development of non-invasive, accessible, and individually tailored tools acquires strategic relevance. The proposed approach lies at the intersection of technological innovation and precision nutrition, aligning with the emerging paradigm of personalized and predictive medicine.

The biofrequency analysis technology employed in this study is based on the detection and digitization of electromagnetic signals emitted by cellular structures, whose vibrational frequencies are associated with their molecular composition and functional state [15,16,18,20]. The use of the hair follicle as a biological matrix is particularly innovative, due to its high mitotic turnover, its role as an epigenetic sensor of the internal and external environment, and its capacity to store metabolic and environmental information longitudinally [26]. The underlying hypothesis suggests that these vibrational patterns may be indirectly correlated with micronutrient imbalances, oxidative stress, food sensitivities, and exposure to environmental contaminants, thereby enabling the development of nutritional profiles without the need for invasive or costly methods.

In terms of expected outcomes, it is anticipated that participants in the experimental group will demonstrate greater improvement in eating patterns (in terms of adherence to the Mediterranean diet), a reduction in disordered eating behaviors, lower levels of stress and affective symptoms, and a stronger sense of control and satisfaction with their health status. High acceptability of the personalized report generated by biofrequency is also expected, along with a positive perception among participants regarding the practical applicability of the recommendations. Collectively, these findings would provide preliminary evidence for the potential of biofrequency technologies as complementary tools for metabolic risk stratification, the design of individualized nutritional interventions, and the promotion of healthy lifestyle habits in community settings.

From a methodological perspective, the protocol is characterized by a rigorous experimental design, including sex-stratified randomization, two longitudinal assessment points, and the application of mixed-effects statistical models for data analysis. This structure will not only allow for the control of potential confounding variables but also facilitate the exploration of differentiated effects by sex, time, and group-intervention interaction. Moreover, the inclusion of multiple dimensions of health status, anthropometric, behavioral, and psychological, enables a comprehensive evaluation of the intervention's impact, going beyond the traditional reduction of clinical trials to unidimensional or exclusively biochemical metrics. The use of validated instruments to assess adherence to the Mediterranean diet, affective symptoms, disordered eating behaviors, and perceived stress further strengthens the study's internal validity.

Nevertheless, this protocol also presents limitations inherent to its preliminary phase. Firstly, the S-Drive system and its biofrequency interpretation algorithm have not yet undergone substantial clinical validation through independent peer-reviewed studies. While the device is certified by regulatory agencies in terms of electromagnetic safety, its diagnostic reliability and predictive value still needs to be verified against standardized biomarkers. Additionally, self-reported anthropometric and behavioral data may introduce information biases, although these may be partially mitigated through the use of standardized questionnaires. The 90-day duration, while sufficient to detect initial behavioral changes, may be insufficient to assess the sustainability of the intervention's effects. Finally, the exploratory nature of the study, while necessary given the novelty of the tool, limits its ability to establish definitive causal relationships beyond the proposed hypothesis.

Despite these limitations, this study constitutes an original and necessary contribution toward the integration of emerging technologies in the field of biomarker-based nutrition. Its user-centered design, the simultaneous consideration of epigenetic and behavioral variables, and its implementation in a naturalistic (non-clinical) setting make it a replicable and scalable model.

Should positive outcomes be observed in terms of dietary adherence, well-being, or reduction of risk indicators, this protocol could serve as a foundation for future research combining objective biomarkers, metabolomic analysis, and digital tools for continuous monitoring.

This protocol represents a structured first step toward the empirical evaluation of biofrequency as a supportive tool in biomarker-based nutrition interventions. Its originality lies in integrating non-invasive epigenetic reading tools with behavioral strategies to improve lifestyle habits, within a controlled experimental framework. Should the study results demonstrate significant clinical or psychosocial benefits, it could open new avenues for the use of portable bioinformatic technologies in primary care, public health programs, and the field of preventive wellness. Overall, the study presents a high-impact hypothesis supported by solid theoretical foundations, offering an opportunity to rethink current models of nutritional assessment through a systemic, transdisciplinary, and person-centered lens.

4. Conclusions

The present study represents an innovative step toward integrating emerging biofrequency technologies into the field of biomarker-based nutrition. By addressing the interaction between micronutrient status, epigenetic signals, and dietary behavior, this research proposes a novel framework for understanding and influencing health-related outcomes through non-invasive and individualized strategies. The potential of biofrequency analysis to identify nutritional imbalances and guide tailored interventions could transform current models of nutritional care, particularly in preventive and community health contexts. If proven effective, this approach may offer a scalable and accessible solution to promote healthier lifestyles, enhance subjective well-being, and reduce the burden of nutrition-related chronic diseases.

Author Contributions: Conceptualization, D.M.-S.; J.F.L.-G. validation, D.M.-S.; investigation, D.M.-S.; L. F. A., and M. A. C.; writing—original draft preparation, E.C.-V.; writing—review and editing, J.F.L.-G., F.Q.-C., D. M. S., L. F. A., and M. A. C.; visualization, J.F.L.-G.; supervision, D.M.-S.; project administration, D.M.-S. and J.F.L.-G. All the authors have read and agreed to the published version of the manuscript.

Funding: This study will be funded by Cell Wellbeing. The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Data availability statement: Not applicable.

Acknowledgments: The authors would like to thank Cell Wellbeing for providing the consumables and technical resources required for the implementation of the biofrequency assessments. The authors also acknowledge the collaboration of DZ Procenter (Murcia) for facilitating the collection of biological samples and the *Grupo Alcaraz Sport Association* for facilitating the sample and expressing their sincere gratitude to all participants for their time and commitment to the study.

Conflicts of interest: Leire Fradua Arteaga reports a commercial relationship with Cell Wellbeing as an external collaborator.

References

1. de Hoogh, I.M.; Winters, B.L.; Nieman, K.M.; Bijlsma, S.; Krone, T.; van den Broek, T.J.; Anderson, B.D.; Caspers, M.P.M.; Anthony, J.C.; Wopereis, S. A Novel Personalized Systems Nutrition Program Improves Dietary Patterns, Lifestyle Behaviors and Health-Related Outcomes: Results from the Habit Study. *Nutrients* **2021**, *13*, doi:10.3390/nu13061763.
2. Lagoumintzis, G.; Patrinos, G.P. Triangulating Nutrigenomics, Metabolomics and Microbiomics toward Personalized Nutrition and Healthy Living. *Human Genomics* **2023**, *17*, 109, doi:10.1186/s40246-023-00561-w.
3. Linseisen, J.; Renner, B.; Gedrich, K.; Wirsam, J.; Holzapfel, C.; Lorkowski, S.; Watzl, B.; Daniel, H.; Leitzmann, M. Data in Personalized Nutrition: Bridging Biomedical, Psycho-Behavioral, and Food Environment Approaches for Population-Wide Impact. *Advances in Nutrition* **2025**, 100377, doi:10.1016/j.advnut.2025.100377.
4. Picó, C.; Serra, F.; Rodríguez, A.M.; Keijer, J.; Palou, A. Biomarkers of Nutrition and Health: New Tools for New Approaches. *Nutrients* **2019**, *11*, doi:10.3390/nu11051092.
5. Budrevičiūtė, A.; Damiati, S.; Sabir, D.; Onder, K.; Schuller-Götzburg, P.; Plakys, G.; Katilevičiūtė, A.; Khoja, S.; Kodzius, R. Management and Prevention Strategies for Non-Communicable Diseases (NCDs) and Their Risk Factors. *Frontiers in Public Health* **2020**, *8*, doi:10.3389/fpubh.2020.574111.
6. Gámez-Calvo, L.; Hernández-Beltrán, V.; Pimienta-Sánchez, L.P.; Delgado-Gil, S.; Gamonales, J.M. Revisión Sistemática de Programas de Intervención Para Promover Hábitos Saludables de Actividad Física y Nutrición En Escolares Españoles. *Archivos Latinoamericanos de Nutrición* **2022**, *72*, 294–305, doi:https://doi.org/10.37527/2022.72.4.007.
7. Kan, J.; Ni, J.; Xue, K.; Wang, F.; Zheng, J.; Cheng, J.; Wu, P.-C.; Runyon, M.; Guo, H.; Du, J. Personalized Nutrition Intervention Improves Health Status in Overweight/Obese Chinese Adults: A Randomized Controlled Trial. *Frontiers in Nutrition* **2022**, *9*, doi:10.3389/fnut.2022.919882.
8. Kimokoti, R.W.; Millen, B.E. Nutrition for the Prevention of Chronic Diseases. *Medical Clinics of North America* **2016**, *100*, 1185–1198, doi:https://doi.org/10.1016/j.mcna.2016.06.003.
9. Donovan, S.M.; Abrahams, M.; Anthony ,Joshua C., J.C.; Ying, B.; Barragan, M.; Bermingham, K.M.; Blander, G.; Keck, A.-S.; Lee, B.Y.; Nieman, K.M.; et al. Personalized Nutrition: Perspectives on Challenges, Opportunities, and Guiding Principles for Data Use and Fusion. *Critical Reviews in Food Science and Nutrition* **2025**, 1–18, doi:10.1080/10408398.2025.2461237.
10. Feijoo, L.; Rey-Brandariz, J.; Guerra-Tort, C.; Candal-Pedreira, C.; Santiago-Pérez, M.I.; Ruano-Ravina, A.; Pérez-Ríos, M. Prevalence of obesity in Spain and its autonomous communities, 1987-2020. *Rev Esp Cardiol (Engl Ed)* **2024**, *77*, 809–818, doi:10.1016/j.rec.2023.12.018.
11. Hawkins Carranza, F.; Corbatón-Anchuelo, A.; Bermejo Pareja, F.; Martín-Arriscado Arroba, C.; Vega-Quiroga, S.; Benito-León, J.; Serrano-Ríos, M. Incidence of Type 2 Diabetes in the Elderly in Central Spain: Association with Socioeconomic Status, Educational Level, and Other Risk Factors. *Primary Care Diabetes* **2022**, *16*, 279–286, doi:10.1016/j.pcd.2021.12.016.
12. Menéndez, E.; Delgado, E.; Fernández-Vega, F.; Prieto, M.A.; Bordiú, E.; Calle, A.; Carmena, R.; Castaño, L.; Catalá, M.; Franch, J.; et al. Prevalence, Diagnosis, Treatment, and Control of Hypertension in Spain. Results of the Di@bet.es Study. *Rev Esp Cardiol (Engl Ed)* **2016**, *69*, 572–578, doi:10.1016/j.rec.2015.11.034.
13. Raymond, J.L.; Morrow, K. *Krause. Mahan: Dietoterapia*; 16 ed.; Barcelona, Spain, 2025; ISBN 978-84-9113-937-9.

14. Galekop, M.M.J.; Uyl-de Groot, C.A.; Ken Redekop, W. A Systematic Review of Cost-Effectiveness Studies of Interventions With a Personalized Nutrition Component in Adults. *Value in Health* **2021**, *24*, 325–335, doi:10.1016/j.jval.2020.12.006.
15. Apollonio, F.; Liberti, M.; Paffi, A.; D'Inzeo, G. Frequency Spectrum Investigations on Detection of Radiofrequency Electromagnetic Fields by Biological Cells. *IEEE MTT-S International Microwave Symposium Digest, 2003* **2003**, *2*, 1431–1434, doi:10.1109/MWSYM.2003.1212641.
16. Cifra, M. Molecular Understanding of Electromagnetic Field-Biomatter Interaction for Rational Bio/Chemical Sensing Device Design. *2021 IEEE Sensors* **2021**, 1–4, doi:10.1109/SENSORS47087.2021.9639510.
17. Huang, P.; Xu, L.; Xie, Y. Biomedical Applications of Electromagnetic Detection: A Brief Review. *Biosensors* **2021**, *11*, doi:10.3390/bios11070225.
18. Kim, N.-Y.; Adhikari, K.; Dhakal, R.; Chuluunbaatar, Z.; Wang, C.; Kim, E.-S. Rapid, Sensitive, and Reusable Detection of Glucose by a Robust Radiofrequency Integrated Passive Device Biosensor Chip. *Scientific Reports* **2015**, *5*, doi:10.1038/srep07807.
19. Lutz, K.; Sabry, S.; Garcia, K.; Patil, S. *Monitoring Human Biomarkers with AO Scan during Lunares Analog Mission Pilot Study*; 2021;
20. Potischman, N. Biologic and Methodologic Issues for Nutritional Biomarkers. *J Nutr* **2003**, *133 Suppl 3*, 875S-880S, doi:10.1093/jn/133.3.875S.
21. Ahmad, A.; Imran, M.; Ahsan, H. Biomarkers as Biomedical Bioindicators: Approaches and Techniques for the Detection, Analysis, and Validation of Novel Biomarkers of Diseases. *Pharmaceutics* **2023**, *15*, doi:10.3390/pharmaceutics15061630.
22. Zheng, C.; Tako, E. Editorial: Biochemical Biomarkers of Nutritional Status. *Frontiers in Nutrition* **2024**, *Volume 11-2024*.
23. Bingham, S.A. Biomarkers in Nutritional Epidemiology. *Public Health Nutr* **2002**, *5*, 821–827, doi:10.1079/phn2002368.
24. Jenab, M.; Slimani, N.; Bictash, M.; Ferrari, P.; Bingham, S.A. Biomarkers in Nutritional Epidemiology: Applications, Needs and New Horizons. *Hum Genet* **2009**, *125*, 507–525, doi:10.1007/s00439-009-0662-5.
25. Cell Wellbeing S-Drive Technology Available online: https://cell-wellbeing.com/ (accessed on 4 June 2025).
26. Lemasters, J.; Ramshesh, V.; Lovelace, G.; Lim, J.; Wright, G.; Harland, D.; Dawson, T. Compartmentation of Mitochondrial and Oxidative Metabolism in Growing Hair Follicles: A Ring of Fire. *The Journal of investigative dermatology* **2017**, *137 7*, 1434–1444, doi:10.1016/j.jid.2017.02.983.
27. Bonenfant, D.; Towbin, H.; Coulot, M.; Schindler, P.; Mueller, D.; Van Oostrum, J. Analysis of Dynamic Changes in Post-Translational Modifications of Human Histones during Cell Cycle by Mass Spectrometry*S. *Molecular & Cellular Proteomics* **2007**, *6*, 1917–1932, doi:10.1074/mcp.M700070-MCP200.
28. Liu, R.; Wu, J.; Guo, H.; Yao, W.; Li, S.; Lu, Y.; Jia, Y.-S.; Liang, X.; Tang, J.; Zhang, H. Post-translational Modifications of Histones: Mechanisms, Biological Functions, and Therapeutic Targets. *MedComm* **2023**, *4*, doi:10.1002/mco2.292.
29. Ramazi, S.; Allahverdi, A.; Zahiri, J. Evaluation of Post-Translational Modifications in Histone Proteins: A Review on Histone Modification Defects in Developmental and Neurological Disorders. *Journal of Biosciences* **2020**, *45*, 1–29, doi:10.1007/s12038-020-00099-2.
30. U.S. Centers for Disease Control and Prevention (CDC) Epigenetics, Health, and Disease Available online: https://www.cdc.gov/genomics-and-health/epigenetics/index.html#:~:text=Epigenetics%20refers%20to%20how%20your,body%20reads%20a%20DNA%20sequence.

31. Choi, S.-W.; Friso, S. Epigenetics: A New Bridge between Nutrition and Health. *Advances in Nutrition* **2010**, *1*, 8–16, doi:10.3945/an.110.1004.
32. Tiffon, C. The Impact of Nutrition and Environmental Epigenetics on Human Health and Disease. *Int J Mol Sci* **2018**, *19*, doi:10.3390/ijms19113425.
33. Zhang, Y.; Kutateladze, T.G. Diet and the Epigenome. *Nature Communications* **2018**, *9*, 3375, doi:10.1038/s41467-018-05778-1.
34. Milagro, F.I.; Martínez, J.A. La Nutrición Personalizada a Través de La Epigenómica. *Mediterráneo Económico* **2015**, 345–361.
35. Celis-Morales, C.; Livingstone, K.M.; Marsaux, C.F.; Macready, A.L.; Fallaize, R.; O'Donovan, C.B.; Woolhead, C.; Forster, H.; Walsh, M.C.; Navas-Carretero, S.; et al. Effect of Personalized Nutrition on Health-Related Behaviour Change: Evidence from the Food4Me European Randomized Controlled Trial. *International Journal of Epidemiology* **2017**, *46*, 578–588, doi:10.1093/ije/dyw186.
36. Manzano-Sánchez, D.; Palop-Montoro, M.V.; Arteaga-Checa, M.; Valero-Valenzuela, A. Analysis of Adolescent Physical Activity Levels and Their Relationship with Body Image and Nutritional Habits. *Int J Environ Res Public Health* **2022**, *19*, doi:10.3390/ijerph19053064.
37. Kernan, W.N.; Viscoli, C.M.; Makuch, R.W.; Brass, L.M.; Horwitz, R.I. Stratified Randomization for Clinical Trials. *J Clin Epidemiol* **1999**, *52*, 19–26, doi:10.1016/s0895-4356(98)00138-3.
38. Cohen, J. *Statistical Power Analysis for the Behavioral Sciences*; 2nd Edition.; New York, 1988;
39. Fewtrell, M.S.; Kennedy, K.; Singhal, A.; Martin, R.M.; Ness, A.; Hadders-Algra, M.; Koletzko, B.; Lucas, A. How Much Loss to Follow-up Is Acceptable in Long-Term Randomised Trials and Prospective Studies? *Arch Dis Child* **2008**, *93*, 458–461, doi:10.1136/adc.2007.127316.
40. Schulz, K.F.; Altman, D.G.; Moher, D.; the CONSORT Group CONSORT 2010 Statement: Updated Guidelines for Reporting Parallel Group Randomised Trials. *BMC Medicine* **2010**, *8*, 18, doi:10.1186/1741-7015-8-18.
41. Popkin, B.M.; D'Anci, K.E.; Rosenberg, I.H. Water, Hydration, and Health. *Nutrition Reviews* **2010**, *68*, 439–458, doi:10.1111/j.1753-4887.2010.00304.x.
42. Ludwig, D.S.; Hu, F.B.; Tappy, L.; Brand-Miller, J. Dietary Carbohydrates: Role of Quality and Quantity in Chronic Disease. *BMJ* **2018**, *361*, doi:10.1136/bmj.k2340.
43. Satija Ambika; Bhupathiraju Shilpa N.; Spiegelman Donna; Chiuve Stephanie E.; Manson JoAnn E.; Willett Walter; Rexrode Kathryn M.; Rimm Eric B.; Hu Frank B. Healthful and Unhealthful Plant-Based Diets and the Risk of Coronary Heart Disease in U.S. Adults. *JACC* **2017**, *70*, 411–422, doi:10.1016/j.jacc.2017.05.047.
44. Babio, N.; Becerra-Tomás, N.; Martínez-González, M.Á.; Corella, D.; Estruch, R.; Ros, E.; Sayón-Orea, C.; Fitó, M.; Serra-Majem, L.; Arós, F.; et al. Consumption of Yogurt, Low-Fat Milk, and Other Low-Fat Dairy Products Is Associated with Lower Risk of Metabolic Syndrome Incidence in an Elderly Mediterranean Population1, 2, 3. *The Journal of Nutrition* **2015**, *145*, 2308–2316, doi:10.3945/jn.115.214593.
45. Mozaffarian, D.; Wu, J.H.Y. Flavonoids, Dairy Foods, and Cardiovascular and Metabolic Health. *Circulation Research* **2018**, *122*, 369–384, doi:10.1161/CIRCRESAHA.117.309008.
46. Zong, G.; Lebwohl, B.; Hu, F.B.; Sampson, L.; Dougherty, L.W.; Willett, W.C.; Chan, A.T.; Sun, Q. Gluten Intake and Risk of Type 2 Diabetes in Three Large Prospective Cohort Studies of US Men and Women. *Diabetologia* **2018**, *61*, 2164–2173, doi:10.1007/s00125-018-4697-9.
47. Hafiz, M.S.; Campbell, M.D.; O'Mahoney, L.L.; Holmes, M.; Orfila, C.; Boesch, C. Pulse Consumption Improves Indices of Glycemic Control in Adults with and without Type 2 Diabetes: A Systematic Review and Meta-Analysis of Acute and Long-Term Randomized Controlled Trials. *European Journal of Nutrition* **2022**, *61*, 809–824, doi:10.1007/s00394-021-02685-y.

48. Mozaffarian, D.; Rimm, E.B. Fish Intake, Contaminants, and Human HealthEvaluating the Risks and the Benefits. *JAMA* **2006**, *296*, 1885–1899, doi:10.1001/jama.296.15.1885.
49. Wirth, J.; Hillesheim, E.; Brennan, L. The Role of Protein Intake and Its Timing on Body Composition and Muscle Function in Healthy Adults: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *The Journal of Nutrition* **2020**, *150*, 1443–1460, doi:10.1093/jn/nxaa049.
50. Fuller, N.R.; Sainsbury, A.; Caterson, I.D.; Markovic, T.P. Egg Consumption and Human Cardio-Metabolic Health in People with and without Diabetes. *Nutrients* **2015**, *7*, 7399–7420, doi:10.3390/nu7095344.
51. Guasch-Ferré Marta; Liu Xiaoran; Malik Vasanti S.; Sun Qi; Willett Walter C.; Manson JoAnn E.; Rexrode Kathryn M.; Li Yanping; Hu Frank B.; Bhupathiraju Shilpa N. Nut Consumption and Risk of Cardiovascular Disease. *JACC* **2017**, *70*, 2519–2532, doi:10.1016/j.jacc.2017.09.035.
52. Hewlings, S.J.; Kalman, D.S. Curcumin: A Review of Its Effects on Human Health. *Foods* **2017**, *6*, doi:10.3390/foods6100092.
53. Bray, G.A.; Heisel, W.E.; Afshin, A.; Jensen, M.D.; Dietz, W.H.; Long, M.; Kushner, R.F.; Daniels, S.R.; Wadden, T.A.; Tsai, A.G.; et al. The Science of Obesity Management: An Endocrine Society Scientific Statement. *Endocrine Reviews* **2018**, *39*, 79–132, doi:10.1210/er.2017-00253.
54. Nyaradzo Moyo, H. The Impact of Food Processing Techniques on Nutrient Retention and Bioavailability. *Iconic Research And Engineering Journals* **2024**, *8*, 435–460.
55. Holick, M.F. Sunlight, UV Radiation, Vitamin D, and Skin Cancer: How Much Sunlight Do We Need? In *Sunlight, Vitamin D and Skin Cancer*; Reichrath, J., Ed.; Springer International Publishing: Cham, 2020; pp. 19–36 ISBN 978-3-030-46227-7.
56. Monteiro, C.A.; Cannon, G.; Levy, R.B.; Moubarac, J.-C.; Louzada, M.L.; Rauber, F.; Khandpur, N.; Cediel, G.; Neri, D.; Martinez-Steele, E.; et al. Ultra-Processed Foods: What They Are and How to Identify Them. *Public Health Nutrition* **2019**, *22*, 936–941, doi:10.1017/S1368980018003762.
57. Schulze, M.B.; Martínez-González, M.A.; Fung, T.T.; Lichtenstein, A.H.; Forouhi, N.G. Food Based Dietary Patterns and Chronic Disease Prevention. *BMJ* **2018**, *361*, doi:10.1136/bmj.k2396.
58. Weir, C.B.; Jan, A. BMI Classification Percentile and Cut Off Points. In *StatPearls*; StatPearls Publishing: Treasure Island, 2023.
59. Stommel, M.; Schoenborn, C.A. Accuracy and Usefulness of BMI Measures Based on Self-Reported Weight and Height: Findings from the NHANES & NHIS 2001-2006. *BMC Public Health* **2009**, *9*, 421, doi:10.1186/1471-2458-9-421.
60. Valles-Medina, A.M.; Castillo-Anaya, S.I.; Sevilla-Mena, T.L.; Aadahl, M. Validity of the Danish Physical Activity Scale, Adapted to Spanish Speaking Population. *Atención Primaria* **2021**, *53*, doi:10.1016/j.aprim.2020.09.008.
61. Ainsworth, B.E.; Haskell, W.L.; Whitt, M.C.; Irwin, M.L.; Swartz, A.M.; Strath, S.J.; O'Brien, W.L.; Bassett, D.R.J.; Schmitz, K.H.; Emplaincourt, P.O.; et al. Compendium of Physical Activities: An Update of Activity Codes and MET Intensities. *Med Sci Sports Exerc* **2000**, *32*, S498-504, doi:10.1097/00005768-200009001-00009.
62. Martínez-González, M.Á.; Corella, D.; Salas-Salvadó, J.; Ros, E.; Covas, M.I.; Fiol, M.; Wärnberg, J.; Arós, F.; Ruíz-Gutiérrez, V.; Lamuela-Raventós, R.M.; et al. Cohort Profile: Design and Methods of the PREDIMED Study. *Int J Epidemiol* **2012**, *41*, 377–385, doi:10.1093/ije/dyq250.
63. Sanz, J.; Navarro, M.E. Propiedades Psicométricas de Una Versión Española Del Inventario de Ansiedad de Beck (BAI) En Estudiantes Universitarios. *Ansiedad y Estrés* **2003**, *9*, 59–84.

64. Löwe, B.; Decker, O.; Müller, S.; Brähler, E.; Schellberg, D.; Herzog, W.; Herzberg, P.Y. Validation and Standardization of the Generalized Anxiety Disorder Screener (GAD-7) in the General Population. *Med Care* **2008**, *46*, 266–274, doi:10.1097/MLR.0b013e318160d093.
65. Spitzer, R.L.; Kroenke, K.; Williams, J.B.W.; Löwe, B. A Brief Measure for Assessing Generalized Anxiety Disorder: The GAD-7. *Arch Intern Med* **2006**, *166*, 1092–1097, doi:10.1001/archinte.166.10.1092.
66. Remor, E. Psychometric Properties of a European Spanish Version of the Perceived Stress Scale (PSS). *Span J Psychol* **2006**, *9*, 86–93, doi:10.1017/s1138741600006004.
67. Remor, E.; Carrobles, J.A. Versión Española de La Escala de Estrés Percibido (PSS-14): Estudio Psicométrico En Una Muestra VIH+. [Spanish Version of the Perceived Stress Scale (PSS-14): Psychometric Study in a HIV+ Sample.]. *Ansiedad y Estrés* **2001**, *7*, 195–201.
68. Garcia-Campayo, J.; Sanz-Carrillo, C.; Ibañez, J.A.; Lou, S.; Solano, V.; Alda, M. Validation of the Spanish Version of the SCOFF Questionnaire for the Screening of Eating Disorders in Primary Care. *Journal of Psychosomatic Research* **2005**, *59*, 51–55, doi:10.1016/j.jpsychores.2004.06.005.
69. World Health Organization Noncommunicable Diseases Available online: https://www.who.int/news-room/fact-sheets/detail/noncommunicable-diseases (accessed on 24 January 2025).