

Information needs on precision medicine: a survey of Italian health care professionals

Antonio Addis¹, Francesco Trotta¹, Giovanni Tafuri² and Luca De Fiore³

¹Dipartimento di Epidemiologia del Servizio Sanitario Regionale, Regione Lazio, Rome, Italy

²Agenzia Italiana del Farmaco (AIFA), Rome, Italy

³Associazione Alessandro Liberati, Rome, Italy

Abstract

Background. Despite advances in technology development for precision medicine, obstacles remain as barriers to progress and change. In this context simple questions arise: what is the level of understanding of precision medicine among healthcare professionals? We tried to address this question with a survey whose objective was to explore the perception and understanding of precision medicine.

Methods. A questionnaire was administered to a sample made of oncologists, clinical and hospital pharmacists, pharmacologists and infectiologists in the context of five different Italian national congresses. Participation in the survey was voluntary and anonymous.

Results. The questionnaire was filled-in by a total number of 1113 professionals out of 3670 registered participants in the congresses. About half of respondents stated they were not sufficiently informed about precision medicine, and infectiologists were the ones who felt less informed. Most respondents agreed with the basic principles and definitions of precision medicine and believed this new approach is going to require deep changes in healthcare.

Conclusions. Our findings show that healthcare professionals have partial knowledge on this topic and that there is a significant association between respondents' knowledge and their clinical specialty. However, despite some misconceptions about precision medicine, a genuine interest and familiarity with its basic principles seems to emerge.

Key words

- precision medicine
- survey
- questionnaire
- healthcare professionals

BACKGROUND AND OBJECTIVES

Personalized medicine is the tailoring of therapies to defined subsets of patients based on their likelihood to respond to therapy or their risk of adverse events. This emerging approach holds great promise for improving human health and optimizing the development and clinical use of medications. New medicines targeting discrete molecular subclasses of tumours have been recently approved aiming to treat and monitor patients more precisely and effectively and in ways that better meet their needs. A new report from the Personalized Medicine Coalition shows that in 2016, for the third year in a row, personalized medicines accounted for more than 20 percent of the new molecular entities approved by the US Food and Drug Administration (FDA) [1].

Precision medicine – the use of comprehensive genomic, proteomic or even “pan-omic” characterization of patients to guide medical decisions – is a key step

towards truly personalized medicine, implying the combination of biomarker and molecular information with a specific clinical phenotype at the individual patient level [2, 3].

This new approach has drawn increasing interest in the past few years in the medical and scientific communities and efforts are underway to promote its development. Indeed in 2015 the former President of the United States, Barack Obama, announced the “Precision Medicine Initiative”, a research investment plan aiming to accelerate progress towards precision medicine (<https://obamawhitehouse.archives.gov/node/333101>). The goal, he said, was “delivering the right treatment at the right time, every time, to the right person”. Similarly in the European Union both Europe-wide (e.g. the Innovative Medicine Initiative (www.imi.europa.eu/) supported by the European Medicines Agency) and country-specific projects on precision medicine have been successfully developed in the last years [4].

However, despite the advances in technology development and the emerging clinical applications for precision medicine, significant practical obstacles remain as barriers to progress and true change. Contributing forces are both cultural and technological: medical practice does not easily keep pace with rapid technological advances and uptake into clinical care will necessitate a change in culture and perception, whereby genomic information is seen as routine for health care [5]. Moreover, a simple question arises: what is the level of understanding of precision medicine among health care professionals? Are there health care professionals less or more exposed/informed than others? Are their information needs adequately addressed? We tried to address these key questions with a survey whose objective was to explore the perception and understanding of precision medicine among health care professionals, including other related challenges, such as patients' expectations, funding and organizational issues.

METHODS

This is the first survey conducted within the "Forward" project (<http://forward.recentiproggressi.it/>) involving both public and private stakeholders and collecting the opinions of a number of different health care professionals with a dedicated issue on Precision Medicine in 2016. A short report of this analysis was previously published in Italian on the Forward project website (<http://forward.recentiproggressi.it/numero-1/i-risultati-della-survey/>). To this purpose, a questionnaire was prepared by the Forward working group and administered to a sample made of oncologists, clinical and hospital pharmacists, pharmacologists; infectiologists were also chosen as an additional group of professionals since they are expected to be less exposed to precision medicine than others. The questionnaire consisted of 20 questions, organized in 3 sections covering the general perception of precision medicine, general concerns on this field, and finally personal and professional characteristics of respondents (see *Table 2*). Participation in the survey was voluntary and anonymous. Given the nature of the study, exclusively based on the administration of a questionnaire and the collection of anonymous data with no disclosure of confidential/sensitive information by respondents, formal approval by ethics committees was not required.

The questionnaires were administered in the context of five different Italian national congresses. During each event, there was an information desk dedicated to the Forward project, where the project staff provided general information and distributed copies of the questionnaire.

The national congresses involved were:

1. the 17th National Congress of the Italian Association of Medical Oncology (AIOM) held in Rome from 23 to 25 October, 2015;
2. the 3rd National Congress of the Italian Society of Clinical Pharmacy and Therapy (SIFaCT), held in Rome from 8 to 10 October, 2015;
3. the 36th National Congress of the Italian Society of Hospital Pharmacy (SIFO), held in Catania from 22 to 25 October, 2015;

4. the 37th National Congress of the Italian Society of Pharmacology (SIF), held in Naples from 27 to 30 October, 2015;

5. the 14th National Congress of the Italian Society of Infectious and Tropical Diseases (SIMIT), held in Catania from 8 to 11 November 2015.

The reason for choosing these events was that they were all major national and consecutive conferences. The first step of the study was a descriptive analysis, including the calculation of absolute and relative frequencies. The second step consisted of a bivariate analysis using the Chi-square test, in order to assess possible statistical correlations of the different variables using a statistical significance level of 0.05.

RESULTS

The questionnaire was filled-in by a total number of 1113 professionals out of 3670 registered participants in the five congresses (30.3%).

Characteristics of respondents are summarized in *Table 1*.

The first item of the questionnaire explored to what extent respondents felt familiar with the concept of precision medicine (Question 1, see *Table 2*). This allowed a first grouping of respondents based on their answers: 52.6% stated they were not sufficiently informed and 40.7% stated they were only partially informed. Only 6.7% of respondents considered themselves as appropriately informed on this topic (*Figure 1*).

The difference among answers is due to the presence of a significant association ($p < 0.05$) between the respondents' degree of information on precision medicine and their clinical specialty. Infectiologists (the group that appeared to be less inclined to answer to the questionnaire) felt they did not know enough on this topic, whereas oncologists and pharmacologists felt sufficiently informed. On the other hand, no significant associations were found between the respondents' degree of information and their age, gender and geographical region of work.

Another question (Question 2, see *Table 2*) tested the level of knowledge on the initiative on precision medicine launched by the US Government. Almost

Table 1
Characteristics of study respondents

	Number	%
Oncologists	307	28
Clinical/hospital pharmacists	428	38
Pharmacologists	277	25
Infectiologists	101	9
Males	380	34
Females	733	66
Northern Italy	376	34
Central Italy	325	29
Southern Italy	272	24
Islands	149	13

Table 2
Complete set of questions and possible answers administered to each respondent

Question 1. Do you feel informed enough about precision medicine?
Yes/No/Partially.
Question 2. Which institution has launched an important research investment in precision medicine in January 2015?
World Health Organization/European Union/The Government of the United States of America/The National Institute for Health and Care Excellence/I don't know.
Question 3. Do you agree with the following statement: "Precision medicine implies health care decision-making tailored on patients characteristics"?
I fully agree/I partially agree/I partially disagree/I completely disagree.
Question 4. Do you agree with the following statement: "Precision medicine implies the development of therapies targeting individual patients characteristics"?
I fully agree/I partially agree/I partially disagree/I completely disagree.
Question 5. Do you agree with the following statement: "Precision medicine implies the identification of subpopulations with different susceptibility to certain diseases and different response to specific therapies"?
I fully agree/I partially agree/I partially disagree/I completely disagree.
Question 6. Do you agree with the following statement: "Precision medicine and personalized/individualized medicine are synonyms"?
I fully agree/I partially agree/I partially disagree/I completely disagree
Question 7. Do you agree with the following statement: "Precision medicine greatly emphasizes the importance of the individual patient. This contrasts with the typically difficult relationship between patients and physicians"?
I fully agree/I partially agree/I partially disagree/I completely disagree.
Question 8. Do you agree with the following statement: "Precision medicine, shifts the emphasis on disciplines such as molecular biology, or immunology. This may potentially distract health care professionals from their core business i.e. curing patients"?
I fully agree/I partially agree/I partially disagree/I completely disagree.
Question 9. Do you agree with the following statement: "Precision medicine is an alternative to evidence-based medicine. Indeed focusing on the individual patient implies the overcoming of population-medicine"?
I fully agree/I partially agree/I partially disagree/I completely disagree.
Question 10. Do you agree with the following statement: "Precision medicine can be successful in treating limited types of diseases with a strong genetic component"?
I fully agree/I partially agree/I partially disagree/I completely disagree.
Question 11. Do you agree with the following statement: "Resource allocation in precision medicine will subtract resources from sectors more strategically important, such as prevention or rehabilitation"?
I fully agree/I partially agree/I partially disagree/I completely disagree.
Question 12. How would you rate the outcomes reached so far in certain therapeutic areas e.g., oncology, through precision medicine?
Very promising/Sufficiently promising/Not sufficiently promising to justify investment/Not promising.
Question 13. Do you think that precision medicine will require changes in the hospital organization?
Certainly yes/Probably yes/Probably no/Certainly no.
Question 14. Do you think that precision medicine will create excessive expectations among patients and their families?
Certainly yes/Probably yes/Probably no/Certainly no.
Question 15. Do you think that precision medicine will require a different training of physicians and pharmacists?
Certainly yes/Probably yes/Probably no/Certainly no
Question 16. Are there additional topics that should have been included, but were not covered in this survey?
Yes (if yes, elaborate which topics you would add)/No/I don't know.

the totality of respondents (89.8%) ignored that the institution launching this investment plan was the White House. About 70% (68.8%) of respondents admitted they did not know, 15.2% thought the institution was the World Health Organization, for 2.9% it was National Institute for Health and Care Excellence (NICE), while for 3.1% the European Union. Only 10.2% gave the right answer. Oncologists were the most informed specialists on this initiative, while pharmacologists and infectiologists were the ones who

more frequently attributed the initiative to the World Health Organization.

Of note, most of the respondents who felt sufficiently informed about precision medicine gave the right answer.

In this first section of the questionnaire respondents were also asked to express their agreement/disagreement (full agreement, partial agreement, partial disagreement, complete disagreement) on a number of statements about precision medicine.

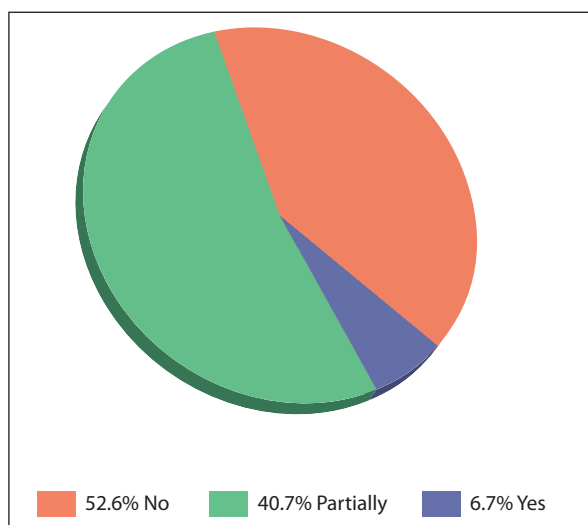


Figure 1
Answers to Question 1: "Do you feel informed about precision medicine?"

Question 3 (see *Table 2*) explored the level of agreement on precision medicine as an approach implying health care decision-making tailored on patients characteristics. Almost all respondents (95.3%) fully or partially agreed with this statement (43.5% were in full agreement with this statement, while 51.8% were in partial agreement). Only 4.7% expressed overall disagreement (3.3% partially disagreed and only 1.4% completely disagreed).

When asked about the agreement on precision medicine for the development of therapies targeting individual patients characteristics (Question 4, see *Table 2*), respondents showed a high level of agreement (96.2%): 50.5% fully agreed with the statement, and 45.7% partially agreed. Only 3.7% expressed negative opinions: 3.2% in partial disagreement, and 0.6% in complete disagreement.

Another question (Question 5, see *Table 2*) tested the level of agreement on precision medicine implying the identification of subpopulations with different susceptibility to certain diseases and different response to specific therapies: 92.6% of respondents agreed (45.5% in full agreement, 47.1% in partial agreement), 6.2% partially disagreed and 1.2% completely disagreed.

With regard to Question 6 (see *Table 2*), respondents were supposed to express their agreement on precision medicine and personalized/individualized medicine as synonyms. 70.4% of respondents overall agreed (22.1% fully agreed, 48.3% partially agreed), while 20.8% of respondents partially disagreed and 8.8% answered they completely disagreed.

Question 7 (see *Table 2*) investigated whether respondents agreed with the idea that precision medicine greatly emphasizes the importance of the individual patient, despite the well known challenging interactions between patients and physicians. Most respondents (72.9%) agreed (30.2% fully agreed, 42.7% partially agreed). A negative opinion was expressed by 27.1% of

respondents (18.5% partially disagreed, and 8.6% completely disagreed).

Another question (Question 8, see *Table 2*) aimed at highlighting a critical aspect of precision medicine, i.e. the emphasis on disciplines such as molecular biology, or immunology – which may represent a potential distraction from curing the patients. In this case only 12.2% fully agreed with this statement, 37.2% partially agreed, 32.4% partially disagreed and 18.2% completely disagreed.

Another question (Question 9, see *Table 2*) dealt with a particularly sensitive and delicate aspect, namely if the paradigm shift imposed by precision medicine may decrease the importance of the traditional evidence-based approach to medicine. 66.5% tended to agree with this statement (19.1% fully agreed and 47.4% partially agreed). The remaining 33.5% expressed their disagreement on this statement (23.6% partially disagreed and 9.9% completely disagreed).

The idea that precision medicine can be successful in treating limited types of diseases with a strong genetic component (Question 10, see *Table 2*) was agreed by the majority of respondents (75.5%), in particular 29.1% fully agreed, 46.4% partially agreed, 18.2%, partially disagreed, and 6.3% fully disagreed.

The following question (Question 11, see *Table 2*) focused on funding issues. Indeed respondents' agreement was measured on the issue that precision medicine may potentially cause a funding reallocation, thus subtracting resources from sectors more strategically important, such as prevention or rehabilitation. The analysis revealed that 35.7% of respondents agreed (9.5% fully agreed and 26.2% partially agreed) and 64.3% overall disagreed (44.5% partially disagreed, and 19.8% completely disagreed).

Another question explored the perception of respondents on the outcomes reached so far in certain therapeutic areas e.g., oncology (Question 12, see *Table 2*) through precision medicine: 75.8% of respondents considered the results obtained as promising (30.9% very promising and 44.9% partially promising). Only 0.4% of respondents considered the results obtained as not promising at all, and 5.6% as not enough to justify the investment. Finally, 18.2% of survey participants believed they were not sufficiently informed to answer this question.

The second set of questions tested doubts and concerns of respondents on the healthcare reorganization potentially caused by precision medicine, about the possible excessive expectations from patients and their families, and on the different education and training needed by healthcare professionals in relation to precision medicine (Questions 13, 14 and 15, see *Table 2*).

Almost all respondents (94.9%) were aware that advances in precision medicine will require changes in terms of hospital organization: 53.6% stated that they will probably lead to changes, while 41.3% declared changes will definitely occur. Only 4.6% stated that no major change of the healthcare organization is expected in relation to precision medicine. Answers to this item were found to be independent from medical specialties, age and geographic area of respondents; possible differences are thus due to chance.

Interestingly, most respondents (79.4%) believed that precision medicine may create excessive expectations in patients and their families: in particular, 60% stated that it will probably create excessive expectations, 19.4% were absolutely sure it will do, 20.6% did not think that precision medicine might create false expectations in patients and their families (probably not 17.7%, certainly not 2.9%). Clinical and hospital pharmacists are more convinced that precision medicine might somehow disappoint patients and their families. "Probably not" is the most frequent answer given by oncologists.

Almost all respondents (95.4%) are aware that the adoption of precision medicine will necessarily require changes in education and training of healthcare professionals. Only 4.2% believed that changes in training will probably not be needed. The positive answers ("Certainly yes", "Probably yes") were found to be independent from age and gender of respondents, while a statistically significant correlation ($p = 0.02$) was identified with the medical specialty of respondents, since it emerged that clinical/hospital pharmacists and experts in infectious diseases more strongly believe in the need

for healthcare professional's education specific for precision medicine.

Last question (Question 16, see Table 2) was an open question to test the comprehensiveness of the survey itself. Most respondents (63.5%) answered the survey was exhaustive, 2.1 % thought some subjects had not been addressed, but did not mention which ones. 28.1% of respondents indicated aspects that should have been included, mentioning the economic sustainability of precision medicine, the relationship with gender medicine, the diseases to which precision medicine can be applicable, the degrees of its applicability within different health care contexts, ethical issues, data bases and registries, issues related to patient's compliance, the relationship with pharmaceutical companies' interests, and biostatistics.

Respondents' answers are summarised in Figure 2 and Figure 3.

DISCUSSION

This analysis represents the first systematic attempt to look into the actual perception of precision medicine, reporting directly the views and information needs

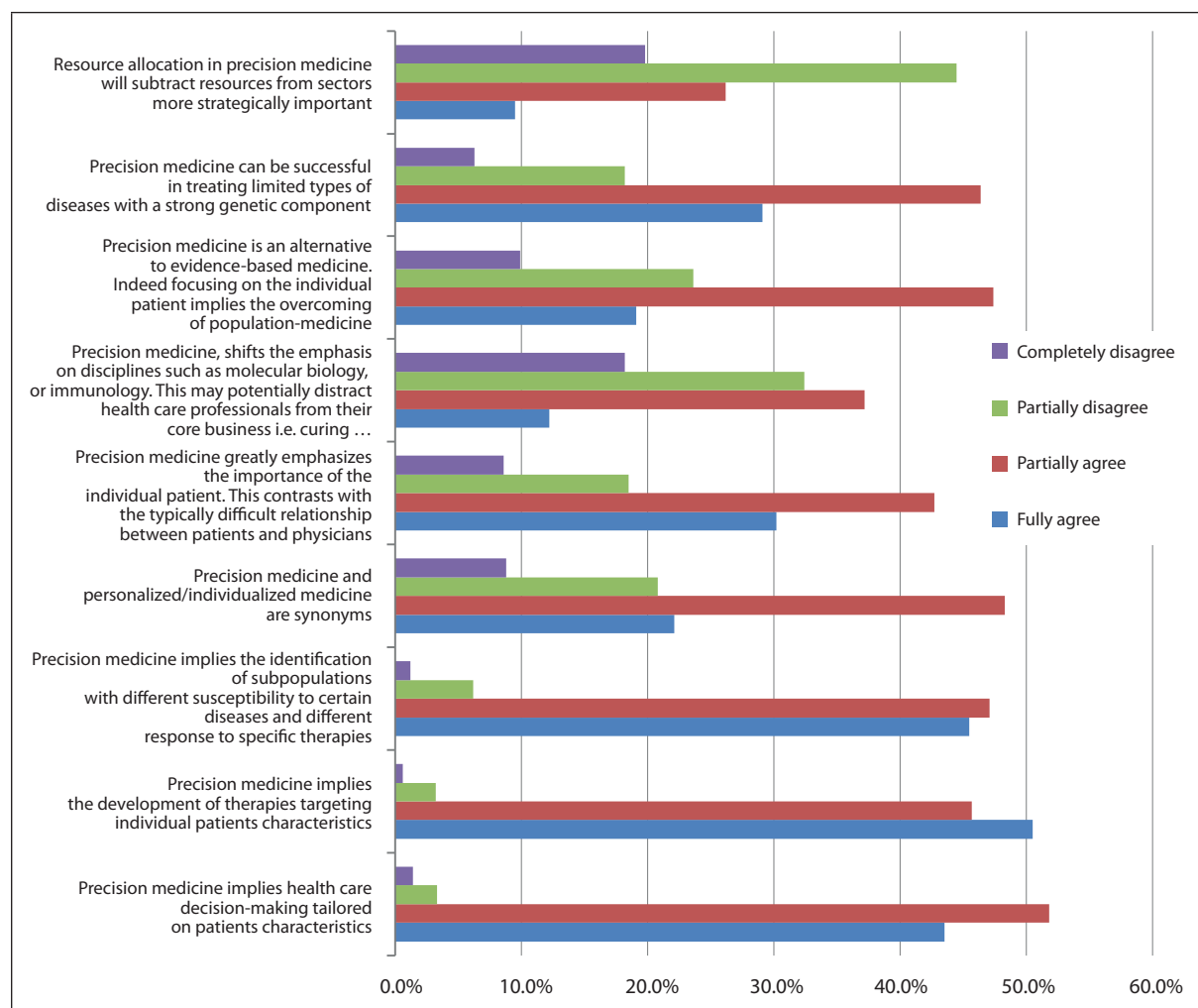


Figure 2
Summary of answers to question 3-11.

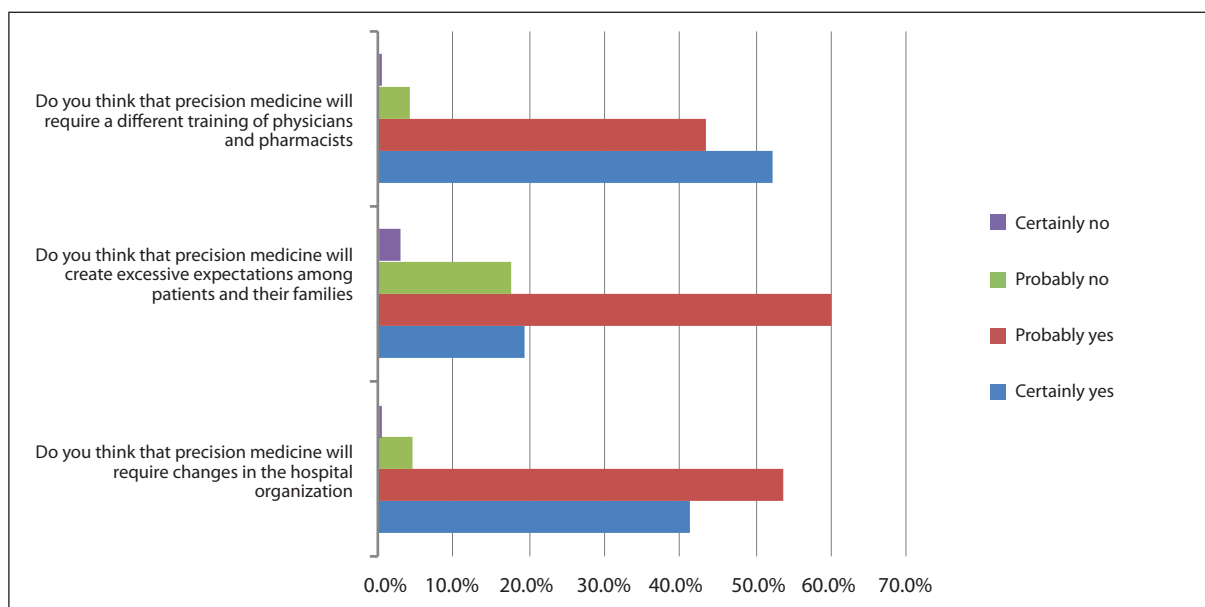


Figure 3
Summary of answers to question 13-15.

of Italian health care professionals. Overall the study findings show partial knowledge of this topic, which may have influenced the willingness of respondents to answer the questions, as well as the quality and reliability of their answers. This, however, does by no means threaten the validity of the study, which still provides a reliable overview on this subject.

Are we informed enough?

Feeling well informed about precision medicine (roughly 7% of respondents) seems to be strongly associated with being aware of the Precision Medicine Initiative and that the US Government was the institution launching this important research project (only 10% of correct answers). Nevertheless, in a context of general misinformation, it is still reassuring to observe a 15% of respondents attributing a coordinating and leading role to the World Health Organization.

Surprisingly, most respondents believed that precision medicine and personalized/individualized medicine are synonyms (70.4%). It is true that the two terms partially overlap and some people still use them interchangeably. Our opinion is that precision medicine, focusing especially on pharmacogenomics, represents the most advanced niche within personalized medicine. Of note, these concepts are not new. "What is new is that advances in a wide range of fields from genomics to medical imaging to regenerative medicine, along with increased computational power and the advent of mobile and wireless capability and other technologies, are allowing patients to be treated and monitored more precisely and effectively and in ways that better meet their individual needs", as Dr. Margaret A. Hamburg, former FDA Commissioner, once stated in a speech [6]. Her words indicate that precision medicine does not "go beyond" – and is still part of – population medicine; whereas one out of three of our respondents sup-

port an opposite view. This strengthens our perception on substantial misunderstandings and misinterpretation of such new concept among respondents.

As previously mentioned, most professionals believe that precision medicine is patient centered, and seems to conflict with the evidence-based medicine which is perceived as the "population (imprecise) medicine", based on the results of large randomized controlled trials. However, a patient centered approach does not conflict with the evidence based medicine. Indeed, evidence based medicine is conceived to deliver the best available care to patients taking into account specificities such as severity of the disease, risk factors etc. The "imprecisions" should rather be identified in the delivery of services by health care facilities.

The survey shows heterogeneity among different medical specialties, highlighting the need of educational pathways tailored on specific categories of health care professionals.

The need for a cultural mindshift

Almost all respondents (94%) believed that precision medicine requires significant organizational changes within the healthcare system. But to what extent and in which sectors? Significant challenges exist to precision medicine's broad implementation in health care, including infrastructure challenges, slow uptake of genomic information into clinical care and research, reimbursement of costly targeted therapies and companion diagnostics, and achieving greater patient's and clinician's engagement and trust [7].

In particular, a cultural change among health care professionals is key to the successful implementation of precision medicine. A number of American Universities have already started to deal with this issue setting up specific courses on diagnosis and treatment of diseases with a strong genetic component. This is the case of the

Harvard Medical School (<https://dbmi.hms.harvard.edu/>), of Duke University (<https://medschool.duke.edu/>) and of Stanford University (<http://med.stanford.edu/>) for example. Italy has no experience of this kind and this is reflected in the answers of our respondents (95% of respondents believe that healthcare workforce education should be reconsidered and a significant proportion of these answers came from residents of Southern Italy and Islands).

Furthermore, more efforts are needed in the framework of continuing medical education, in line with the initiatives implemented at the Genomic Medicine Institute of Cleveland Clinic (<https://my.clevelandclinic.org/departments/genomics/about>) or at the Mayo Clinic's Center for Individualized Medicine (<http://mayor-esearch.mayo.edu/center-for-individualized-medicine/>) for example, which are organizing courses for both healthcare professionals and citizens.

Precision medicine and citizens

Engagement and trust of the public to participate in precision medicine research is necessary for the field to reach its full potential. Intense research has allowed cutting down the costs of human genome sequencing [8]. This constant cost reduction (today, in the US, the cost is more or less US\$ 1000 – excluding the costs for data reading and interpretation) implied a series of consequences: the increasing spread of tests forces doctors to be more competent on the issue and at the same time citizens are more aware of the opportunities that may stem from new treatment options. The personal-genomics screening tests for genetic health risks (including one for Alzheimer's and one for a rare blood disorder) recently approved by the FDA, are a clear example of the impact of precision medicine on people's life and on the radical change expected in the relationship between physicians and their patients [9]. The question of how positive this change is going to be for patients and health care professionals remains still unsolved.

As to the practical impact of precision medicine on citizens, the so-called "Angelina Effect" is often mentioned. In May 2013, US actress Angelina Jolie revealed, in a New York Times editorial, her decision to undergo bilateral mastectomy based on her familiarity for breast cancer, as she was a carrier of a BRCA1 (Breast Related Cancer Antigens) gene mutation. Expectedly, the news spread across the world and, in the immediately following weeks, an impressive increase in the Google search on this matter was registered [10]. At the same time, the number of both tests and consequent surgeries rapidly increased.

A study carried out by a team of the Johns Hopkins University showed that 3 out of 4 US citizens knew Angelina Jolie's story and her decision, but only 10% had all the necessary information to understand the rationale for the higher risk run by the actress [11]. Only 3.4% of the sample had read the editorial on the *New York Times* and the vast majority of people had heard the news from television or entertainment magazines. 57% of interviewed women declared they would undergo surgery and 50% would recommend it to a family member under the same Jolie's circumstances.

Patients' expectations tend to become higher, once "precision" strategies are able to cure severe and life threatening diseases. Our survey respondents seemed to be very well aware of it, since most of them (79%) believed that precision medicine risks to create exaggerated expectations in patients and their families.

CONCLUSIONS

The barriers to developing precision medicines are many. Everyone has a stake in this process; in particular health care professionals, using genomic and other information in routine health care delivery will be crucial to integrating precision medicine into health systems.

Despite some misconceptions about precision medicine, a genuine interest and familiarity with its basic principles seem to emerge among the health care professionals. Based on that, it is reasonable to expect that further investments in educating the health care workforce will lead to rapid positive changes over the next few years. However, challenges to the clinical adoption of precision medicine should be uncovered and potential solutions should be outlined.

Availability of data and materials

Datasets will be made available by authors upon request.

This article is based on an online short report previously published in Italian on the Forward project website available at: <http://forward.recentiproggressi.it/numero-1/i-risultati-della-survey/>.

Conflict of interest statement

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Author contributions

AA and LDF made substantial contributions to conception, design of the survey and data collection, while FT and GT drafted the article. All authors contributed to the analysis and interpretation of data and gave final approval of the version to be submitted and of any revised version.

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The views expressed in this article are the personal

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