Bio-medical research and search for personhood: a 40-year project

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Abstract During our PhD thesis in Leuven (Belgium), we chose the path of biomedical research, not as an intellectual enterprise, but as a concrete full time choice for the person. We worked at Mario Negri, Milan, a non-profit institution, convinced that independent research should offer health benefit to the population, rather than economically exploiting the scientific results obtained. Science communication was also developed as an ethic aspect of research. At Mario Negri Sud, located in a small village far from large cities, we combined excellence in research and attention to the surrounding territory, including schools, elderly people, agricultural products, industry and religious traditions. One of the most consistent features of our research work was to involve young fellows and give them responsibility. A major effort was also performed to diffuse a scientific attitude among young people (e.g. “Summer Student” program). When we moved further down to Southern Italy, namely to Campobasso, human population studies were fully developed. Being in Molise, our main research project had direct impact on the Molisani people. The “MOLI-SANI” project was performed in collaboration with local GPs, regional health authorities, priests in charge of parishes, elderly cultural circles, lay press and television networks, schools. Health promotion, life style and prevention were and still are the preferred targets of the project, rather than diseases, hospitals and drugs. Along whole our life, we believed in research as a preferential way to develop the personhood. If only one of the researchers who worked with us will keep the same faith, we shall feel privileged.

Keywords Science communication · Population studies · Education and training · Southern Italy · MOLI-SANI project · Mario Negri Institute

A rainy month in Belgium

We were both medical students, in that rainy September 1967, when we arrived as fellows of the SISM (Segretariato Italiano Studenti in Medicina) (<http://www.sism.org/>) to Leuven, the ancient Brabant city hosting one of the oldest European Universities (founded in 1425) (Fig. 1). We were supposed to spend 1 month there, at the Laboratory of Coagulation and Proteolysis headed by Professor Marc Verstraete, a medical doctor (42 year-old) strongly believing that myocardial infarction was the consequence of the formation of clots (thrombi) occluding one or more coronary arteries and that a drug (streptokinase) able to induce lysis of such thrombi would have been an effective treatment of coronary heart disease patients [1]. We landed to Belgium from the young but already prestigious Catholic University, in Rome, where we had already become acquainted with blood platelets and fibrinogen. Thus we were not fully surprised by Verstraete’s approach to myocardial infarction. What left us admired was instead the fact that he was receiving us in a lab rather than in a clinical ward and was speaking in such a way to make obvious the power of research beyond his thoughts.

At the end of that memorable month, we both had decided to fully devote ourselves to research for the rest of our life. We went back to Leuven 1 year later (“You will get married before coming here again”, Professor Verstraete had strongly advised us before leaving the first time) and spent 5 years there gaining a unique experience on biomedical research and personhood. The PhD degree we

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Fig. 1 The City Hall (Stadhuis) of Leuven, Belgium

both obtained at the end of our stay in Leuven was certainly an important academic achievement, but the lesson for life we learnt by Professor Verstraete and his Colleagues (in particular our tutor and friend Jos Vermeylen) was the most influential experience for our future work and life.

Nowadays, more than 40 years later (Professor Verstraete is 87 now and he is still active [2] especially in raising research funds for his University), we believe we made a good choice, although (or possibly because) we became more and more free from both money and power, but closer and closer to values of research, which meant for us values of the person.

Bio-medical research: a choice for the person

In Leuven we had chosen the fascinating though difficult path of biomedical research, not as an intellectual enterprise, but as a concrete choice for the person. When we left Leuven and a well established, increasingly famous research laboratory, we started a 40-year trip towards the South and the East (possibly not yet at its final stop...). We

came back to Italy well conscious that our Country had great economic difficulties and could not invest into research, a luxury it could not afford. Moreover, Italian Universities were still under the influence of the so-called “baroni”, old professors who had long managed to change everything so that nothing changed. At that time, a faithful and servile attitude towards one of them rather than being competent and independent was often more useful to obtain an academic position.

In 1973, we established *ex novo* a small research group on thrombosis with a very young technician (who is still successfully doing research) and a Polish medical fellow (who later was appointed as Pro Rector of his University) [3–6]. The context was the Mario Negri Institute for Pharmacological Research in Milan (Table 1). Despite La Scala and the Last Supper, Milan was more than 1,000 km south of the Europe’s centre and several people were still surprised at that time that at Italian meetings we used slides written in English. The Mario Negri Institute was a remarkable exception not only because English was currently spoken there, but mainly because instead of offering academic career, it offered the pleasure to fellows and research personnel to challenge themselves, to explore the intimate mechanisms of the brain or the heart function, to find out new remedies for old or novel diseases. The salaries and the fellowships reached the minimal threshold to survive in a big city like Milan; however, working at Mario Negri could help for getting an easier access to more economically rewarding jobs in the pharmaceutical industries or as school teachers.

During our first years in Milan, it became more and more clear to us that the main objective of our research activity was to produce reliable results to answer clinically relevant questions. To obtain that, we had to rely upon persons combining high professional proficiency and solid ethical principles. We adapted to research for our young coworkers a famous statement of Immanuel Kant: “research should always be viewed as an end and never as simply a means (to progress in your career or to get money or power)”. We would have considered a different attitude a betrayal of their persons on their part.

At Mario Negri Institute, all results—also those negative from the view-point of the financial sponsor—had to be published. Nobody could apply for a patent, as Silvio Garattini, both founder and Director of the Institute, was strongly convinced that it should be a non-profit institution offering health benefit to the population, rather than economically exploiting the scientific results obtained. Instead of being kept secret and unpublished for a patent, data should have been rapidly published and largely diffused, from publications in peer-reviewed international journals up to meetings with medical doctors, students, laymen, mass-media. At that time participating in a radio or a TV

Table 1

The Mario Negri Institute for Pharmacological Research is a not-for-profit biomedical research organization. It was founded in 1961, and started work in Milan on 1 February 1963. There are now research units in Bergamo, at Ranica —near Bergamo—and at Santa Maria Imbaro, near Chieti

The Institute's main aim is to help defending human health and life

To achieve this goal, research is aiming at a fuller understanding of the innermost workings of living organisms and at knowing why and how diseases arise, and what happens inside an organism when foreign substances enter it. The Institute's research programs therefore span from the molecular level to the whole human being and populations, and the findings help building up the basis for developing new drugs, and making existing ones more effective

The main research headings are the battle against cancer, nervous and mental illnesses, cardiovascular and kidney diseases, rare diseases and the toxic effects of environmental contaminants, mother and child's health. The Institute is also involved in research on pain relief and drug addiction

Parallel to its biomedical investigations, the Mario Negri Institute runs training schemes for laboratory technicians and graduate researchers. It takes part in a range of initiatives to communicate information in biomedicine, on a general level and with the specific aims of improving health care practice, and encouraging more rational use of drugs (<http://www.marionegri.it/mn/it/index.html>)

programme was considered inappropriate for a scientist who should only address himself to his peers in scientific contexts. At Mario Negri Institute science communication was developed instead as an ethic aspect of research itself. *Data are not data if they are not communicated*, was one of the statements that both of us accepted with enthusiasm.

Since then, one or more young journalists have always worked with us, not only to disseminate information, but also do research on scientific communication, studying for instance the impact of mass-media information and adherence to Mediterranean diet.

To select young research fellows for our growing laboratories (we had split the original group in two independent labs, already forming a kind of *ante litteram* department), high school or university degrees were not paid great attention, but curiosity, reasoning ability, English language knowledge, brilliant eyes were privileged instead. Each young or old investigator was given full responsibility in his/her research activities, no formal check being made on entry/exit times, vacations, time spent at the lab or at the institute's cafeteria (we considered the latter place indeed the most productive lab of our institute in terms of new ideas, collaborations, friendships).

In the Seventies Europe was divided by an “iron curtain” between Western and Eastern Countries, the latter under the strict control of the Soviet Union. Mario Negri Institute (and later on Mario Negri Sud) were characterized by a generous acceptance of numerous fellows from Poland, Hungary and other “communist” Countries. A Colleague commented few years ago that the Berlin wall had fallen at Mario Negri much earlier than in Berlin itself....

Welcome to the South

At that time, several fellows at Mario Negri were coming to Milan from Southern Italy: Garattini generated the idea,

which we progressively refined, that part of the institute could move to Southern Italy and offer unusual challenges and perspectives to Southern young people. The intelligence—Garattini used to say—is randomly distributed in our Country, while the resources are not. Many potential good investigators live in Milan or Naples; it is necessary to give them a comparable concrete chance to express their talent.

The Mario Negri Sud (Table 2), a consortium jointly established with the Administration of the province of Chieti, in the Abruzzo region, started to operate 25 years ago, after having restored and/or rebuilt the abandoned structures of a psychiatric hospital, whose construction had been stopped by the so-called “Basaglia Law” [7].

Both of us, together with Chiara Cerletti, Andreina Poggi, Cosmo Rossi and a pioneering group of colleagues, decided to move there and take responsibility for this new research experience. The place was a small village, Santa Maria Imbaro, near Lanciano, in the province of Chieti, few kilometers from that Adriatic Coast (Fig. 2) celebrated by Gabriele D'Annunzio [8] and in view of the Majella and Gran Sasso mountains, the two highest Appennines' peaks.

During the first 10 years of activity of Mario Negri Sud, we developed a project trying to combine excellence in research at international level and attention to the surrounding territory, including schools, elderly people, agricultural products, industry, religious traditions.... All senior investigators who joined the Mario Negri Sud (Fig. 3) established their home close to the institute, thus avoiding to travel back and forth between home and work; commuting was instead (and unfortunately still is) a habit quite common among academic people in similar cases.

Research fellows, technicians and administrators were selected among young people living in Abruzzo or other Southern regions.

Table 2

Located in Santa Maria Imbaro (Chieti, Italy) the Consorzio Mario Negri Sud is a non-profit organization for biomedical and pharmacological research. It was founded in the late Seventies as a consortium between the Mario Negri Institute in Milan and the Chieti Province authority, later joined by the Abruzzo Region authority. Scientific activities operatively began on September 1st, 1987. Since then Negri Sud has given a significant contribution to the advancement of research aimed at the prevention and cure of human diseases. Based on a core of senior staff of around 80 scientists, the centre is also engaged in training of pre-doctoral and post-doctoral fellows, including an International PhD Programme (<http://www.negrisud.it/en/>)

Fig. 2 One of the typical “trabocco” along the Adriatic coast, near the Mario Negri Sud

“We need somebody to pull a few strings here”

“We need somebody to pull a few strings here” was an usual expression of many candidates and their relatives wishing to apply to a Mario Negri Sud fellowship or job selection. It reflected the ancient and diffuse belief that nothing may happen in (Southern) Italy without a “raccomandazione” (political support). We resisted this well established habit and remained always free in taking our decisions on people or furniture selection. On one occasion, we had just completed the selection of young laboratory technicians, when we received two letters of political support by two local politicians. We immediately called the already selected technicians to an informal meeting, congratulated them for their success and informed them that two of them had been removed from the list of winners, due to a letter of political support sent in their favour. At the greatest astonishment of all young fellows, we said—we wanted to work only with young people who believed in themselves. However, we continued, as both letters had arrived *after* our list had been completed, we had finally decided to accept the two fellows *notwithstanding* the “raccomandazione”, but not thanks to it. That meeting still remains in our minds as a memorable experience.

On another occasion, someone from the cabinet of an influent Minister called one of us to recommend a medical doctor candidate to a research fellowship at Negri Sud. The fellow had already been excluded from the winners’ list of our selection procedure. As the secretary at the telephone was insisting on his request, we said:

“Would you please ask Mr.....if he would support the request of a young priest to enter the Seminar?”

“I do not think so, it would be a matter of vocation.....”

“Research too is a matter of vocation...”

End of the telephone call.

Bio-medical research for young people

One of the most consistent features of our research work was to involve young fellows.

From a scientific and economical success’ point of view, it would have been preferable to offer few selected post-doc fellows a well-paid salary asking them to produce a number of important papers to be published in highly reputed international journals (high Impact Factor). We used to compare such an approach to that of highly reputed foot-ball teams (such as today that of Paris Saint Germain or Manchester City) buying the best players all over the world. We preferred instead to develop a local seedbed (*vivaio*) of young fellows, as we strongly believed that the major contribution of a research institution to a region such as Southern Italy would have been that of offering to a great number of young people the possibility to challenge themselves in a research environment. This was also in line with our initial objectives. We considered the diffusion on a large scale of a critical attitude and an evidence-based approach, as the best result of the presence of the Negri Sud at Santa Maria Imbaro. A strong orientation to excellence in research was developed in parallel to the training programme mentioned above. Within few years, many papers from Negri Sud investigators appeared in most respected journals such as The New England Journal of Medicine, Blood, Cell, Nature, PNAS [9–32].

Fig. 3 The group of senior investigators at Mario Negri Sud, February 1998. *Upper level*, from the left: Daniela Corda, Silvio Garattini, Giovanni de Gaetano, Maria Benedetta Donati, Chiara Cerletti, Andreina Poggi and Saverio Alberti; *lower level*, from the left: Vittorio Bertelè, Alberto Luini, Gianni Tognoni, Roberto Lorenzet, Antonio De Blasi and Ennio Esposito. Domenico Rotilio, Cosmo Rossi and Cleo Colombo were absent when this picture was taken

Our intention to diffuse a scientific attitude among young people included a number of programmes with local secondary schools: in the early Nineties a couple of schools in Lanciano were connected to internet through a link to our information network (“Negrilink”) (<http://www.cilea.it/tp/pubblicazioni0/convegni-presentaz/archivio-nir/nit-it-1994/atti-del-convegno/negrilink/>). It was apparently the first example in Italy of an electronic connection between a school and internet.

A major effort was performed with the “Summer Student” programme, initiated at Negri Sud and continued in Campobasso (<http://www.cattolicanews.it/2227.html>): a variable number of students having completed the penultimate year of any secondary school was selected to spend 2–4 weeks in a research lab at direct contact with instruments, reagents, and most importantly researchers, and perform a small research project under a tutor’s supervision. The stage in the lab usually occurred in June and July and was followed in September by a public session during which each student briefly presented the results of his/her experience to an audience made by parents, younger brothers, grand-parents, teachers, people from our labs, lay press and TV and a few local administrators and politicians.

At a certain moment, it happened that our relationships with some of our senior colleagues at Negri Sud progressively deteriorated, for a number of scientific and cultural reasons that are beyond the scope of the present article. We should have imposed our views and authority—someone reproached us later on—but we preferred to stop fighting and step back. At an infinitesimal level, and with a different outcome, this story could recall that of the two women

disputing about a small baby, as reported in the Bible (Kings 1; 3: 16–28) (Table 3).

At the moment we both left Santa Maria Imbaro, Licia Iacoviello, a young coworker of ours, had just started IMMIDIET, a EC-funded project (http://www.moli-sani.org/immidiet_site/project.html). The general aim of IMMIDIET was to evaluate the impact of dietary habits on the risk profile of 3 European communities at different risk of myocardial infarction (MI):

- Abruzzo in Italy
- Limburg in Belgium
- South-eastern London in England

As an index of MI, factors under the combined influence of both dietary and genetic determinants were studied. Migration from Italy to Belgium was used as a “natural” human model in this context. Specific objectives included the evaluation of differences in the variables studied in populations at different MI risk and host countries for possible future immigrations; changes in dietary habits and biomarkers of food intake of mixed couples as compared with those of the original population; and the effects of such changes on specific Coronary Artery Disease risk also in relation to their genetic determinants.

This study also provided an integrated multi-language questionnaire for food intake assessment to evaluate dietary habits in multicultural populations and educational support for health care providers and promotion of healthy dietary habits for the prevention of CAD.

Interestingly enough, couples were recruited through networks of Belgian, Italian and British general practitioners suitably organized for that purpose. In a second phase,

Table 3 A story of two women disputing about a baby

- ¹⁶ Now two women came to the king and stood before him. ¹⁷ One of them said, “Pardon me, my lord. This woman and I live in the same house, and I had a baby while she was there with me. ¹⁸ The third day after my child was born, this woman also had a baby. We were alone; there was no one in the house but the two of us
- ¹⁹ “During the night this woman’s son died because she lay on him. ²⁰ So she got up in the middle of the night and took my son from my side while I your servant was asleep. She put him by her breast and put her dead son by my breast. ²¹ The next morning, I got up to nurse my son—and he was dead! But when I looked at him closely in the morning light, I saw that it wasn’t the son I had borne”
- ²² The other woman said, “No! The living one is my son; the dead one is yours”
- But the first one insisted, “No! The dead one is yours; the living one is mine.” And so they argued before the king
- ²³ The king said, “This one says, ‘My son is alive and your son is dead,’ while that one says, ‘No! Your son is dead and mine is alive’”
- ²⁴ Then the king said, “Bring me a sword.” So they brought a sword for the king. ²⁵ He then gave an order: “Cut the living child in two and give half to one and half to the other”
- ²⁶ The woman whose son was alive was deeply moved out of love for her son and said to the king, “Please, my lord, give her the living baby! Don’t kill him!”
- But the other said, “Neither I nor you shall have him. Cut him in two!”
- ²⁷ Then the king gave his ruling: “Give the living baby to the first woman. Do not kill him; she is his mother”

Bible, 1 Kings 3:16–28

mixed pairs, formed in Belgium by a marriage between Italians and Belgians, with the same range of age as the population studied in the first phase were also recruited [33]. Among the numerous data generated by the IMMIDIET project, of particular interest was the observation that cardiovascular risk factors and global risk of fatal cardiovascular disease were positively correlated between partners of the 802 married couples examined, suggesting preventive approaches should be better addressed to families rather than to individuals [34]. Another interesting finding was that alcohol intake was found to be associated with higher plasma and red blood cell concentrations of marine n-3 fatty acids. Components of wine other than alcohol (polyphenols) were possibly exerting these effects. Data suggest that part of the well known alcohol-induced cardio-protection may be mediated through increased marine n-3 FAs levels [35]. The IMMIDIET project was presented at the Italian Consulate in Genk, Limburg, Belgium and was the occasion to meet many Italian emigrants’ families with their second and third Belgium-born generations. It has been a constant aim of our research projects to apply them to broader cultural contexts, privileging persons or groups involved in the research itself.

Campobasso, a... “low-field”, but a high-profile

At the millennium turn, we left Santa Maria Imbaro and accepted a challenging proposal by our *Alma Mater* to contribute at establishing an official seat of the Catholic University of Milan in Southern Italy. A quite ambitious project and a number of former colleagues from Negri Sud decided to join us in this new adventure (Table 4).

We moved further down to Southern Italy, namely to Campobasso, the head town of the Molise region, at 700

meters above the sea, in view of the Matese mountain. Once again, we opened new laboratories, selected new young people from the region, started ex novo new research programmes. This time, independently of a decision of our Centre not to host any animal facilities, we straight-forwardly moved towards direct human/population studies. As mentioned above, we had already addressed our interest to this kind of approach with the IMMIDIET project. We decided that, being in Molise, our main research project should have been of large, direct, concrete impact for the Molisani people.

A first study aimed at investigating the adherence to Mediterranean diet and at measuring anthropometric and metabolic parameters in an observational study in the ‘Alto Molise’ region, a rural setting, in the context of a health screening initiative: the MOLI-SAL project [36]. It was the first time that an epidemiological study was performed in that part of the Molise region. Altogether more than 600 healthy participants were studied in eight different villages, each visited on a Summer Sunday morning. Blood pressure, glucose, and total cholesterol were measured using automatic devices. Food intake was evaluated with a semi-quantitative food-frequency questionnaire, and the Mediterranean adequacy index (MAI) was calculated. Adherence to the Mediterranean diet was found to depend on age, possibly because in younger people the traditional Mediterranean style diet is decreasing, even in rural areas of southern Italy. Age also influences the association between MAI and metabolic variables such as systolic blood pressure in women.

The MOLI-SANI project: when research meets people

The “MOLI-SANI” project (www.moli-sani.org) was conceived, under the energetic impulse of Licia Iacoviello, as a great research effort to be performed by our

Table 4 A mad flight (il folle volo)

Remember who you are, what you were made for: not to live like brutes, but for the quest of knowledge and the good. I said no more	Considerate la vostra semenza: fatti non foste a viver come bruti, ma per seguir virtute e canoscenza
For, encouraged by this brief address, my comrades were so keen to journey on I scarce could hold them from the final test	Li miei compagni fee' io sì aguti, con questa orazion picciola, al cammino, che a pena poscia li avrei ritenuti
And with our stern set firmly towards the dawn, we made wings of our oars for that mad flight, forever gaining on the port horizon	e volta nostra poppa nel mattino, de' remi facemmo ali al folle volo, sempre acquistando dal lato mancino

Dante Alighieri, *Inferno*, canto XXVI, vv: 118–126

Laboratories in collaboration with local GPs, the regional health authorities, the priests in charge of the different parishes, the elderly cultural circles, the lay press and television networks, the schools. The Medical School of the local state University (Università del Molise) had not yet been established at that time. The study received the initial generous support of the Italian Pfizer Foundation, that left us absolutely free to plan, run and analyse the study, without interfering at any stage with it.

Health promotion, life style and prevention were the preferred targets of the project, rather than diseases, hospitals and drugs.

We made the first official announcement of the study at the end of 2002, on the occasion of the Opening Ceremony of the newly established Research Centre of the Catholic University in Campobasso, but the project was first presented at an elderly public during an open air meeting held in the small beautiful square of Roccavivara, a small village (870 residents) at 650 meters above the sea level. It is of note that Roccavivara was not included by chance among the villages or towns randomly selected for the project. Notwithstanding that, each year in August, at the

occasion of the annual “Giornata dell’Anziano” the progress and interim results of the study are presented by one of us in the same square.

During the last 10 years it was not always easy to establish fruitful contacts with potential public or private sponsors or to attract the interest of the regional Health Department for the results of the study. It had been easier to interact with lay people especially within the 30 villages/towns randomized to participate in the planned recruitment of the 25,000 participants (Fig. 4). During the past 3 years in particular we have visited by invitation many of these 30 villages, presenting there the first data obtained in the whole population, but also the peculiarities recorded in each single village and commenting with the local GPs and the numerous people present at our meetings how to improve their health and to prevent major diseases.

A brief description of the MOLI-SANI project (Table 5)

“MOLI-SANI” is a population-based cohort study aiming at evaluating the risk factors linked to chronic-degenerative

Fig. 4 The front page of the MOLI-SANI calendar 2011, showing a picture of the thirty villages participating to the study. “Campanili della Salute” means “Health bell-towers”

Table 5 Main methods used in the MOLI-SANI project

The MOLI-SANI project	
<i>The recruitment procedures</i>	
All subjects were asked to answer three different questionnaires, namely a case history, a food frequency (FFQ) and a quality of life (FS36) questionnaire; they underwent psychometric tests to evaluate any depressive status, stress response and attitude to suicide	
<i>The case history questionnaire</i>	
Beyond personal data, information was collected on social status and childhood, physical activity, smoking habits, hormonal status in women, body weight history, inflammatory disease in the past year, antibiotics and influenza vaccine, hypertension, diabetes and dyslipidemia and relative dietary and pharmacological treatments, ischemic cardiovascular disease and relative treatment (type of medication, dosage and compliance) and possible hospitalization, pulmonary diseases (relative treatment and possible hospitalization), depressive status or anxiety with relative previous and current treatment, haematological, kidney, gastrointestinal or endocrine disease, Alzheimer disease, tumours (malignant or benign), surgical interventions and radiological tests in the past 5 years (with indication of the Clinical Centres where they were performed)	
Finally, the questionnaire included a detailed pharmacological interview on each chronic or acute medication taken in the past 15 days, with indication of commercial name, type of packaging, dosage, frequency, compliance and clinical indication (people were asked to bring with them the GPs' prescription or the drug packaging of the medication they used to consume)	
<i>The dietary assessment</i>	
The European Prospective Investigation into Cancer and Nutrition (EPIC) FFQ was used to determine daily nutritional intakes consumed in the past year. This questionnaire was previously validated in a multicenter study performed in 10 European Countries, to evaluate the relation between diet and cancer. The questionnaire, computerized with a tailor-made software, allowed researchers to interview participants in a fully interactive way, including illustrations of sample dishes of definite sizes or by reference to standard portion sizes. All the answers provided by the participants were recorded in a database in real time. The NAF software (Nutritional Analysis of Food Frequency Questionnaires, National Cancer Institute, Milan, Italy) was used to transform information about food composition into daily intake of food items (g/d), energy (kcal or kJ/d), and macro- and micro-nutrients (g or mg/d). Nutrient data for specific foods were obtained from the food composition database for epidemiological studies in Italy	
On the basis of the recorded data, each subject was given his own cardiovascular risk score according to the <i>cuore.exe</i> algorithm elaborated within the Cuore Project (http://www.cuore.iss.it/)	
<i>Biochemical measurements</i>	
Venous blood samples were obtained by clean vein-puncture between 07:00 and 09:00 a.m. from participants who had fasted overnight and had refrained from smoking for at least 6 h. Blood glucose, cholesterol, HDL, LDL, C-reactive protein, D-dimer levels and blood cell counts were measured within 3 h from blood sampling, on fresh samples in the centralized MOLI-SANI clinical chemistry laboratory built up in both recruiting centers. Quality control was maintained using internal laboratory standard in-house plasma pool. Inter and intra-day CV was 5.4 and 7.6 %, respectively	
Blood cell counts included platelets, white and red blood cells, mean platelet volume, mean corpuscular volume and haemoglobin	
Citratated plasma, EDTA plasma, serum, cellular pellet and urinary spots were stored in liquid nitrogen in a dedicated biobank (Moli-bank, http://biobank.moli-sani.org/)	
<i>Anthropometric and blood pressure measurements</i>	
Body weight and height were measured with subjects wearing no shoes and only light indoor clothing. BMI was calculated as kg/m ² . Waist circumferences were measured according to the NIH, Heart, Lung, and Blood guidelines	
Blood pressure was measured by an automatic device (OMRON-HEM-705CP) three times on the non-dominant arm and the average of the last two values was recorded	
<i>Definition of risk factors</i>	
<i>Hypertension</i> was defined by values of systolic BP ≥ 140 mm Hg and/or diastolic BP ≥ 90 mm Hg, or current pharmacological treatment. <i>Hypercholesterolemia</i> was defined by levels of cholesterol ≥ 200 mg/dL or current pharmacological treatment. Diabetes was defined by fasting glucose level >126 mg/dL or current treatment with antidiabetic drugs	
Subjects were classified as non-smokers if they had never smoked cigarettes or had smoked less than 100 cigarettes life-long, ex-smokers if they had smoked more than 100 cigarettes in the past but had stopped smoking for at least 1 year, and current smokers those who reported having smoked more than 100 cigarettes in their lifetime and either still smoked or had quit smoking by less than 1 year	
<i>Socio-economic status</i> was defined by a score based on 8 variables (income, education, job, housing, ratio between the number of live-in partners and the number of rooms—both current and in the childhood—and availability of hot water at home in the childhood); the highest the score, the highest the level of socio-economic status. Physical activity was assessed by a structured questionnaire and expressed as daily energy expenditure in metabolic equivalent task-hours (MET-h)	

Table 5 continued

The MOLI-SANI project	
<i>Metabolic syndrome</i> was defined according to Adult Treatment Panel III criteria. Global individual CVD risk was calculated applying the risk equations of the CUORE project. Subjects older than 69 years or with a history of cardiovascular events were excluded from this analysis	
<i>The electrocardiograms</i>	
Standard 12-lead resting ECG was measured using a Cardiette® ar2100-view electrocardiograph, an electrocardiographic acquisition unit able to transmit the ECG signal to the PC in real time via a	
USB cable and storing ECG in SCP format. The ECG was then digitally processed by the “University of Glasgow 12-Lead ECG Analysis Algorithm”	
<i>Pulmonary function tests</i>	
Pulmonary function manoeuvres were performed by trained operators, according to American Thoracic Society/European Respiratory Society recommendations, with 3 V-Max Encore 22D equipped with plethysmographyc V62 J Autobox and 2 V-Max Encore 20, all with the same Mass Flow Sensor model (Sensormedics® Viasys). Daily volume calibration was performed with a 3-L syringe. Volume variability higher than 0.5 % from the real value (3 L) was discarded and calibration was repeated. At the end of each tests session, technicians evaluated the acceptability (including start, duration and end of test) and the reproducibility of the maneuvers. Subjects with HQ spirometry randomly performed plethysmography and diffusion test. All tests were performed in the morning after technical explanation, with subjects in a sitting position and with the use of a nose-clip	

disease with particular regard to cardiovascular disease (CVD) and cancer. Intermediate metabolic phenotypes such as hypertension, dyslipidemia, diabetes, obesity and metabolic syndrome are also investigated. A complex equilibrium does exist between genetics and lifestyle often setting the border between health and sickness. To better understand such an equilibrium and its consequences on cardiovascular, cancer and metabolic diseases is a major aim of the MOLI-SANI project.

Studying either cardiovascular, cancer or metabolic risk factors in the light of their relationships and mutual influence, might offer a powerful tool for exploring the concept of a “common soil” for these diseases [37], an approach that is attracting increasing attention. Moreover, the MOLI-SANI project aims at identifying easy-to-use and relatively low-cost tools that could be used in public health and in the clinical practice for an early identification of subjects at risk of developing chronic disease.

The study population

The cohort of the MOLI-SANI study was randomly recruited in the Molise region from city hall registries by a multistage sampling. First, townships were sampled in major areas by cluster sampling; then, within each township, participants aged ≥ 35 years were selected by simple random sampling. Recruitment was based on household to allow household and large pedigree construction for genetic analysis. The few exclusion criteria were pregnancy at the time of recruitment, disturbances in understanding or willingness, current poly-traumas or coma, or refusal to sign the informed consent. Thirty percent of subjects refused to participate; these were generally older and had a higher prevalence of CVD and cancer.

Between March 2005 and April 2010, 24,318 subjects were recruited in two different centres: the Catholic University at Campobasso ($n = 19,211$; 79 %) and San Timoteo Civil Hospital in Termoli ($n = 5,107$; 21 %), by research personnel, accurately trained. The recruitment strategies were carefully defined and standardised across the two recruiting centres. Structured digitalized questionnaires were administered to collect personal and clinical information.

We started a follow-up based on linkage with hospital discharge records (SDO) and mortality regional registry in May 2010 after a mean period from the recruitment visit of 2.5 years. Such a follow-up is being up-dated every 6 months. In July 2010 a telephone follow-up on the whole cohort was also completed.

The MOLI-SANI study complies with the Declaration of Helsinki and was approved by the Catholic University ethical committee. All participants enrolled provided written informed consent.

The first few data

The first data from the observational part of the MOLI-SANI study include the relationship between pulmonary function and 10-year risk for cardiovascular disease, the pandemic and seasonal vaccine coverage and effectiveness during the 2009–2010 pandemic influenza, the influence of mass-media information on the adherence to Mediterranean diet, the relationship between total dietary antioxidant capacity and lung function, the distribution in the general population of short and lifetime risks for cardiovascular disease, the role of white blood cell count, sex and age as major determinants of heterogeneity of platelet indices, the methodology for plasma profiling measurements, breakfast food consumption, dietary patterns and risk factors for cardiovascular disease, and—last but not least—the good news that regular consumption of dark chocolate is associated with low serum concentrations of C-reactive protein, a sensitive bio-marker of cardiovascular risk [38–47].

Moreover, MOLI-SANI offered us the chance to focus our attention on the role of Mediterranean diet on health thanks to the large amount of data collected on dietary habits of the population. Beyond the scientific papers published on this topic, we have also recently published a book on the epidemiology of Mediterranean diet which is raising great interest not only in the scientific community but also among the general public. In the wake of the belief that science is poor without people being involved [48].

In the context of the relationships between food and health, we developed an increasing interest in wine/beer/alcohol consumption, cardiovascular risk and total mortality, a matter of great concern at institutional, popular and scientific level. A couple of meta-analyses performed by our group are considered as a valuable reference in the international debate on this topic [49–51].

Ultimo folio

The rest of this story is a chronicle of the present days and is of no interest to this article.

It is better ended by a paraphrase of St. Paul (*Second epistle to Timothy*; 4:7): “We have fought a good fight, we have kept the faith in research and on the personhood. If only one of the researchers who worked with us will keep the same faith, we shall feel privileged. But we believe there will be many more...”

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Conflict of interest The authors declare that they have no conflict of interest.

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