A Data-Driven Methodology and Workflow Process Leveraging Research Electronic Data Capture (REDCap) to Coordinate and Accelerate the Implementation of Personalized Microbiome-Based Nutrition Approaches in Clinical Research

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Abstract. In the rapidly evolving field of precision medicine, personalized nutrition is taking over as well. As individuals respond differently to diet, personalized nutrition engages the idea of going from delivering lifestyle and nutritional recommendations from the population to the individual level, allowing thus a better adherence to the diet, an achievement of nutritional goals, and an effective behavior change. The main factor contributing to the development of personalized nutrition in healthcare is the increase in the availability of large patient data that offers the opportunity to explore and investigate the relationship between various patient features, going from integrating simple data host to metagenomics data. Therefore, using microbiome data as a component of personalized nutrition can be substantial given the close relationship of the gut microbiome with nutrition and the host's health. However, shifting recommendations from the population to the individual level requires a robust data collection and management strategy. In this paper, we aim to describe the methodology and workflow process that uses Research Electronic Data Capture (REDCap) to facilitate the implementation of personalized microbiome-based nutrition approaches in clinical research.

Keywords: personalized nutrition · microbiome data · clinical research · electronic data capture

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1 Introduction

As stated by Van Ommen et al. [1] “Personalized nutrition tailors dietary recommendations to specific biological requirements based on a person’s health status and goals”. The personalized nutrition care model [2] reflects the different aspects used to allow patients to benefit from tailored interventions, with regular and continuous monitoring to reach specific outcomes. It includes: *(1)* The assessment with quantitative and qualitative host data such as diet, biochemistry, metagenomics, etc., *(2)* The interpretation of the personalized data through scientific evidence, *(3)* The intervention developed using guidance and therapeutics to design actionable interventions such as changes to diet and lifestyle factors, and *(4)* The ongoing monitoring and evaluation along the care process for regular feedback, and therapeutic interventions refinement to achieve self-efficacy and behavior change. The therapeutic intervention adherence, represented here by the adherence to an adequate diet, is an important indicator of self-efficacy and health behavior change [3]. Adherence is defined by the World Health Organization (WHO) as the degree to which a person complies with agreed recommendations from a healthcare practitioner, whether taking medication, adhering to a diet, or implementing other lifestyle changes [4]. Across all therapeutic areas, patient non-adherence represents an issue. The lack of patient treatment adherence can be associated with poorer health outcomes, lower quality of life, death, and a burden on healthcare costs [5]. In Medical nutritional therapy (MNT), we understand adherence issues as mainly poor adherence to the nutritional plan. Research indicates that individuals facing different barriers are less likely to comply with a long-term dietary plan [6]. With tailored nutritional recommendations that address patient’s needs and barriers, considering the perspectives of personalized nutrition can be a great strategy for facilitating and improving nutrition adherence, and as variations in how each individual responds to diet are always present [7], personalized nutrition engages the idea of going from delivering lifestyle and nutritional recommendations from population to individual level, allowing thus a better adherence and achievement of nutritional goals, and effective behavior changes [8].

For this reason, richer data can help to achieve more targeted interventions and recommendations: from nutritional intake assessment, routine lab testing, and targeted lab testing to omics analysis, the tailored evidence-based strategies and interventions will go from generalized to more personalized for individuals [2]. As an example of the gut microbiome that is unique to each individual and can be influenced by several factors, our diet greatly impacts it, therefore, manipulating this latter with dietary approaches will consist of using gut microbiome markers to optimize dietary interventions, to modulate diet and using diet to modulate the gut microbiome [9]. Personalized nutrition is therefore considered one of the greatest advances in modern medicine, especially with the development of omics and digital technologies.

However, shifting recommendations from the population to the individual level to achieve personalized nutrition requires extensive clinical and omics data, which comes with the need for a robust data collection and management system. As defined in the FAIR (Findable, Accessible, Interoperable, Reusable) data guiding principles [10], making the data collected easily searchable, accessible, integrated, and used in combination with other data and reusable is also a crucial element for supporting personalized nutrition. Moreover, the advancement in information technologies (IT) has led to the development of health data management systems to provide to a greater extent accurate and better patient care [11]. Researchers have designed and implemented a data management system to manage patient data and support clinicians in their decision-making to diagnose genetic diseases [12]. Some worked on capturing data related to patients with inflammatory joint diseases directly from an electronic health record system and transferring them into an electronic data capture system, helping in transitioning from paper format to electronic system [13]. Another study proposed an integrated data management system to support and manage data of patients with Parkinson's disease, preventing, therefore, data loss, and offering patients clinical follow-up and monitoring [14]. In nutrition care, dietary assessment and nutritional monitoring can be challenging for healthcare professionals and nutritionists as the available methods are time-consuming and susceptible to human errors [15]. Leveraging digital health technology may now offer a new way to provide medical nutritional therapy on a more accurate, personal, and accessible level. There is evidence for example that computerized patients' data management systems can improve nutritional care and monitoring, with better data visibility and adequate nutrition delivery [16].

One of the easily accessible data collection and management systems is the Research Electronic Data Capture (REDCap) [17]. REDCap is a secure, web-based application designed for research teams as a tool to collect, manage, and store research data in a secure environment. Because of its user-friendly interface, it has been used in several domains, and more importantly in clinical research as a tool to support precision medicine in oncology [18] and support clinicians in assessing the probability of patient outcomes after surgery for pancreaticoduodenectomy [19]. The field of nutrition research is known for its huge amount and complex data, which makes it one of the healthcare fields that are advancing in the use and application of computational techniques to its important data [20]. REDCap can be an important part of data-driven projects related to nutrition, as data collected and managed using REDCap can be later processed and analyzed using various computational techniques, including machine learning (ML) and artificial intelligence (AI), evolving the field of personalized nutrition.

Therefore, given the close relationship of the microbiome with nutrition and its key role in modulating health and disease, it is important to integrate the gut microbiome as a component of a personalized nutrition intervention along with other individuals' information. With the ability to modulate the gut with diet, it is appealing to target the gut microbiome with diet-based strategies and to harness digital technologies, such as REDCap's data management features to efficiently collect and integrate data, leading to more tailored dietary interventions, which can be of interest for both healthcare professionals and patients for providing targeted and actionable nutritional approaches and receiving recommendations for achieving sustainable results, respectively. To this end, this paper aims to describe the methodology and workflow process deployed to manage and integrate data at different scales using digital health (REDCap) to advance the field of personalized nutrition and facilitate the implementation of personalized microbiome-based nutrition approaches in clinical research.

2 Materials and Methods

2.1 Ethical Statement

The study protocol was approved by the Ethics Committee of Reference of the Regional Health Service of Segovia, Spain, as well as the Ethics Committee from Hospital Clínico San Carlos of Madrid, Spain, which also approved the related data management processes (17/183-E-BS and 19/409-E).

2.2 Data Source

The Hospital Clínico San Carlos of Madrid, together with the Primary Care Centre of the province of Segovia (Autonomous Community of Castilla y León) in Spain are carrying out a collaborative study to investigate the metabolic syndrome and cardiovascular risk factors in a cohort of patients: the SEGOVIA cohort study. This study is a longitudinal population-based study with a long follow-up of 20 years involving a cohort of 809 subjects aged between 35 and 74 years, enrolled in the study between January 2000 and January 2003. Assessments were carried out at three points in time, in which the study variables are collected: a baseline visit from 2000, a second visit with a median follow-up of 7 years in 2008, and, finally, a third visit with a median follow-up of 20 years in between 2021–2023. The work presented in this paper focuses on the sub-cohort of patients with a median follow-up of 20 years, where a sub-study of metabolic syndrome, diet and characterization of the intestinal microbiota is being conducted.

2.3 Data Collection

The patient clinical information was gathered by means of a written questionnaire in a face-to-face interview with an interviewer, where an individual code was assigned to each patient. The report form includes extended questions to gather the necessary information about the patient, related among others, to his personal data, medical history, clinical data, and daily habits.

The nutritional assessment and the dietary data collection of patients were carried out using two types of evaluation tools: *(1)* a 14-item Mediterranean Diet Adherence Screener (MEDAS) [21] integrated into the general questionnaire, where the level of adherence to the Mediterranean diet is assessed using a 14-item questionnaire (12 questions on food consumption frequency and 2 questions on food intake habits considered characteristic of the Spanish Mediterranean diet), and *(2)* a Food Frequency Questionnaire (FFQ) from the University of Navarra (Spain) that consists of a list of foods and beverages with categories of response to estimate the frequency of consumption over a specified period of time. Both the patient clinical information and the nutritional data were given in a Microsoft Excel spreadsheet file in an anonymized way, with the patient ID as the identifier.

Finally, the characterization of the composition of the gut microbiota was done after the collection of feces samples provided by the patients and their analysis by the Microbiota Laboratory of the Hospital of Madrid using Next Generation Sequencing (NGC) technologies. The results were given in a tabular representation of the gut microbiome composition: Operational Taxonomic Units (OTUs) table. OTUs table summarizes the composition of the microbial communities present in each sample, where each column represents a different sample, and each row represents the taxonomic identification of the bacterial taxa from the level of phylum, class, order, family, genus to species. The abundance of each taxonomic unit in each sample is represented by the relative abundances in the cells.

2.4 Setting up the REDCap Database and Data Entry Workflow

The collected patient data was transferred to a REDCap database created on the REDCap web-based application accessed through the hospital network, with only the research team having user rights. The digitization workflow included:

Selecting the relevant variables for defining the block of variables.
Patient clinical information gathered from the general questionnaire consisted of extensive information on patient health where several types of data were collected. For now, and based on the purpose of the research team and the study, only the data of interest was captured and digitized. The selection was made by the research team based on a mapping of common variables from the different questionnaires of each of the visits at the three points of time, i.e., 2000, 2008, and 2021. The interest behind this procedure is to be able later to investigate and establish the relationship between these variables over time, in a longitudinal way, as the data of the two previous studies projects is stored in a separate REDCap repository. In the end, only the relevant data has been selected, and the block of variables has been defined and captured in REDCap, as presented in the results part.

The nutritional information to be digitized covered on one hand, the data gathered from the answers to the 14 questions of the Mediterranean Diet Adherence Screener and its total score, and on the other, the data gathered from the Food Frequency Questionnaire, that is the result of the automatic calculations of estimated daily intakes of different nutrients and food groups from the respondent-reported information.

Finally, the gut microbiome information, given the large size of the initial OTUs table and the complexity of gut microbiome data, data will be captured as the relative abundance at each phylum level for every sample (i.e., patient) to enable simple and efficient data capture.

Completing the required metadata information
The worksheet with all the defined data elements is used to complete the requirements for data entry, by filling in the specific information related to *the type of variable (field type), the field label, and the variable name in REDCap* to prepare the data entry in the software for building the environment.

Creating the environment via the Online Designer
The online designer in REDCap allows the creation of the environment via the instrument collection page, where data collection instruments, referring to the block of variables defined, can be created and the variables can be added.

Capturing the data
Once the environment has been added to REDCap, it is possible to upload the data directly into REDCap using the Data Import Tool.

3 Results

3.1 Defining the Block of Variables and Integrating Data

Our data source included 113 patients (58,4% women and 41,6% men). Overall, after the selection of variables, we were able to define five blocks of variables that represent the instruments to be created on REDCap, with their associated metadata. We integrated multiple data types, including *(1) demographic data, (2) clinical data, (3) dietary records and nutritional data, (4) analytical data, and (4) omics data*, as detailed in Table 1.

Table 1. Block of variables retrieved with the associated metadata

Demographic data
Personal ID Gender Clinical center Date of interview Age Year of revision The starting time of the questionnaire Marital status Place of residence Professional activity
Clinical data
Medical history, including *history of diabetes, hypertension, cholesterol, cardiovascular and intestinal diseases, other diseases, birth delivery, and physical examination* Anthropometric measurements *Weight, Height, Waist circumference, Hip circumference* Blood pressure measurements Electrocardiogram measurements
Nutritional data
14 items questionnaire of MEDAS Food Frequency Questionnaire *Macronutrients intake (per day)* *Micronutrients intake (per day)* *Vitamins* *Minerals* *Total intake by food groups (g/day)*

(*continued*)

Table 1. (*continued*)

Analytical parameters
Diabetes diagnostic *Basal capillary glycemia (fasting glycemia)* *Capillary glycemia 2 h after glucose tolerance test* *Glycated hemoglobin HbA1c* Lipids profile: total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides Kidney and hepatic functions Urine: microalbuminuria
Gut microbiota data (relative abundance by phylum)
Overall characterization of 26 phyla; relative abundance of each phylum for each patient

3.2 Clinical REDCap Workflow

After designing and creating the environment on REDCap, one can either import the data using the data import tool option or add records directly via the record dashboards as the surveys and the required components have been created to facilitate the capture of data. By adding a new record, we are creating a new patient profile with its personal ID. We can then start capturing the demographic data, the phenotype-based information data, including anthropometrics, clinical information and clinical biomarkers, and nutritional information by filling the dietary record related to the FFQ, as well as the survey related to the Mediterranean questionnaire that will automatically retrieve the total score of the survey. Finally, the microbiome profile will be integrated as the relative abundance of each phylum present in each sample.

Figure (1) briefly shows the clinical REDCap workflow setup to enable the deployment of the digitization of the needed data for a personalized nutrition strategy in clinical care. The data management system created on REDCap allows us to capture the data directly by filling in the information in the appropriate fields. Once capturing data is completed, reports and statistics can be accessed, as well as initiating the data export.

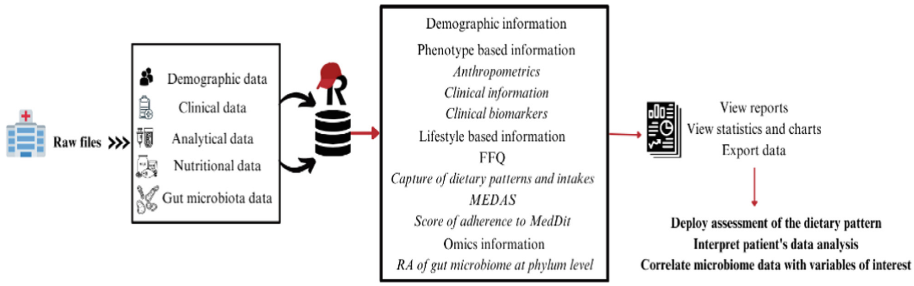

Figure. 1. Clinical REDCap workflow for supporting the implementation of personalized microbiome-based nutrition approaches in clinical research. *Abbreviation: RA. Relative abundance*

3.3 Impact of Digitization in the Clinical Setting

The digitization of the available data contributed to having an efficient process, compared to paper-based data collection, to limit the number of manual tasks and automatically capture the relevant data from capturing individual dietary records to integrating omics data and calculating the score for adherence to the Mediterranean diet. The use of the REDCap platform ensured a standardized collection of patient data, minimizing missing data and ensuring high-quality data collection. It offers hospital practitioners a practical option to easily export the data, generate reports, statistics, and charts that can help in comprehensively presenting data, as well as overviewing the included patients and the availability of their data, combining clinical and omics data, offering a support tool for clinicians to inform clinical decision making related to providing personalized nutrition strategy in a novel way that could be adopted in a clinical setting.

4 Discussion and Conclusion

The study associated with this work, the Segovia study, is a longitudinal population-based study that was at the beginning a study representative of the Segovia province resident population in urban and rural areas aiming at estimating the prevalence of the Metabolic Syndrome [22]. The present paper focuses on the sub-cohort of patients with a median follow-up of 20 years (i.e., third visit) that aims at studying the Metabolic Syndrome, diet and characterization of the intestinal microbiota. Given the importance of digital health, and to leverage the use of digital tools in clinical settings like REDCap and its advanced data storage features, we were able to create a detailed patient profile by integrating multiple data types, from dietary, and clinical data to microbial profiles. This comprehensive patient profile is important for designing nutritional recommendations that are more likely to be adhered to. The microbiome profile of the patient is provided by the relative abundance of the microorganisms at the phylum level. It gives us information on how many proportions of the microbiome are made up of bacterial taxa at the phylum level. This allows us to evaluate further if the relative abundance of the bacteria is associated with one of the variables of interest such as dietary pattern or adherence to the Mediterranean diet.

Ensuring efficient data collection and enhancing data accessibility can be relevant for supporting actionable nutritional recommendations. Tools for data management systems like REDCap have a valuable contribution and have found larger use in several domains including research projects and clinical environments. As in the study of Brauer et al., [23] where they aimed to assess whether personalized nutrition in metabolic syndrome can be associated with diet quality changes, the data capture system was used to enter the nutrition process data, including data restrictions and real-time data integrity checks. Moreover, REDCap [24] has found its use in clinical trials where included subjects can complete an online self-screening form and a survey in the application, and where the completed case report forms and demographic information will be stored and updated. Related to that, researchers [25] have designed and implemented a web-based data management system for diabetes clinical trials that had a good rating among researchers using it, showing that electronic systems can facilitate the clinical data management process in diabetes and endocrinology research. These support the extensive use of electronic data capture systems in clinical research and their ability to improve and facilitate the data management process.

Having access to data with real-time monitoring and reporting can facilitate the process of informed decision-making making, therefore be valuable for (1) achieving a proper assessment by identifying patient inputs that will help to gain a better understanding of the individual's behavior and distinctive characteristics ranging from general host data, biological data to the more advanced assessment of complex data such as gut microbiome, (2) interpreting the analysis of the patient's data gathered to derive actionable information from them and identify patterns and relationships between the different factors, (3) producing actionable interventions tailored to the specific patient's needs and goals, and (4) monitoring and evaluating to track progress and adjust recommendations as needed throughout the time, in an iterative process, and guarantee further refining in the intervention, enhancing thus patient's adherence and engagement to the personalized nutrition plan. One interesting study [26] reported the substantial contributions to patient care from using REDCap, where demographic, epidemiologic, and clinical data of HIV-positive and negative patients with or without liver and cervical cancer were accessible in REDCap, and have helped healthcare professionals in providing more personalized care, as well as promoting patients' involvement in their health care.

Overall, the data-driven methodology and workflow process leveraging REDCap has been deployed to structure the collection of data relevant for coordinating and implementing personalized nutrition in clinical practice, emphasizing the importance and value of the insights gained from data in providing efficient solutions. The digitization process and integration offer real-time accessible information to healthcare providers to inform clinical decisions for personalized nutrition purposes and improve individual health outcomes by leveraging an approach of patient-centered care, with a special focus on improving adherence to nutritional treatment plans. This study, however, has some limitations due to its design (i.e., observational) and due to the individuals lost in the follow-up assessments. Nevertheless, death causes will be available for the 20-year period of follow-up, as well as some clinical information of those subjects that were not revised during the first and second follow-up waves which will be extracted from medical registries in the coming months. Future work will eventually emphasize on making available sequenced data for genome-wide association studies (GWAS) to help achieve more targeted interventions and recommendations.

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