Implementation of Precision Oncology in the National Healthcare System: A Statement Proposal Endorsed by Italian Scientific Societies

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ABSTRACT

PURPOSE Precision oncology (PO) promises positive results for patients. To date, in Italy, the effort to implement PO has been made autonomously by regional health institutions in a top-down fashion. This approach is not very efficient and jeopardizes patients' equal access to PO. Similar outcomes have been recorded in other Western countries. We tested a method of collaboration among professionals, scientific societies, and government institutions to facilitate the delivery of PO innovation to patients' bedsides.

METHOD We designed an organizational research project on the basis of a bottom-up approach. We started by observing PO-related activities in five health care authorities (HCAs) in one Italian region. We then compared the issues that emerged with those of three additional HCAs in other Italian regions. Using the results of the initial observation and adopting validated multiple-step consensus methods, we finally derived 14 statements that were approved by the four main scientific societies of oncology and pathology at the national level.

RESULTS The 14 statements addressed the main issues linked to the implementation of PO in clinical practice. The strong professional consensus advocated for prompt adoption within the national healthcare system.

CONCLUSIONS The consensus on the statements that were obtained shows the importance of a synergistic effort among professionals, scientific societies, and health care institutions in defining homogeneous solutions for innovation implementation within the health care system.

ACCOMPANYING CONTENT

Appendix

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INTRODUCTION

In recent years, the introduction of precision oncology (PO) in clinical practice has reshaped cancer management, offering novel diagnostic and treatment strategies for a growing number of patients with cancer and presenting new challenges for national healthcare systems (NHSs). Although initially relevant for few tumor types, PO has progressively garnered attention and currently plays a central role in cancer treatment along with the fast-increasing genome sequencing capability and the development of new target drugs. Large investments in research are accelerating the pharmaceutical and technological evolution in oncology: in 2020, almost one third of all medical experimentation was in the oncology field.[1] Thus, we foresee an increasing expansion of knowledge and opportunities that will hopefully further reduce the mortality of patients with cancer.[2] However, many patients do not receive the most effective personalized treatments because of the challenges associated with integrating predictive biomarker testing into clinical practice. Currently, it is reported that many patients with cancer never receive genomic testing according to guidelines, and even for those who do, only 60%-75% with actionable mutations receive the targeted treatments that are indicated by their test results.[3] Patients are lost at various steps along the PO pathway because of operational inefficiency, limited understanding of biomarker strategies, inappropriate testing result usage, and access barriers.[4] If the implementation of precision medicine is slow or inadequate, the promise of genomics will be only partially realized.[5]

Some elements, such as workflows including protocols for automatic next-generation sequencing (NGS) testing for patients with advanced solid tumors, the presence of molecular tumor boards (MTBs) for result interpretation, and administrative assistance for the matching of clinical trials

and fast access authorizations, have been shown to be key factors in the successful implementation of precision medicine programs.[6]

The Italian Parliament has recently recognized the importance of this challenge and approved a law for PO implementation at the national level within the *National Recovery and Resilience Plan* (PNRR art. 8 law 233), which is part of the postpandemic European development project Next Generation EU. This law gives the National Agency for Health Services and the Conference of Regions a mandate to define the criteria, methods and procedures for the establishment of MTBs, and the identification of the specialist centers dedicated to extended parallel sequencing analysis in each region. To date, the rules are not yet issued.

The public Italian NHS is region-based, and following indication of the Ministry of Health, cancer patient care should be delivered within regional oncology networks. Differences in population sizes, geographic extension, and organization complicate the adoption of a unique model of PO delivery. Applying a method could aid in the pursuit of the same outcome and objectives even in different organizational frameworks. We think that other universalistic health care systems could be facing similar challenges in implementing PO in cancer care pathways.

To date, while regulatory indications are still pending, efforts to implement and regulate the application of PO innovation have been made autonomously by some regional health institutions that decreed the aim, role, and organization of MTBs in a top-down fashion. This approach was not very efficient in answering all the clinical and organizational needs, as was revealed by a national survey that was conducted as a part of this research project.[7]

To face the complexities linked to PO, we believe that a method rather than one model is needed and that collaboration between scientific societies and government institutions is the only possible way to bring innovation efficiently, efficaciously, sustainably, and homogeneously to the patient's bedside.

To accomplish this aim, the four most representative Italian oncology and pathology scientific societies (Associazione Italiana di Oncologia Medica—AIOM, Collegio Italiano Primari Oncologi Medici Ospedalieri—CIPOMO, Collegio Oncologi Medici Universitari—COMU, and Società Italiana di Anatomia Patologica e Citologia—SIAPeC) jointly developed an organizational research project, using a bottom-up approach to identify possible solutions to emerging needs by pursuing an interassociation consensus on some fundamental principles. In the following sections, we present our method and results.

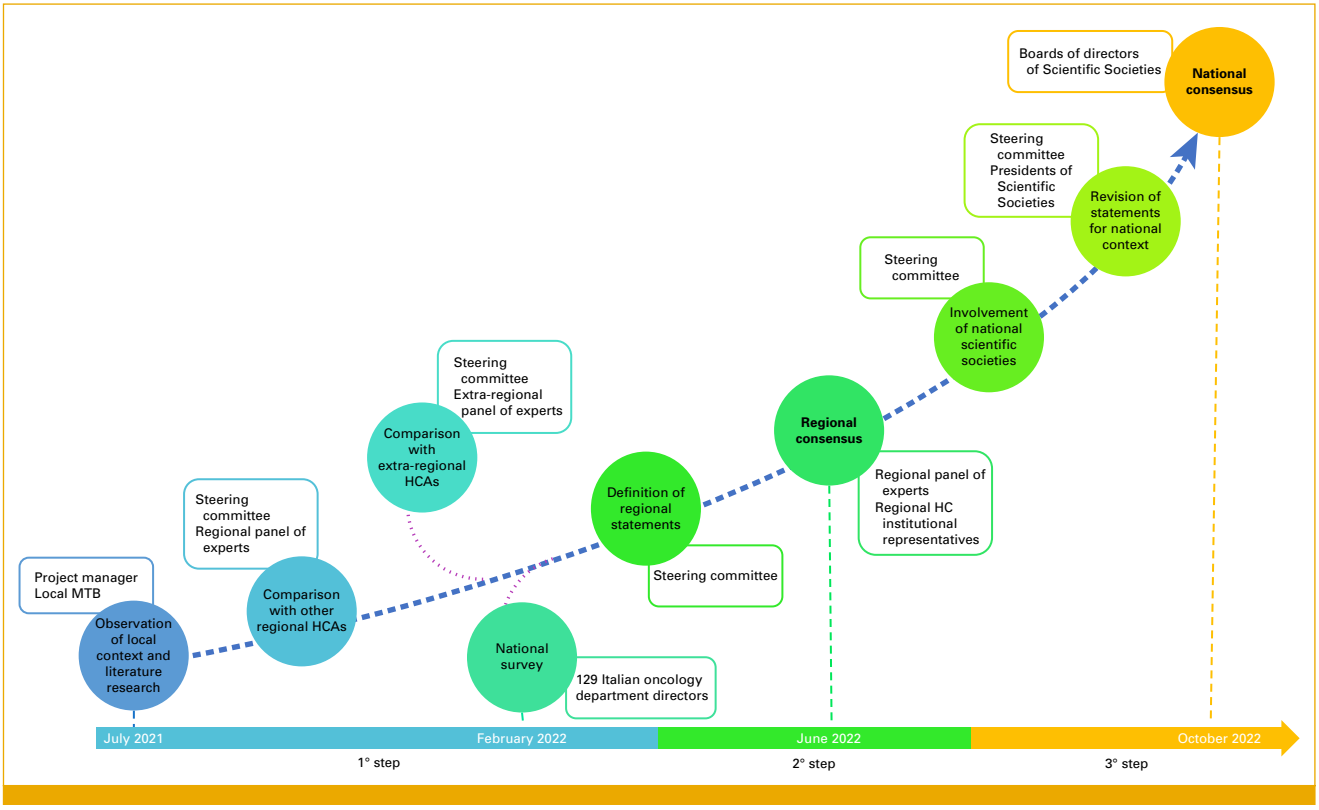

FIG 1. The phases of the bottom-up approach from the local context to the national level. HC, health care; HCA, health care authority; MTB, molecular tumor board.

METHOD

To understand how to support the integration of PO and the activity of an MTB within the current oncology pathways, we designed an organizational research project with the aim of implementing PO following a bottom-up approach (Fig 1). A steering committee, including an oncologist, a chief medical officer, an associate professor in health care management, and a project manager, was instituted. The research project was approved by the local ethical committee.

The project started in the Friuli Venezia Giulia region (Northeast Italy) with the aim of defining indications for PO implementation to be adopted homogeneously by the five health care authorities (HCAs), including two Istituto di ricerca e cura a carattere scientifico (IRCCSs).

Three other HCAs from different regions in Northern Italy (Veneto, Emilia Romagna, and Lombardia) were involved in this project to broaden the observations and to better understand the PO-related challenges in different contexts. Each HCA was represented by a panel of experts including oncologists, pathologists, and chief medical officers to simultaneously analyze the clinical, administrative, and managerial aspects of the topic.

These partners represent regions with different population sizes and different organizational models within the Italian NHS (Table 1). The project was led with the support of the Centre for Research in Healthcare and Social Management of the Scuola di Direzione Aziendale Bocconi University School of Management.

First Step: Identifying the Priorities and Needs of PO

We began direct observations with one of the HCAs of the Friuli Venezia Giulia region, where an MTB was first established in October 2020 and included oncologists, hematologists, pathologists, biologists, geneticists, and pharmacists. The MTB clinical discussions also revealed the methodological, technological, and organizational needs to build a good workflow. These aspects were collected by the project manager who oversaw the involvement of experts to design and implement the solutions.

In addition to technical and organizational needs, several other challenges of PO implementation emerged:

- The integration of the new agnostic approach into the current histology-based clinical pathways.
- The fine tuning between innovation (what is new and shows benefit compared with previous practice) and appropriateness (what is effective, efficient, and in line with ethical principles of fair allocation).[10]
- The sustainability of high-cost treatments.
- The professional reconciliation between diagnostic potential and therapeutic impact.
- The need for new and high-quality standards for laboratories.
- The interpretation of the data.
- The management of a massive amount of data.

All these topics were then discussed by all eight HCAs who participated in the project, comparing the way in which these activities were being managed in different contexts and collecting the opinions of professionals from different disciplines (oncologists, pathologists, and medical directors) to better understand whether the challenges that were perceived where the MTB was established were context-specific or general.

A comparison of the different approaches and levels of implementation recorded by the involved HCAs revealed a need to depict the state of the art of PO at the national level. To do this, we designed a national survey focusing on two major topics: (1) the diffusion, use, and impact of NGS technology and (2) the diffusion, activity, and organization of MTBs. The survey was submitted to 169 heads of medical oncology departments affiliated with CIPOMO.

Second Step: Regional Statement Definition and Consensus

Combining the information gained from the initial observations of MTB activity, the structured comparison with the professionals of the other HCAs involved and the results of the national survey enabled us to define some general needs and tendencies in the approach to PO in various contexts. Starting from these findings, we launched a second step of the project aimed at presenting solutions to the current needs for a homogeneous implementation of PO among the various HCAs. The propositions were

TABLE 1. Characteristics of the Regions Involved in the First Step of the Project

Characteristic	Population, Mln	Surface, km^2	HCA and Public IRCCS	Regional Oncology Network Model
Friuli Venezia Giulia	1.2	7.9	5	Comprehensive cancer care network/hub and spoke
Emilia Romagna	4.4	22.5	9	Comprehensive cancer care network
Lombardia	9.9	23.9	31	Comprehensive cancer center
Veneto	4.8	18.3	10	Hub and spoke

NOTE. Data modified.[8,9]
Abbreviations: HCA, health care authority; IRCCS, Istituto di ricerca e cura a carattere scientifico.

formulated by the steering committee as 10 statements (Appendix Table A1).

The statements were then submitted to the regional panels of experts (including 14 professionals all belonging to the five HCAs of the Friuli Venezia Giulia region: five chief medical officers, four oncology directors, and five pathology directors) for evaluation following the Delphi method using a five-point Likert scale (where 1 = completely disagree, 2 = slightly disagree, 3 = partially agree, 4 = agree, and 5 = completely agree).[11,12]

Third Step: Involvement of Scientific Societies for a National Consensus

After the implementation of feedback in the first regional experience, we decided to test the contents of the statements at the national level. The regional statements and their production process were presented to the presidents of the four more representative Italian oncology and pathology scientific societies, AIOM, CIPOMO, COMU, and SIAPeC, which joined the original steering committee, thus establishing a national board for the project. This group examined the results of the work that began with the eight HCAs initially involved at the regional level and the results of the national survey.

National Statement Definition and Evaluation

After the discussion within this national board, the statements were integrated and slightly modified by the steering committee to better fit the national perspective while retaining the core concepts derived from the bottom-up approach followed from the beginning.

The resulting 14 statements were then submitted to a national panel of experts composed of the 45 members of the boards of directors of the four scientific societies for a round of evaluation using a five-point Likert scale.

The result of this evaluation was shared during a national workshop involving the eight HCAs who initially joined the project, the four national scientific societies of oncology and pathology, five of the most representative oncology patients' associations, the National Agency for Health Services, and the Conference of Italian Regions. After the public presentation and discussion about the contents of the statements, the final document was undersigned by the presidents of the four scientific societies and delivered to the institutions that, according to the PNRR art eight law 233, have the mandate to produce national guidance documents for a homogeneous implementation of PO in the NHS.

In this article, we present the 14 statements, each of which was validated with a high consensus level, representing the position of the provisional Societies Boards of Directors about PO implementation in this phase (while waiting for future developments). The statements are grouped into four main areas: equity and accessibility, quality and sustainability of laboratories, clinical and organizational appropriateness of MTBs, and data handling and transparency.

RESULTS

First Step Results: Survey's Highlights

One hundred twenty-nine directors from 19 of 21 regions participated. The 113 sets of answers that were analyzed

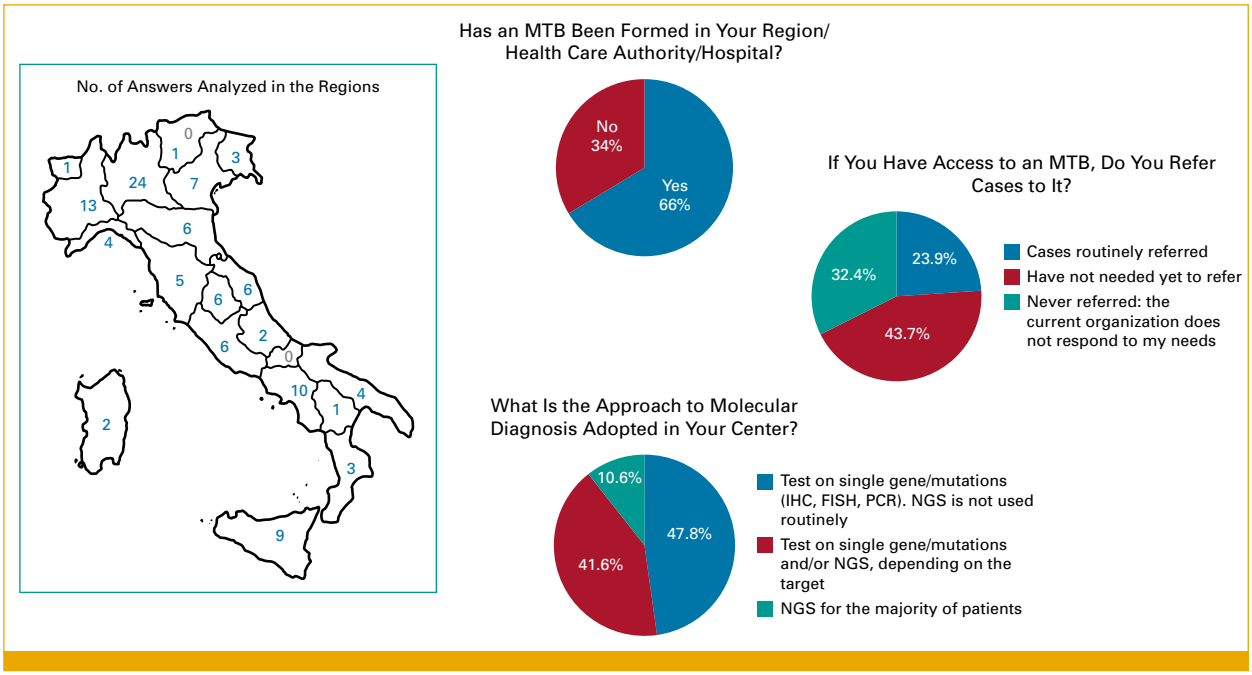

FIG 2. Distribution of answers analyzed from the national survey and main findings.[7] FISH, fluorescence in situ hybridization; IHC, immunohistochemistry; MTB, molecular tumor board; NGS, next-generation sequencing; PCR, polymerase chain reaction.

revealed a heterogeneous implementation of PO at the national level, confirming the complexity of the subject. The main findings showed that the use of NGS was unequally distributed at the national level; informed consent and clinical reports were managed differently, as the integration of medical, biologic, and informatic domains in a patient-centered workflow was inconsistent; and a heterogeneous MTB environment emerged with one third of the responding professionals reporting that they did not have access to MTBs and among those who did, many did not refer cases to MTBs because of organizational issues (Fig 2).[7]

Second Step Results: Regional Consensus

A large and stable consensus was recorded in two rounds. The consensus results were officially presented in a dedicated workshop held in June 2022 and were eventually shared with the regional HCAs as references for future measures. The contents of these statements have been adopted and integrated into health care policies by the Friuli Venezia Giulia region. These preliminary results indicated that the bottom-up approach allowed for the formulation of solutions fitting the context of the region in which they were generated.

Third Step Results: National Statements

In Table 2, we present the 14 statements (left column) grouped under four main topics: equity and accessibility, quality and sustainability of laboratories, clinical role and organization of MTBs, and data handling and transparency. Each statement is supported by a comment (right column) highlighting the impact according to recent literature.

Thirty-six of 45 (80%) representatives of the boards of directors of the scientific societies took part in the consensus round (Table 3). A strong professional consensus was reached for each statement (Table 4).

DISCUSSION

Comprehensive genomic profiling enables a new strategy for PO to be offered to patients with cancer. As usually happens with fast clinical innovation, health care professionals are the first to perceive its impact, whereas policy-makers, especially in a public health services system, need to follow a complex process involving multiple factors (including feasibility considerations, stakeholder interests, and political values)[50] and may struggle to give prompt indications to meet emerging needs. This often results in the fragmentation of the clinical activity and uneven allocation of services influenced by the professional culture and the resources present in different centers. When government indications are formulated, there is a high chance that they may contrast with the activities and experiences that have already been developed. Because it is difficult to conciliate the fast nature of innovation with policy-making, the most effective approach may be to coordinate the bottom-up initiatives using a shared method. This could also be useful for facing the issue of poor availability and restricted access to targeted therapies, which are the problems affecting health care systems worldwide and for which most professionals are asking for a common solution from policy-makers.[51]

In fields where it is difficult to obtain scientific evidence, such as public policy and health services organizations,[50,52] the solicitation of expert opinion generating a formal consensus through validated tools (such as the Delphi consensus group method) has been recognized as a reliable problem-solving process.[53]

In this project, we collected high-level professionals' consensus on matters influencing the rapidly evolving topic of PO implementation in a public NHS. Following a bottom-up approach, we first observed a single HCA context; subsequently, we compared the initial observations with those from seven other HCAs; we then reached a professional agreement on statements addressing the highlighted issues at the regional level; and finally, we obtained a strong consensus on statements about PO implementation within the national framework.

The final document includes 14 statements. It was undersigned by the presidents of the four scientific societies that were involved in this project and was delivered to the institutions (the National Agency for Health Services and the Conference of Regions) that have the mandate to produce national guidance documents for a homogeneous implementation of PO in the NHS. To support an optimal application of these proposals in clinical practice, we suggest different levels of responsibilities following the Italian NHS institutional setup. For example, the selection of the centers for the advanced analysis (statement 5) and the monitoring of the activity (statement 11) should be the responsibilities of the National Coordinating Group. The Regional Oncology Networks where the MTBs are embedded must be in charge of the application of statements 3, 4, 9, and 10. The recommendations that are more focused on operation (eg, 12 and 13) should be handled within the HCAs where the activities are run. The National Agency for Health Services is in charge of monitoring the Regional Cancer Network development and might play the role of assuring the implementation of these indications.

With this initiative, supported by a structured method, the four most representative Italian scientific societies of oncology and pathology provided policy decision-makers with shared indications about PO implementation in our national health service.

We are all aware that innovation does not automatically reach the patient's bedside in an appropriate timeframe. To overcome barriers and to improve quality of care, the oncology community should advocate for the following actions: additional research in genomics, cancer outcomes, and health care use; education of health care providers and patients; rapid and iterative technology assessment; and policy-level interventions to ensure access to precision cancer care for patients who can benefit from such an

TABLE 2. Statements Endorsed by the Italian Scientific Societies

Statement	Background and Context's Analysis
Equity and accessibility	
1. The access to molecular diagnostic tests with multigenic sequencing techniques should be available to all patients treated in a medical oncology center, regardless of its geographical position and its role within the network	Today, NGS assays are widely available and considered to be part of the standard of care in specific clinical situations.[13] The rising disease burden is paired with a widening disparity in access to the most effective targeted therapies.[14] Limited access to cancer diagnostics is a critical bottleneck to efficiently tailoring available treatments.[15] Across Europe, many patients with cancer cannot benefit from NGS-driven approaches because of gaps in its implementation,[16] and in Italy, the results obtained with NGS technologies are heterogeneously implemented and distributed.[17] This statement advocates a homogeneous implementation of technology to guarantee equal treatment chances for patients in Italy
2. An MTB is a consultation tool for the diagnostic and therapeutic pathway, it should be accessible for all cases with an indication, regardless of the geographical position and the role of the center within the network, and it should guarantee adequate response time	MTBs are teams of multidisciplinary experts working together to translate a patient's unique tumor molecular profile into evidence-based, genomic-driven, patient-tailored treatment recommendations.[18] The role of MTBs in defining criteria for patient's selection, material to be tested, and tests to be used and in the interpretation of complex molecular profiles allowing access to matched therapies has been widely reported in the literature.[19-23] An MTB has been documented to be an independent positive predictor of overall survival regardless of residence location among 956 patients with NSCLC.[24] In a recent systematic review on 14 studies, MTBs appear to improve clinical outcome for patients with cancer.[25] Despite the positive impact on clinical outcomes for patients, the implementation of these boards is very heterogeneous in the national context, as highlighted in the national survey, affecting the equity of patients' access. We believe that the advent of PO should be sustained by processes that allow a broader and faster access to therapeutic options, while ensuring appropriateness. The two sides of the coin could be guaranteed by the MTBs as the space where patients' referral to clinical trials is systematized and encouraged. Moreover, the access to off-label therapies could be eased by recognizing to MTBs the mandate of prescribing these types of drugs after evaluation, ensuring real-world data collection through national databases in the NHS context. Preliminary experiences have been led in Italy with the Rome trial (which has just concluded the accrual) and the Rational trial[26] This statement addresses the topic of care disparities, proposing a principle that should inform policy-makers' choices
3. To guarantee equity of access to MTBs, depending on the population and the organizational model of the region, it could be appropriate to differentiate two activity levels a. Within HCA for managing clinical issues b. Regional for coordination, managing, and governance issues	In a regional-based NHS, it is important to consider the peculiarities of each context to guarantee concentration of skills, in relation to volume of activities, together with chances for equal access to care. The number of MTBs should follow analog criteria, on the basis of the volume-outcome ratio indicated in the decree that the Italian Ministry adopted in 2015 with the intention of reviewing the high-complexity services placement[27] Considering these criteria and the varying sizes of the regions, it could be possible for some highly populated regions to establish several MTBs, whereas smaller ones could rely on extra-regional MTBs Where more MTBs are present in the same region, the need for homogeneity and integration could be met with the foundation of a higher-level (regional) coordinating group
Quality and sustainability of laboratories	
4. The laboratories designated for ensuring first-level molecular diagnostic (analysis established by guidelines) are identified by the regions and should have available next-generation (multigenic) sequencing technologies and follow expertise standards linked to catchment areas and guaranteed by the participation in national and international quality control programs	The growing diffusion of NGS technology for the diagnosis of different pathologies is making extended biomarkers analysis more accessible in laboratories around the nation. There is a wide agreement on the importance of focusing on the implementation and maintenance of quality systems to guarantee high-level analytical performance.[28] The transparent and efficient accreditation of qualified laboratories performing NGS molecular tests, with either an ISO9001 or an ISO15189,[29] to ensure adequate training for all the professionals involved is considered crucial.[30] This statement emphasizes the relevance of ensuring access to new generation molecular diagnostics while supporting the authorization, by designated health authorities, of this type of analysis for centers with recognized quality standards
5. Panels containing between 20 and 50 genes are currently adequate to meet first-level diagnostic needs (analysis established by guidelines), avoiding information redundancies and ensuring appropriateness	The lack of national norms and the rapid diffusion of NGS technologies brought heterogeneity in the choice of panels and their extension. The use of extended panels (>50 genes) from the first diagnosis generates much information that is not useful for matching patients with an appropriate therapy and that is linked to drawbacks such as more complicated interpretation and communication to patients. Clinical interpretation of NGS results often relies on manual procedures, which poses considerable challenges to the medical teams undertaking this task. Clinical decision support systems can tackle these challenges by implementing efficient data analysis and reporting processes.[31] It is reported that a 50-gene panel can detect most of the genomic abnormalities matched to FDA-approved

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TABLE 2. Statements Endorsed by the Italian Scientific Societies (continued)

Statement	Background and Context's Analysis
	therapies.[32] This statement suggests an indication to match the analytical appropriateness according to clinical guidelines and the standardization of the laboratory's workflows
6. The extension of first-level diagnostic panels should be periodically updated by professionals identified at the regional level depending on the coordination model developed	The fast development of knowledge requires rapid implementation of the clinical offer to guarantee appropriateness and homogeneity. This statement not only is strongly linked to the principles of appropriateness in the previous one but also considers the perspectives of this fast-evolving field[33,34]
7. Advanced analysis requiring large panels (exceeding 50 biomarkers) should be run in a limited number of high-volume, qualified laboratories identified by national health authorities	Even if it is possible to analyze more than 500 genes for multiple samples in a run, currently, the scientific evidence does not support the use of extended sequencing in clinical practice because of the limited availability of molecular target drugs.[35,36] Managing large amounts of data involves higher complexity and specific expertise that are likely to be guaranteed in only a few centers. Moreover, a structured collection and sharing of these data can be better managed in a network with few reference centers. This statement endorses the needs of indication at the national, rather than the regional, level for the identification of reference laboratories to support a more appropriate use of resources and the concentration of competences
Clinical role and organization of MTBs	
8. The request for advanced analysis with extended panels (exceeding 50 biomarkers) should be evaluated by an MTB	MTBs address gaps in knowledge and clinical utility by providing a forum for individuals with wide-ranging expertise to review patient medical histories and mutation profiles to guide patient-specific treatment options.[13] Another function of these groups is to help avoid the clinical and financial toxicities of prescribing inappropriate targeted therapy.[37] This statement emphasizes the need of MTB evaluation for the appropriateness of the whole PO pathway, including diagnosis
9. MTB composition should be functional to the activities and reasonably agile: an MTB should include a core team (oncologists, molecular biologists, pathologists, geneticists, pharmacists, case managers) plus professionals on demand depending on the needs	A variability in the composition of MTBs is reported both in international literature[38-41] and in Italian regional decrees. In Italy, high-level managers with no strictly clinical competences are often included within MTBs. Their presence could result in a waste of their time and make the organization of clinical meetings more complicated. This statement suggests the presence of an agile clinical core team that could be integrated on demand when necessary. This solution is also reported in the literature,[29,42] and the proposed composition was derived from the answers of the national survey. Even if a lean core team is needed, it could happen that not all institutions would be able to operate an MTB with such a configuration. Nevertheless, it is of primary importance to organize a group with the available experts, consulting at least a pathologist and an oncologist to guarantee equal patient access to PO[42]
10. Where established, the regional coordination group composition should involve representatives of each intraregional MTB and referents of the regional institutions	In highly populated regions, where the establishment of more MTBs is needed, coordinating groups to guarantee activity homogeneity should be formed and include representatives of the institutions and of each MTB. This would allow for efficient communication of the emerging needs from professionals to authorities, which could facilitate the implementation of measures at the institutional level. In this way, a bottom-up approach would be followed to make the changes needed to guarantee more fluent innovation delivery
11. A national coordination group for PO activities should be created with the aim of analyzing the functioning of the different configurations adopted and supporting government institutions in the definition of GL	Considering the strong role that regions play in the Italian health care system, a national monitoring of PO-linked activities is needed to avoid disparities among territories, eg, heterogeneity in the selection criteria of patients, the molecular profiling technology or molecular test proposed, and the choice of medical therapies across different institutions.[30] The aim of this group is to guarantee a fast interception of emerging needs and to ensure prompt solutions. This should be performed through periodic checks, reports, and direct communication with regional MTBs or coordinating groups and the organization of annual meeting to verify the level of achievements of objectives and discuss the improvements needed
Data handling and transparency	
12. Informed consent, conveniently modified, should be considered implicit for first-level molecular diagnosis (analysis established by guidelines), regardless of the technology used for the analysis, whereas it should be explicitly submitted for analysis with the chance of highlighting mutations with germinal implications or for analysis run with panels exceeding 50 biomarkers extension	To ensure a lean process, the consent, given by a patient at the beginning of the diagnostic and therapeutic pathway, should cover all the biomolecular tests needed for the treatment definition, independent of the technique used for the analysis When the analysis could highlight germinal mutations, an ad hoc consent is already expected because of the impact this information could have on patients' families. Up to 12% of tumor genomic profiling reports will reveal a germline pathogenic variant,[43] and ASCO guidelines from 2015 recommended that oncology providers communicate the potential for

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TABLE 2. Statements Endorsed by the Italian Scientific Societies (continued)

Statement	Background and Context's Analysis
	incidental and secondary germline information to patients before they conduct somatic mutation profiling[44] Running analyses with an extended panel of biomarkers (>50) increases the chance of highlighting mutations with low or not-yet-known significance for a pathology. This brings out the need for an accurate communication to the patient about the impact and the purpose of these extended analyses and requires the submission of an informed consent[45,46]
13. The report should contain the results of all the tested biomarkers, highlighting the ones linked to the patient's condition with their clinical significance, according to GL	NGS reports contain much information that must be interpreted carefully before being used to make treatment recommendations.[47] Even small panels (<50 genes) could report more information than is necessary for choosing a treatment, but because it is patient's right and in their interest, the complete results of the analysis must be reported.[48] This increases the complexity of the communication between clinicians and patients when mutations that are not specific to the pathology are found. It could be helpful to highlight the biomarkers reported in the guidelines as relevant for the pathology from the unsolicited findings to facilitate a better understanding of the laboratory report and lower the chances of controversies
14. It is necessary to ensure the correct collection, storage, and management of the data produced by the sequencing analysis and the MTB evaluations, contributing to the connection between informatic systems and the chance to use the data for treatment and real-world research	Genomic data are among the most valued data types available to precision medicine, but they need elaborated intermediation to be used as medical evidence. These workups are becoming more complex as the amount of data produced increases.[49] As the complexity of cancer biomarkers continues to grow, automating the interpretation and reporting of sequencing results decreases the need for manual procedures and facilitates rapid, comprehensive, and consistent clinical decision making.[31] Alongside the management of data, the foundation of an accessible databank to maximize real-world evidence studies is of utmost importance

Abbreviations: FDA, US Food and Drug Administration; GL, guidelines; HCA, health care authority; MTB, molecular tumor board; NGS, next-generation sequencing; NHS, national healthcare system; NSCLC, non–small-cell lung cancer; PO, precision oncology.

approach.[5] In fact, the improvement of science does not translate immediately to improvement of care: it could take up to 20 years for a new product to reach from bench to bedside.[54] The implementation of every advancement should be supported by the collaboration, coordination, and organization of the various stakeholders within the health care system. The same synergistic effort should be the basis for the management of the innovation impact on the system,[55] including the effects of the growing cancer patient prevalence on NHS human resources need and sustainability.[56,57]

Clinical governance is the main vehicle for continuously improving the quality of patient care and developing the capacity of the universalistic NHS.[58] As health care professionals, we have to develop a better capacity to represent the needs of the cancer care system to public decision-makers and governmental institutions to achieve the homogeneous delivery of high-quality care. Innovation should be an integral part of strengthening the health system. This means developing not only new capacities in technology, medicine, and diagnostics but also creative and new ways of thinking and providing care to patients.[59]

TABLE 3. Number of People on Each Scientific Society Board of Directors and Their Participation Rate in the National Consensus Round

Scientific Society	Board of Directors	Answer	% of Answers
AIOM	11	8	72
CIPOMO	13	13	100
COMU	5	4	80
SIAPeC	16	11	69
Total	45	36	80

Abbreviations: AIOM, Associazione Italiana di Oncologia Medica; CIPOMO, Collegio Italiano Primari Oncologi Medici Ospedalieri; COMU, Collegio Oncologi Medici Universitari; SIAPeC, Società Italiana di Anatomia Patologica e Citologia.

The implementation of PO-related innovation to ensure equitable and efficient delivery to patients with cancer is indeed difficult. Across Europe, each country presently demonstrates different degrees of efficiency and deficiency in its approach to NGS, with widely varying practices in its use and access, which results in many patients not benefiting from the potential of NGS-driven approaches.

Achieving the transformation of patient care with an NGS approach requires the conditions for implementation to be met. This depends on collaboration among multiple stakeholders, including payers, policy-makers, the medical and scientific community, and patient organizations, at both the national and international levels.[16]

Furthermore, the challenges of PO push health care systems to find a new balance between concentrating activity volumes and expertise and diffuse access to care across the whole territory.

Addressing practice gaps in the PO approach can lead to improved clinical care and outcomes for patients.[6]

TABLE 4. Level of Consensus Achieved in the 14 Statements Using a Five-Point Likert Scale

Statement Number	S1	S2	S3	S4	S5	S6	S7	S8	S9	S10	S11	S12	S13	S14
Mean	4.7	4.7	4.4	4.8	4.3	4.3	4.3	4.4	4.6	4.4	4.6	4.4	4.7	4.8
Median	5.0	5.0	4.0	5.0	4.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0

Therefore, an increased understanding of the impact of practice gaps can inform strategies to deliver more fully on the promise of personalized medicine.[4]

In conclusion, these statements are an operational guide shared by the main scientific societies of oncology and pathology for the implementation of PO in the NHS. The strong consensus obtained makes them a solid support for professionals, health care management, and policymakers. We hope that our work could contribute to facing and overcoming the difficulties brought by PO implementation in practice. Moreover, we believe that active collaboration among professionals, scientific societies, and health care government institutions is necessary, especially in such complex contexts and even more so in the near future.

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APPENDIX

TABLE A1. Regional Statements Resulted From the Second Step

Statement Number	Content
Statement 1	The laboratories in the hubs ensure the ordinary molecular diagnostic with massive parallel sequencing technologies for patients in their catchment area
Statement 2	It is appropriate that extended sequencing analyses (ie, panels exceeding 50 biomarkers) are managed in one regional reference laboratory to guarantee adequate expertise and quality levels linked to case numbers
Statement 3	MTBs established in each hub ensure the current clinical consultation activity, involving the Spoke
Statement 4	MTB core composition should be lean and include professionals from the most relevant areas for PO (oncologists, pathologists, molecular biologists, geneticist, pharmacists, case managers). The group can be integrated on demand with other professionals if needed
Statement 5	It is recommended to establish a regional coordination group for PO and diagnostic, involving representatives for each Hub MTB and representatives of the health care institutions with the aims of (1) aligning practice, approach, and organizational tools; (2) addressing and coordinating solutions for complexities emerging from current Hub MTB activities (eg, data management); (3) consulting on management aspects in clinical and scientific areas; (4) promoting education and research; and (5) supporting decisions about regional competence and technological and IT upgrade
Statement 6	Since molecular analysis is necessary to assess treatment planning, to facilitate processes of taking charge of the patient, informed consent should be considered implicitly acquired within the one already provided for the current procedures, independent of the technology used for the analysis, and adjusted accordingly
Statement 7	Informed consent must be acquired explicitly with an ad hoc document for analysis, which could highlight germinal mutations or whenever panels with a broader extension than the ones for first-level diagnosis are used (ie, panels exceeding 50 biomarkers)
Statement 8	The laboratory report must contain the results of all the analyzed biomarkers, highlighting the ones relevant to the patient's pathology and their clinical relevance, identified by the guidelines
Statement 9	Panels containing between 20 and 50 biomarkers are (until now) adequate for first-level diagnostic needs, enabling adherence to national and/or European guidelines with a lean and sustainable management of laboratory processes, while avoiding information redundancy
Statement 10	The indication for the use of an extended panel (ie, panels exceeding 50 biomarkers) is subjected to a formal evaluation by the MTB

Abbreviations: MTB, molecular tumor board; PO, precision oncology.