Genomic-driven personalized nutrition: science, concept and case study on antioxidant supplementation

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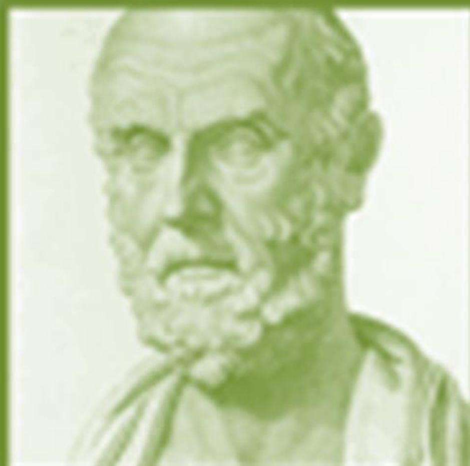


Let food be thy medicine and medicine be thy food

~ Hippocrates

- Individual genetic variation can influence how nutrients are assimilated, metabolized, stored and excreted by the body.
- The exploration of the complex interaction food ~ genes promises a real revolution in the way and concepts of nutritional treatment of diseases.

↓

Personalized nutrition (PN)

enhance human health by tailoring dietary recommendations to individuals

Keyword **”personalized nutrition”**

Google search:

~ 1.530.000.000 rezultate; ~ 1.680.000.000 rezultate (”personalized nutrition#”)

WoS:

5481 results (1986-2023)

SCOPUS

3738 document results

Projects, H2020

2011-2015 Food4Me *Personalised nutrition: An integrated analysis of opportunities and challenges*

2018-2022 *Empowering consumers to prevent diet-related diseases through omics sciences*

2018-2022 *Personalized nutrition for healthy living*

2018-2023 *Fact-based personalised nutrition for the young*

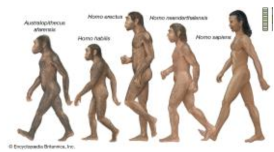
2018-2023 *Smart technologies for personalised nutrition and consumer engagement*

- Personalized nutrition: science and concept
- Strategies in personalized nutrition.
  Case study on antioxidant supplementation
- Perspectives on personalized nutrition

1. Personalized nutrition – science and concept

❑ Why is PN needed?

Nutritional factors



affected the gene expression → phenotypes that responded properly to environmental changes	provided the metabolic support for the development of motor functions → better exploitation of food resources in the new habitat

❑ To whom is PN addressed?

- healthy individuals, general public → information about genetic variants used for targeted dietary and lifestyle recommendations

- people with rare metabolic diseases arising from gene mutations/ *inborn errors of metabolism* (glucosemia, hereditary fructose intolerance, phenylketonuria), and more common disorders (lactose intolerance, celiac disease).

- Currently, increasing importance is given to the involvement of genetics in multifactorial diseases (hypertension, diabetes, dyslipidemias, cancers, obesity)

WHO estimates that

~ 80% of premature heart disease cases, strokes, type 2 diabetes, and

~ 40% of cancers

could be avoided if unhealthy diets were eliminated.

Concept, descriptors and definitions of PN

American biochemist *Roger J. Williams* (1893–1988), article published in 1950 “Concept of genetotrophic disease”: ‘*a genetotrophic disease is one which occurs if a diet fails to provide suffcient supply of one or more nutrients required at high levels because of the characteristic genetic pattern of the individual concerned*’.

The concept remained in a dormant stage until the *human genome sequencing (1990-2003)*. From this point, a lot of studies emerged on 2 main disciplines:

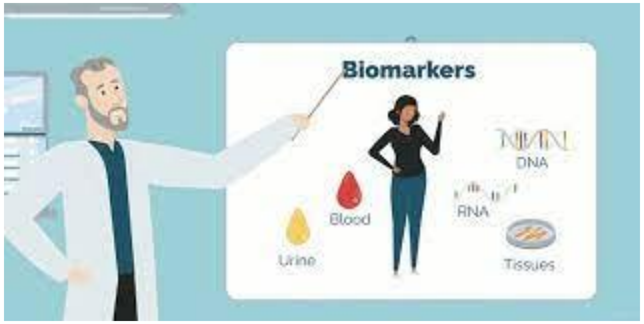
“*nutrigenetics*” - how genetic background affects the response to dietary components, nutrient requirement, and predisposition to certain diseases;

“*nutrigenomics*” - how diet affects gene transcription, translation and metabolism

Generic nutritional recommendations	Personalized nutrition
→ **Initially**, to ensure a proper intake of nutrients (minerals, trace elements and vitamins) to prevent malnutrition → **Nowadays**, to ensure an adequate intake of nutrients and sufficient physical activity to reduce risk factors (*hypertension, overweight, obesity, hyperglycemia, hyperlipidemia*). "one-size-fits-all" approach	→ developed based on information collected on: **1. the individual's diet** *dietary records, 24-h recalls, questionnaires, modern technology, food preferences, sensory preferences* **2. the phenotype** *weight, height, hip and waist circumference measurements, BMI calculation, questionnaires on physical activity and lifestyle, physical activity monitors and devices for measuring blood pressure, pulse rate or blood oxygen saturation, analysis of metabolites in blood, cholesterol, glucose, biomarkers of nutrient status, disease status, physiological state, etc.* **3. the individual's genotype** *nutrigenetics by DNA analysis e.g. from buccal cell samples*

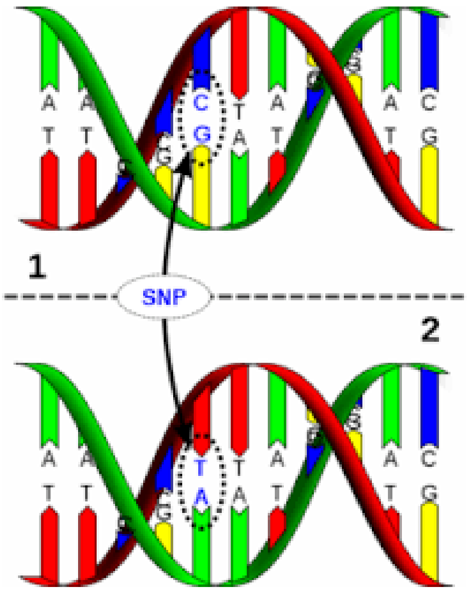
For effective and sustainable PN practices, the following are required:

■ a *consensus* PN definition,
■ established *standards* for PN approaches,
■ *biomarkers* that predict responses.



PN involves:
- multiomics analyses
- machine learning tools

Opportunities and Challenges in Nutrigenetics/ Nutrigenomics and Health



Individuals differ from each other in their gene sequence.

Genetic variation - naturally occurring genetic differences

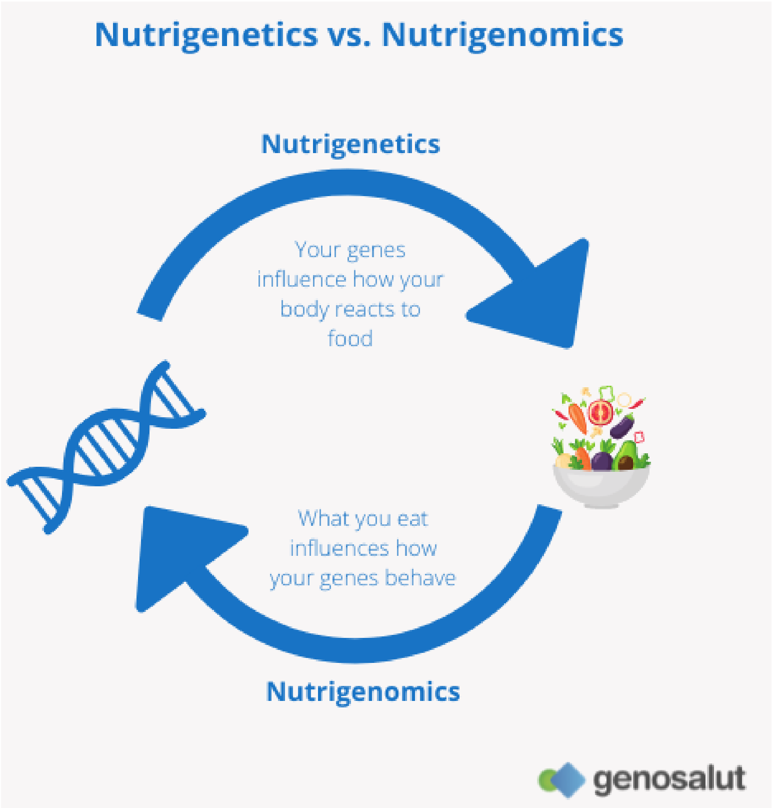
- assures survival of a population under environmental changes
- affects uptake, transport, metabolism and elimination of food components
- influences the individual daily requirements for nutrients
- variation of DNA gene sequence between 2 individuals is 0.1%
- a large genetic variation= single-nucleotide polymorphism (SNP).

	NUTRIGENETICS	NUTRIGENOMICS
DEFINITION	■ how genetic variability modulates the individual response to nutrients (macro-/micro-/non-essential)	■ how nutrients affect gene expression and metabolic profiles; effects on: - genome stability, - epigenome alterations, - RNA and protein expressions - metabolites
EXAMPLES	■ LCT gene ~ lactose intolerance ■ AMY1 gene ~ high-starch diet	■ Resveratrol can prevent cancer by modulating gene products resveratrol markedly reduces the cytokine-induced expression of pro-inflammatory mediators (IL-8, iNOS and TNF-α), as result of the resveratrol-mediated reduction of mRNA stability; ■ Glucose and selenium influences the stability of mRNA for specific enzymes (fatty acid synthetase, glutathione peroxidase)
ASSESSMENT	■ Genetic analysis + conventional standard nutritional guidelines + other info	Multi-omics approach: ■ Transcriptomics (microarray technology, PCR) ■ Proteomics (2D electrophoresis, MS) ■ Metabolomics (MS, NMR)

Methods for determining genetic variations (genotyping)

1. **PCR method**
2. **Micro-array platforms**
3. **Sequencing methods**

What does the nutrigenetic test tell you?



Nutrigenetics and nutrigenomics are of major importance for the national health systems and for the food industry.

Problems/ challenges:

- the complexity of the human genome;
- the complexity of food composition induced geographically, seasonally, culturally, gastronomically, but also variable components' interactions.

2. Strategies in personalized nutrition
Case study on antioxidant supplementation

Measuring what individuals eat

Indicator	Edible portion	Water	Energy (kcal)	Protein	Fat	Carbohydrate, available	Dietary fibre
Combined unit of measure	percent	g	kcal	g	g	g	g
Food category							

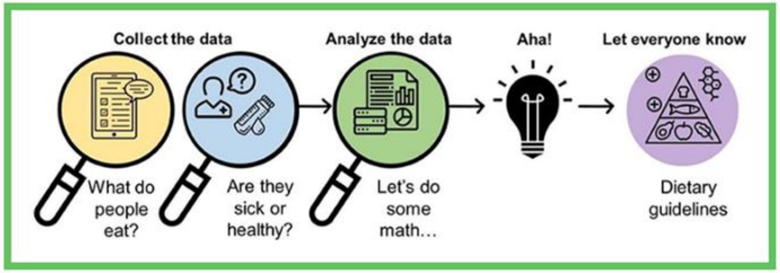
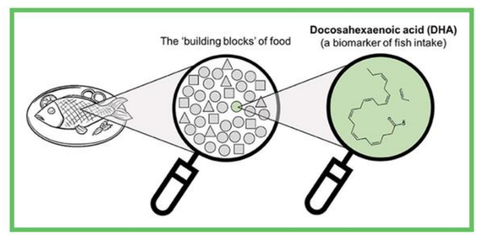
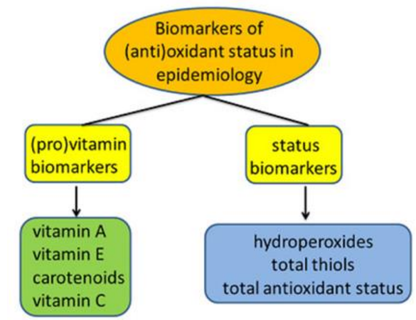


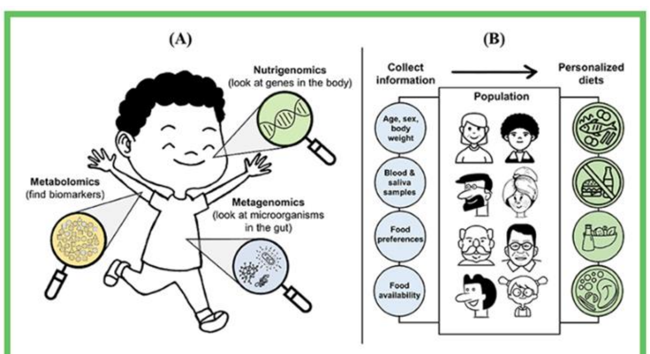
Figure 1 - How researchers in nutritional epidemiology investigate links between food and health.

Investigating the link between food and health

Investigating biomarkers of food intake



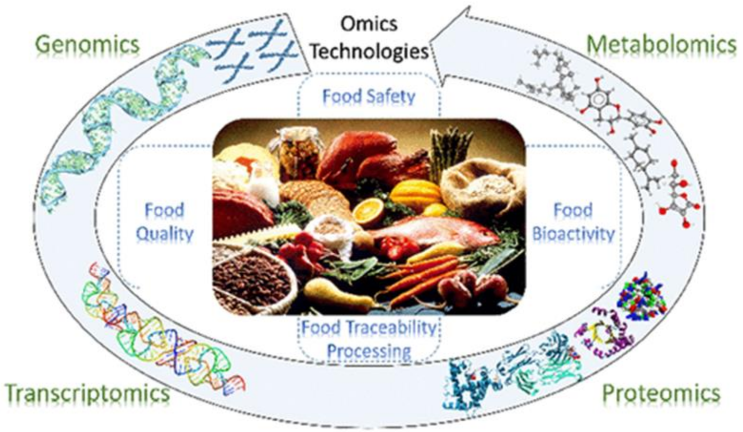




Collect genetic data
Integrate omic tools

FOODOMICS

omics-technologies used to quantify food compounds with the purpose to improve health



1. **Foodomics applications related to food safety and quality:**

- ❑ GMO detection in maize by DNA microarray (genomics);
- ❑ crop improvement of melon by gene expression microarray (transcriptomics);
- ❑ authenticity of fruit juices by NMR (metabolomics).

2. Foodomics applications related to Nutrigenomics:

- ❑ **sulforaphane** – studied on mice by DNA microarray (transcriptomics) for cancer protection;
- ❑ **isoflavones** from soya – studied on human serum by LC-MS/MS, 2DE (proteomics) for vascular protection;
- ❑ **polyphenols** from grape juice – studied on human feces by NMR (metabolomics) for prevention of the inflammatory bowel disease.

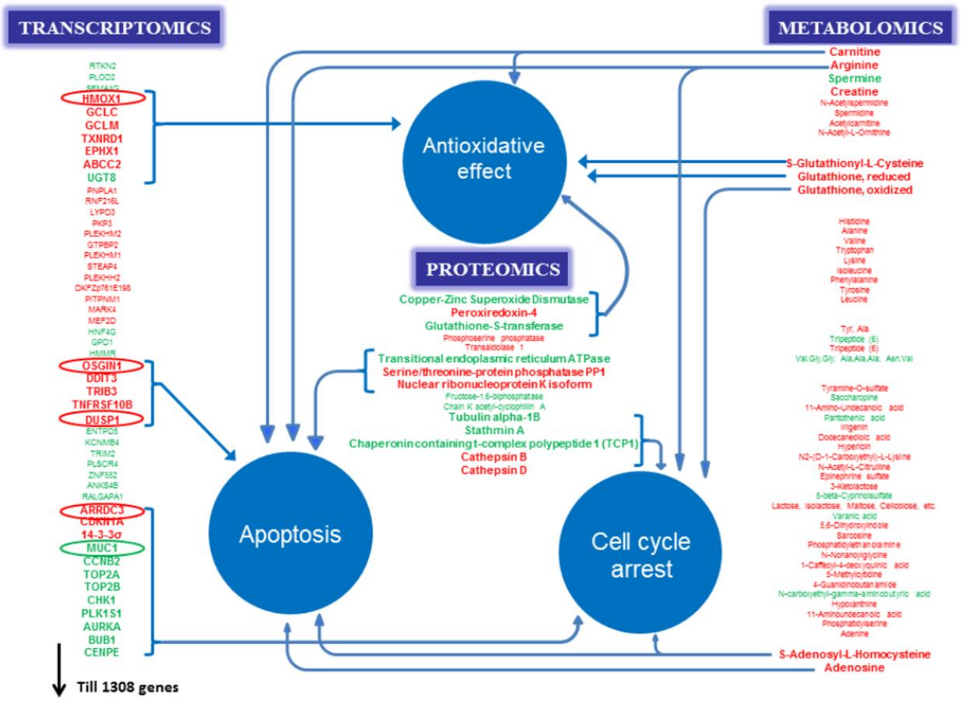
Nutrigenomics and antioxidants

Study of Nasséra Chalabi et al. (2006, 2007):

- investigated the **effects of lycopene against breast cancer**
- tested the differences between lycopene-treated and untreated cells on 202 genes interacting with the two major breast cancer genes (BRCA1, BRCA2), and on the whole genom
- results showed an *effect of lycopene on cell cycle, apoptosis and DNA repair mechanisms*.

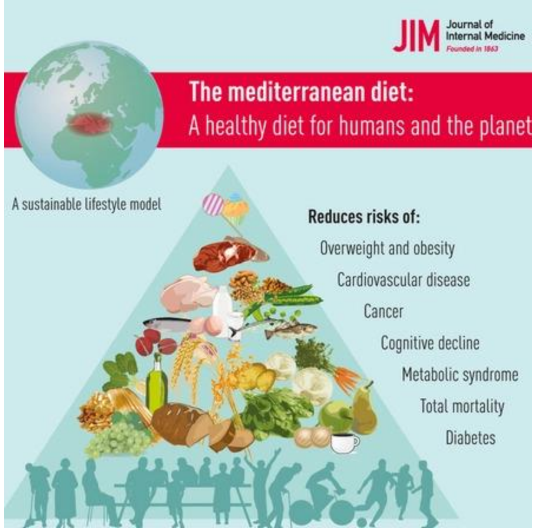
Study of Clara Ibáñez et al. (2012):

- investigated the **effects of dietary rosemary polyphenols** against HT29 colon cancer cells
- described the identified genes, proteins and metabolites that are involved in the principal biological processes altered in HT29 colon cancer cells after the treatment with polyphenols.

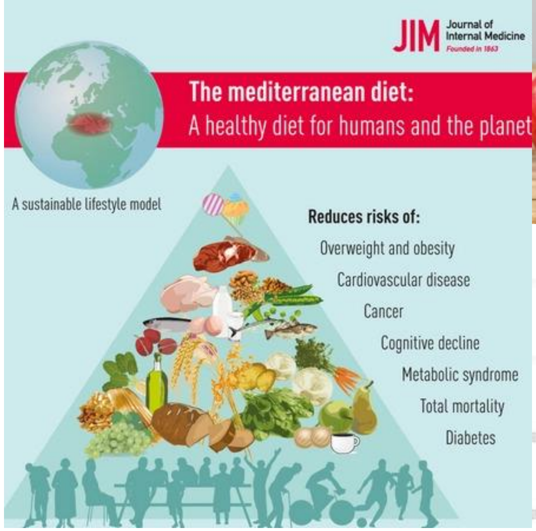


Study of Paola Gualtieri et al. (2023):

- investigated a **2-week supplementation of a Med.Diet with a mixed apple and bergamot juice**
- results show a positive impact on:
  - body composition - *gain in lean mass*
  - biochemical profile - *significant reduction in total cholesterol/ HDL index*
  - oxidative and inflammatory gene expression - *increase in Macrophage Migration Inhibitory Factor, Peroxisome Proliferator-Activated Receptor γ, Superoxide dismutase, and Vitamin D Receptor expressions*



versus



Antioxidants in Personalized Nutrition and Exercise – studies of the *Greek and Cypriot group of researchers (Margaritelis, Paschalis, Theodorou, Kyparos, Nikolaidis)*

Antioxidant supplementation is beneficial, detrimental, or neutral?

It largely depends on the baseline antioxidant profile of the individuals who receive the treatment.

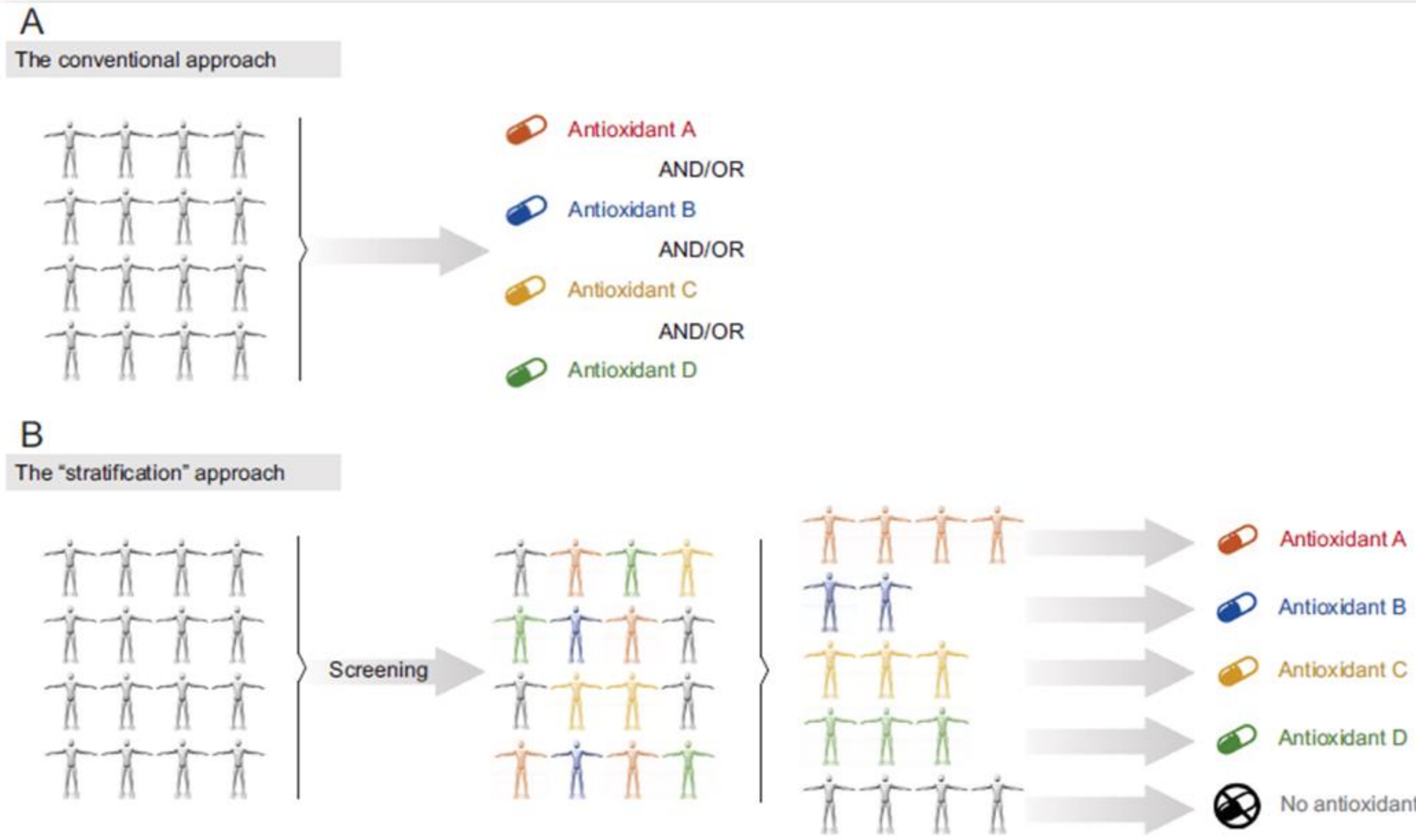


FIGURE 1 The conventional (A) and the novel "stratification" (B) approach with regard to antioxidant supplementation. The conventional approach is characterized by the indiscriminate administration of antioxidants irrespective of the redox profile of the individual. On the contrary, the stratified approach aims to identify potential antioxidant deficiencies in order to tailor the most suitable treatment (if needed).

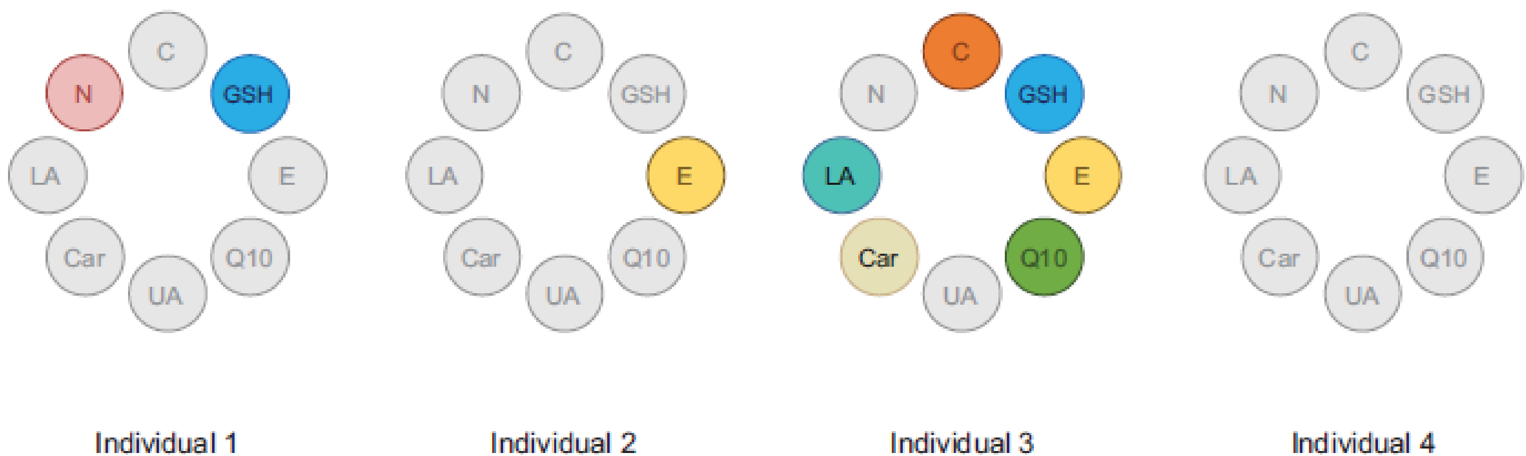
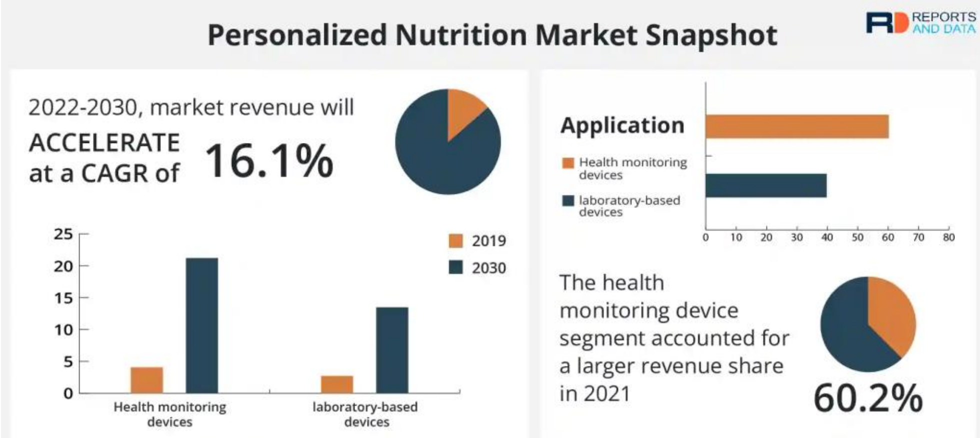


FIGURE 4 An "idealized" analytical tool to assess (e.g., via a capillary blood sample) an individual's systemic antioxidant profile in order to tailor the most optimal nutritional redox treatment. Individual 1 represents a person with low concentrations of GSH and NAD(P)H [e.g., due to dysregulated NAD(P)H redox metabolism]; individual 2 represents a vitamin E–deficient person (e.g., due to malnutrition); individual 3 represents a person with a highly disturbed antioxidant profile (e.g., due to severe illness); individual 4 represents an apparently healthy person with normal antioxidant status who does not need any exogenous antioxidant supplement. C, vitamin C; Car, carotene; E, vitamin E; GSH, reduced glutathione; LA, lipoic acid; N, NAD(P)H; Q10, coenzyme Q10; UA, uric acid.

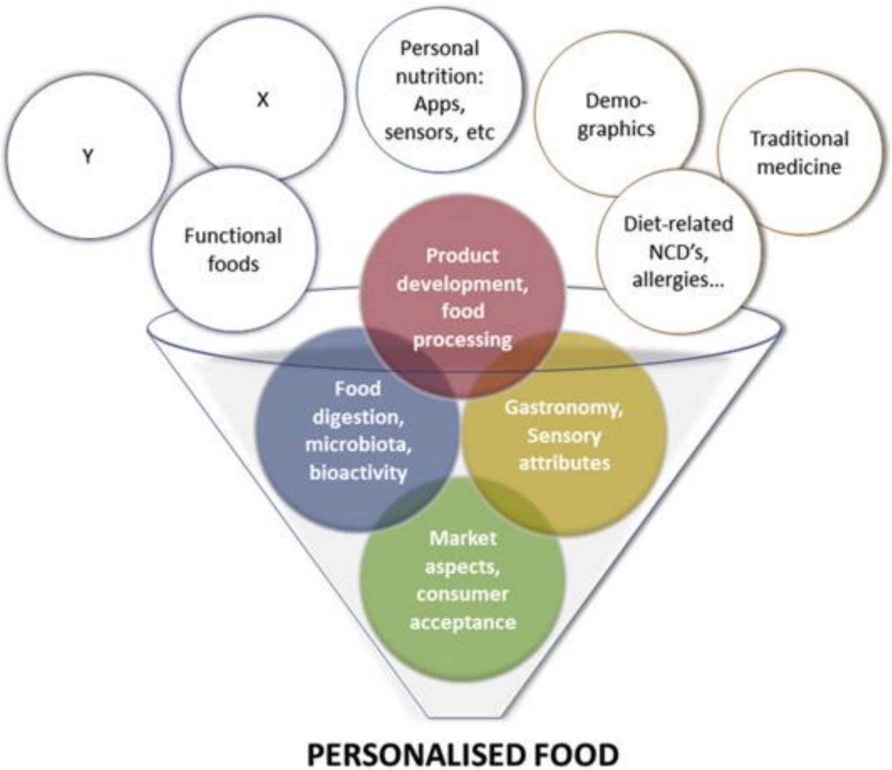
Global/ standard recommendation	Personalized dietitian recommendation based on an <u>individual's history and preferences</u>	Personalized recommendation based on <u>individual history, preferences, and genetic information</u>
Zn (8 mg/day): Consume a wide variety of foods containing zinc, in particular red meat and poultry. Other good food sources: beans, nuts, certain types of seafood, whole grains, fortified breakfast cereals, and dairy products.	Recommendations <u>vary according</u> to age, sex, pregnancy and lactation (2-13 mg/ day) → PN In addition, <u>consideration should be given to</u>: • People who have had **gastrointestinal surgery or digestive disorders** (ulcerative colitis, Crohn's disease). Both these conditions can decrease the amount of zinc that the body absorbs and increase the amount lost in the urine • **Vegetarians**, because they do not eat meat, which is a good source of zinc. For this reason, vegetarians *might need to eat as much as 50% more zinc than the recommended amounts* • **Older infants who are breastfed** because breast milk contains insufficient zinc for infants aged >6 months. Infants taking formula receive sufficient zinc. Older infants who do not take formula should be given foods that contain zinc, such as pureed meats • **Alcoholics**, because alcoholic beverages decrease the amount of zinc absorbed by the body and increase the amount lost in the urine. Also, many alcoholics eat a limited amount and variety of food, so they may not get enough zinc • People with **sickle cell disease**, because they might need more zinc	The **SLC30A8 gene** encodes a protein called zinc transporter 8 (ZNT8), which is responsible for transporting zinc around the body, primarily in beta-cells of the pancreas. Carriers of the **gene variant, the "A" allele of rs11558471 of SLC30A8**, need supplements containing zinc in addition to a healthy diet, to maintain proper glucose homoeostasis → Zn supplementation. The 'A' allele of rs11558471 is associated with impaired zinc transport and a higher risk of type 2 diabetes in *Chinese, Punjabi, and Malay populations*.

3. Perspectives on personalized nutrition



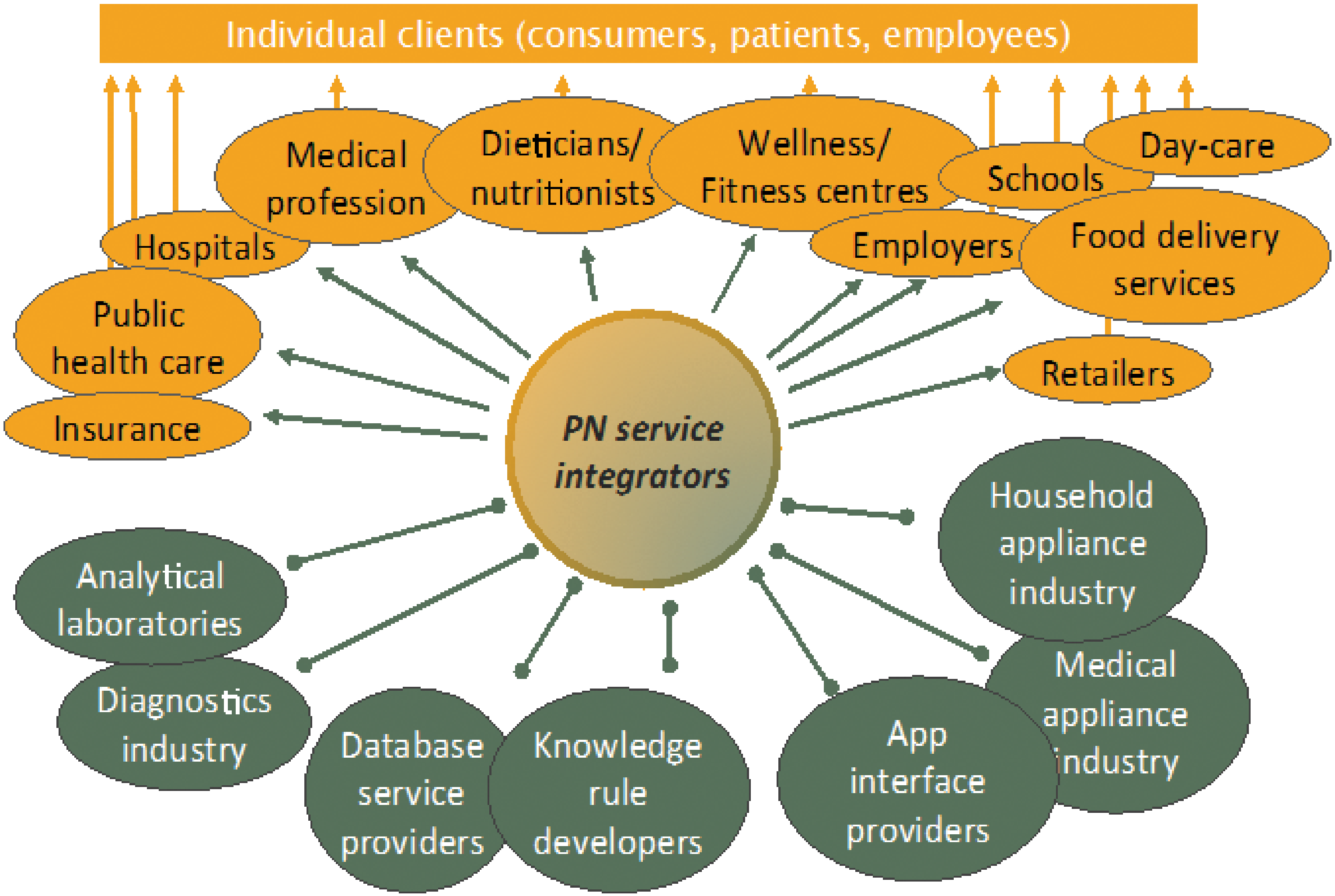
Potential market :

- PN is addressed to both diseased and healthy people;
- eating is a daily activity → opportunities for personalization are continuous;
- through PN a person may feel able to improve or maintain its health.



Food industries & nutrigenomic research

- developing the concept of 'personalized diets'
- identifying molecular biomarkers
- identifying new bioactive food ingredients for validation as functional food components or nutraceuticals


Individual clients (consumers, patients, employees)
Medical profession
Dieticians/ nutritionists
Wellness/ Fitness centres
Schools
Day-care
Hospitals
Employers
Food delivery services
Public health care
Retailers
Insurance
PN service integrators
Household appliance industry
Analytical laboratories
Medical appliance industry
Diagnostics industry
Database service providers
Knowledge rule developers
App interface providers

- Complex human, complex food;
  nutrigenomics= expensive and time-consuming process

- very few companies propose personalized food based on health biomarkers and genetic information

- some companies provide only advices on what foods are right for the customers leaving them the buying of ingredients, food preparation and choice of cooking

- in other cases the consumers are helped to cook by using app which contains hundreds of recipes to accurately follow

- even in a case of a well design of personalized food, very few companies are capable to create and to deliver the meals at home

Although nutrigenomics is important, genetic is not the only factor that influences our overall health → *behavioral, environmental, physical, cultural and social factors*.

Advancement of PN

- development of a strong theoretical basis
- more robust study designs
- multidisciplinary research teams, from academics, policy makers, civil society, relevant industry and market actors
- scientific evidence for efficiency and cost effectiveness of the studies
- introduction of a regulatory framework/ control
- integration of other “omics” (epigenomics, microbiomics) to provide better interpretation of the evidence.

Conclusions

During human evolution, food interacted bidirectionally with genes;

Dietary guidelines require additional data; *combined individual diet+phenotype+genotype= personalized nutrition*;

Technology will help advancement of personalized nutrition;

Oxidative stress plays a key role in nutrition research – case studies on antioxidants in PN, “stratification” approach;

Huge potential market for personalized nutrition/ foods; other determinants of health should be considered.

Happy personalized meal!