

Transforming Regional Agrifood Productions to Challenge NCDs—From the DiMeSa Study to the PASSI Project and Beyond

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1. Foreword: Can Two Emergencies Make an Opportunity?

In our country, like in many other regions worldwide, two major, apparently unrelated, crises are deeply impacting the wellbeing and health of the population and the economy. There is, however, substantial indication that these two distinct emergencies are strictly interdependent, if not faces of the same coin, and that, thereof, systemic, cross-sectional strategies, implemented for and merging critical issues of both sides, could be highly effective in providing an answer, in the medium- and long-term, to this highly demanding, global occurrence.

The Italian agrifood system is of considerable importance both in terms of turnover and number of businesses and employment for the characterization of the Made in Italy and, more in general, the Italian lifestyle across the world. The Italian food industry faces today a phase of profound evolution based, on one hand, on the internal dynamics of the system and, on the other, on the more general process of globalization that profoundly affects the entire world economy. These changes are influenced by and, in turn, influence new consumer behavior trends, though factors associated with regional level and individual cultural diversities significantly and systematically impact impulsive purchasing behavior (Kacen and Lee 2002).

The radical changes in the production, commercial and distribution systems related to food products have generated socio-economic changes that have in turn modified consumers' eating habits (Greendex 2014). In recent decades, we have witnessed weighty social phenomena, such as the destructuring of the family nucleus, the increasing inclusion of women in both the labor market and economic activities, the spread of the market nonstop opening hours and the steady increase in out-of-home food consumption, which have all determined a profound reorganization of life rhythms and contributed to generating significant changes in eating patterns. The latter are also featured by an ever increasing degree of processing, hence favoring a decrease in the time allocated for food preparation and consumption and determining

a consequential preference for products with a higher content of additional services that consumers are willing to purchase at higher prices.

Another phenomenon that has expanded in recent years is the demand for safe food products with stable quality over time, providing the consumer with a high level of satisfaction based on taste (Grunert 2005). This is, in turn, closely connected to other important aspects, such as the impact on both individual and collective health status and well-being, the genuineness and naturalness of the agricultural raw materials used, the link with the territory, its history and traditions, factors that have all contributed to the realization of systems for the traceability of food products and the valorization of different food and wine cultures dispersed throughout the national and regional territories, including our own.

Furthermore, recent changes in the Italian agrifood system originate from the transformation of the distribution systems, which have become increasingly similar to those already established in most advanced European countries, whereby, along with the considerable gigantism of major companies in the large-scale retail trade that compete on prices and dictate the conditions for other companies to enter the market, there are small/medium-sized agricultural and agrifood enterprises, generally characterized by low bargaining power and limited capacity to occupy significant market segments. Moreover, these companies, being generally based on atomistic structures, suffer the ensuing difficulty of developing innovative, competitive products on the market at large.

As far as our regional agrifood sector is concerned, although it has the highest number of enterprises in the country, with the greatest percentages of agricultural area used for vineyards, fruits and vegetables cultures, it has, on average, one of the lowest company dimensions, in terms of either hectares or employees per company (ISTAT 2010). Furthermore, regional investments in the agrifood sector lie well below the national average (nearly 50%), with the agriculture added value in Sicily plateauing and occupation units in the agroindustry having decreased over the last decade (INEA 2013). Additionally, small/medium enterprises (SMEs) in the field are often featured by a limited innovation potential, a poor integration with public-private research institutions and an insufficient systematization and organization of the existing resources in an extended territorial networking. This results in increasing difficulties for SMEs to run both domestic and foreign markets with characteristics of quality and competitiveness.

According to WHO, noncommunicable diseases (NCDs), mostly represented by cardiovascular disease, cancer, chronic respiratory disease and diabetes, accounted for 71% of the 57 million deaths worldwide in 2016 (WHO 2018a). In our own region,

NCDs account for nearly 80% of all causes of death in both sexes (ReNCaM 2014). However, the global risk of dying from any one of these four major NCDs in people aged 30 to 70 years has steadily decreased in the last two decades (from 22% in 2000 to 18% in 2016) (WHO 2018b). On the other hand, several epidemiological studies clearly indicate that all Western countries, including Italy, are witnessing real epidemics of these NCDs and both adult and childhood obesity, mostly because of the dramatic changes that have occurred in both food systems and consumer eating habits and behavior globally (Hunter and Reddy 2013). Furthermore, the appearance of many chronic diseases is occurring today at an average age earlier than ever, with a progressive leftward shift in the onset age of various illnesses, including diabetes, cancer and obesity (Gale 2002).

Paradoxically, or subsequently if you like, these changes have produced the most profound and rapid consequences in Southern European countries, including Italy, Greece, Portugal and Spain, eventually leading to a significant increase in incidence rates of NCDs, along with high percentages of overweight and/or obese children (Wijnhoven et al. 2014), as a result of cultural, social, economic and genetic transformations. The progressive decline in mortality from NCDs, combined with the rise in their incidence worldwide, has produced an alarming “scissor” phenomenon, consisting in a remarkable and continuous increase in the total number of chronically ill individuals, that is to say of NCD prevalence (Hunter and Reddy 2013). This trend causes economic, social and health issues of outstanding relevance worldwide and eventually led the World Health Organization (WHO), along with all major health institutions, to launch a pluriannual action plan (2013–2020) for the primary prevention and control of NCDs based on intersectorial strategies targeting the removal of key risk factors for these diseases, including tobacco use, air pollution, physical inactivity, harmful use of alcohol and, notably, unhealthy diet (WHO 2013).

In this framework, the increasingly high prevalence of NCDs is basically a consequence of the transition from traditional to contemporary dietary patterns and physical activity. This shift, often named nutritional transition, is based on the increasingly large availability of inexpensive, high calorie-dense food, quite often at the expense of biodiverse, local and healthier products. In particular, processed and ultra-processed food, rich in salt, refined sugar or sweeteners, saturated and trans fats, is largely outpacing healthy food, rich in micronutrients, including fresh fruits, vegetables, legumes and nuts. Furthermore, while the intake of unrefined, whole grains is fading and that of fruits and vegetables remains largely insufficient, the consumption of meat, dairy products and sweetened drinks has markedly expanded in most regions around the world. In a recent Italian study, Giampaoli and

colleagues compared the food consumption of a self-reported survey recorded in 1960 in a southern Italian village (Nicotera) with that of an OEC/HES survey carried out in 2008–2012 on 1968 men and 2062 women, aged 40–59 years. The authors found that the consumption of cereals has dropped to less than 40% in both sexes, while the intake of meat, dairy products, milk and sweets has increased from 2- up to 4-fold (Giampaoli et al. 2015).

By definition, a food system comprises “all the elements (environment, people, inputs, processes, infrastructure, institutions) and activities that relate to the pre-production, production, processing, distribution, preparation and consumption of food and the outputs of these activities, including socioeconomic and environmental outcomes” (High Level Panel of Experts on Food Security and Nutrition 2017). In this wider context, individuals procure and consume food in the food environment, defined as “the interface that encompasses external dimensions such as the availability, prices, vendor and product properties, and promotional information, as well as personal dimensions such as the accessibility, affordability, convenience and desirability of food sources and products” (Turner et al. 2018).

A number of disparate factors determine the structure of food systems (see Figure 1).

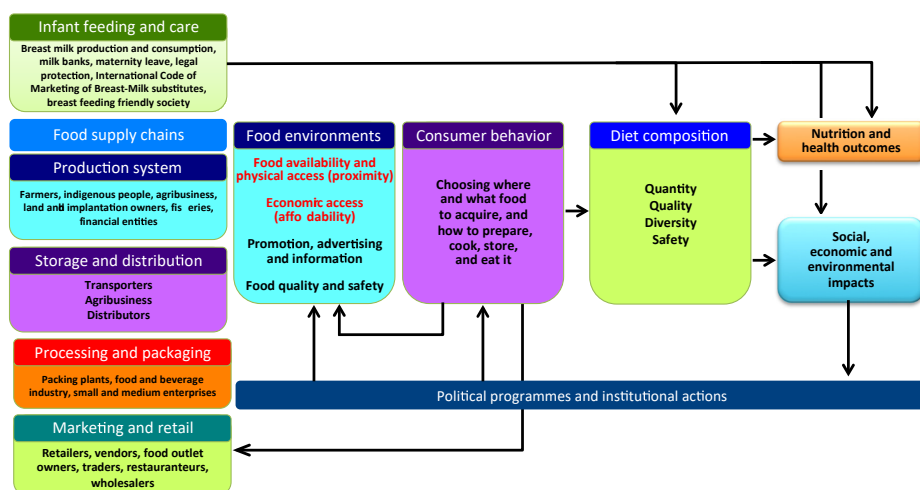


Figure 1. Schematic representation of food system and its outcomes. Source: Modified from Branca et al. (2019), used with permission.

They relate to a vast array of drivers and policies, as described by Branca and colleagues (Branca et al. 2019). The former include demographic issues, globalization,

urbanization and climate changes. The latter comprise environmental, agricultural, commercial and economic policies, either locally or globally. According to Turner and associates (Turner et al. 2018), food environments consist of both external and personal domains, whereby a variety of dimensions coexist and shape the environment: the external domain comprises subjects relevant to food availability and prices, characteristics of vendors and products, marketing and its regulation; the personal domain is based on individual dimensions, including food accessibility, affordability, convenience and desirability. The authors consider that people's food acquirement and consumption is generated by a series of intricate interactions between these domains and their assorted dimensions.

In the food environment, consumer behavior has a central role and is subjected to a multiplicity of influencing factors, belonging to cultural background and individual knowledge; personal preferences; food availability and accessibility, either physical (reachability) or economic (affordability); time and effort allocable for food purchase; preparation; cooking; and consumption. In recent decades, consumer behavior has been the primary target of aggressive marketing strategies of major food companies and large retail chains, eventually corrupting the food system and delivering mostly inexpensive, unhealthy food, with devastating effects on public health, especially for low-income, developing countries and vulnerable and marginalized populations. Today, although citizens are literally soaked in a liquid milieu of innumerable news, information, reports, forums, blogs, advertisements and mass and social media, all available on the internet, quite often most of them come from an extremely large and doubtful variety of sources that can heavily affect and/or undermine consumer behavior and beliefs. Luckily enough, however, the basic idea that food is important for human health has pervaded the general population at large and generated an increasingly greater demand for healthy food, with a greater intake of fruits and vegetables and a growing interest in products containing superfoods as healthful ingredients. In this highly fragmented and complicated context, there is an urgent need to develop policies, programs and campaigns for the nutritional counseling and education of citizens based on scientific, solid evidence and shared, verifiable information.

Based on this combined consideration, promoting both the production and competitiveness of traditional food products—in regional, domestic and international markets, through a series of activities aimed at increasing their health and/or nutraceutical potential, to clinically validate their effects on both health and chronic disease(s); to enable the rapid technological transfer and industrial development of either processes or products; and to exploit large, population-based interventions

of nutritional and behavioral education to develop individual knowledge and competences (empowerment) concerning lifestyle, nutrition and health—would represent a systemic strategy of high impact in the short, medium and long term for important expected outcomes from an economic, technological and healthcare standpoint.

2. The DiMeSa Study

The DiMeSa study¹, where DiMeSa stands for **Dieta Mediterranea e Salute**, simply Mediterranean Diet and Health, was funded by the Italian Ministry of University and Research (MIUR) to the leader Institution, the AgroBioPesca Technology Cluster. The project, which ran from October 2012 up to December 2015, was named “DiMeSa—Valorization of typical products of Mediterranean Diet and their use for health and nutraceutical purposes” and aimed at increasing the attractiveness and competitiveness, in either the domestic or international market, of traditional products from major regional agrifood chains. In particular, the main objective of the DiMeSa project was, using different approaches, to develop and exploit innovative industrial research and experimental activities that would eventually lead to improving the health potential of traditional food products and that, at the same time, would scientifically validate the existing relationship between these products or their components and health, both in terms of maintaining, both individually and collectively, a wellbeing condition and, especially, of the primary prevention of NCDs.

As illustrated in Figure 2, the DiMeSa project was arranged into 4 major objectives, precisely:

1. the analysis and identification of traditional food processes and the development of innovative biotechnological protocols for the production of food with high nutritional and health potential, including extra virgin olive oil, cereals or vegetables and their transformed derivatives;
2. the definition and implementation of procedures and methodological approaches for the production of functional foods (extra virgin olive oil, pasta, juices) through their combination (functionalization) with natural substances and/or plant/byproducts extracts with high health potential and their distribution through innovative vending machines;

¹ Based also on previously published work by Carruba et al. (2016).

3. the clinical validation of specific health claims through the implementation of randomized, controlled clinical trials to assess the health effects of selected functional food products on cohorts of either healthy, high-risk or diseased study-subjects through the evaluation of the impact of dietary intervention on some clinical and biomolecular end-points, such as: (a) anthropometric measures; (b) immunological markers of inflammation; (c) oxidative stress and endothelial function; (d) hormonal profiles and gene/miRNA expression;
4. the economic evaluation of the concept, traceability and industrial scale-up of either prototypal products or processes aiming to allow their immediate industrialization and successful marketing.

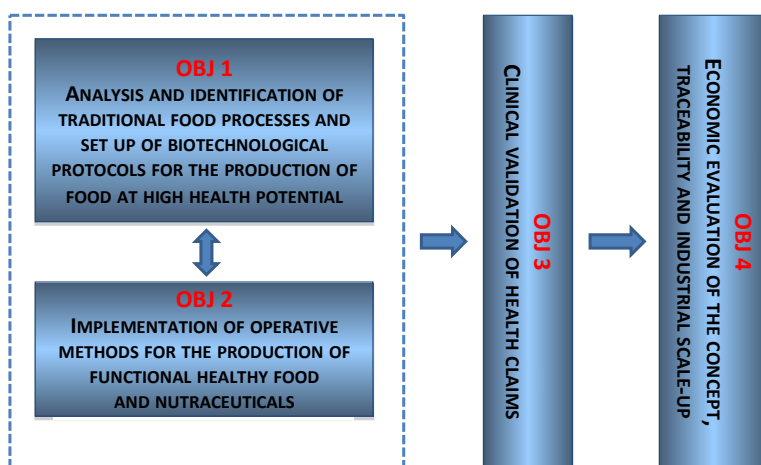


Figure 2. Framework of the Dieta Mediterranea e Salute (DiMeSa) project and its 4 major objectives. Source: Figure by the author.

The DiMeSa project was a multicenter study, characterized by a large regional partnership, which included universities and other public research institutions, on one hand, and small/medium enterprises (SMEs) in the field, on the other (see Figure 3).

PUBLIC	SMES
University of Palermo <ul style="list-style-type: none"> – SAF – DIFI – DIBIMEF – SEMBIO – CGA – DICGIM 	CoRiSvl <ul style="list-style-type: none"> – Oleificio San Calogero – Az. Agr. Angela Consiglio – Azienda “GeOlive” Belice – Pastificio Tomasello SpA – Laboratorio di Ricerche Locorotondo
University of Catania <ul style="list-style-type: none"> – Dip. Clinico-Sperimentale di Medicina e Farm. – D3Di 	Innova Agro Sicilia <ul style="list-style-type: none"> – Molino di Sicilia SrL – Agriplast SrL – Medivis
National Research Council (CNR) <ul style="list-style-type: none"> – IBF-Palermo – IBIM-Palermo – ICAR-Palermo – ISAFOM-UOS-Catania 	Agroindustry Advanced Technologies (AAT)
Ballatore Consortium CoRiSSIA IZSS	

Figure 3. Partnership of the DiMeSa project, including public research bodies and small/medium enterprises (SMEs). Source: Figure by the author.

In the framework of the DiMeSa project, we conducted two main clinical trials, both belonging to Objective 3 of the project.

In the first randomized study, we assessed the health impact of monocultivar extra virgin olive oils (EVOs) on 2 cohorts of study subjects represented by healthy postmenopausal women and patients with breast cancer. All study subjects were recruited at the Azienda di Rilievo Nazionale e di Alta Specializzazione (ARNAS)—Civico, Di Cristina, Benfratelli (CDB). Overall, 103 healthy postmenopausal women and 35 breast cancer patients were enrolled in the study. Two different mono-cultivar EVOs, one at a lower (*Biancolilla* cultivar, BL) and one at a higher (*Cerasuola* cultivar, CS) content of polyphenols and oleocanthal, were used in the study; both EVOs were produced by the Department of Agriculture and Forestry Sciences (SAF) of Palermo University, under the supervision of Prof. Tiziano Caruso. As regards healthy women, after an initial one-week wash-out period (“no EVO” week), the subjects consumed a daily amount of 30 mL of the BL EVO for 4 weeks, followed by another one week wash-out period (“no EVO”) and an additional 4 weeks intervention with the CS EVO, as illustrated in Figure 4. Conversely, breast cancer patients were randomized into one BL EVO and one CS EVO intervention group that consumed daily amounts of 30 mL of either BL or CS EVO for 4 weeks (see Figure 4). Both healthy and breast cancer study subjects, before and after any EVO intervention, undertook the following: (a) compiled a food frequency questionnaire originally developed for the EPIC study (Pisani et al. 1997);

(b) measured anthropometric indexes, including height, weight and waist-to-hip ratio; (c) were administered psychometric tests (HADS, SF-36); (d) collected both fasting blood samples and 12 h urine samples. The latter samples were used to determine the potential effect of dietary intervention on an array of both plasmatic and serum biomarkers, the expression profiles of a set of previously selected genes, the whole miRNome and the urinary profile of sex steroid hormones.

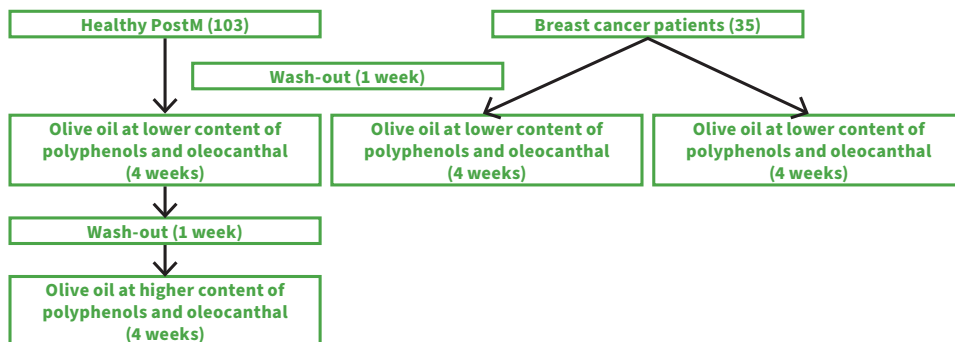


Figure 4. Flow chart of a randomized clinical trial in the DiMeSa project to assess the effects of selected monocultivar extra virgin olive oil on selected parameters in both healthy postmenopausal women and breast cancer patients. For explanation, see text. Source: Figure by the author.

Biological samples (plasma, serum and urine) were collected and stored in a biobank until analyses. A web-based study database was also created and data processed using advanced statistical analysis and appropriate software.

As reported in Table 1, the consumption of BL EVO resulted in significant changes of various plasmatic biomarkers in both healthy subjects and breast cancer patients. In particular, the reduction in glycemia, insulinemia and total cholesterol levels appears to be of special interest.

On the other hand, the consumption of CS EVO produced several modifications in selected biomarkers (see Table 1), including a significant increase in HDL cholesterol and reduction in LDL cholesterol. Interestingly, this EVO also induced a marked decrease in the plasmatic levels of estradiol. It appears noteworthy that, when comparing the two EVOs, BL EVO appeared to be more effective in reducing glycemia, while CS EVO proved to be more effective in decreasing plasmatic estradiol (see Table 2).

Table 1. Effects of BL and CS extra virgin olive oil (EVO) on plasmatic biomarkers in both healthy postmenopausal women and breast cancer patients.

BL Extra Virgin Olive Oil				CS Extra Virgin Olive Oil			
Variable	Baseline	After	<i>p</i> -Value *	Variable	Baseline	After	<i>p</i> -Value *
Azotemia	30.85	28.48	0.002	Cretininemia	0.69	0.63	<0.001
Uricemia	4.17	4.29	0.001	Uricemia	4.23	4.43	0.002
Glycemia	85.35	83.59	0.021	Glycemia	89.16	88.48	0.023
Insulinemia	10.33	8.79	<0.001	Glycated hemoglobin	5.64	5.51	<0.001
Total cholesterol	207.48	197.12	<0.001	HDL cholesterol	57.87	59.31	0.023
Gamma GT	21.90	24.50	0.001	LDL cholesterol	119.62	102.12	0.047
Total Proteinemia	7.00	6.91	0.005	Testosterone	0.39	0.36	0.033
Sideremia	76.95	67.02	<0.001	Estradiol	31.40	23.95	0.002

* paired T test, ANOVA. BL, *Biancolilla* cultivar; CS, *Cerasuola* cultivar. Source: Carruba et al. 2016.

Table 2. Comparison of the effects of BL and CS EVO on glycemia and estradiol levels in both healthy postmenopausal women and breast cancer patients.

Variable	BL EVO	CS EVO	<i>p</i> -Value
Glycemia	83.59	88.48	0.023
Estradiol	37.21	23.95	0.027

BL, *Biancolilla* cultivar; CS, *Cerasuola* cultivar. Source: Carruba et al. 2016.

This would imply that different EVOs may have distinct impacts on either glycemic control or hormonal (sex steroid) status, also depending on the cultivar and on the phenology of fruit ripening (the earlier the stage, the greater the content of polyphenols).

The results of gene expression, microRNA profiling and patterns of urinary sex steroids are currently under complex analysis and are awaited with great expectation and interest.

In the context of the DiMeSa project, we conducted another clinical trial to assess the impact of a pasta product supplemented with an extract of cladodes of *Opuntia Ficus Indica* (OFI) on the lipid profiles of subjects presenting with at least one component of the metabolic syndrome (MS).

As illustrated in Figure 5, eighty-six healthy subjects of both sexes, among over 2500 employees, participated voluntarily in the study at the Division of Research and Internationalization of the ARNAS-Civico, Di Cristina, Benfratelli healthcare comprehensive center (Palermo, Italy) for 8 months.

Out of these 86 subjects, 52 aged 40–65 years (13 male and 36 female; age: 56 ± 5 years) were recruited in the study based on the inclusion criterion of presenting with one or more risk factors of MS according to the American heart Association (AMA), precisely: (a) fasting glucose ≥ 100 mg/dL (or receiving drug therapy for hyperglycemia); (b) blood pressure $\geq 130/85$ mm Hg (or receiving drug therapy for hypertension); (c) triglycerides ≥ 150 mg/dL (or receiving drug therapy for hypertriglyceridemia); (d) HDL-C < 40 mg/dL in men or < 50 mg/dL in women (or receiving drug therapy for reduced HDL-C); (e) waist circumference ≥ 102 cm in men or ≥ 88 cm in women.

Dietary intervention consisted in the weekly consumption of 500 g of the dried pasta functionalized with a 3% soluble extract of OFI cladodes for a total of 4 weeks and was maintained as an add-on to the cardio-metabolic therapies already in use. At baseline and at the end of dietary intervention, all study subjects underwent the following: (1) anthropometric measures; (2) psychometric tests; (3) medical examination; (4) biochemical assessment of circulating biomarkers, with special emphasis on the LDL-C subfractions (conducted at the Unit of Diabetes and Cardiovascular Prevention at the University of Palermo, Italy—Proff. G. Montalto and M. Rizzo).

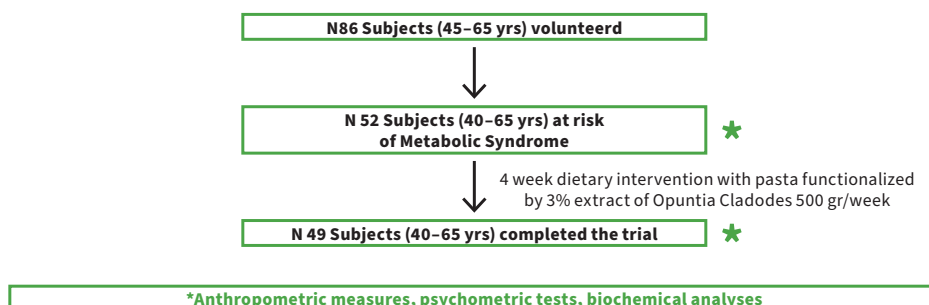


Figure 5. Flow chart of a randomized clinical trial in the DiMeSa project to assess the effects of pasta supplemented with a 3% extract of cladodes of *Opuntia Ficus Indica* on selected parameters in subjects at risk of metabolic syndrome. For explanation, see text. Source: Figure by the author.

In particular, the LipoPrint System (Quantimetrix Corporation, Redondo Beach, CA, USA) was used to separate and measure LDL-C subclasses, as described elsewhere

(Hoefner et al. 2001). LDL subclasses were divided into seven bands (LDL-1 to LDL-7, respectively), LDL-1 and -2 being defined as large LDL, while LDL-3 to -7 were defined as small LDL (Rizzo and Berneis 2006). At baseline, all participants were asked not to vary their food and/or physical activity during the period of the study. After a complete description of the study, written informed consent was obtained from all participants. The procedures adopted were approved by the Ethics Committees (EC) of both ARNAS-Civico (EC2) and the Policlinico University of Palermo (EC1). Overall, 49 subjects completed the study.

After 4 weeks dietary intervention with the OFI-supplemented pasta, a limited but significant decrease in waist circumference was observed, while neither body weight nor body mass index (BMI) showed any significant change (Table 3).

Table 3. Changes of biometric parameters after 4 weeks dietary intervention with *Opuntia Ficus Indica* (OFI)-supplemented pasta.

Variable	Baseline	4 Weeks	<i>p</i> Value *
Weight (kg)	69.5 (14.6) 67.8 (47.9–125.4)	69.8 (14.1) 69.1 (47.8–123.4)	0.8665
Waist circumference (cm)	92.3 (12.3) 92 (73–132)	91.4 (10.5) 91 (72–129)	0.0297
BMI (kg/m ²)	25.9 (3.9) 25.3 (20.8–41.4)	26.1 (3.7) 25.5 (20.8–40.8)	0.8788

Values are mean (\pm SD) and median (min–max). * Wilcoxon paired test. Source: Carruba et al. 2016.

Furthermore, dietary intervention resulted in a statistically significant modification of several biochemical plasmatic parameters, including a significant reduction in blood urea nitrogen (BUN), creatinine, glucose, triglycerides, aspartate transaminase (AST) and sideremia; conversely, some hormonal parameters, including estrogens (estradiol and estrone) and sex hormone binding globulin (SHBG), showed a significant increase. As far as plasma lipids are concerned, total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C) remained unchanged (see Table 4).

Interestingly, dietary intervention with the OFI-enriched pasta produced a significant increase in LDL-1 (from 49.6 ± 0.3 to $65.1 \pm 0.2\%$, $p = 0.0002$) and a concomitant reduction in LDL-2 (40.1 ± 0.3 to 29.7 ± 0.2) and LDL-3 (8.3 ± 0.2 to $4.6 \pm 0.1\%$, $p = 0.0004$). In addition, LDL-4 and LDL-5 also subclasses decreased, though differences were not statistically significant (see Table 5). No correlation was found between changes in sdLDL and any other metabolic parameter.

Table 4. Changes of plasmatic parameters after 4 weeks dietary intervention with OFI-supplemented pasta.

Variable	Baseline	4 Weeks	<i>p</i> Value
BUN (mg/dL)	32.7 (7.9) 33 (17–51)	43.3 (9.3) 43 (23–68)	<0.0001 *
Creatinine (mg/dL)	0.74 (0.1) 0.71 (0.52–1.33)	0.72 (0.1) 0.71 (0.43–1.25)	0.0244 *
Glycemia (mg/dL)	84.6 (12) 84 (58–128)	74.4 (14.2) 72 (60–158)	<0.0001 *
HbA1c (%)	5.4 (0.4) 5.3 (4.7–7.6)	5.4 (0.4) 5.3 (4.7–7.5)	0.9516 **
Total Cholesterol (mg/dL)	208.3 (36.1) 210 (115–267)	209.9 (35.6) 208 (129–266)	0.9620 **
HDL (mg/dL)	60.7 (13.9) 61 (30–88)	60.6 (13.3) 61 (30–88)	0.6672 **
LDL (mg/dL)	139.3 (32.9) 138 (65–195)	139.3 (33.6) 139 (78–200)	0.5274 **
Triglycerides (mg/dL)	104.6 (53.6) 82 (36–271)	92.8 (54.7) 71 (44–300)	0.0137 *
AST (mU/mL)	28.3 (8.2) 26 (17–63)	23.7 (8.4) 21 (15–62)	<0.0001 **
ALT (mU/mL)	22.2 (11.4) 18 (8–65)	22.6 (13.0) 19 (8–69)	0.8830 **
Gamma GT (U/L)	31.5 (27.5) 27 (11–167)	33.6 (39.2) 25 (11–268)	0.3855 **
Sideremia (µg/dL)	87.3 (21.3) 87 (45–134)	78.8 (28) 78 (26–158)	0.0255 *
Estradiol (pg/mL)	34.1 (27.2) 22 (7–102)	56.4 (58) 43 (25–432)	0.0055 **
SHBG (nmol/L)	66.5 (30.8) 60 (18–143)	81 (44) 66 (21–195)	<0.0001 **
Estrone (pg/mL)	23.7 (23.2) 15 (4–123)	77.7 (35.2) 64 (45–250)	<0.0001 **

Values are mean (±SD) and median (min–max). * Student's paired *t* test; ** Wilcoxon paired test. Source: Carruba et al. 2016.

Table 5. Effects of OFI-supplemented pasta on LDL-C subfractions.

LDL-C Fraction	Baseline	4 Weeks	<i>p</i> Value
LDL-1	49.6 ± 0.3	65.1 ± 0.2	0.0002
LDL-2	40.1 ± 0.3	29.7 ± 0.2	<0.0001
LDL-3	8.3 ± 0.2	4.6 ± 0.1	0.0004
LDL-4	1.3 ± 0.1	0.6 ± 0.0	0.2987
LDL-5	0.7 ± 0.1	0.0 ± 0.0	0.3223

Data represent average ± SD of percent values. Source: Carruba et al. 2016.

3. The PASSI Project

As a natural development of the DiMeSa project, we recently designed a new project called the Produzioni Agroalimentari Sostenibili Salutistiche e Identificabili in Sicilia—Sustainable, Healthy and Identifiable Agrifood Productions in Sicily (123 PASSI). The general framework of this project is illustrated in Figure 6.

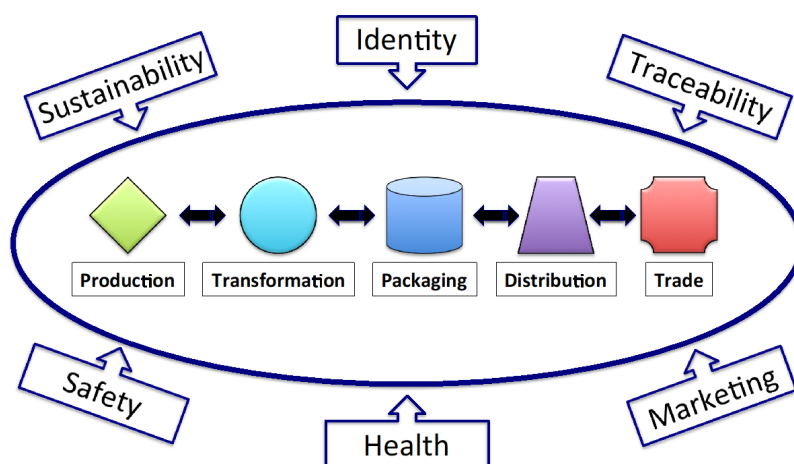


Figure 6. The conceptual framework of PASSI project. This picture portrays the overall goal of the project and its domains, from farm to market, that will be primary focus of the project’s activities across major food chains. Additionally, the potential impact of key issues (from sustainability to marketing) on food system is also here highlighted as addressed in the project.

The general goal of the PASSI project consists not only of the systematization of experimental evidence and results accomplished with the DiMeSa project, both in

terms of processes and products, but also to overcome its intrinsic limits by creating a collection of functional food products, traditionally belonging to the regional agrifood system, through research and development actions set up in different domains (production, processing, packaging, distribution and trade) throughout each supply chain (horizontal objectives)—along with those relevant to sustainability (environmental and industrial), traceability, food security, health potential and equity of access (vertical objectives)—generating knowledge of the supply chain and its identity value and, therefore, increasing consumer skills and decision-making capacities (empowerment) also through the use of algorithms (Blockchain, Distributed Ledger Technology) for the traceability of food supply chains and their health value (see Figure 7). The general objective of this project consists of the promotion and valorization in either domestic or international markets of high-quality functional food products typical of the traditional region, which are sustainable, traceable and safe, and whose health effect is proven in controlled and randomized clinical trials. The specific objectives comprise the development and exploitation of supply chain programs (from field to table; from farm to fork) that allow the production, processing, packaging, distribution and marketing of high-quality foods with a high health potential in major regional agrifood chains, precisely: (a) the extra virgin olive oil (EVO) chain; (b) cereal chain; (c) citrus chain; (d) fresh and dried fruit; (e) vine and wine chain. The activities to be developed consist of industrial research and experimental development activities, structured according to an immediate transfer of technologies and competences to the industrial setting for the production and realization/marketing of processes/products widely used and consumed in the Sicilian agro-industry. The project is divided into 8 implementation objectives (ORs), of which the first 5 (OR1–5) relate to food chain programs, while the remaining 3 (OR 6–8) to transversal research activities (see Figure 7).

The PASSI project is now being developed through its 9 implementation objectives and also integrated with additional, though highly relevant, aspects, with special emphasis on the use of agricultural byproducts and co-products to functionalize food of high consumption in the general population.

4. Conclusions and Perspectives

Doubtlessly, the primary prevention of NCDs through dietary interventions, in the wider context of health promotion through a life-course approach, as endorsed by WHO, requires the design and exploitation of systemic strategies, implemented both locally and globally, that would include radical changes in food systems and environments in order to provide identifiable, safe, healthy and affordable food to

the current population. Virtually all aspects of food chains, including pre-production, productive processes, transformation, packaging, distribution, marketing and retail, should be renovated according to comprehensive approaches and policies shared at regional, national and international levels.

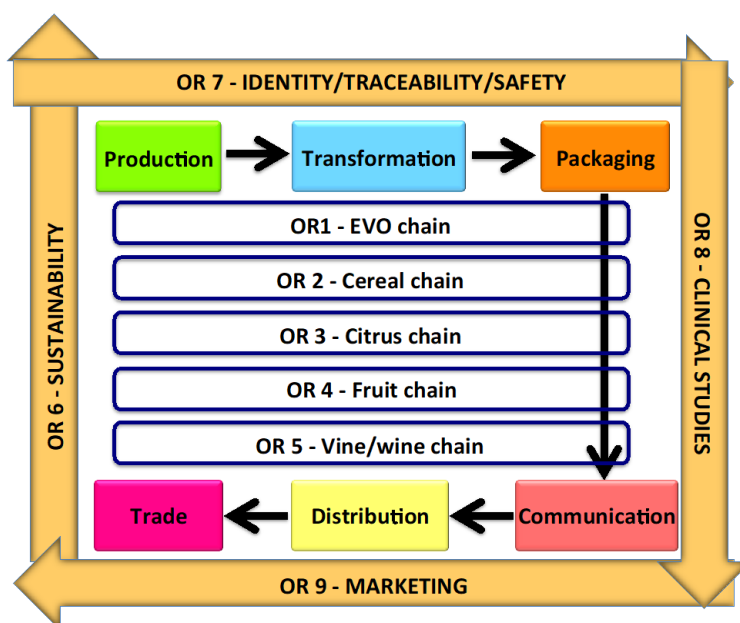


Figure 7. Structure of the 123 PASSI project. The project is divided into “horizontal” objectives (the traditional Mediterranean food chains: OR 1 to 5) and “vertical” objectives (from sustainability to marketing: OR 6 to 9), bridged by a sequential succession of activities (from production to trade) featuring the whole system. OR: implementation objective. Source: Figure by the author.

In particular, the adoption of incentives for primary producers and suppliers to produce and distribute healthy food sustainably should be accomplished. Conversely, fiscal policies to tax unhealthy, processed or ultra-processed food should also be implemented. Changes in food storage, transportation and distribution, aimed at providing easy access to nutritionally valuable, perishable food, should be introduced.

It is well recognized that health determinants consist of a vast array of personal, relational, social, economic and environmental factors that influence, individually and collectively, health status. According to Dahlgren and Whitehead (1991), socio-economic, cultural and environmental conditions include education, agriculture

and food production as important pillars of wellbeing. In other words, health (in its broadest sense) cannot be considered as an issue belonging solely to the welfare sector; conversely, it must be dealt with using intersectoral, multidimensional approaches and systemic strategies. In this paper, the PASSI project proposes a cross-sectoral model for the production and marketing of high health potential food products, addressing either internal (production, processing, packaging, distribution and trading) or external (sustainability, identity, traceability, safety, functionality and marketing) factors of major food chains. This approach, intrinsically, impacts various SDGs included in the 2030 Agenda for Sustainable Development, precisely: (1) Goal 2: end hunger, achieve food security and improved nutrition and promote sustainable agriculture; (2) Goal 3: ensure healthy lives and promote wellbeing for all at all ages; (3) Goal 12: ensure sustainable consumption and production patterns. Furthermore, it is indirectly related to the following SDGs: (4) Goal 4: ensure inclusive and equitable quality education and promote lifelong learning opportunities for all; (5) Goal 8: promote sustained, inclusive and sustainable economic growth, full and productive employment and decent work for all; (6) Goal 15: protect, restore and promote sustainable use of terrestrial ecosystems, sustainably manage forests, combat desertification and halt and reverse land degradation and halt biodiversity loss.

We recently designed an innovative, multi-actor approach based on the integration of a variety of data, skills, expertise and competences to create a knowledgeable platform and a strategic plan for the sustainable consumption and production of healthy, identifiable, safe and traditional food products. This project, with the SHAPE acronym standing for Sustainable, Healthy and identifiable Agri-food Production Enterprise, represents the natural evolution of the PASSI project, as it is molded upon a consumer-centered food system model that comprises individual taste and preferences; equitable access and affordability; socio-economic, psychosocial and behavioral determinants of food behaviors; cultural identity; innovative marketing strategies; and comprehensive nutrition education all with the goal of strengthening the valorization of the health benefits of the Mediterranean diet in different populations groups. This innovative model could be developed and implemented in a series of “Mediterranean” countries, including Italy, Greece, Malta, Lebanon, Jordan (partners of the project), Portugal and Spain, where the dramatic changes that have occurred in both food systems and consumer eating habits and behavior in recent decades have led to a significant increase in the incidence rates of NCDs, along with high percentages of overweight and/or obese children. In this respect, the innovative SHAPE approach could also be used, in the short and medium

term, as a primary prevention strategy to tackle the increasingly large prevalence of noncommunicable diseases in Mediterranean regions.

Importantly, food environments should be transformed, before anything, culturally, by defining and implementing measures of nutritional education, from primary schools to adulthood, to seminally diffuse healthy behaviors not only in term of eating patterns but also regarding physical activity.

In this respect, the Department of Health (DASOE) of the Sicilian Region initiated the Program named “Formazione Educazione Dieta” (FED), aimed at the promotion and diffusion of healthy lifestyles, according to the Mediterranean Diet (Requirez et al. 2016). The major methodological strength of the FED program consists of an intervention of health prevention and promotion based on two strategic elements: a centralized planning, adjustable according to outcome indicators, and a multiyear action plan, with cyclic activities throughout three regional networks (health, education and agribusiness). The program is synergistically focused on: (a) a cascade training program, aimed at qualifying people to become expert trainers/educators able to influence the cultural changes, behaviors and lifestyles of the population, by acting specifically on the various recipients, in accordance with appropriate methodologies and evidence-based content; (b) the activation of local networks built to promote capillary activities in the regional territory (see Figure 8).

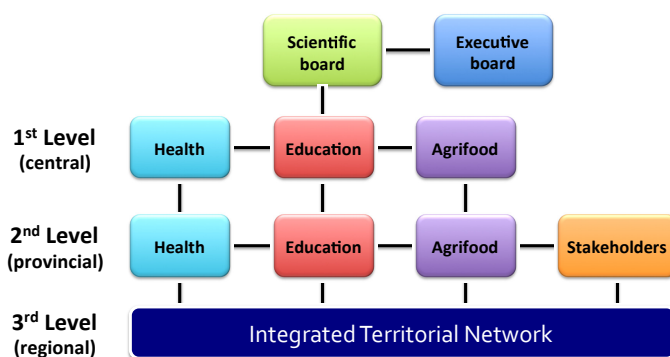


Figure 8. The FED operational model. The program is based on a cascade training system, governed by the Scientific Board and divided into 3 levels: (a) central, addressed to beneficiaries from Health, Education and Agrifood macroareas (1st level trainers); (b) provincial, addressed to beneficiaries from selected macroareas and stakeholders (2nd level trainers); (c) regional, with the creation of an Integrated Territorial Network consisting of representatives from the Scientific Board, 1st and 2nd level trainers for seminal diffusion of education activities throughout the region. Source: Figure by the author.

Using an integrated multiprofessional approach, the experts develop an operational and training program with centrality and uniqueness, making it uniformly applicable to the distinct organizational realities of the Sicilian territory.

Today, just ten multinational companies control over 70% of the food supply on the planet, owning nearly 500 different brands and providing the largest market ever of unhealthy, high-calorie food. Against their economic and organizational supremacy, governments should put in place strict policies to protect the production and marketing of traditional food through investments in short-chained, territorial healthy products.

In this framework, outstanding importance is also assigned to the transition from a linear economy to a circular economy in the agrifood industry, providing an array of opportunities at all stages, from primary production using precision agriculture techniques, to the recycling and use of agricultural byproducts or waste to produce functionalized, healthy food.

In a holistic view, global efforts are being made through several international initiatives, notably the 2030 Agenda for Sustainable Development including its 17 Sustainable Development Goals (SDGs), to radically modify food systems and environments with the ambitious objective of preventing NCDs while protecting the human right of equitable, accessible and affordable nutritious food.

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