Nutrigenomic Information in the openEHR Data Set

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Abstract

Background  The traditional concept of personalized nutrition is based on adapting diets according to individual needs and preferences. Discussions about personalized nutrition have been on since the Human Genome Project, which has sequenced the human genome. Thenceforth, topics such as nutrigenomics have been assessed to help in better understanding the genetic variation influence on the dietary response and association between nutrients and gene expression. Hence, some challenges impaired the understanding about the nowadays important clinical data and about clinical data assumed to be important in the future.

Objective  Finding the main clinical statements in the personalized nutrition field (nutrigenomics) to create the future-proof health information system to the openEHR server based on archetypes, as well as a specific nutrigenomic template.

Methods  A systematic literature search was conducted in electronic databases such as PubMed. The aim of this systemic review was to list the chief clinical statements and create archetype and templates for openEHR modeling tools, namely, Ocean Archetype Editor and Ocean Template Design.

Results  The literature search led to 51 articles; however, just 26 articles were analyzed after all the herein adopted inclusion criteria were assessed. Of these total, 117 clinical statements were identified, as well as 27 archetype-friendly concepts. Our group modeled four new archetypes (waist-to-height ratio, genetic test results, genetic summary, and diet plan) and finally created the specific nutrigenomic template for nutrition care.

Conclusion  The archetypes and the specific openEHR template developed in this study gave dieticians and other health professionals an important tool to their nutrigenomic clinical practices, besides a set of nutrigenomic data to clinical research.

Background and Significance

The nutrigenomics nutrition field uses molecular tools to clarify and understand different responses from nutrient intake by individuals and population groups.1 It is related to the influence from dietary factor (bioactive molecules) and gene interactions that potentially change the gene expression.2,3 Hence, the human genome sequencing enabled the emergence of the so-called "personalized nutrition."4

Hesketh4 defined personalized nutrition as the ability to detect thousands of stable genetic differences occurring in humans and their impact on nutritional sciences. Accordingly, a new vision of nutritional-advice delivery has emerged as a result of it5; in other words, it is nowadays consensus that nutrigenomics is the "future of nutrition."6 Therefore, some authors suggested that it is necessary to study the particular genotype of an individual to prescribe a correct dietary advice to him/her. Such study would be
effective to prevent chronic diseases\textsuperscript{2,4,7,8} and to prescribe personalized dietary nutrient-intake recommendations.\textsuperscript{9,10}

Thus, nutrigenomics has used science to encourage the development of a genetic-tests marketing.\textsuperscript{11,12} However, despite the benefits of applying nutrigenomics, some points such as the lack of knowledge presented by health professionals and experts about how to convey the nutrigenomic information remain significant barriers to its use in clinical practices.\textsuperscript{13,14} Although nutrigenomic studies have shown significant benefits,\textsuperscript{15–17} we are aware of its vast field and of points still requiring further investigation.\textsuperscript{18} Therefore, genetic data, particularly from the nutritional genomics field, should be collected and stored in medical records to be further used to improve the collection of robust data and to be integrated into clinical practices.\textsuperscript{19}

Hence, the electronic health record (EHR) is an essential tool for the aforementioned process, although the nutrition-support content in EHR is yet reported as insufficient and demands significant improvement.\textsuperscript{20} The main causes for such results come from the fact that dieticians have not been deeply involved in the EHR modeling process and from the lack of organizational commitment to encourage health professionals to participate in EHR modeling.\textsuperscript{21}

Some authors have reported timelessness, availability, completeness, legibility, and accuracy as the benefits from electronic records.\textsuperscript{22–24} Some of the points identified by Beale\textsuperscript{25} regarding ideal EHR systems were: providing information and efficient-use interface to reflect multiple hierarchical, biological, and social organization levels; following multilanguage approach; integrating knowledge-bases such as terminologies and clinical guidelines; providing wide geographical availability of a given record to multiple careers and applications; being consent-based—privacy rules on information use (except for emergency access); etc. Hard efforts have been made to address issues concerning EHR modeling and implementation as a way to allow the development of future-proof EHR systems\textsuperscript{26} and these efforts have resulted in openEHR, among others.\textsuperscript{27}

The openEHR is a community focused on turning physical-form health data into an electronic form and on assuring the universal interoperability of all electronic data. It is mainly focused on EHR and on related systems.\textsuperscript{27} This community assumes two framework levels known as reference and archetype models; both used to separate knowledge from information models. Such separation enables reliable clinical-meaning sharing in addition to assure data interoperability.\textsuperscript{26} Moreover, openEHR holds part of the data structure used to represent the instanced data named “Archetype.”\textsuperscript{28}

Archetype is a computable expression given to a domain content model offset in structured constraint statements based on a reference (information) model.\textsuperscript{29} In other words, archetype is a pattern applied to store complete clinical information capable of being interpreted through EHR.\textsuperscript{30} It provides specifications from unique concepts such as body mass index and body temperature to complex concepts such as positive family history.\textsuperscript{31}

Archetypes allow the creation of a template formed by a directly, locally, and usable definition. This template turns archetypes into a larger structure often corresponding to a screen form, document, report, or message. Templates are used for data construction and validation.\textsuperscript{29}

The openEHR archetypes and templates turn clinicians into active openEHR participants. Therefore, health professionals will simultaneously create and improve these tools; consequently, they will influence EHR functioning and patient care quality.

**Objective**

The aim of this study was to create the future-proof health information system to the openEHR server based on archetypes, as well as a specific nutrigenomic template resulting from a literature review on publications about nutrigenomics.

**Methods**

The present research was developed based on the following six stages (Fig. 1).

**Literature Review**

A literature search was performed in PubMed database to find articles published in the nutrigenomics field and to identify the main variables (clinical concepts) used in these studies.

The search was based on the following index terms: “nutrigenomics” AND “diet” AND “intervention,” and “nutrigenomics” AND “nutrition.” Studies complying with the following inclusion criteria were included in the research: (1) intervention studies; (2) intervention using nutrient or food; (3) nutrigenomic studies; (4) human studies; (5) English language; (6) studies published in the last 5 years (2013–2017); and (7) original articles (Table 1).

**Archetype-Friendly Concept Identification**

Bacelar et al were the references followed at this step.\textsuperscript{32} Our team created a list of clinical concepts, which compose a clinical statement defined as the minimal indivisible information unit to be record by clinicians\textsuperscript{33} and of organized clinical statements classified according to the nature of the statement. These concepts were identified in the “methods” and “result” section of each study; moreover, we used all the variables taken into consideration in the studies. Statistical methods were not used to analyze the clinical statements; content was manually interpreted according to team expertise by assessing whether the clinical statements could be model for an archetype.

We organized clinical statements in a structured form after listing them and gathered possible archetype-friendly concepts, mainly those considered objectives and the ones similar to them. We can cite an example to better describe how the clinical statements were assessed. A study presented variables such as “carbohydrate,” “dietary fat,” “polymorphism,” “vitamin C,” and “vitamin D,” and these concepts were gathered into archetype-friendly concepts. Thus, clinical concepts such as vitamin C and D were grouped as “micronutrient” (which is a possible archetype proposition);
"carbohydrate" and "dietary fat" were added as "macronutrient" (which is another archetype proposition).

**Clinical Knowledge Manager Analysis**

The Clinical Knowledge Manager (CKM) is an international clinical-knowledge resource repository that supports international domain knowledge governance, besides being a library of openEHR archetypes and templates. We searched for all archetype-friendly concepts in the repository, because CKM avoids archetype duplication; however, it was necessary to include the concept name and core data items in it. Archetype concepts lacking availability in the CKM were created by the authors.

**Archetype Modeling in openEHR**

It is hard for developers to perform archetype modeling processes, but we used the Ocean Archetype Editor Software, which is available at the openEHR Web site, to model the archetypes. Classifying the archetypes in entries such as observation, evaluations, instructions, or actions is the first step to model them. Entry types are responsible for solving medical problems such as diseases healed through medication prescription (action) or through symptom observation. Each entry presents specific structure in clinical recording processes; for instance, observation entry holds classes such as concept description, purpose, use, misuse, data (main clinical statements), events (moments when the collected data become important), protocol (information about data collection), and state (details about the patient at the time to get the data). On the other hand, the instruction entry presents classes such as concept description, purpose, use, misuse activities, and protocol. The archetype must be containing complete information, thus, the authors researched for information in journals, papers, books, and in instruction manuals. Moreover, all rules set for archetype creation were followed by the authors according to specific manuals. Finally, the new archetype was recorded in Archetype Definition Language (ADL), which is a formal language used to express the openEHR archetype.

**Clinical Knowledge Manager Subjection to Review**

The modeled archetypes were subjected to CKM at the Web site (www.openehr.org/CKM). The authors have created an account in the Web site to submit the archetype. We clicked in "propose new archetype" to upload the file after login in. Then, we added a new resource proposition and a brief description of the new archetype. Our archetypes were included in an area called "open archetype proposals" after the submission, and all CKM editors' doubts and communications were answered in there.

In this moment, openEHR editors assessed whether the suggested archetypes were necessary for the CKM repository. Archetypes were included as "draft" in an incubator or project after their approval. Incubators are spaces used in initial archetype development stages. Finally, the archetypes will be exhaustively reviewed by the international clinical community to be approved and published in the CKM.

**Nutrigenomic Template**

It was possible to create a specific nutrigenomic template (in which the archetypes were arranged) from the herein created archetypes and from the existing archetypes. The Ocean Template Designer Software was used to generate the template; this tool allowed including archetypes in the template.

It was not necessary to subject the project to the Ethics Committee in this study, since it did not use patients' clinical and demographic data.

**Results**

**Literature Review**

The bibliographic search followed predefined strategies and resulted in 51 articles. Of those, 25 articles were excluded after the abstracts were analyzed, because they did not present predefined criteria; therefore, the final sample comprised of 26 articles.

**Identifying the Archetype-Friendly Concept**

The performed critical analysis led to 117 clinical statements, which are the most used variables in nutrigenomic studies. These statements were represented in 27 possible archetypes.
<table>
<thead>
<tr>
<th>Article</th>
<th>Year</th>
<th>Clinical statements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lang et al[51]</td>
<td>2013</td>
<td>EPA - DHA - height - body weight - WC - BMI - FFQ - dietary recalls - n-3 - n-6 - PUFA - vit A - vit E - vit C - selenium - total fat intake - polymorphism</td>
</tr>
<tr>
<td>Nielsen and El-Sohemy[56]</td>
<td>2014</td>
<td>SNP - energy - sugars - variants - genes - FFQ - vitamin C - genotype - age - sodium</td>
</tr>
<tr>
<td>Gahete et al[58]</td>
<td>2014</td>
<td>Age - TC - isocaloric diet - protein - carbohydrate - total fat - SFA - MUFA - food diary - FFQ - α-tocopherol - ascorbic acid - fiber</td>
</tr>
</tbody>
</table>
international CKM health community; however, the other
was approved (August 2017) for review by editors in the
it in November 2017. The
Fig. 2
Classifying archetypes and entries.

Table 1 (Continued)

<table>
<thead>
<tr>
<th>Article</th>
<th>Year</th>
<th>Clinical statements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fallaize et al68</td>
<td>2016</td>
<td>Age = gender = PA - phenotype = genotype = FFQ = gene variants = SFA = scoring of polymorphism = genotype = allele frequency = BMI - body weight = WC - height - cholesterol = n3-fat = SFAs = MUFAs = PUFAs</td>
</tr>
<tr>
<td>Pu et al70</td>
<td>2016</td>
<td>WC = HDL-c = glucose = SFA = MUFA = PUFA = SNP - BMI = age = TC - HCL-c = body weight = SBP = DBP = gene = alleles = genotype = n3-n6</td>
</tr>
<tr>
<td>De Lorenzo et al71</td>
<td>2017</td>
<td>PBF = TBFat = body fat mass = LDL-ox = genes = BMI = energy = calories = proteins - carbohydrates = fats = dietary fibre = age = height = body weight = glucose = TC - HDL-c - TG</td>
</tr>
</tbody>
</table>

Abbreviations: BMI, body mass index; BMR, basal metabolic rate; CRP, C reactive protein; DASH, Dietary Approaches to stop Hypertension; DBP, diastolic blood pressure; DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; FFQ, Food frequency questionnaire; HC, hip circumference; HDL, high-density lipoprotein; Hg, hemoglobin; LDL, low-density lipoprotein; MUFAs, monounsaturated fatty acid; NC, neck circumference; PA, physical activity; PBF, percentage of body fat; total body fat percentage; PUFA, polyunsaturated fatty acid; SBP, systolic blood pressure; SFA, saturated fatty acid; SNP, single-nucleotide polymorphism; SQFFQ, semi-quantitative food frequency questionnaire; SUFA, saturated fatty acid; TBBone, total body bone; TBfat, total body fat; TC, total cholesterol; TEE, total energy expenditure; TG, triglycerides; TL, telomere length; WC, waist circumference; WHr, waist–hip ratio.

Clinical Knowledge Manager Analysis
However, of the 27 possible archetypes identified in the CKM search, 23 were available in the international CKM repository, so we modeled four archetypes (Fig. 2).

Archetype Modeling in openEHR
Finally, we created four archetypes, namely, waist-to-height ratio, genetic test results, genetic summary, and diet plan, which were subjected to CKM between July and August 2017—except for the “genetic summary,” which was subjected to it in November 2017. The “waist-to-height ratio” archetype was approved (August 2017) for review by editors in the international CKM health community; however, the other archetypes remain under editors’ review. All archetypes were created in English language. The purpose of the modeled archetypes was:

- **Genetic test results** (Observation)—Recording results and interpreting individuals’ genetic tests. Submitted to and under analysis by the editors. Fig. 3 represents the proposed archetype.
- **Genetic summary** (Evaluation)—Recording summary genetic information about an individual’s genetic details. Fig. 4 represents the proposed archetype.
- **Diet plan** (Cluster)—Recording information about an individual’s diet. Submitted to and under analysis by the editors. Fig. 5 represents the proposed archetype.

A specific nutrigenomic template was created after modeling the four archetypes. Fig. 6 represents the nutrigenomic template.

Discussion
This article describes the openEHR archetypes and template-based structure development process. It is used to represent clinical concepts from the nutrigenomics field, which assesses the influence from nutrients and bioactive food compounds on the gene expression.38

According to modern researchers, nutrigenomics presents significant results. However, registered dieticians (RDs) do not think that such researchers have the basic knowledge to
integrate nutrigenomics to their clinical practices.\textsuperscript{13} Accordingly, this study becomes relevant to create openEHR archetypes and a specific template capable of providing health professionals with the best information available in the nutrigenomics field.

Our group analyzed the selected articles and identified 117 clinical concepts to the nutrigenomics field, which made it possible to distinguish 27 archetypes. Four archetypes were created from these 27 ones. It is necessary to describe a complete clinical concept to model clinical statements into archetypes; however, the archetype creation process does not follow an established criterion; it is unlimited and depends on the researchers’ imagination.\textsuperscript{30} Therefore, and because nutrigenomics is rarely used in clinical practices, our group was careful and detailed in the conduction of the experiment performed to create these archetypes. Assembling similar clinical concepts was the number one step in this modeling process, although it is a difficult step, mainly if one takes into account broader fields such as genetics and nutrition.

The American Society for Parenteral and Enteral Nutrition (ASPEN) studied the current situation of the nutrition data

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**Fig. 3** Mindmap of archetype genetic test results.

**Fig. 4** Mindmap of archetype genetic summary.
Fig. 5  Mindmap of diet plan archetype.

Fig. 6  Nutrigenomic template.
found in the EHR by checking the safety and effectiveness of the nutrition documentation. The ASPEN members scored the EHR nutrition component as “fair.” Such grade is possibly associated with the fact that dieticians must be involved in EHR content creation. This result shines the light on the EHR developer health care system. These ASPEN members reassessed EHR nutrition safety and efficacy 4 years later and reached the same conclusions. However, the authors reinforced that nutrition societies and organizations need to provide education on clinical informatics to their members, as well as templates for standard nutrition care processes.\(^\text{21}\)

Thus, it is essential to encourage professional’s involvement in openEHR archetype creation, since these archetypes present well-described advantages in the literature.\(^\text{39}\) One example is that archetypes can be created and revised, thus making it possible reformulating whenever needed. This is an essential advantage, mainly when it comes to genetic data, because new data are always found and archetypes always need reformulation. The systematic discovery of new syndromes each year is an example of content being needed to be updated mainly because contents and terminologies need to be revised.\(^\text{40}\)

Actually, we aimed at creating openEHR archetypes and a specific template to the nutrigenomics field to facilitate EHR use by health professionals and to help storing correct and future-proof contents; however, health care professionals, mainly RD, are not familiar with the nutrigenomics field, and it impairs EHR development.\(^\text{13,14}\)

However, RDs appear to be the most qualified health professionals to talk about nutrigenomics with patients. Accordingly, they must acquire the knowledge and skills necessary to integrate this science to their practices.\(^\text{13}\) The present archetypes and template could provide correct information capable of mitigating difficulties and of improving the nutrigenomic care.

Therefore, we have recently modeled nutrition information to prevent and treat childhood obesity based on clinical guideline recommendations.\(^\text{41}\) It was possible to herein create 14 new archetype concepts to improve nutrition care. These archetypes can be incorporated to different EHR systems. Other authors have also focused on developing openEHR-based structures to improve clinical care and EHR system in different fields.\(^\text{31,32,42}\)

Moreover, archetype validation and its publishing is not an easy process. Braun et al proved that creating, validating, and publishing them was a hard work. It is possibly so because of lack of domain expertise and modeling experience, as well as because of the large number of steps to be taken. However, although this is a complicated process, mainly in the genetic field, it is worth emphasizing that it is essential to assure the quality of the medical information model.\(^\text{31}\)

The multiplicity of genetic data becomes a challenge at the time to identify the main data and the specific information type to be inserted in EHR. Recently, Mascia et al\(^\text{39}\) suggested the following genetic archetypes: “genetic findings” and “sequence variation,” among others. However, the development of the “genetic test results” archetype is in process. In our opinion, some data in this archetype are not related to “results” as “interpretation summary” and “recommendation” data. Besides, the “laboratory identifier” archetype is not enough data to record genetic content and requires “laboratory scope” data to determine whether it is a diagnostic or a research laboratory. Accordingly, in our opinion, the archetype suggested by Mascia et al still presents points to be improved.

Our decision about the clinical genetic statements was to model two archetypes to solve the addressed matter, namely, genetic test results and genetic summary. Our genetic archetypes were based on Marsolo and Spooner,\(^\text{40}\) who identified the points needed in genomic EHR, namely, genetic information stored as structured data; data interoperability; phenotypic information stored as structured data and associated with relevant genetic information; data availability for use by rule-based decision-support engines; and EHR use to display the information needed by clinicians to interpret genotypic and phenotypic data.

However, we faced important challenges to model the genetic archetypes:

- **Genetic protocol:** The stored genetic information does not follow any standard protocol\(^\text{43}\); although the Electronic Medical Records and Genomics (eMERGE) Network comprise researchers presenting a wide range of expertise in genomics, clinical informatics medicine, statistics, ethics, etc. to develop the best practice for EHR use as genomic tool.\(^\text{44}\) We used guideline recommendations and articles that described the minimum genetic EHR requirements to solve this problem.\(^\text{40,45}\)

- **Extensive genetic data:** Stored genetic data are extensive and complex; EHR is able to save all genome data. It is possible to include extensive data in openEHR by the electronic path and can be added to archetype, making possible that all the EHR content be genetic data.

- **EHR categories:** Much of the EHR content is collected in free text notes, and it increases data variability; therefore, only the indispensable contents were created in free text notes.

We aim to have health professionals presenting good quality nutrition and genetic data, and to have archetypes presenting all the current important data, as well as data that may be essential in the future. A specific nutrigenomic template was developed from archetype creation; however, the new template can be built from our archetypes, as well as from archetypes available at CKM, and meet health professionals’ demands.

**Limitations**

Results in this article reported the archetypes developed through nutrigenomic clinical statements based on literature review. However, it is worth knowing health professional’s opinion about the main clinical statements used in nutrigenomic clinical practices. Moreover, many nutrition professionals lack knowledge about this field, and it justifies the difficulty we had to get specialized opinions.

Finally, not all the herein suggested archetypes were approved for review by CKM editors. We know that
archetype validation is a hard process in CKM, but we believe that all archetypes built by us are essential to clinical practices; therefore, they will soon be approved.

Conclusion

This article describes the process to create new openEHR archetypes and a specific template based on the literature review. Hence, the new archetypes and the template can be incorporated to different EHR systems and help health professionals in nutrigenomic data collection to improve their clinical practices. The most significant result concerned the fact that all health professionals will have complete nutrigenomic data in the EHR system; these data can be used in further clinical research. We reinforce the importance of having health and information technology (IT) professionals involved in EHR creation, because it would result in a complete and structured EHR system.

Clinical Relevance Statement

The openEHR archetype modeled to EHR (in a specific field) is an important point to improve health care. It contains complete and structured data capable of minimizing data collection errors and of improving the quality of the collected data. Therefore, archetype creation is of significant importance when it comes to providing the best care to patients.

Multiple Choice Question

Archetype creation is linked to design principles; thus, is it possible to say that a correct archetype design principle concerns is:

a. Archetypes used to define aggregates of information suitable for particular local uses.
b. Archetypes that do not create new constraints to the data they refer to.
c. An archetype that cannot be a specialization of another archetype.
d. An archetype that defines constraints to the structure of instances from a reference model.

Correct Answer: The correct answer is option d, there are 14 archetype design principles. According to the “Archetype Definitions and Principles,” letters A and B are wrong, because they are related to a template design used to define aggregates of archetypes suitable for “particular uses,” and to “templates that cannot create new constraints to the archetypes they refer to; they can only further constrain in a compatible way. Letter C is wrong because the archetype can be a specialization of another archetype. Archetypes can be defined at higher or lower detail levels at a given ontological level. Thus, a “biochemistry result” archetype would define the general shape and constraints to all the biochemistry results, whereas a “cholesterol result” archetype could be defined as a specialization of it, to further constrain data to only comply the shape of a cholesterol test.

Protection of Human and Animal Subjects

Not required.

Conflict of Interest

None.

Acknowledgments

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