BMJ Oncology

Patient-reported outcomes (PROs) in clinical trials and in clinical practice: report from the XXI national conference of the Italian Association of Medical Oncology (AIOM)

Alberto Puccini,[1,2] Giuseppe Viscardi,[3] Oriana Ciani,[4] Fabio Efficace,[5] Angela Piattelli,[6] Giordano Domenico Beretta,[7] Davide Petruzzelli,[8] Patrizia Popoli,[9] Francesco De Lorenzo,[10] Francesco Longo,[11] Marco Zibellini,[12] Lara Gitto,[13] Antonella Brunello,[14] Evaristo Maiello,[15] Alberto Servetto ,[16] Martina Pagliuca,[17] Alessandra Raimondi,[18] Laura Marandino,[19] Saverio Cinieri,[20] Elisabetta Iannelli,[21] Carla Ida Ripamonti,[22] Paolo Bossi,[1,2] Gianmauro Numico ,[23] Tiziana Latiano,[15] Carmine Pinto,[24] Silvana Quaglini,[25] Laura Locati,[26] Gualberto Gussoni,[27] Gianluca Mignone,[28] Pricivel M Carrera,[29] Ethan Basch,[30] Massimo Di Maio ,[31] Francesco Perrone[32]

To cite: Puccini A, Viscardi G, Ciani O, *et al*. Patient-reported outcomes (PROs) in clinical trials and in clinical practice: report from the XXI national conference of the Italian Association of Medical Oncology (AIOM). *BMJ Oncology* 2025;**4**:e000783. doi:10.1136/bmjonc-2025-000783

AP and GV are joint first authors. MDM and FP are joint senior authors.

Received 11 February 2025
Accepted 21 May 2025

► http://dx.doi.org/10.1136/bmjonc-2025-000879

For numbered affiliations see end of article.

Correspondence to
Professor Massimo Di Maio; massimo.dimaio@unito.it

ABSTRACT

Objective Patient-reported outcomes (PROs) are considered the gold standard for the assessment of subjective symptoms, quality of life (QoL) and patient well-being in both clinical trials and clinical practice. Here, we report key discussions and findings from the 21st National Conference of the Italian Association of Medical Oncology, held in Bologna on 21–22 June 2024, with a focus on the integration and impact of PROs in oncology research and clinical practice.

Methods and analysis Leading national and international experts presented and analysed data regarding the use of PROs in clinical trials and routine oncology care. Topics included the role of electronic PROs (ePROs), digital therapeutics, financial toxicity as a PRO and methodologies for standardising QoL assessment. Insights were drawn from expert presentations, consensus discussions and practical experiences shared during the conference sessions.

Results Experts emphasised that PROs should be included as key endpoints in clinical trials, with timely publication of results and standardised methodologies for analysis and interpretation. The conference highlighted the critical importance of incorporating PROs and QoL measures throughout the cancer care continuum—from screening to survivorship. In clinical practice, PROs improve patient-centred care and communication, particularly when oncologists are trained to interpret QoL data. The use of ePROs was noted as a valuable tool to support digital health interventions. Financial toxicity emerged as a significant PRO, with screening tools recommended to identify and support at-risk patients. Key organisational challenges were identified, including technological barriers,

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Patient-reported outcomes (PROs) are widely recognised as the gold standard for assessing symptoms, quality of life (QoL) and overall well-being from the patient's perspective in oncology. Despite their proven value, their integration into clinical trials and routine care remains inconsistent. Methodological heterogeneity, lack of standardisation and limited clinician familiarity with PRO data interpretation have hindered their full adoption.

WHAT THIS STUDY ADDS

⇒ This study summarises expert consensus from the 21st Italian Association of Medical Oncology (AIOM) National Conference, emphasising the necessity of including PROs as endpoints in all phases of cancer care and clinical research. It identifies electronic PROs and financial toxicity as emerging areas of importance, advocates for methodological standardisation and highlights practical and organisational challenges to implementation. It also underscores the growing role of digital solutions and clinician education in enhancing the use of PROs.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The findings support a more structured and widespread use of PROs in both research and practice. They call for healthcare systems to invest in digital infrastructure, provide clinician training in QoL data interpretation and adopt policy frameworks that prioritise patient-centred metrics, including financial toxicity. These steps could drive a shift towards more responsive and equitable oncology care.

resource constraints and the need for responsive infrastructure to support real-time PRO integration.

Conclusion The implementation of PROs, including ePROs and financial toxicity assessments, is essential for advancing quality cancer care. Standardisation, digital innovation and targeted clinician education are critical to integrating PROs effectively in both research and clinical settings. Addressing infrastructural and technological challenges will be vital for optimising patient outcomes and ensuring optimal care across the cancer journey.

INTRODUCTION

A patient-reported outcome (PRO) is a direct report of a patient's condition, not interpreted nor modified by a clinician or anyone else. PROs are considered the gold standard for the assessment of subjective symptoms, quality of life (QoL), functional scales and patient well-being in both clinical trials and clinical practice.[1 2]

PROs were the topic of the 21st National Conference of the Italian Association of Medical Oncology (AIOM), which was held in Bologna on 21–22 June 2024. Leading national and international experts in the field reported on findings about the implementation of PROs into clinical trials and clinical practice, the measurement of financial toxicity (FT) in cancer care as an example of PRO, the growing role of electronic PROs (ePROs) in enhancing patient care and digital PROs as digital therapeutics.

This paper presents a synthesis of the topics discussed in Bologna. Key messages from the expert discussion are reported in box 1.

Box 1 Recommendations from the consensus of experts

- ⇒ Assessment of quality of life (QoL) is relevant in all disease settings, from screening to metastatic disease.
- ⇒ In clinical trials, QoL should be included among endpoints and its results should be timely published.
- ⇒ In both clinical trials and clinical practice, instruments that can be used to measure PROs and QoL should be selected among validated tools.
- ⇒ Methodology of analysis and interpretation of PROs in clinical trials needs to be standardised, adherence to specific reporting checklist is recommended.
- ⇒ Medical oncologists should be familiar with the reading and interpreting QoL results, to better interpret the results of clinical trials and to use these results for optimal communication with patients in clinical practice.
- ⇒ In clinical practice, symptoms may be underestimated and underreported and potentially undertreated without the use of PROs. Adoption of PROs can improve quality of care for patients with cancer.
- ⇒ The attention to QoL and PROs, both in clinical practice and in clinical trials, should not be limited not only to active treatment but also to subsequent phases of the patient journey, including survivorship care.
- ⇒ Screening tools for financial toxicity should be implemented at various stages of cancer treatment to identify at-risk patients and mitigate financial burden.
- ⇒ PROs should be integrated into daily oncology practice, with the aim of improving patient outcomes and symptom management.
- ⇒ The effective implementation of PROs in daily practice should address challenges for healthcare organisations, including the need to overcome technological barriers, develop digital infrastructure, ensuring resources to promptly respond to PRO data and provide flexible interventions.
- ⇒ Compliance with General Data Protection Regulation and Data Security Protocols should be ensured; Data Protection Impact Assessment should be provided for high-risk operations, and patients should be adequately informed on the use of PROs and on their rights when artificial intelligence systems are used in healthcare.

IMPLEMENTING PROS IN CLINICAL TRIALS

PROs are measured using instruments collectively known as patient-reported outcome measures (PROMs), which allow the perspective of the individual living with the disease or receiving a given treatment to be captured in terms of physical, emotional, cognitive, social functioning, psychological well-being and health-related QoL.

There are several reasons for including PRO assessment in the clinical development programme for oncology medicinal products. These may encompass: (a) to provide a patient-focused assessment of the burden and impact of the disease by understanding how a treatment impacts patients' functioning and well-being; (b) to add information about the clinical benefit of a therapy by complementing efficacy and safety data with patient-reported evaluation; (c) to assess the relationship and/or concordance between clinician-reported and patient-reported endpoints; (d) to attempt to differentiate between two treatments in the setting of a non-inferiority trial, where the primary endpoint is an objective measure; (e) to provide information to facilitate more accurate future patient–physician communication.[3]

Unfortunately, QoL data are not available for many clinical trials.[4] Indeed, most QoL data from trials go unpublished or published with a substantial delay, even when the primary study results are positive.[5–7]

In response to growing concerns about the clinical value and cost-effectiveness of new oncology drugs, the European Society for Medical Oncology (ESMO) established a standardised framework to aid healthcare professionals, policymakers and patients. Introduced in 2015, the ESMO—Magnitude of Clinical Benefit Scale (MCBS), was designed to objectively assess the magnitude of clinical benefit from cancer therapies by examining factors such as survival gain, QoL and treatment toxicity. After its development and validation, the ESMO-MCBS has been increasingly used to score the clinical benefit of cancer medicines reported in clinical trials.[8] When QoL is assessed as a secondary outcome in clinical studies, QoL results impact the scoring of the ESMO-MCBS. When QoL benefits are reported in studies applying a validated tool, with an adequately complete dataset and using valid statistical criteria, the ESMO-MCBS score is increased by one point in the non-curative setting. When the primary outcome is progression-free survival (PFS) with secondary outcomes of overall survival (OS) and QoL, the value of

the PFS improvement depends on the QoL results in the absence of an OS benefit. Non-publication or delayed publication of QoL data subverts this important score adjustment, which does not account for these issues.[9] Indeed, QoL and PROs in oncology are underrated and under-reported. Although an improvement has been reported with an absolute increase of 15% in the inclusion of QoL among trial endpoints from 2012 to 2016 to 2017–2021,[10] the time to secondary publication of QoL results is long (even several years).

QoL data are crucial to evaluate a trial that is already positive for other endpoints. Indeed, in positive trials, we should know what the 'cost' to patients in terms of tolerability is to offset the OS or PFS benefit.[11–13] Furthermore, in trials showing a PFS benefit, QoL data are essential to determine whether this benefit translates into a meaningful clinical improvement for patients, rather than being purely instrumental. Unfortunately, a relevant proportion of positive trials do not report QoL data and only a minority of positive trials, both those with primary endpoint of OS and PFS, also report positive QoL data.[14 15]

In Italy, the PRO4ALL working group was set up in 2021 with the aim of understanding the role of the 'patient voice' in clinical research and regulatory pathways, with a specific focus on PROs and their measurement. The PRO4ALL project has conducted several research studies over the last 2 years, from the evaluation of the role of PROs in European Medicines Agency (EMA) assessment reports between 2017 and 2022,[16] to the analysis of the association between PROs and the reimbursement class and innovative status of drugs[17] assigned by the Italian Medicines Agency (AIFA). Among reports on authorised medicines for neurological[18] or oncological indications,[19] 57% and 51% reported any use of PROMs, respectively. The working group concluded that there is a need for harmonisation and standardisation of the use of PROs and PROMs in clinical research, together with an institutional commitment to ensure that patients are at the centre of evaluation throughout all stages of drug development. The project developed a comprehensive archive of PROMs in oncology and identified their main characteristics and target outcome domains.[20] This archive represents a useful tool to guide researchers and practitioners in selecting the most suitable measures and to foster a patient-centred approach in clinical trials, clinical practice and regulatory activities.

Indeed, selecting the appropriate PROMs for clinical research and practice requires a trade-off between information needs, logistics and patient burden. Ultimately, the selection of PROMs must take into account which and how many domains to target, the extent to which the recall period may be a critical factor, combined with the timing of instrument administration and the cancer treatment schedule. To ensure the reliability of PROMs, it is essential to use validated tools that include a defined minimal clinically important difference,[21] which helps interpret whether changes in scores reflect meaningful clinical improvement. Furthermore, selecting an appropriate PROM should involve consideration of the preferences and needs of end users—such as patients, clinicians and healthcare providers—to ensure the results are both relevant and actionable.[22]

PROs and methodology

In certain areas of oncology, significant advances in treatment have made the inclusion of PROs essential for informed clinical decision-making.

Given the significant progress in cancer treatment and the chronic nature of oral anticancer medications, the monitoring of symptomatic adverse events (AEs) in routine practice is crucial, as these can directly influence clinical responses. Even low-grade symptomatic AEs can have a substantial impact on QoL.[23–25]

PROs need to be sensitive enough to capture the effects of newer drugs in clinical trials. The use of PRO item libraries to complement traditional PRO questionnaires offers a valuable strategy, as several such libraries are now available.[26] The use of item libraries for PRO measurement in oncology allows for the customisation of PRO assessment to measure key health-related QoL concepts of relevance to the target population and intervention. A recent international working group provided recommendations for the use of item libraries in oncology trials. These recommendations address methods to drive item selection, plan the structure and analysis of item lists and facilitate their use in conjunction with other measures.[27]

For these reasons, regulatory agencies provided guidance documents to address how stakeholders can collect and submit patient experience data and other relevant information from patients and caregivers for medical product development and regulatory decision-making (ie, FDA Patient-Focused Drug Development—PFDD[28] and EMA Appendix 2[29]).

Incorporating PROs into clinical trials is a crucial step towards understanding the full impact of treatments from the patients' perspective. However, this integration comes with a host of methodological challenges that can complicate the process and affect the reliability of the findings.[22 30–34] The SPIRIT-PRO guidelines provide recommendations for items that should be addressed and included in clinical trial protocols in which PROs are a primary or key secondary outcome. Improved design of clinical trials including PROs could help ensure high-quality data that may inform patient-centred care.[22]

Data collection methods pose significant challenges. Researchers must decide on the most effective way to collect PRO data. Moreover, the potential for response bias has been raised by some authors (eg, over-reporting problems for attention, under-reporting to avoid treatment changes/discontinuation), when collecting PRO data.[35] We agree that this variability in self-reporting can complicate the analysis, making it difficult to draw accurate conclusions, but we are strongly convinced that, despite these potential issues, PROs and QoL measurement are a relevant part of the definition of treatment value.

Interpreting and reporting PRO data also involve complexity. It is essential to differentiate between statistical significance and clinical relevance. The Setting International Standards in Analyzing Patient-Reported Outcomes and Quality of Life Endpoints in Cancer Clinical Trials-Innovative Medicines Initiative Consortium builds on the existing SISAQOL work to establish recommendations on design, analysis, presentation and interpretation for PRO data in cancer clinical trials, with an expanded set of topics, including more in-depth recommendations for randomised controlled trials (RCTs) and single-arm studies, and for defining clinically meaningful change.[36 37]

The integration of PRO data with clinical outcomes is another methodological hurdle. Researchers need to analyse how PRO measures correlate with clinical endpoints, such as survival or objective response rates. There may be discrepancies between patient-reported symptoms and clinical assessments, leading to confusion about the overall effectiveness of a treatment. In addition, despite their benefits, there are concerns that the potential burden on respondents may reduce their willingness to complete PROs, with potential impact on the completeness and quality of the data for decision-making. Recently, an international effort developed consensus-based recommendations to facilitate the minimisation of respondent burden for individuals completing PROs in both healthcare research and clinical practice.[38]

Another important resource is The Patient-Reported Outcomes Tools: Engaging Users and Stakeholders (PROTEUS)-Trials Consortium, which aims to help researchers generate patient-reported outcome data from clinical trials to (1) enable investigators, regulators and policy-makers to take the patient perspective into account when conducting research and making decisions; (2) help patients understand treatment options and make treatment decisions; and (3) inform clinicians' discussions with patients regarding treatment options. In these ways, the PROTEUS Consortium promotes patient-centred research and care.[39]

Finally, ethical considerations surrounding the use of PROs in clinical trials cannot be overlooked. Ensuring that patients fully understand the purpose of PRO assessments and how their data will be used is critical to informed consent. Researchers must be transparent about the potential risks and benefits associated with participation to foster an environment of trust. The PRO ethics guidelines were developed following the Enhancing the Quality and Transparency of Health Research Network's guideline development framework. The PRO ethics guidelines provide recommendations for ethical issues that should be addressed in PRO clinical research. Addressing ethical issues of PRO clinical research has the potential to ensure high-quality PRO data while minimising participant risk, burden and harm and protecting participant and researcher welfare.[40]

In summary, while the inclusion of PROs in clinical trials is essential for capturing the patient experience, it is fraught with methodological challenges. Addressing these issues requires a thoughtful and systematic approach to ensure that the resulting data truly reflect the realities faced by patients.[41] As the landscape of clinical research continues to evolve, ongoing dialogue and innovation will be necessary to improve the utility of PROs and ultimately improve patient-centred care.

PRO application and value of PROs in patients with different types of cancer

Lung cancer

In patients with non-small cell lung cancer (NSCLC), QoL is significantly affected by the symptom burden, treatment-induced toxicities, psychological and social implications, ultimately impacting emotional well-being. Although assessment of QoL is relevant in all disease phases, from screening to metastatic disease, no specific tools exist for each setting.

From the aforementioned PRO4ALL project, Servetto *et al* identified a detailed archive of 17 available lung cancer-specific PROMs; 13/17 (76.5%) PROMs do not include items related to the global QoL domain.[42] In some cases, a novel drug may significantly improve cancer-associated symptoms, while not showing an impact on global QoL, eventually due to the toxicity profile. For instance, this is the case with dacomitinib, which significantly improved PFS over gefitinib in first-line treatment of patients with Epidermal Growth Factor Receptor (EGFR)-mutation-positive NSCLC.[43] In this trial, the dacomitinib group showed a significant improvement in chest pain compared with the gefitinib group, while global QoL was significantly in favour of gefitinib. Thus, further studies are needed to clarify whether the assessment of disease-related symptoms may be more relevant than global QoL. Unfortunately, as already described above, a large proportion of RCTs does not report QoL outcomes in their primary publications, revealing an attitude of underestimating the importance of QoL data in clinical oncology research. Salomone *et al* recently showed that only 2/172 (1.2%) trials in NSCLC included QoL as a primary study endpoint, and 40/172 trials (23.3%—profit 17.7%; no profit 40.5%) did not include QoL assessment as an endpoint at all. Furthermore, the majority of RCTs (102/172, 59.3%) did not report QoL results in primary publications.[6 44] Finally, Servetto *et al* recently investigated whether QoL results correlated with PFS and OS outcomes in phase III RCTs investigating new systemic treatments in metastatic NSCLC.[45] The authors showed a positive association of QoL results with PFS, whereas in trials where OS was improved, 53.3% of the results showed no difference in QoL

Breast cancer

In early breast cancer, QoL issues can be very relevant. For instance, Franzoi *et al* showed that 78.1% among 7895 patients reported at least one sexual concern between diagnosis and 4 years' follow-up.[46] However, >50% of patients with sexual dysfunction did not receive adequate

supportive care, highlighting the need for proactive evaluation of sexual health across the care continuum is needed, to promptly identify patients suitable for multidisciplinary counselling, referral and supportive interventions. In addition, several other symptoms side effects such as joint pain, musculoskeletal symptoms cognitive side effects, hot flushes and night sweats and the consequent loss of sleep are often underestimated and overseen in follow-up visits.[47]

In advanced breast cancer, PROs have emerged as important independent prognostic factors for both survival and AEs, helping to identify patients at risk and predict potential complications. The CLEOPATRA,[48] EMILIA[49] and MARIANNE[50] clinical trials collected data from a total of 2894 patients using the Functional Assessment of Cancer Therapy-Breast (FACT-B) questionnaire to assess PROs. The study focused on the associations of pretreatment PROs with OS, PFS and the incidence of grade ≥3 AEs, analysed using Cox proportional HR. The results revealed that patient-reported physical well-being, functional well-being and the breast cancer subscale of the FACT-B questionnaire were all significantly associated with both OS and PFS as well as with the occurrence of grade ≥3 AEs ($p<0.05$). This highlights the importance of these PRO domains as independent predictors of clinical outcomes in breast cancer treatment, suggesting that patient-reported experiences of their physical and functional health may provide valuable prognostic information beyond traditional clinical measures.[51]

Moreover, PROs can be instrumental in developing predictive risk models,[52] which aim to enhance the care pathway for patients with early-stage breast cancer. By analysing PRO data, healthcare providers can better anticipate patient needs, tailor interventions and optimise treatment plans. Novel technologies and remote monitoring are increasingly being used to gather PRO data in real time, enabling continuous tracking of patient progress.[53] This integration of digital tools enhances the ability to manage breast cancer care more effectively, ensuring a more patient-centred approach.[54]

Gastrointestinal cancer

In gastrointestinal cancer, QoL is crucial across all stages of the disease, from the metastatic setting to curative treatment scenarios. PROs play an essential role in this evaluation, whether they are non-specific or more disease-specific tools, such as the FACT-C or European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire (QLQ)-CR29 for colorectal cancer[55] or several tools specific for gastro-oesophageal cancer.[56] A striking observation from 67 phase III trials conducted between 2012 and 2018 is that 61.2% of studies did not include QoL as part of the trial endpoints.[57] This underscores a persistent gap in considering QoL as a central factor in treatment evaluation, despite its clear relevance for patient well-being. In addition, there is high heterogeneity among PROMs used in clinical trials.[58]

Anti-EGFRs showed efficacy benefit in combination with first-line chemotherapy in *RAS* wildtype (and *BRAF* wt, left-sided) metastatic colorectal cancer (mCRC). However, there was no significant difference in the change in EQ-5D HSI and VAS scores between treatment groups in first-line and second-line trials,[59] and no significant differences in the EORTC QLQ-C30 GHS/QoL and social functioning scores between the arms.[60] In addition, oxaliplatin-based induction plus anti-EGFRs induces a transient significant QoL deterioration and treatment deintensification determines an overall recovery of QoL.[61 62] However, there is often a disagreement between doctors and patients regarding the impact of treatment, particularly in the context of therapies such as anti-EGFR agents. While physicians may focus on clinical endpoints, patients might experience side effects or QoL concerns that are not immediately apparent in medical assessments.

Taking into consideration the impact of immunotherapy, in DNA Mismatch Repair deficient/microsatellite instability mCRC first-line pembrolizumab provided a meaningful and statistically significant benefit in PFS, lower AEs and improvement in QoL versus chemotherapy.[63] In advanced oesophageal cancer, pembrolizumab plus chemotherapy conditioned survival benefit and improvement in disease-related symptoms from baseline to week 18 in PROs.[64]

In the palliative setting in advanced gastrointestinal disease, the maintenance of QoL and reduced deterioration of ECOG PS is a crucial endpoint.[65] Several reports suggest an association between PRO score at baseline and survival outcomes. For instance, in more than 900 patients with gastro-oesophageal cancer, global health status and individual items were independently associated with OS in curable disease and non-significantly in advanced disease.[66] In 159 patients with advanced gastrointestinal cancers, the results of a prospective study suggested that 1-month changes in PROs can be associated with treatment response and survival, while variations in tumour markers (CEA and CA19.9) were not.[67]

As per the curative setting, due to the efforts in improving cure rates of patients with gastrointestinal cancers, the number of survivors is increasing and the topic of treatment sequelae is crucial, thus there is an unmet need of identification and reporting late and long-term effects.[68 69]

Genitourinary cancer

Many of the existing questionnaires were developed to assess QoL among genitourinary cancer patients receiving chemotherapy or other old standards. The new era of treatment with immunotherapy, targeted therapies and antibody–drug conjugates is associated with a different side-effect profile and thus QoL measures will probably need to be recalibrated or refined to fully understand the patient's experience and facilitate informed patient discussion.[70 71] Achieving consistency in the integration and reporting of PROMs in clinical trials for advanced renal cell carcinoma (RCC) remains challenging and

represents an important unmet need. A systematic review by Motzer *et al*[72] showed that a wide variety of PROMs have been included in clinical studies for patients with advanced/metastatic RCC: 19 different PROMs, 3 kidney cancer-specific scales, 2 cancer-specific scales, 2 generic scales and 12 symptom-specific scales, with the Functional Assessment of Cancer Therapy-Kidney Symptom Index-19 (FKSI-19) (RCC-specific) being the most frequently used (14/33). Several novel combinations are available in the first-line setting for RCC; however, the use of multiple tools, different analyses and reporting makes challenging to interpret the results and it is not appropriate to compare the effect of treatments across trials.[73] In the adjuvant setting, although there was a numerically higher QoL deterioration with pembrolizumab compared with placebo in the KEYNOTE-564 trial, no clinically meaningful differences between treatment arms were observed.[74] There are currently no PROs specifically developed for use in the RCC adjuvant setting, making this an area for future research.

Another important issue is PROs and survivorship, as we could observe in testicular cancer.[75] When comparing all testicular cancer survivors with controls, no clinically important difference in physical and mental QoL was observed. However, the study revealed that individuals with a history of high-dose platinum-based chemotherapy are at a high risk of experiencing a significantly increased prevalence of long-term adverse health outcomes (AHOs) (peripheral sensory neuropathy, Raynaud's phenomenon, tinnitus and hearing loss), which subsequently leads to diminished QoL. Thus, before starting standard platinum-based chemotherapy, patients with testicular cancer should be informed about the long-term development of typical post-treatment AHOs and be aware that their long-term global QoL will generally not differ from that of age-matched men from the general population, except for those patients treated with high-dose platinum-based chemotherapy. For these patients, multidisciplinary post-treatment rehabilitation should be started early and maintained during long-term follow-up.

Finally, in prostate cancer as well as in other tumours, there are suggestions on implementing electronic PROs, which may be crucial for the proper management of the treatment journey.[76] There is uncertainty about the feasibility of adopting ePROs in certain patient population such as patients with prostate cancer. Older patients could be less familiar with technology, and this may represent one of the issues when adopting ePROs both in clinical trials and in clinical practice. However, evidence from prostate cancer research suggests that this approach might also be acceptable, engaging and satisfactory in this context.[77]

PROS AND COMMUNICATION

Effective doctor–patient communication is critical in healthcare.[78 79] It ensures that patients feel heard and understood, which can significantly influence their satisfaction with care, adherence to treatment and overall health outcomes. By actively involving patients in the conversation through the use of PROs, healthcare providers can create a more collaborative environment that empowers patients to express their concerns, preferences and experiences.[80 81]

The implementation of PROs in clinical trials can enhance the communication of results and support shared decision-making by providing insights into the patient's perspective on treatment benefits and side effects. Furthermore, integrating PROs into routine clinical practice facilitates patient-centred communication by helping clinicians identify and address issues most relevant to patients, thereby fostering trust and improving the overall quality of oncological care.[82]

Indeed, oncologists must face several communication issues: How to communicate the diagnosis and prognosis of a disease? How to deal with family members who ask not to communicate the diagnosis of serious illnesses to the patient? How to understand one's own and others' feelings and emotional reactions? What strategies should be implemented to address particularly difficult questions? Are there communication techniques to collect information from the patient? How to share patient information between colleagues?

Physicians can improve his/her communication skills by participating in training courses that allow the acquisition of a series of communication skills (empathy, active listening) aimed at a better understanding of both the cognitive and emotional contents of the patient and the caregiver, with the aim of building a good therapeutic alliance by creating a new relationship to promote the best compliance with treatments and make the best use of the PROs.[83]

One of the key benefits of using PROs is that they facilitate a more realistic understanding of a patient's experience and especially they can disclose patients' preferences in the content of the communication.[84] Moreover, incorporating PROs into clinical practice can improve the quality of communication. When doctors use structured questionnaires or surveys to gather PROs, they can focus conversations on specific areas of concern. This structured approach helps to ensure that important topics are not overlooked, fostering a more thorough discussion. Patients are more likely to engage in conversations about their treatment if they feel that their input is valued and considered in the decision-making process.[85]

Additionally, the use of PROs can build trust between doctors and patients. This trust is essential for encouraging patients to be open about their experiences, leading to more accurate diagnoses and effective treatment plans. Integrating digital tools, such as patient portals or mobile apps, can streamline the collection and analysis of PROs. These tools can facilitate real-time feedback and keep the lines of communication open, even between appointments.[86]

However, the implementation of PROs is not without challenges. Some healthcare providers may feel that

collecting PROs adds extra time and complexity to their already busy schedules. As the healthcare landscape evolves, the emphasis on PROs is likely to increase, underscoring the importance of patient-centred care in achieving holistic and effective treatment strategies.

PATIENT-REPORTED OUTCOMES AND VALUE OF TREATMENTS IN ONCOLOGY FROM THE PERSPECTIVE OF HEALTH TECHNOLOGY ASSESSMENT

Health technology assessment (HTA) is a systematic and multidisciplinary process that evaluates the impact and effects of healthcare technologies, including drugs, devices, and procedures, on health, social, economic and ethical aspects.[87]

HTA agencies are also increasingly involving patients in their processes, considering their experiences with medical interventions, their views on health-related QoL measures and value assessments that inform reimbursement decisions.[88]

In the HTA setting, the perception of value differs from the need for positive results of critical endpoints assessed by regulators. Particularly, HTA focuses on comparative analysis to guarantee that the intervention reimbursed can diminish burden in the system, while facilitating access. In this sense, there is an opportunity to use PROMs in HTA to gather information on a treatment's added value, which, in turn, can inform market access, reimbursements and pricing negotiations. Incorporating PRO data in HTA can be essential in assessing the effectiveness and value of health technologies and ultimately improve efficiency in resource allocation.[89 90] Indeed, as mentioned before, the FDA,[28] the EMA,[29] the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use[91] and the UK's Medicines and Healthcare Products Regulatory Agency,[92] all consider PRO data derived robustly using fit-for-purpose PRO instruments as key components of decision-making during the benefit–risk appraisal of new drugs and biologic products in oncology.[93]

The use of PROMs is important for several reasons. First, they help to focus patient care on the aspects that matter most to the individual. By encouraging patients to think about specific issues, PROs allow healthcare professionals to better tailor treatment plans, address side effects and manage the overall patient experience. The choice of what to measure is crucial because PROs define the 'lens' through which patients assess their health. Whether for research, treatment optimisation, daily management, improving adherence or supporting patients in coping with their vulnerabilities, PROs play a critical role in refining care strategies.

Several initiatives are ongoing at a global level, implemented by the various stakeholders, particularly by regulatory agencies, to enhance the use of PROs in decision-making, while taking into consideration how PROs can also contribute to HTA and clinical decisions.[93 94] A study analysed HTA appraisal reports that contained PROs as endpoints between January 2018 and March 2020 and that were submitted to the Canadian, French, German, Scottish and British HTA agencies. PRO data were found in 77% (48 out of 62) of the reimbursement submissions (62 medicinal products assessed in total). PROs were included in 23 appraisals as a primary or a key secondary endpoint and 43% of these assessments (10 out of 23) received approval for reimbursement from at least three agencies. However, the authors reported that most of the PRO data submitted received unfavourable assessments from various agencies. The main reasons listed were the absence of a predefined analysis for responders, utilisation of a non-validated tool for collecting PROs, uncertainty in PRO measurements and meaningful changes in scores. Thus, the study showed that there is a considerable variability in HTA assessment of PROs and there is room for companies to better prepare their submissions.[95]

An important aspect of using PROs is understanding 'who is involved in the process'. Every day, input from patients—whether through surveys, consultations, or feedback—helps shape the care they receive. This direct patient feedback provides a means of generating value that can enhance the efficiency and resource allocation within the healthcare system. Patient organisations have long been ahead of the curve in recognising the value of PROs. In fact, oncology patient associations were advocating for PROs long before healthcare institutions fully understood their importance. As early as 2003, these associations were highlighting patient needs that had been overlooked by healthcare professionals, and the European Commission has recognised QoL as a central pillar of its Mission on Cancer.[96]

The use of PROs is also key in assessing the value of medicines. For pharmaceutical companies, this shift in focus is particularly relevant in the development of drugs for chronic conditions. Developing a new drug is not just about producing a 'me-too' therapy; it can be about offering a better QoL for patients, either by reducing side effects or improving treatment adherence. These benefits have the potential to realise savings for the healthcare and welfare systems in terms of lower utilisation of healthcare services and higher productivity of individuals in the labour market. PROs offer even more valuable insights when they show how drugs perform not only within clinical trials but also in the 'real life'.

For oncologists and the pharmaceutical industry, it is crucial to adopt a mindset that prioritises patient QoL as much as the clinical efficacy of the treatment. This is where HTA plays an essential role, especially when assessing the value of drugs. When determining the price or value of a treatment, the social value, in terms of the impact on a patient's life—such as their ability to work or carry out daily activities—needs to be considered. HTA bodies, such as the AIFA, do consider QoL measurement in their guidelines and are already engaging with patient associations to ensure these perspectives are included in evaluations. However, the real potential lies in valuing

PROs, not just QoL questionnaires, during the HTA process, allowing for a more comprehensive view of how a drug affects patients' lives, both immediately and in the long term, through validated instruments recognised by the different stakeholder groups.

Indeed, recently a strong call to action to harmonise PRO evidence requirements across key European HTA bodies in oncology has been made,[97] since HTA bodies have provided varying levels of detail regarding PRO evidence requirements in their current method guidance. Furthermore, there is a lack of consistency across HTA bodies on how PRO evidence is reviewed and considered in oncology HTAs.

Ultimately, using PROs in the HTA process allows to evaluate not just the clinical benefits of a treatment but also its economic and social value—how it impacts patients' QoL and their ability to participate fully in society. In doing so, the healthcare system will be more patient-centred, truly reflecting the needs and experiences of those it aims to serve.

FINANCIAL TOXICITY (FT) IN CANCER CARE AS AN EXAMPLE OF PATIENT-REPORTED OUTCOME

Cancer patients face not only the physical burden of the disease but also the financial and subjective distress due to cancer diagnosis and its treatment.[98] FT is a measurable and clinically relevant PRO, representing a major concern in cancer care. While national health services generally shield patients from the high cost of anticancer drugs, out-of-pocket expenses and financial challenges persist even in universal healthcare systems. Patients with cancer are more likely to face financial hardship than the general population.[99] As a reliable predictor of poor prognosis, financial insolvency was associated with a higher risk of death among individuals with cancer.[100] Moreover, as reported using question 28 of the EORTC QLQ C30 to score financial difficulties, 26% of patients enrolled in 16 academic clinical trials in Italy reported baseline FT, and 22.5% developed FT during treatment, which was associated with increased risk of death (HR 1.20, 95% CI 1.05 to 1.37, p=0.007).[101] To mitigate FT, it has been emphasised that assessment of FT at various stages of cancer treatment is crucial. The first instrument developed, the COmprehensive Score for financial Toxicity (COST), has 12 items and a scoring system ranging from 0 to 44. It was designed to measure financial distress and the overall economic burden that cancer patients face during their treatment, being developed in the USA and validated in many languages.[102] The Patient-Reported Outcome for Fighting FInancial Toxicity (PROFFIT) instrument was subsequently developed with a focus on the Italian healthcare context and public health systems in general. Besides seven items estimating the level of FT, PROFFIT includes nine individual items exploring possible determinants of FT.[103] The instrument has been validated in a prospective cohort of patients receiving cancer treatment in 10 Italian centres.[104]

Implementing financial counselling and screening tools could help identify at-risk patients, allowing potential cost-saving measures. The value of universal health coverage and social security to offset the burden of both direct medical and indirect costs was underlined during the discussion.

BEYOND CLINICAL TRIALS: BENEFITS AND CHALLENGES FOR PRO INTEGRATION IN DAILY ONCOLOGY PRACTICE

PROs have the potential to shift the focus from clinician-centred to patient-centred assessments, allowing symptoms and treatment-related toxicities reporting as well as timely interventions to prevent complications and improve treatment adherence. The various implementation modalities, as well as the challenges faced by a healthcare system such as the Italian one, were discussed.

PRO detection can be paper-based, smart technology-driven or also involve machine learning systems. Reading may be provided either during scheduled visits or continuously via integrated data entry and alert systems. Interventions vary from phone calls to direct unplanned visits, involving nurses, oncologists or emergency services, depending on symptom severity and urgency. A phone-based model offers immediacy and a personalised response but can be more expensive in terms of resources and less efficient due to potential subjectivity in trigger detection. The app-based model, on the other hand, allows for guided triggers and filtered queries.

As studied by Cherny *et al*, only 6.4% of app-based reports required in-person evaluation, with most being managed via nurse calls.[105] A hybrid system, integrating app-based symptom tracking with phone-based follow-up for complex cases, could probably optimise both responsiveness and resource efficiency.

Using PROs not only improves symptom management but also decreases the need for acute care services. In terms of hospitalisation, a pivotal study indicated reduced emergency department visits (34% vs 41%) and hospital admissions (45% vs 49%) with regular monitoring of patients' symptoms through ePROs.[106] However, comparing standard follow-up care with a model that included weekly web-based PRO assessments, Denis *et al* showed a 70% increase in planned visits and a greater number of unplanned visits when using the PROs system.[107 108] Moreover, the benefit of using PROs without immediate referral to the treating centre was not demonstrated.[109]

PROs have also shown significant promise in managing treatment-related toxicities. Studies discussed at the conference highlighted that early detection of AEs via PROs and supportive interventions allow for faster clinical responses, which may reduce the severity or duration of symptoms or unplanned healthcare utilisation.[110] In the Symptom Tracking and Reporting for Patients (STAR) randomized clinical trial, patients undergoing chemotherapy for metastatic solid tumours were asked to report 12 common symptoms through a web-based

system, being clinicians notified via email alerts of severe symptoms. As a result, more patients in the intervention group experienced QoL improvements (34% vs 18% in the usual care group), fewer emergency department visits (34% vs 41%) and hospitalisations (45% vs 49%), longer chemotherapy duration (8.2 vs 6.3 months), ultimately leading to improved survival. Namely, the study found a 5-month increase in median OS for the intervention group (31.2 vs 26.0 months), with a higher percentage of patients surviving at 1 year (75% vs 69%), benefiting also the computer-inexperienced group.[106 111] A trial conducted by the Italian Network for Supportive Care in Cancer (NICSO) in 29 Italian centres, aimed to assess the impact of a weekly phone-based nurse monitoring system on managing chemotherapy-related toxicities in patients with breast, colon, or lung cancer receiving adjuvant chemotherapy. The intervention group experienced less time with both severe toxicities, particularly often unreported symptoms, such as fatigue, and mild-to-moderate side effects, such as diarrhoea, mucositis, and pain, compared with the control group. The time spent without any AEs was significantly longer in the phone-monitored group, without additional need for special medical care.[112]

The PRO-TECT cluster-randomised trial evaluated the impact of ePRO symptom monitoring during cancer treatment across 52 oncology practices. Patients with metastatic cancer in the intervention group completed weekly symptom surveys, with severe or worsening symptoms generating alerts to the care team. While OS did not differ significantly between groups, the ePRO group experienced a delay in time to first emergency visit, reduced emergency visit rates, and delayed deterioration in physical function, symptoms, and health-related QoL.[113]

In summary, despite the benefits, implementing PROs in daily practice comes with challenges. One of the key concerns is the burden on patients and the technological barriers for those who are less familiar with technology, particularly older individuals. Additionally, there is a need for healthcare providers to establish systems that can enable a timely collection of alerts and a proactive response, as the positive impact of PROs largely depends on the timing of reading and the following intervention. In resource-limited settings, the introduction of PROs also raises concerns about the potential burden on healthcare services.

Future implementations must ensure PRO systems are designed to be accessible and inclusive across diverse populations and care contexts, including paediatric oncology. Emerging literature underlines the importance of equitable data collection[114] and patient engagement among diverse backgrounds[115] to avoid increasing health disparities. Age-appropriate instruments like Patient-Reported Outcomes Measurement Information System (PROMIS) Pediatric and Pediatric PRO-Common Terminology Criteria for Adverse Events (CTCAE) are also being developed to address the gap between child self-report and caregiver-proxy report for symptoms of children undergoing cancer treatment.[116]

Moreover, the role of the pharmaceutical industry is critical in driving broader implementation of PROs. As most clinical trials are industry-sponsored, meaningful progress relies on the inclusion of robust, patient-centred outcomes from the earliest phases of development. The 2024 PRO4ALL Manifesto, endorsed by AIOM and a broad coalition of Italian healthcare stakeholders—including non-oncology scientific societies and patient organisations—supports this perspective within the context of the Italian National Health Service (SSN). It promotes coordinated action between industry, regulatory bodies, and academia to integrate PROs not only in clinical practice, but also along the entire clinical research and development pipeline.[117] This national effort aligns with the work of the PREFER Consortium, a European public-private partnership funded by Horizon 2020 and European Federation of Pharmaceutical Industries (EFPIA), which brought together regulators, HTA bodies, academia, patient groups, and industry. PREFER developed comprehensive recommendations to guide the systematic inclusion of patient preferences in decision-making across the medical product life cycle[118]

EPROS AND DIGITAL THERAPEUTICS

The conference highlighted the increasing role of ePROs and digital health technologies in oncology care, providing a comprehensive guide to navigating the complex intersection of healthcare, digital platforms, and data privacy.

Digital Therapeutics (DTx) are evidence-based therapeutic interventions driven by software used to prevent, manage, or treat a medical disorder or disease.[119] DTx are delivered via digital platforms such as apps or devices and may be integrated with conventional treatments for application in chronic disease management, mental health and oncology. However, clinical validation through rigorous trials, and regulatory approval and monitoring are required for their large-scale implementation.

Digital PROs, particularly those integrated into routine clinical practice through electronic health records (EHRs), have been shown to improve patient outcomes in different trials. In addition to findings from the STAR study,[106 111] in a French lung cancer trial, weekly web-mediated PRO monitoring resulted in improved OS (median OS, 23.0 vs 14.8 months, HR 0.62, 95% CI 0.39 to 0.995, p=0.048) when added to usual CT scan as follow-up in patients with advanced lung cancer.[107 108] The large Canadian Population Study, including over than 1 28 000 patients, showed that symptom monitoring via ePROs was associated with significantly better outcomes, including a higher 1-year survival rate (81.9% vs 76.4%, p=0.0001), fewer emergency department visits and reduced hospitalisations.[120] In addition, reimbursement opportunities for

PROs are expanding in the US and Europe. The Cancer Patients Better Life Experience (CAPABLE) project, financed within the European Union's Horizon 2020 research programme, builds on the growing body of evidence supporting the use of ePROs. Italian and Netherlands patients with various cancer types are provided with technologies, including a smartphone app and a smartwatch. Using an interface terminology inspired by both CTCAE and PRO-CTCAE, patients diagnosed with melanoma or metastatic RCC (mRCC) report symptoms more frequently through CAPABLE app than in control group. The CAPABLE app also provides personalised recommendations based on clinical guidelines and offers mental well-being activities and virtual coaching. Pilot studies indicated that the app enhances the QoL in mRCC patients compared with standard care. In Italy, CAPABLE app achieved better performance than in the Netherlands, possibly due to better patient engagement and technical support to care for PRO management, highlighting the importance of organisational aspects for the success of these initiatives.[121]

The integration of ePROs and digital therapeutics into clinical practice holds significant promise for enhancing patient care. However, the successful implementation of these technologies requires careful consideration of several methodological aspects. Key challenges include determining appropriate thresholds for triggering interventions based on ePRO data, establishing optimal recall periods for symptom reporting and identifying clinically meaningful PRO items tailored to specific patient cohorts and disease contexts.[122] Despite the growing adoption of ePROs, there remains a notable gap in national-level readiness, particularly concerning the standardisation of these parameters.[123] This gap underscores the need for comprehensive methodological research to ensure the effective and equitable integration of digital health solutions into routine clinical practice.

LEGAL FRAMEWORK AND PRIVACY ISSUES

Both the General Data Protection Regulation (GDPR), adopted by the European Parliament in April 2016, and the Italian Legislative Decree No. 70 of May 2011, establish the need for explicit consent from individuals for the processing of health data through digital platforms such as EHRs and online medical reports.[124]

The use of sensitive data concerning vulnerable subjects, large-scale processing and the use of new technologies are among the criteria defining high-risk processing operations, requiring a Data Protection Impact Assessment under the GDPR.

In this context, the Italian national EHR system, named Fascicolo Sanitario Elettronico (FSE), aims to provide both patients and healthcare professionals with access to digital health data generated from clinical events, while ensuring strict privacy protection, with the patients controlling who can access their data. The GDPR has also significant implications for the practice of telemedicine. Several data security protocols need to be implemented, such as the use of strong authentication methods, data encryption and storage limit. In addition, organisations that collect and process personal data must be able to demonstrate compliance with the GDPR.

Moreover, pursuant to GDPR, the Italian Data Protection Authority adopted guidelines on web scraping in May 2024, with the aim to provide guidance to providers acting as data controllers and prevent the massive collection of personal data for the purpose of training generative artificial intelligence (AI) models. Finally, Italian legislation aligns with the European Parliament's AI Acts by establishing rules on data protection when AI is used for healthcare purposes and ensuring that individuals are informed when AI systems are used in their medical treatment.

CONCLUSIONS

In conclusion, the 2024 AIOM conference on PROs underscored the transformative potential of such tools and digital health technologies in oncology. By addressing the challenges of improving symptom management through PROs, of adequately describing and fighting FT, and of harnessing the power of digital therapeutics, the healthcare system can enhance the quality of cancer care. However, successful implementation will require careful consideration of patient needs, resource allocation and regulatory compliance to ensure that these innovations are both effective and sustainable.

Author affiliations
[1]Department of Biomedical Sciences, Humanitas University, Pieve Emanuele, Italy
[2]IRCCS Humanitas Research Hospital, Rozzano, Italy
[3]Department of Pneumology and Oncology, PO Monaldi-AORN Ospedali dei Colli, Ospedali dei Colli Monaldi Cotugno CTO, Naples, Italy
[4]SDA Bocconi School of Management, Center for Research on Health and Social Care Management, Bocconi University Department of Economics Ettore Bocconi, Milan, Italy
[5]Data Center and Health Outcomes Research Unit, Italian Group for Adult Haematologic Diseases (GIMEMA), Fondazione GIMEMA, Rome, Italy
[6]UOC Oncologia Medica—Dipartimento Oncoematologico Azienda Ospedaliera di Cosenza, Azienda Sanitaria Provinciale di Cosenza, Cosenza, Italy
[7]Medical Oncology, Hospital, Pescara Hospital, Pescara, Italy
[8]La Lampada di Aladino, Brugherio (MB), Italy
[9]Centro Nazionale Ricerca e Valutazione Preclinica e Clinica dei Farmaci, Istituto Superiore di Sanità, Rome, Italy
[10]Italian Federation of Oncological Voluntary Associations (FAVO), Rome, Italy
[11]Centre for Research on Health and Social Care Management-Scuola di Direzione Aziendale, Department of Social and Political Sciences, Bocconi University, Milan, Italy
[12]Direzione Tecnico Scientifica, Farmindustria, Roma, Italy
[13]Department of Economy, Università degli Studi di Messina, Messina, Italy
[14]Department of Oncology, Medical Oncology 1 Unit, Istituto Oncologico Veneto IOV—IRCCS, Istituto Oncologico Veneto IRCCS, Padua, Italy
[15]Unit of Oncology, Fondazione IRCCS "Casa Sollievo della Sofferenza", IRCCS Ospedale Casa Sollievo della Sofferenza, San Giovanni Rotondo, Italy
[16]Department of Clinical Medicine and Surgery, University of Naples Federico II, Naples, Italy
[17]Clinical and Translational Oncology, Scuola Superiore Meridionale, Naples, Italy

[18]Medical Oncology Department, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy
[19]Skin and Renal Units, The Royal Marsden NHS Foundation Trust, London, UK
[20]U.O.C. Oncologia Medica and Breast Unit, Ospedale Senatore Antonio Perrino, Ospedale Antonio Perrino Divisione di Oncologia Medica, Brindisi, Italy
[21]Italian Federation of Oncological Voluntary Associations, Rome, Italy
[22]Department of Medical and Surgical Specialties, Radiological Sciences and Public Health, University of Brescia, Brescia, Italy
[23]Medical Oncology, AO S.Croce e Carle, Cuneo, Italy
[24]Medical Oncology, Comprehensive Cancer Centre IRCCS-AUSL, Azienda USL—IRCCS di Reggio Emilia, Reggio Emilia, Italy
[25]Department of Electrical, Computer and Biomedical Engineering, University of Pavia, Pavia, Italy
[26]Department of Internal Medicine and Therapeutics, University of Pavia, Pavia, Italy
[27]Clinical Research Department, Italian Scientific Society of Internal Medicine, Milan, Italy
[28]Studio Legale Mignone, Benevento, Italy
[29]German Cancer Research Center, Heidelberg, Germany
[30]Division of Oncology, University of North Carolina at Chapel Hill, University of North Carolina Research Opportunities Initiative, Chapel Hill, North Carolina, USA
[31]Department of Oncology, University of Turin, AOU Città della Salute e della Scienza di Torino, Turin, Italy
[32]Istituto Nazionale Tumori IRCCS Fondazione Pascale, Napoli, Italy

X Giuseppe Viscardi @giusvisc and Massimo Di Maio @MassimoDiMaio75

Contributors All authors actively contributed as Invited Speakers or Chairperson during the 21st National Conference of the Italian Association of Medical Oncology (AIOM), held in Bologna on 21–22 June 2024. AP, GV, MDM, FP: Conceptualisation; data curation; methodology; resources; supervision; writing—original draft; writing—review and editing. MDM: guarantor. All other authors: resources, writing—review and editing.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests FP: reports honoraria from Pfizer, Glaxo, Bristol Myers Squibb, Menarini, Roche, Viatris Italia for consultancy or participation to advisory boards; AIOM President. MDM reports honoraria from AstraZeneca, Boehringer Ingelheim, Janssen, Merck Sharp institutional funding for work in clinical trials/contracted research from Beigene, Exelixis, MSD, Pfizer and Roche. SC: reports honoraria from Lilly oncology, Menarini Stemlines, Lilly oncology, past president AIOM and Presidente AIOM Foundation. AP: reports honoraria from GlaxoSmithKline, Takeda Pharmaceuticals USA, Takeda Italia, Bayer, Daiichi Sankyo Italia, MSD Italia for consultancy or participation to advisory boards; from Pierre Fabre, Servier, Amgen as Invited Speaker; institutional funding for work in clinical trials/contracted research from GlaxoSmithKline, Amgen; from AstraZeneca, Amgen, Merck Serono for Travel, Accommodations, Expenses. All not related to this manuscript. AR: reports honoraria for speaker bureau and advisory board participation: Elma Academy, Servier, MSD, Nordic Pharma. PB: Participation to advisory board or conference honoraria for Merck, Sanofi-Regeneron, Merck Sharp from Pharmamar for travel and accommodation expenses. FE: consultancy or advisory role for AbbVie, Incyte, Novartis and JAZZ Pharmaceuticals. Research funding (institution) from Daiichi Sankyo. All are not related to this manuscript. MP: reports honoraria from Ipsen for travel and accomodation expenses; from Gilead for Research funding (to institution). GV: reports honoraria from MSD, Novartis for consultancy or participation to advisory boards; From Astra Zeneca, Novartis, Sanofi for Travel accommodation; from AstraZeneca, BMS, Merck, MSD, Regeneron, Roche, Takeda for Speaker fee CP: outside the submitted work personal fees for the advisory role, speaker engagements, and travel and accommodation expenses from Amgen, Astellas, AstraZeneca, Bayer, Bristol Meyer Squibb, Celgene, Daiichi Sankyo, Eisai, Ipsen, Janssen, Incyte, Merck-Serono, Merck Sharp and Dohme, Novartis, Roche, Sandoz, Sanofi, and Servier. LM: outside the submitted work personal fees for Speakers' Bureau: Gilead Sciences, Merck; Research Funding: AstraZeneca; Travel, Accommodations, Expenses: Janssen, Immunocore.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval Not applicable.

Provenance and peer review Not commissioned; externally peer-reviewed.

Data availability statement No data are available.

ORCID iDs
Alberto Servetto http://orcid.org/0000-0003-3624-224X
Gianmauro Numico http://orcid.org/0000-0003-3253-2960
Massimo Di Maio http://orcid.org/0000-0001-8906-3785

REFERENCES

1 Di Maio M, Basch E, Bryce J, *et al*. Patient-reported outcomes in the evaluation of toxicity of anticancer treatments. *Nat Rev Clin Oncol* 2016;13:319–25.
2 Di Maio M, Basch E, Denis F, *et al*. The role of patient-reported outcome measures in the continuum of cancer clinical care: ESMO Clinical Practice Guideline. *Ann Oncol* 2022;33:878–92.
3 European Medicines Agency. EMA/CHMP/292464/2014.
4 Hwang TJ, Gyawali B. Association between progression-free survival and patients' quality of life in cancer clinical trials. *Int J Cancer* 2019;144:1746–51.
5 Marandino L, La Salvia A, Sonetto C, *et al*. Deficiencies in health-related quality-of-life assessment and reporting: a systematic review of oncology randomized phase III trials published between 2012 and 2016. *Ann Oncol* 2018;29:2288–95.
6 Salomone F, Di Costanzo F, Pecoraro G, *et al*. Health-related quality of life is underestimated and underreported in phase III clinical trials in NSCLC. *Lung Cancer (Auckl)* 2022;174:36–44.
7 Blackstone EC, Efficace F, Meyerhardt JA, *et al*. Timely Reporting of Patient-Reported Outcomes in Cancer Clinical Trials: An Ethical Imperative. *J Clin Oncol* 2025;43:1176–9.
8 Cherny NI, Dafni U, Bogaerts J, *et al*. ESMO-Magnitude of Clinical Benefit Scale version 1.1. *Ann Oncol* 2017;28:2340–66.
9 Gyawali B, de Vries EGE, Dafni U, *et al*. Biases in study design, implementation, and data analysis that distort the appraisal of clinical benefit and ESMO-Magnitude of Clinical Benefit Scale (ESMO-MCBS) scoring. *ESMO Open* 2021;6:100117.
10 Marandino L, Trastu F, Ghisoni E, *et al*. Time trends in health-related quality of life assessment and reporting within publications of oncology randomised phase III trials: a meta-research study. *BMJ Oncol* 2023;2:e000021.
11 Mosele F, Di Maio M. Trastuzumab deruxtecan for breast cancer: do patients experience a comprehensive benefit? *Ann Oncol* 2023;34:567–8.
12 Hurvitz SA, Hegg R, Chung W-P, *et al*. Trastuzumab deruxtecan versus trastuzumab emtansine in patients with HER2-positive metastatic breast cancer: updated results from DESTINY-Breast03, a randomised, open-label, phase 3 trial. *Lancet* 2023;401:105–17.
13 Curigliano G, Dunton K, Rosenlund M, *et al*. Patient-reported outcomes and hospitalization data in patients with HER2-positive metastatic breast cancer receiving trastuzumab deruxtecan or trastuzumab emtansine in the phase III DESTINY-Breast03 study. *Ann Oncol* 2023;34:569–77.
14 Paratore C, Schiavone R, Zichi C, *et al*. Health-related quality of life (QoL) in randomized phase III trials in oncology: Association between results of QoL, results of primary endpoint and drug approval. *JCO* 2024;42:11109.
15 Paratore C, Zichi C, Schiavone R, *et al*. Association between health-related quality-of-life results, outcomes of efficacy and drug approvals: a meta-research study of randomized phase III trials in oncology. *ESMO Open* 2024;9:103654.
16 Meregaglia M, Malandrini F, Angelini S, *et al*. The Assessment of Patient-Reported Outcomes for the Authorisation of Medicines in Europe: A Review of European Public Assessment Reports from 2017 to 2022. *Appl Health Econ Health Policy* 2023;21:925–35.
17 Malandrini F, Borroni C, Meregaglia M, *et al*. Il ruolo degli esiti riferiti dal paziente nelle decisioni di rimborso e innovatività dei farmaci in Italia. *Glob Reg Health Technol Assess* 2023;10:12.
18 Ciani O, Meregaglia M, Battaglia MA, *et al*. Patient-reported outcome measures in drugs for neurological conditions approved by European Medicines Agency 2017-2022. *Neurol Sci* 2023;44:2933–7.
19 Ciani O, Meregaglia M, De Lorenzo F, *et al*. Patient-Reported Outcome Measures in Oncology Drugs Approved by the

European Medicines Agency, 2017-2021. *JAMA Netw Open* 2023;6:e2251564.
20 Malandrini F, Meregaglia M, Di Maio M, *et al*. The development of an archive of patient-reported outcome measures (PROMs) in oncology: The Italian PRO4All project. *European Journal of Cancer (Oxford, England* 2024;207:S0959-8049(24)00817-7:114161:.
21 McGlothlin AE, Lewis RJ. Minimal clinically important difference: defining what really matters to patients. *JAMA* 2014;312:1342–3.
22 Calvert M, Kyte D, Mercieca-Bebber R, *et al*. Guidelines for Inclusion of Patient-Reported Outcomes in Clinical Trial Protocols: The SPIRIT-PRO Extension. *JAMA* 2018;319:483–94.
23 Guérin A, Chen L, Dea K, *et al*. Association between regular molecular monitoring and tyrosine kinase inhibitor therapy adherence in chronic myelogenous leukemia in the chronic phase. *Curr Med Res Opin* 2014;30:1345–52.
24 Efficace F, Rosti G, Aaronson N, *et al*. Patient- versus physician-reporting of symptoms and health status in chronic myeloid leukemia. *Haematologica* 2014;99:788–93.
25 Efficace F, Baccarani M, Breccia M, *et al*. Chronic fatigue is the most important factor limiting health-related quality of life of chronic myeloid leukemia patients treated with imatinib. *Leukemia* 2013;27:1511–9.
26 PRO-CTCAE measurement system. 2024. Available: https://healthcaredelivery.cancer.gov/pro-ctcae/overview.html
27 Piccinin C, Basch E, Bhatnagar V, *et al*. Recommendations on the use of item libraries for patient-reported outcome measurement in oncology trials: findings from an international, multidisciplinary working group. *Lancet Oncol* 2023;24:e86–95.
28 FDA patient-focused drug development guidance series. 2025. Available: https://www.fda.gov/drugs/development-approval-process-drugs/fda-patient-focused-drug-development-guidance-series-enhancing-incorporation-patients-voice-medical
29 EMA. Appendix 2 to the guideline on the evaluation of anticancer medicinal products in man - the use of patient-reported outcome (PRO) measures in oncology studies - Scientific guideline. 2016. Available: https://www.ema.europa.eu/en/appendix-2-guideline-evaluation-anticancer-medicinal-products-man-use-patient-reported-outcome-pro-measures-oncology-studies-scientific-guideline
30 Calvert M, Blazeby J, Altman DG, *et al*. Reporting of Patient-Reported Outcomes in Randomized Trials. *JAMA* 2013;309:814.
31 Basch E, Abernethy AP, Mullins CD, *et al*. Recommendations for Incorporating Patient-Reported Outcomes Into Clinical Comparative Effectiveness Research in Adult Oncology. *JCO* 2012;30:4249–55.
32 Efficace F, Feuerstein M, Fayers P, *et al*. Patient-reported outcomes in randomised controlled trials of prostate cancer: methodological quality and impact on clinical decision making. *Eur Urol* 2014;66:416–27.
33 Fayers PM, Hopwood P, Harvey A, *et al*. Quality of life assessment in clinical trials—guidelines and a checklist for protocol writers: the U.K. Medical Research Council experience. *Eur J Cancer* 1997;33:20–8.
34 Efficace F, Cottone F, Yanez B, *et al*. Patient-reported symptom monitoring and adherence to therapy in patients with newly diagnosed chronic myeloid leukemia. *Cancer* 2024;130:287–99.
35 Haverman L, Luijten MAJ, Blackford AL, *et al*. Truth and dare: patients dare to tell the truth when using PROMs in clinical practice. *Qual Life Res* 2024;33:3299–307.
36 Pe M, Alanya A, Falk RS, *et al*. Setting International Standards in Analyzing Patient-Reported Outcomes and Quality of Life Endpoints in Cancer Clinical Trials-Innovative Medicines Initiative (SISAQOL-IMI): stakeholder views, objectives, and procedures. *Lancet Oncol* 2023;24:e270–83.
37 Cremante M, Pastorino A, Ponzano M, *et al*. Reliability of patient-reported toxicities during adjuvant chemotherapy. *Eur J Cancer* 2023;182:115–21.
38 Aiyegbusi OL, Cruz Rivera S, Roydhouse J, *et al*. Recommendations to address respondent burden associated with patient-reported outcome assessment. *Nat Med* 2024;30:650–9.
39 Snyder C, Crossnohere N, King M, *et al*. The PROTEUS-Trials Consortium: Optimizing the use of patient-reported outcomes in clinical trials. *Clin Trials* 2022;19:277–84.
40 Cruz Rivera S, Aiyegbusi OL, Ives J, *et al*. Ethical Considerations for the Inclusion of Patient-Reported Outcomes in Clinical Research: The PRO Ethics Guidelines. *JAMA* 2022;327:1910–9.
41 Mercieca-Bebber R, King MT, Calvert MJ, *et al*. The importance of patient-reported outcomes in clinical trials and strategies for future optimization. *Patient Relat Outcome Meas* 2018;9:353–67.
42 Servetto A, Malandrini F, Meregaglia M, *et al*. MA14.13 Analysis of Lung Cancer-Specific Patient-Reported Outcome Measures (PROMs): Results from the PRO4All Project. *J Thorac Oncol* 2024;19:S115–6.
43 Wu Y-L, Cheng Y, Zhou X, *et al*. Dacomitinib versus gefitinib as first-line treatment for patients with EGFR-mutation-positive non-small-cell lung cancer (ARCHER 1050): a randomised, open-label, phase 3 trial. *Lancet Oncol* 2017;18:1454–66.
44 Servetto A, Salomone F, Di Costanzo F, *et al*. Inadequate health-related quality of life assessment and reporting in phase III clinical trials of immune checkpoint inhibitors in solid cancers: A systematic review. *Crit Rev Oncol Hematol* 2022;172:103649.
45 Servetto A, Di Maio M, Salomone F, *et al*. Analysis of phase III clinical trials in metastatic NSCLC to assess the correlation between QoL results and survival outcomes. *BMC Med* 2023;21:234.
46 Franzoi MA, Aupomerol M, Havas J, *et al*. Investigating sexual health after breast cancer by longitudinal assessment of patient-reported outcomes. *ESMO Open* 2024;9:102236.
47 Andreu Y, Soto-Rubio A, Ramos-Campos M, *et al*. Impact of hormone therapy side effects on health-related quality of life, distress, and well-being of breast cancer survivors. *Sci Rep* 2022;12:18673.
48 Swain SM, Baselga J, Kim S-B, *et al*. Pertuzumab, trastuzumab, and docetaxel in HER2-positive metastatic breast cancer. *N Engl J Med* 2015;372:724–34.
49 Verma S, Miles D, Gianni L, *et al*. Trastuzumab emtansine for HER2-positive advanced breast cancer. *N Engl J Med* 2012;367:1783–91.
50 Perez EA, Barrios C, Eiermann W, *et al*. Trastuzumab Emtansine With or Without Pertuzumab Versus Trastuzumab Plus Taxane for Human Epidermal Growth Factor Receptor 2-Positive, Advanced Breast Cancer: Primary Results From the Phase III MARIANNE Study. *J Clin Oncol* 2017;35:141–8.
51 Modi ND, Danell NO, Perry RNA, *et al*. Patient-reported outcomes predict survival and adverse events following anticancer treatment initiation in advanced HER2-positive breast cancer. *ESMO Open* 2022;7:100475.
52 Di Meglio A, Havas J, Soldato D, *et al*. Development and Validation of a Predictive Model of Severe Fatigue After Breast Cancer Diagnosis: Toward a Personalized Framework in Survivorship Care. *JCO* 2022;40:1111–23.
53 Kikawa Y, Uemura Y, Taira T, *et al*. A randomized study comparing electronic patient-reported outcome (ePRO) monitoring with routine follow-up during trastuzumab deruxtecan treatment in patients with metastatic breast cancer (PRO-DUCE study). *JCO* 2024;42:1504.
54 Coles CE, Earl H, Anderson BO, *et al*. The Lancet Breast Cancer Commission. *Lancet* 2024;403:1895–950.
55 Besson A, Deftereos I, Chan S, *et al*. Understanding patient-reported outcome measures in colorectal cancer. *Future Oncol* 2019;15:1135–46.
56 Rowsell A, Sodergren SC, Vassiliou V, *et al*. Systematic review of health-related quality of life (HRQoL) issues associated with gastric cancer: capturing cross-cultural differences. *Gastric Cancer* 2022;25:665–77.
57 Lombardi P, Marandino L, De Luca E, *et al*. Quality of life assessment and reporting in colorectal cancer: A systematic review of phase III trials published between 2012 and 2018. *Crit Rev Oncol Hematol* 2020;146:102877.
58 Winkelmann C, Mezentseva A, Vogt B, *et al*. Patient-Reported Outcome Measures in Liver and Gastrointestinal Cancer Randomized Controlled Trials. *Int J Environ Res Public Health* 2023;20:6293.
59 Bennett L, Zhao Z, Barber B, *et al*. Health-related quality of life in patients with metastatic colorectal cancer treated with panitumumab in first- or second-line treatment. *Br J Cancer* 2011;105:1495–502.
60 Láng I, Köhne C-H, Folprecht G, *et al*. Quality of life analysis in patients with. *Eur J Cancer* 2013;49:439–48.
61 Raimondi A, Maio M, Morano F, *et al*. Health-related quality of life in patients with. *Eur J Cancer* 2020;135:230–9.
62 Ballhausen A, Karthaus M, Fruehauf S, *et al*. Health-related quality of life in patients with RAS wild-type metastatic colorectal cancer treated with fluorouracil and folinic acid with or without panitumumab as maintenance therapy: a prespecified secondary analysis of the PanaMa (AIO KRK 0212) trial. *Eur J Cancer* 2023;190:112955.
63 Andre T, Amonkar M, Norquist JM, *et al*. Health-related quality of life in patients with microsatellite instability-high or mismatch repair deficient metastatic colorectal cancer treated with first-line pembrolizumab versus chemotherapy (KEYNOTE-177): an open-label, randomised, phase 3 trial. *Lancet Oncol* 2021;22:665–77.
64 Shah MA, Sun J-M, Shen L, *et al*. First-line pembrolizumab (pembro) plus chemotherapy (chemo) for advanced esophageal

cancer: 5-year outcomes from the phase 3 KEYNOTE-590 study. *JCO* 2024;42:250.
65 Shitara K, Doi T, Dvorkin M, *et al*. Trifluridine/tipiracil versus placebo in patients with heavily pretreated metastatic gastric cancer (TAGS): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet Oncol* 2018;19:1437–48.
66 Van Cutsem E, Amonkar M, Fuchs CS, *et al*. Health-related quality of life in advanced gastric/gastroesophageal junction cancer with second-line pembrolizumab in KEYNOTE-061. *Gastric Cancer* 2021;24:1330–40.
67 Jarnagin JX, Saraf A, Baiev I, *et al*. Patient-Reported Outcomes, Tumor Markers, and Survival Outcomes in Advanced GI Cancer. *JAMA Netw Open* 2023;6:e2343512.
68 Frick MA, Vachani CC, Hampshire MK, *et al*. Survivorship after lower gastrointestinal cancer: Patient-reported outcomes and planning for care. *Cancer* 2017;123:1860–8.
69 van Erning FN, Nieuwenhuijzen GAP, van Laarhoven HWM, *et al*. Gastrointestinal Symptoms After Resection of Esophagogastric Cancer: A Longitudinal Study on Their Incidence and Impact on Patient-Reported Outcomes. *Ann Surg Oncol* 2023;30:8203–15.
70 Bergerot CD, Gupta S. Time to Rethink Quality of Life Assessment in Patients with Urothelial Cancer in the Current Therapeutic Era? *Eur Urol* 2023;83:329–30.
71 Gupta S, Loriot Y, Van Der Heijden MS, *et al*. Patient-reported outcomes (PROs) from a randomized, phase 3 trial of enfortumab vedotin plus pembrolizumab (EV+P) versus platinum-based chemotherapy (PBC) in previously untreated locally advanced or metastatic urothelial cancer (la/mUC). *JCO* 2024;42:4502.
72 Motzer RJ, Rane PP, Saretsky TL, *et al*. Patient-reported Outcome Measurement and Reporting for Patients with Advanced Renal Cell Carcinoma: A Systematic Literature Review. *Eur Urol* 2023;84:406–17.
73 Bergerot CD, Castro DV, Bergerot PG, *et al*. Development of a patient-centered health-related quality of life (HRQOL) measure for metastatic renal cell carcinoma (mRCC): A three-phase study. *JCO* 2024;42:365.
74 Choueiri TK, Tomczak P, Park SH, *et al*. Patient-Reported Outcomes in KEYNOTE-564: Adjuvant Pembrolizumab Versus Placebo for Renal Cell Carcinoma. *Oncologist* 2024;29:142–50.
75 Fosså SD, Haugnes HS, Dahl AA, *et al*. Adverse health outcomes and global quality of life in long-term testicular cancer survivors: a longitudinal 30-year perspective. *Ann Oncol* 2023;34:1165–74.
76 Cacho D, Congregado B, Rivero Belenchon I, *et al*. PRO-WAVE1: Monitoring patient reported outcomes (PROs) in prostate cancer through Wave Health, a novel ePRO health platform. *JCO* 2024;42:114.
77 Lashey MD, Linares Espinos E, Basterretxea L, *et al*. PRO-WAVE1: Monitoring patient reported outcomes (PROs) in prostate cancer through Wave Health, a novel ePRO health platform. *JCO* 2024;42:192.
78 Berardi R, Parisi A, Maruzzo M, *et al*. Communication in oncology between healthcare providers, patients, the scientific community, and the media: recommendations from the Italian Association of Medical Oncology (AIOM). *Support Care Cancer* 2024;32:613.
79 Stiefel F, Bourquin C, Salmon P, *et al*. Communication and support of patients and caregivers in chronic cancer care: ESMO Clinical Practice Guideline. *ESMO Open* 2024;9:103496.
80 NCCN clinical practice guidelines in oncology (NCCN guidelines®) distress management version 2.2024. 2024. Available: https://www.nccn.org/guidelines/guidelines-detail?category=3&id=1431
81 Italian Association of Medical Oncology (AIOM) National Guidelines: Assistenza psicosociale e dei malati oncologici. 2023. Available: https://www.aiom.it/linee-guida-aiom-2023-assistenza-psico-sociale-dei-malati-oncologici
82 Chen J, Ou L, Hollis SJ. A systematic review of the impact of routine collection of patient reported outcome measures on patients, providers and health organisations in an oncologic setting. *BMC Health Serv Res* 2013;13:211.
83 Banerjee SC, Haque N, Bylund CL, *et al*. Responding empathically to patients: a communication skills training module to reduce lung cancer stigma. *Transl Behav Med* 2021;11:613–8.
84 Yang LY, Manhas DS, Howard AF, *et al*. Patient-reported outcome use in oncology: a systematic review of the impact on patient-clinician communication. *Support Care Cancer* 2018;26:41–60.
85 Lavallee DC, Chenok KE, Love RM, *et al*. Incorporating Patient-Reported Outcomes Into Health Care To Engage Patients And Enhance Care. *Health Aff (Millwood)* 2016;35:575–82.
86 Licqurish SM, Cook OY, Pattuwage LP, *et al*. Tools to facilitate communication during physician-patient consultations in cancer care: An overview of systematic reviews. *CA Cancer J Clin* 2019;69:497–520.
87 Bertelsen N, Dewulf L, Ferrè S, *et al*. Patient Engagement and Patient Experience Data in Regulatory Review and Health Technology Assessment: A Global Landscape Review. *Ther Innov Regul Sci* 2024;58:63–78.
88 Almeida D, Umuhire D, Gonzalez-Quevedo R, *et al*. Leveraging patient experience data to guide medicines development, regulation, access decisions and clinical care in the EU. *Front Med (Lausanne)* 2024;11:1408636.
89 Brogan AP, DeMuro C, Barrett AM, *et al*. Payer Perspectives on Patient-Reported Outcomes in Health Care Decision Making: Oncology Examples. *J Manag Care Spec Pharm* 2017;23:125–34.
90 Inotai A, Jakab I, Brixner D, *et al*. Proposal for capturing patient experience through extended value frameworks of health technologies. *J Manag Care Spec Pharm* 2021;27:936–47.
91 International Council for Harmonisation of technical requirements for pharmaceuticals for human use. ICH reflection paper on patient focused drug development (PFDD). 2020. Available: www.ich.org/page/reflection-papers#1-1
92 Medicines & Healthcare Products Regulatory Agency. Patient involvement strategy 2021–25. 2021. Available: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1022370/Patient_involvement_strategy.pdf
93 Gnanasakthy A, Barrett A, Evans E, *et al*. A Review of Patient-Reported Outcomes Labeling for Oncology Drugs Approved by the FDA and the EMA (2012-2016). *Value Health* 2019;22:203–9.
94 Bouvy JC, Cowie L, Lovett R, *et al*. Use of Patient Preference Studies in HTA Decision Making: A NICE Perspective. *Patient* 2020;13:145–9.
95 Sharma G, Naujoks C, Booneti S, *et al*. POSC260 Evaluating the Impact of Patient Reported Outcomes Data on HTA Reimbursement Decisions. *Value Health* 2022;25:S184–5.
96 EU mission: cancer. 2025. Available: https://research-and-innovation.ec.europa.eu/funding/funding-opportunities/funding-programmes-and-open-calls/horizon-europe/eu-missions-horizon-europe/eu-mission-cancer_en#more-information
97 Chassany O, Engen A van, Lai L, *et al*. A call to action to harmonize patient-reported outcomes evidence requirements across key European HTA bodies in oncology. *Future Oncol* 2022;18:3323–34.
98 Carrera PM, Kantarjian HM, Blinder VS. The financial burden and distress of patients with cancer: Understanding and stepping-up action on the financial toxicity of cancer treatment. *CA Cancer J Clin* 2018;68:153–65.
99 Ramsey S, Blough D, Kirchhoff A, *et al*. Washington State cancer patients found to be at greater risk for bankruptcy than people without a cancer diagnosis. *Health Aff (Millwood)* 2013;32:1143–52.
100 Ramsey SD, Bansal A, Fedorenko CR, *et al*. Financial Insolvency as a Risk Factor for Early Mortality Among Patients With Cancer. *J Clin Oncol* 2016;34:980–6.
101 Perrone F, Jommi C, Di Maio M, *et al*. The association of financial difficulties with clinical outcomes in cancer patients: secondary analysis of 16 academic prospective clinical trials conducted in Italy. *Ann Oncol* 2016;27:2224–9.
102 de Souza JA, Yap BJ, Wroblewski K, *et al*. Measuring financial toxicity as a clinically relevant patient-reported outcome: The validation of the COmprehensive Score for financial Toxicity (COST). *Cancer* 2017;123:476–84.
103 Riva S, Arenare L, Di Maio M, *et al*. Cross-sectional study to develop and describe psychometric characteristics of a patient-reported instrument (PROFFIT) for measuring financial toxicity of cancer within a public healthcare system. *BMJ Open* 2021;11:e049128.
104 Arenare L, Porta C, Barberio D, *et al*. Confirmatory validation analysis of the PROFFIT questionnaire to assess financial toxicity in cancer patients. *ESMO Open* 2023;8:102192.
105 Cherny NI, Parrinello CM, Kwiatkowsky L, *et al*. Feasibility of Large-Scale Implementation of an Electronic Patient-Reported Outcome Remote Monitoring System for Patients on Active Treatment at a Community Cancer Center. *JCO Oncol Pract* 2022;18:e1918–26.
106 Basch E, Deal AM, Kris MG, *et al*. Symptom Monitoring With Patient-Reported Outcomes During Routine Cancer Treatment: A Randomized Controlled Trial. *JCO* 2016;34:557–65.
107 Denis F, Basch E, Septans A-L, *et al*. Two-Year Survival Comparing Web-Based Symptom Monitoring vs Routine Surveillance Following Treatment for Lung Cancer. *JAMA* 2019;321:306.

108 Denis F, Lethrosne C, Pourel N, *et al*. Randomized Trial Comparing a Web-Mediated Follow-up With Routine Surveillance in Lung Cancer Patients. *J Natl Cancer Inst* 2017;109:109.
109 Taarnhøj GA, Johansen C, Carus A, *et al*. The iBLAD study: patient-reported outcomes in bladder cancer during oncological treatment: a multicenter national randomized controlled trial. *J Patient Rep Outcomes* 2023;7:99.
110 Harrison JM, Stella PJ, LaVasseur B, *et al*. Toxicity-Related Factors Associated With Use of Services Among Community Oncology Patients. *JOP* 2016;12:e818–27.
111 Basch E, Deal AM, Dueck AC, *et al*. Overall Survival Results of a Trial Assessing Patient-Reported Outcomes for Symptom Monitoring During Routine Cancer Treatment. *JAMA* 2017;318:197.
112 Antonuzzo A, Ripamonti CI, Roila F, *et al*. Effectiveness of a phone-based nurse monitoring assessment and intervention for chemotherapy-related toxicity: A randomized multicenter trial. *Front Oncol* 2022;12:925366.
113 Basch E, Schrag D, Jansen J, *et al*. Symptom monitoring with electronic patient-reported outcomes during cancer treatment: final results of the PRO-TECT cluster-randomized trial. *Nat Med* 2025;31:1225–32.
114 Calvert MJ, Cruz Rivera S, Retzer A, *et al*. Patient reported outcome assessment must be inclusive and equitable. *Nat Med* 2022;28:1120–4.
115 Rocque GB, Caston NE, Hildreth K, *et al*. Engagement Among Diverse Patient Backgrounds in a Remote Symptom Monitoring Program. *JCO Oncol Pract* 2024;20:1426–35.
116 Mack JW, McFatrich M, Withycombe JS, *et al*. Agreement Between Child Self-report and Caregiver-Proxy Report for Symptoms and Functioning of Children Undergoing Cancer Treatment. *JAMA Pediatr* 2020;174:e202861.
117 Fondazione AIOM. Manifesto PRO4ALL – Per una sistematica integrazione dei Patient Reported Outcomes (PROs) nella pratica clinica e nella ricerca oncologica. AIOM; 2024. Available: https://www.aiom.it/manifesto-pro4all-pazienti-protagonisti-per-la-salute-di-tutti/
118 Consortium TP. PREFER recommendations - Why, when and how to assess and use patient preferences in medical product decision-making. 2022.
119 Hong JS, Wasden C, Han DH. Introduction of digital therapeutics. *Comput Methods Programs Biomed* 2021;209:106319.
120 Barbera L, Sutradhar R, Seow H, *et al*. The impact of routine Edmonton Symptom Assessment System (ESAS) use on overall survival in cancer patients: Results of a population-based retrospective matched cohort analysis. *Cancer Med* 2020;9:7107–15.
121 Locati LD, Rizzo M, Gabanelli P, *et al*. Electronic patient-reported outcome measures (E-Proms): Results of the H2020 CAPABLE project for patients with metastatic renal cell cancer (mRCC). *JCO* 2024;42:11045.
122 Paudel R, Enzinger AC, Uno H, *et al*. Effects of a change in recall period on reporting severe symptoms: an analysis of a pragmatic multisite trial. *J Natl Cancer Inst* 2024;116:1137–44.
123 Nielsen AS, Hanna L, Larsen BF, *et al*. Readiness, acceptance and use of digital patient reported outcome in an outpatient clinic. *Health Informatics J* 2022;28:14604582221106000.
124 Available: https://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:32016R0679