Improving access to innovation:

A global vision for how to evolve value and access in oncology

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Foreword

In the last few decades, we have witnessed a paradigm shift to earlier diagnoses in many cancers.[1] This shift, in tandem with therapeutic innovation, means we are moving towards treating cancer at earlier stages than before and better meeting the needs of people living with the disease.[2,3,4]

Despite the emergence of new oncology medicines, disparities in patient access remain a critical issue. The time from marketing authorization to patient availability varies significantly across the world. Within Europe, between 2019 and 2022, newly authorized oncology medicines were available to people living with cancer in Germany around 700 days before the same treatments were available to people in Latvia and Lithuania.[5] Furthermore, access to many of these innovative medicines is limited in low and middle-income countries (LMICs), where even essential medicines can be difficult to obtain.[6]

We know that the cancer burden will grow in coming years. Global deaths from cancer are set to increase from 9.7 to 18.5 million between 2022 and 2050 – almost doubling in under 30 years.[7] The majority of these will occur in LMICs.[8]

It is therefore urgent that the cancer community and health systems around the world collaborate to promote earlier and more equitable access to oncology medicines, while managing budget impact and affordability. This means methods to assess the value of cancer medicines need to evolve to embrace new perspectives of value that are informed by people living with cancer and consider societal impact. Otherwise, cancer medicines may not reach the people who could benefit.

Access to Innovative Medicines in Cancer (AIMC), a group of 27 multidisciplinary global experts and organizations, was formed to improve timely and equitable access to oncology medicines across the globe by evolving value assessment to ensure it keeps pace with advancing science. Through a collaborative approach, we identified key barriers and policy solutions to tackle them which can be taken forward by stakeholders from across the cancer community. These recommendations and stakeholder actions, accompanied by case studies, are outlined in this report – *Improving access to innovation: A global vision for how to evolve value and access in oncology.*

This report's release coincides with numerous national and international initiatives looking to tackle these issues. In Europe, the European Commission's Regulation on Health Technology Assessment (HTAR) aims to improve use of resources and ensure availability of innovative health technologies for people across the European Union (EU).[9] Similarly, the Inflation Reduction Act in the United States (US) aims to reduce healthcare costs,[10] and other initiatives reflect broader shifts in the oncology policy landscape.[11,12] While our report does not address pricing, we hope that it provides a global blueprint for evolving how value is assessed in oncology that recognizes the budget impact considerations, incentivizes innovation and supports timely access.

We need a concerted, collaborative effort from the cancer community and health systems to ensure lived experiences and outcomes are put at the heart of every decision. It is time for value assessments to reflect what matters most to people living with cancer and their families, while also recognizing the value - not just the costs - of oncology care.

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Executive summary

Value assessment needs to keep pace with scientific advancements in oncology. With the move towards earlier diagnosis and treatment, we have seen improved survival rates and better quality of life (QoL). However, the growing global cancer burden and disparities in health outcomes necessitate an updated approach to value assessment to ensure that decisions reflect the full spectrum of societal benefits provided by innovative therapies.

We need to evolve how we measure:

- **Clinical value,** by moving beyond traditional endpoints like overall survival (OS) to include measures such as disease-free survival (DFS), relapse-free survival (RFS), event-free survival (EFS), progression-free survival (PFS), and other oncology endpoints. Perspectives on clinical outcomes from people with cancer, health practitioners, industry and caregivers must also be included in evaluations.
- **Quality of life and wellbeing value,** by analyzing the physical, emotional, and psychological impacts of cancer and its treatments on people with cancer.
- **Economic value,** by including a broader range of direct and indirect costs to healthcare systems, individuals, and society. Long-established components of value assessments can be complemented by methodologies to consider aspects such as the value of hope and choice as well as insurance value.

Making this a reality

Redefining value in oncology will require concerted action and collaboration across many different stakeholders:

We need to refocus HTA and payer decisions on the needs of people living with cancer and caregivers

Actions

» Patient advocacy groups (PAGs) and caregiver groups need to be supported to proactively engage in health technology assessment (HTA) and payer decision-making processes.

» HTAs and payers need to actively invite PAGs and caregivers to incorporate their insights and inform the decision-making process.

» The clinical, research, PAG, and health economics communities need to co-develop international standards and consensus on patient reported outcomes (PROs).

» Health economists, in collaboration with other stakeholders, need to find consensus on, and develop new metrics for, wider value that complement the quality-adjusted life year (QALY).

Facilitating action in LMICs

» National and regional PAGs should seek support from international PAG networks operating in the same or similar disease areas in the form of sharing best practice, knowledge, or resources.

» Where they exist, HTAs and payers should take a more active role in sourcing insights from lived experience. Where possible, they should seek support from HTAs in other countries to learn about and facilitate PAG participation.

» National and regional members of the clinical, research, and PAG communities should work together to adapt current and future standards for PROs, so insights from people with cancer in LMICs are collected and available to support decision-making.

We need appropriate infrastructure to support assessment, reimbursement, and reassessment of innovative oncology therapies

Actions

» Policymakers need to create appropriate legislative and governance frameworks for innovative contracting mechanisms.

» Pharmaceutical developers should commit to undertaking and facilitating data collection to support innovative contracting mechanisms.

» Payers and pharmaceutical developers need appropriate value-based infrastructure to enable the calculation and processing of specific payments or rebates.

» Health system decision-makers need to invest in capacity and infrastructure to ensure timely adoption of effective treatments once approved and reimbursed.

Facilitating action in LMICs

» Countries with experience with innovative contracting models should share best practices so that LMICs can learn about the challenges, minimum requirements, and potential best practices to introduce these models in the future.

» Initial roll-out of smaller pilot schemes could allow LMIC payers to trial new medicines at a smaller investment rate and scale up successful schemes once the value of investment has been demonstrated.

» National and regional policymakers, scientific agencies, pharmaceutical developers and the wider scientific community should look to develop interoperable data collection infrastructure for long-term data collection and analysis.

» Pharmaceutical developers should actively support access in LMICs and offer pricing flexibility or logistical support for medicine distribution.

We need to advance science policy and collaboration among government entities	**Actions** » Policymakers, scientific agencies, pharmaceutical developers, and the wider scientific community need new mechanisms to bridge the gap between the science of innovative therapies and their application within health systems. » National HTAs, payers, regulators, and pharmaceutical developers need to align more closely on the evidence they accept. » HTAs and regulators around the world need to improve global collaboration and coordination. **Facilitating action in LMICs** » National and regional policymakers, scientific agencies, pharmaceutical developers, and the wider scientific community should facilitate greater access to clinical trials in their countries. » International collaborations should include LMIC HTAs and payers, or at least share information with them, so they can benefit from shared knowledge. » Payers in LMICs should proactively use overseas assessments from well-established HTA agencies to inform decision-making. However, they should not rely solely on these, as their decisions should also be informed by local population needs and culture.
We need to use data to mitigate uncertainty and inform reimbursement and pricing decisions	**Actions** » Payers and pharmaceutical developers need to develop a reliable data generation model to inform contract development, agreement and implementation. » Public and private bodies need to invest in building data collection capabilities. » HTA agencies, the research community, and pharmaceutical developers need to build trust in the use of real-world data. **Facilitating action in LMICs** » Members of the national and regional clinical and research communities should utilize internationally standardized datasets and contribute to international and regional databases where possible. » Health systems across the globe can take steps to support real-world data collection by broadening the use of electronic health records (EHRs). » Pharmaceutical developers should continue to have some flexibility on pricing so that LMICs are not expected to reimburse at the same rates as high-income countries (HICs).
We need to secure alignment on clinical value with clear, timely guideline updates and communication	**Actions** » Medical societies and PAGs need to collaborate and align on the clinical value of different endpoints and publish guidance on their use for different types and stages of cancer. » Medical societies and the scientific community need to regularly update guidelines with input from PAGs and pharmaceutical developers to ensure they remain up to date on the latest innovations. **Facilitating action in LMICs** » International medical societies and the scientific community should consider how to prioritize their recommendations and guidelines to ensure that their work is easily accessible and usable for LMICs. » National and regional PAGs, medical societies and members of the scientific community should develop their own consensus positions and resources to support regulatory decision-making and priority-setting in LMICs.

We need to incorporate broader perspectives and measures of economic value

Actions

» Payers and HTAs need to proactively communicate and ensure a balance of consistency and flexibility in the evidence they accept.

» Payers and HTAs need to introduce longer-term analyses and include the indirect economic impact of medicines, particularly for early-stage disease.

» HTAs should prioritize innovative treatments, including for cancers with high unmet need, for expedited review.

Facilitating action in LMICs

» LMICs should manage limited regulatory and HTA agency capacity by prioritizing the review and assessment of medicines targeting disease areas with the greatest unmet need.

» LMIC payers should carefully consider broader economic costs, such as gross domestic product (GDP) reductions due to health-related productivity loss, in order to prioritize medicines with the greatest potential impact in their countries.

The growing cancer burden means we must act now to improve access to oncology medicines. These recommendations offer a global blueprint for evolving how value is assessed in oncology so that value assessments reflect what matters most to people living with cancer and their families, while recognizing the budget considerations this may have.





01
Case for change

1.1.
Why is it important to evolve value assessment?

We stand at the forefront of science, research and innovation in oncology, The oncology landscape is perpetually evolving, driven by scientific advancements that promise to redefine how we understand, diagnose, treat, and support people living with cancer.

Recent decades have seen a paradigm shift to earlier diagnoses in many cancers.[1] Early diagnosis and timely access to effective cancer treatment can support better survival rates and better QoL for people living with cancer.[13,14] In the US, the rate of people with some cancers receiving their diagnosis at the localized or early stage is steadily increasing.[15] For example, over 94% of women in the US are diagnosed with breast cancer before it has metastasized.[16] Screening, early diagnosis, and intervention lead to improved outcomes and reduced financial strain on healthcare systems since cancer treatments are generally less expensive when the disease is diagnosed earlier.[17,18] The economic benefit is clear: screening and detection for early-stage breast, colorectal, cervical and lung cancers, has delivered estimated savings of between $8.2 and $11.3 trillion in the US.[19]

Medical innovations present promising opportunities to treat the disease at earlier stages of progression and better meet the needs of people living with cancer and health systems. With the advent of more innovative, targeted, and personalized approaches, some of which may be suitable for early cancer stages, treatments may not only be more effective but may in some cases come with fewer side effects.[2,3,20] This can have the potential to improve the overall physical and mental wellbeing of people living with cancer during their treatment. In HICs with earlier diagnosis and timely access to these innovations, 1-year and 5-year survival rates have markedly increased across almost all cancer types.[21]

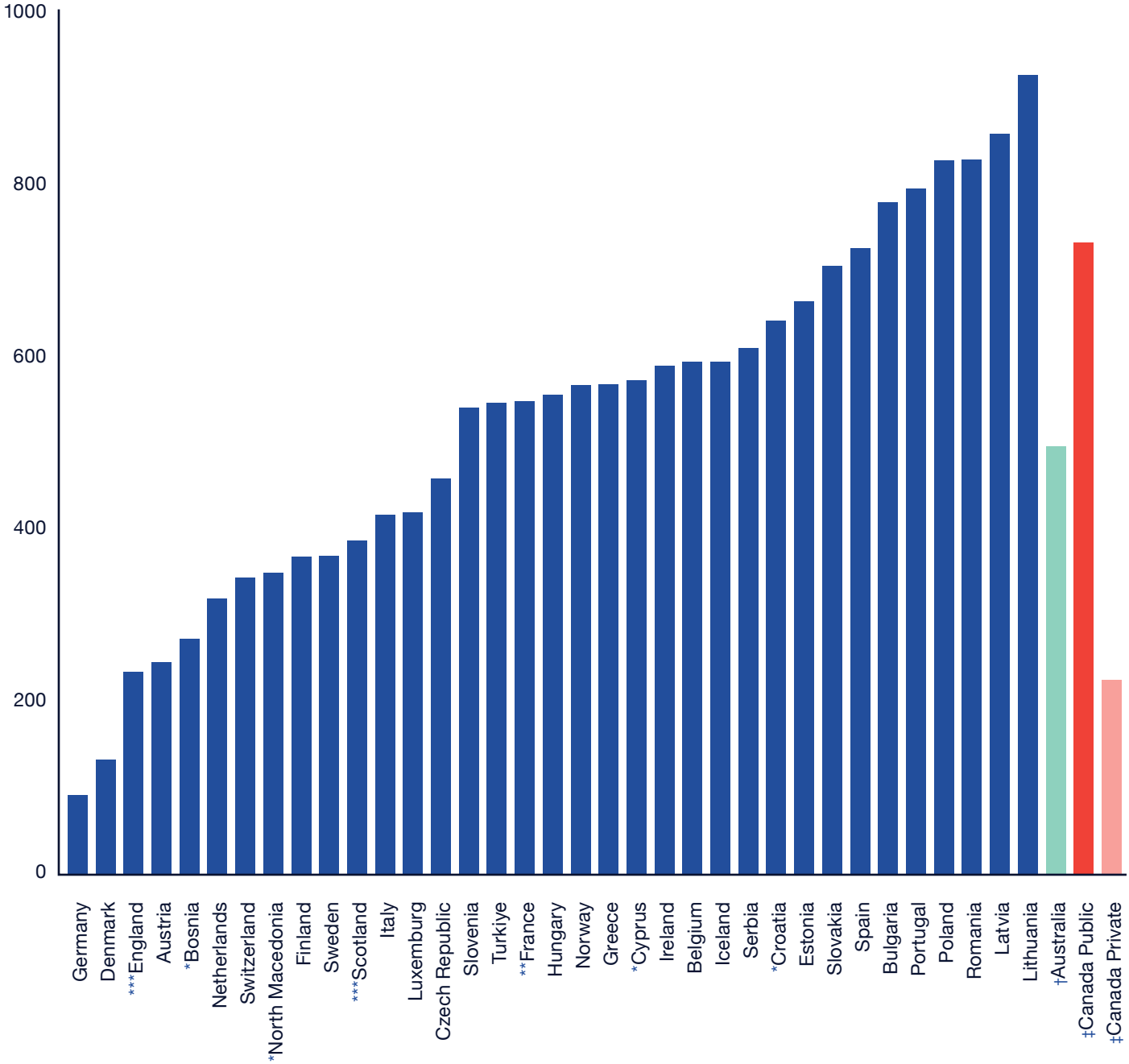
However, despite advancements, the global burden of cancer remains high and health systems around the world are unable to keep up with this growing need. The burden of cancer is growing in almost every country around the world,[22] and it is the leading cause of death in over 50 countries.[23] It is estimated that cancer will cost the global economy $25.2 trillion between 2020 and 2050.[24] However, this burden is not equal: 70% of total global deaths from cancer occur in LMICs.[8] HICs face the highest economic impact from cancer at a national level, but LMICs still experience a significant economic burden.[24] Furthermore, a large proportion of people with cancer in LMICs receive a diagnosis of advanced disease, limiting their chances for curative intent treatment,[25] and further contributing to disparities in outcomes.

There is still significant global disparity in access to oncology medicines.[26, 27, 28] Between 2019 and 2022, the average time to availability of oncology medicines across all 27 EU member states was 559 days, up from 526 days between 2018 and 2021.[5] However, a 'drug lag' also exists within and between countries. The average delay from marketing authorization to patient access to oncology medicines varied from 3 months to more than 2.5 years across European countries between 2019 and 2022.[5] People living with cancer were waiting 93 days on average in Germany and 134 days in Denmark for newly authorized oncology medicines to be available – whereas in Romania, Latvia and Lithuania people were waiting 828, 858, and 926 days on average, respectively.[5] However, the European Commission's Regulation on Health Technology Assessment (HTAR) aims to tackle this issue and improve the availability of health technologies in Europe.[9] It is important to note that LMICs have considerably lower access to oncology medicines than other countries.[29] For example, in LMICs, up to 57.7% of the cancer medicines on the essential medicines list are only accessible to people if they can pay the entire cost themselves.[30]

We must ensure that all people living with cancer can benefit from these scientific advances. More people than ever are living with cancer. In 2022, the International Agency for Research on Cancer estimated that there were 20.0 million new cases worldwide, but this is set to increase by 76.5% by 2050 to 35.3 million new cases per year.[7] As cancer treatments become more targeted and complex, we must understand their full value and ensure they quickly and equitably reach the people who could benefit.

Time to availability of cancer medicines 2019-2022[5,31,32]

- Europe – time to oncology access and reimbursement across all EU states at time of publication.
- Australia – time to oncology access and reimbursement is 496 days.
- Canada – time to access and reimbursement for all drugs.



European country data is correct to 5th January 2024

* Countries that did not complete a full data set and therefore availability may be unrepresentative;

** For France, some innovative products without competitors can be made available prior to market authorization under the system of Temporary Authorizations. As these are not taken into account in the analysis, the average would be lower.

*** In the UK, MHRA's Early Access to Medicines Scheme provides access prior to marketing authorization, but is not included within this analysis, and would reduce the overall days for a small subset of medicines;

† Australian data is the average number of days it takes for medicine to be reimbursed on the PBS after it is registered (2015-2020);

‡ Canada data apples to all therapy areas as they do not have specific data for oncology.

1.2.
Why is it important to measure patient benefit differently?

Our understanding of the biology of cancer has rapidly evolved in recent years, leading to innovation. This means we have a better understanding of how to treat cancer at a molecular level than ever before.[25,33] This has led to new classes of therapies and increasingly targeted approaches being developed and tested in clinical trials.[34] Furthermore, tools like Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) and Artificial Intelligence (AI) could continue to transform the research and development process in oncology and lead to newer and more effective therapies in the coming years.[35,36]

Given these advances, now and in the future, methods to understand the effectiveness of an oncology treatment need re-assessment. The traditional endpoint used to assess the effectiveness of cancer treatments is overall survival (OS). However, this metric is not always appropriate for early-stage cancer treatments due to the time required or feasibility challenges of collecting these data.[3,37] Furthermore, the effect of a treatment on OS may be impacted by subsequent treatments for the cancer, and death unrelated to the cancer.[38,39] HTA agencies and payers must therefore work with this uncertainty when assessing value in these cases where OS is not available at the time of reimbursement. However, it is important to weigh up the potential benefits of comprehensive, more complete data against delayed patient access to more treatment options.[3] Some non-OS endpoints – including disease-free survival (DFS), relapse-free survival (RFS), event-free survival (EFS), and progression-free survival (PFS) – are being used to help address these concerns and collect valuable efficacy data earlier than OS.[39]

We need to rethink our approach to measuring value in oncology. The current emphasis on OS and other long-term outcomes, cost-effectiveness analysis, and short-term budget impact means value assessment often fails to capture the full benefit of medicines to people living with cancer and society. These broader components of value include lower symptom burden, improved QoL, reduced hospitalization rates, and increased productivity.[3,40,41,42] The need to consider all aspects of value and measure value differently is not just compelling – it is critical.

1.3.
What is the vision for the future?

Evolving value assessment processes can help mitigate the significant level of unmet needs in oncology care. With the global cancer burden estimated to rise by 76.5% between 2022 and 2050,[7] we must realize the potential of these scientific advances to address the needs of the cancer community globally. By adapting how we value new oncology medicines, particularly for early-stage cancers, we can facilitate earlier treatment, improve outcomes, and significantly reduce the growing burden that oncology care and treatment places on health systems around the world.[43]

Measuring value differently means embracing new, more societal perspectives on clinical and economic value. It means integrating endpoints that reflect real-world outcomes, considering the psychosocial dimensions of care, and accounting for the broader economic and societal implications of innovative therapies. These models need to be flexible for each cancer type. But in doing so, we must ensure that the metrics by which we measure value are as sophisticated and multifaceted as the treatments they seek to evaluate.

The next sections of this report outline the opportunities presented by these increased scientific capabilities and the pressing need for systemic change to address the barriers that impede the delivery of these advancements to people living with cancer.

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02

How can we achieve change at a global scale?

2.1. Clinical value

2.1.1. What is clinical value?

Although there is no singular definition,[44] clinical value can broadly be defined as the quantitative measurement of changing health indicators as a result of undergoing a given treatment(s), encompassing aspects such as efficacy and safety.[45,46]

2.1.2. What should we value?

Many people value survival as a fundamental outcome when assessing the benefits of new cancer medicines. Across multiple surveys and different cancer types, survival is the most important clinical metric for people living with cancer.[45,47,48]

However, people living with cancer also place high importance on other clinical outcomes related to their cancer. Disease progression, relapse or recurrence, and management of post-treatment side effects are also important.[45,49] They help to understand not just how long a person might live, but how long they might live without experiencing significant complications related to their disease or treatment. Certain studies note that some people may decline treatments that may prolong survival at the expense of symptom burden, side-effects, QoL,[50,51,52] and financial toxicity for their families.[53]

In the context of expanding treatment choices, patients and clinicians must navigate a delicate balance of clinical value and personal preferences to determine the optimal treatment strategy. As targeted and immuno-oncology therapies emerge, early-stage interventions become increasingly common.[54] This may mean better clinical outcomes and a shift in treatment goals.[55,56] People living with cancer and clinicians therefore need to understand the clinical value of all treatment options to jointly identify the right treatment path which fully aligns with the person's needs and preferences.

"Clinical value is a multifaceted concept that requires a comprehensive evaluation of various factors. By systematically assessing efficacy, safety, quality of life, economic impact, and other critical dimensions, healthcare providers and policymakers can make informed decisions that maximize patient outcomes and resource utilization."

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2.1.3.
How do we measure what we value?

OS is a commonly used metric to understand how long people live after treatment.[57] This definitive and precise endpoint is the gold standard for measuring the treatment benefit of cancer therapy,[58] and is the mainstay of how many HTAs and payers assess clinical value.[3,59,60]

As therapies became more advanced, and people with cancer started surviving for many years after treatment, limitations of OS data have emerged. OS data become increasingly hard to collect if treatments are potentially curative or if the cancer displays slow clinical progression.[61] As many people with early-stage cancer undergo long-term maintenance treatment, OS measures in this setting can be confounded by subsequent therapies. Furthermore, OS data collection requires operational capabilities and associated investment over a certain time frame,[62] which is not always feasible.

When OS data are not available or feasible, we need new and more dynamic approaches to look at clinical value. Endpoints were developed and are now being utilized to assess clinical benefit beyond survival.[63] These endpoints aim to better reflect aspects that both patients and healthcare professionals value: the time during which people on treatment can maintain a certain level of QoL without disease progression.[43,64]

Examples include*:

- **DFS** or **RFS** is the length of time after primary treatment for cancer ends that the patient survives without any signs or symptoms of that cancer.[65]
- **EFS** is the length of time after primary treatment for cancer ends that the patient remains free of certain complications or events that the treatment was intended to prevent or delay. These may include the return of the cancer or the onset of certain symptoms.[66]
- **PFS** is the length of time during and after cancer treatment that a person lives with the disease, but it does not get worse.[67]

As we learn more about cancer and new scientific techniques have emerged, we find even better ways of looking at clinical value. Given further research, these new metrics could facilitate even earlier, more personalized treatment choices, continual monitoring, quicker treatment optimization, and ultimately improved outcomes.[68,69]

- Metrics already under use in certain settings include:
  - **Pathologic complete response (pCR).** This metric looks for the signs of cancer in tissue samples removed during surgery or biopsy after treatment.[70] It is increasingly being used in conjunction with other non-OS endpoints, however, further research is required for greater and more consistent use.[71,72]
  - **Minimal residual disease (MRD).** This metric refers to the number of cancer cells that are left in the body after cancer treatment.[73] Studies have found that undetectable MRD strongly correlates with favourable outcomes in people with multiple myeloma, including PFS and OS.[74] Further research is needed to understand how it can be optimally used in clinical settings.[75]
- Biomarkers on the horizon include:
  - **Circulating tumour DNA (ctDNA).** This approach uses a blood test to measure the amount of DNA from cancerous cells and tumours found in the blood of the person with cancer.[76] It can be measured via a process called liquid biopsy. It is highly sensitive[77] and could be valuable in detecting cancer before symptoms emerge and monitoring the earliest possible response to therapies.[78] Further research is required to better understand how this could be used in the future.[79]

*These definitions are from the National Cancer Institute (NCI) Dictionary of Cancer Terms

2.1.4.
How do we currently use these metrics?

Endpoints from clinical trials are used to understand clinical benefits and inform decisions about new cancer therapies. HTA bodies systematically evaluate the clinical, social, economic, organizational, and ethical impacts of a health technology and recommend or decide if it should be available at a regional or national level.[80] Payers then assess whether the benefits, risks and value of the treatment justify the costs, and how the new treatment compares to the existing standard of care before deciding if the technology should be reimbursed and negotiating a price with the pharmaceutical developer.[37] Both HTA agencies and payers currently consider endpoints other than OS, but there isn't a uniform approach to the weight these endpoints carry in decision-making.[37]

Endpoints are not 'one size fits all' and the clinical context of each cancer should be assessed to ensure an appropriate endpoint is used. Relevant endpoints for each type of cancer need to be chosen based on the stage, subtype, life expectancy, and treatment goals.[60,81] For example, for early-stage cancers, where the aims of treatment may be curative intent, non-OS endpoints need to be chosen. Genetics also need to be considered as oncology treatments become increasingly personalized.[82] This complexity and variability means that HTAs must consider information on a case-by-case basis, with limited transferability from one cancer treatment to the next. This analysis requires highly skilled teams working across a high volume of very complex cases.

The relationship between OS and other endpoints is unclear at the time of reimbursement decision-making, leading to inconsistent access decisions between different countries. For payers, this uncertainty can be challenging and requires a careful balance.[61,83] Either reimburse a medicine without knowing its full clinical benefit, allowing people to access the potential value observed in other clinical trial endpoints; or wait for mature, possibly statistically significant OS and have people miss out on the new treatment for the intervening years. It is a challenging situation and one that often ends with payer reluctance to move beyond the use of OS in their decision-making frameworks.[37,81] The ESMO-Magnitude of Clinical Benefit Scale (ESMO-MCBS) has been used by payers to tackle this challenge, contextualizing likely treatment benefits to support reimbursement decision-making.[84,85]

Additional endpoints may help to alleviate uncertainty, define value, and improve access to more therapeutic options for people living with cancer. Some examples of how this works in specific cancers are outlined below:

- Leukaemia-free survival has recently been shown to be an alternative to OS for people with acute myeloid leukaemia.[86,87]
- EFS can be used to support the approval of treatments for breast cancer and neuroblastoma and adjuvant treatment of melanoma.[88,89]
- DFS has been used as an alternative endpoint for OS in clinical trials for colon cancer, breast cancer and in an adjuvant setting in lung cancer.[39]
- The US Food and Drug Administration (FDA) Oncology Drugs Advisory Committee voted to adopt MRD as an endpoint in accelerated approvals of medicines for multiple myeloma.[90]
- The FDA has approved drugs in several cancers, including non-small cell lung cancer (NSCLC), colorectal cancer, and head and neck cancer, using PFS rather than OS as the surrogate endpoint.[88]

There is a lack of consistency and alignment on the clinical value of these different endpoints between regulators and payers. Regulators and payers have specific remits and utilize different evidence requirements to assess therapies. Regulators employ benefit-risk frameworks to support marketing authorization; whereas HTA agencies utilize comparative effectiveness and cost-effectiveness frameworks to support reimbursement.[83] As such, regulators might approve drugs based on various oncology endpoints, while payers often seek more evidence on added clinical value, ethics, and quality of life before reimbursing.[83,91] More needs to be done to support payers with evidence that can be utilized in reimbursement decisions. This may help to tackle noted access challenges following marketing authorization, particularly when regulators approve drugs using accelerated approval pathways.[92,93] By reducing evidence misalignment between regulators and payers, challenges to timely patient access and affordability of new medicines may be reduced.

The scientific and medical communities may also contribute to this fragmented landscape. Limited consensus and guidance on which endpoints are the most valuable in specific situations and how to use them in a practical way may also further challenge HTA and payer decision-making.[94] It is important to tackle the misconception that endpoints are universally applicable and establish guidance on which endpoints should be used based on the type of cancer, genetics driving the disease, if applicable, and stage of disease alongside other relevant factors.[59,95]

2.2. Quality of life and wellbeing value

2.2.1. What is quality of life and wellbeing?

The World Health Organization (WHO) defines QoL as an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns.[96] Many clinical trials measure QoL aspects of an individual's sense of wellbeing and ability to carry out activities of daily living.[97]

Wellbeing is a holistic concept that goes beyond physical health and includes an individual's emotional, social, and psychological health.[98,99]

2.2.2. What should we value?

The physical, emotional, and psychological impact of cancer and cancer treatment can be significant and wide-ranging.[100,101,102] Approximately 30% to 40% of cancer patients experience some mental health or psychiatric issues.[101,102] In the past, improved survival outcomes were achieved at the expense of QoL and health-related QoL (HRQoL), but now some more targeted therapies offer treatment with fewer side effects.[103] Therefore, it is important to consider the person with cancer an individual, listen to what matters to them and consider their QoL when looking at value. This will benefit not just the person living with cancer and their family, but society more widely.

The value of wellbeing, particularly in the context of healthcare and oncology, is increasingly recognized as essential for comprehensive person-centered care. It encompasses physical, emotional, mental, and social dimensions, aiming to improve overall QoL, especially for those facing chronic or life-threatening conditions such as cancer.

There are many aspects to QoL and wellbeing which are valued by people living with cancer, regardless of cancer type or treatment plan.

These include:

- **Functional independence** to perform activities of daily life and maintain independence, autonomy, and participation in work.[104]
- **Social integration** to maintain social connections and fulfil roles within their family and community.[105]
- **Psychological and mental health** to support and address the emotional challenges of living with cancer, and navigate the complexities of the disease and treatment.[106]

Cancer can lead to social isolation and loneliness that impact QoL and wellbeing. Reducing social isolation, loneliness, and the psychosocial impacts of cancer are not only important for QoL, but also improve health outcomes.

For example:

- In a study of five different cancer types involving 20,582 patients, there was an increased mortality risk in those with severe depression compared to those without, across all five cancer types.[107]
- In a study of 123 participants with stage IV NSCLC or small cell lung cancer, the mean survival for those with versus without depression was 323.6 days compared to 558 days.[108]

Some clinical values – such as safety, efficacy, and symptom relief – are also relevant to QoL and wellbeing, feeding into the components outlined above.[50,109,110]

People living with cancer may value broader aspects of treatment which also impact wellbeing.

These include:

- The **value of choice** recognizes the ability to choose between different treatment options and choose an approach which aligns with a person's health goals.[41] Therefore, it emphasizes having as many choices of treatments as possible.

"Measuring quality of life and wellbeing recognizes that the experience of each individual impacted by cancer is unique and respects the dignity of each person. Quality of life and wellbeing go beyond the diagnosis to focus on uplifting and strengthening people living with cancer--and their caregivers-- by embracing hope, connection, and whole person care."

Daneen Sekoni, MHSA
Vice President, Policy & Advocacy, Cancer Support Community, USA

» The **value of hope** acknowledges the psychological benefit of having a possibly effective treatment.[111] Many severely ill patients may be willing to trade some survival – for example by undertaking a risky procedure – for a chance at a "cure", even only for a small probability of increased survival or cure.[112]

Cancer and cancer treatment also impact family members and caregivers. Caregivers can experience physical and emotional challenges, many reporting significant issues with their physical and psychological wellbeing. Some studies have found that the effect of a cancer diagnosis can be more profound on family members than the patients themselves – both emotionally and due to increased caregiving responsibilities and financial costs.[113] Taking caregiver and family member wellbeing into consideration is therefore paramount, and efforts are being made by some HTA agencies to bring family member experiences into assessments.[114]

2.2.3. How do we measure what we value?

Many quantitative and qualitative metrics have been developed to understand and value patient wellbeing.

These metrics and categories of metrics include:

» **Patient Reported Outcomes (PROs)** gather a person's perspective of their health, the impact of disease, and the effect of treatments through questionnaires.[115] They look to evaluate symptoms, side effects, functionality, and overall QoL.[115] PROs need to capture insights into diverse populations and cultures.[116] This data offers important insights into the cancer's influence on daily life, mental health, and social wellbeing.[117]

Example PRO Tool:

» The Organization for Economic Cooperation and Development (OECD) has established the Patient-Reported Indicator Surveys (PARIS) initiative, where countries work together on developing, standardizing, and implementing new indicators that measure the outcomes and experiences of healthcare, largely focusing on primary care.[118]

» **QoL Assessments**, evaluate overall wellbeing and satisfaction with life and look to evaluate the impact of their health condition and treatments as well as other non-health factors.[96] QoL assessments are one type of PRO. A subset of QoL is health-related QoL, which focuses specifically on assessing the direct impact of health conditions and their treatments on aspects of life that are related to physical, mental, and social wellbeing.[119] These are used as a valuable metric alongside survival.[120,121]

Examples of these tools include:

» European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30)[122]

» Functional Assessment of Cancer Therapy – General (FACT-G)[123]

» The World Health Organization's Quality of Life (WHOQOL) instrument[96]

» EuroQol Group's EQ-5D-3L instrument[124]

Payers often prefer the more generic measures or health utility measures that give one simple score for QoL.[125] However, these do not always capture cancer specific impacts or nationally specific preference.[126,127]

Despite the wide variety of tools, the type of PRO instruments used can be variable. HTA agencies and payers often do not accept these instruments or hold the same weight against them as compared to other outcome measures. This can be because the data may be incomplete or low quality.[128,129] The multitude of PRO tools, each with unique methods, adds additional complexity to data collection and leads to a disjointed environment that challenges the incorporation of PRO data into clinical and policy decisions.[130,131,132] Furthermore, people living with health conditions frequently express concerns about these tools: they may not be engaged in their development,[133] or the process is burdensome or not transparent.[134,135] Therefore they feel that the tools do not always fully encapsulate the nuances of their lived experiences or the outcomes they deem most significant.[133] This ultimately leads to significant inconsistencies in the patient-perceived value of treatments, potentially impacting which treatments are recommended or reimbursed.[136] HTA agencies and payers should develop a broad approach to patient and caregiver engagement, including the development, validation, and application of PRO tools.[132]

Other elements of value that are important to people living with cancer are difficult to measure. Alongside the value of choice and hope, there are other measures which are increasingly being recognized as important components of value assessment.[112] These include the real option value, which captures the value of having flexibility in making future treatment decisions,[112] and may have an impact on psychological components and mental health. However, these metrics are not readily quantifiable, challenging their use in decision-making.[41] Work is underway by various groups, including the International Society for Pharmacoeconomics and Outcomes Research (ISPOR),[137] the European Society of Medical Oncology (ESMO),[138] the Center for Innovation and Value Research,[139] and the OECD[140] to implement these metrics and support their wider use in the future.

2.2.4.
How do we incorporate these measures in current HTA frameworks?

The implementation of these new metrics can be seen in various national health systems. Table 1 outlines this and the following case studies provide further detail on how additional metrics are utilized:

» **England** utilizes the EQ-5D instrument to routinely measure PROs as part of a National Health Service (NHS) PRO Measures program.[141,142] However, there is a focus on generic instruments,[143] which means the full benefit of treatments for early-stage cancer is not always captured.

» In **Sweden**, the Swedish Dental and Pharmaceutical Benefits Agency (TLV) has been exploring the inclusion of wider social values in their assessments, taking into account the impact on caregivers and the person living with cancer's ability to participate in work and social life.[114,144]

To see how other countries have ingrained wellbeing metrics into their decision-making process, please see Table 1.



Table 1. Table 1. Comparison of the extent to which PROs and health-related QoL are included in national HTA decision-making

Country	HTA body	Valuation of health-related QoL and preferred source*	What is formally included in the HTA guidelines? Note, that these guidelines are not oncology-specific.	Are PROs used in other parts of the HTA assessment?
Australia	Pharmaceutical Benefits Advisory Committee (PBAC)	Public[145]	PROs are mentioned within guidelines to be included as details to inform clinical health outcomes in models for economic evaluation.[128] However, they are not mentioned as relevant efficacy endpoints. And no standardized instrument is recommended.[128,146]	No specific recommendations but examples provided.[147]
Brazil	National Committee for Health Technology Incorporation (CONITEC)	Public[148]	PROs are used in the HTA process in cost-utility analysis.[148]	There are examples of EQ-5D-3L and other instruments being used and included in the REBRATS's guideline.[149] EQ-5D validated in Brazil, based on local population norms, increasing its applicability in national assessments.[150]
Canada	Canada's Drug Agency (CDA)	Public[151]	A generic system for utility scoring like EQ-5D and other measures is recommended.[145]	No formal guidance for their use, but there is evidence of these being used in practice.[128,151]
England	National Institute for Health and Care Excellence (NICE)	Public[151]	PROs are included as part of the cost-effectiveness evaluation and EQ-5D is the preferred instrument.[152]	No formal guidance for their use, but there is evidence of these being used in practice.[151]
France	Haute Autorité de santé (HAS)	Public[151]	Health-related QoL is explicitly included. However, the methodological standards are as high as for efficacy data and other endpoints, which may be a barrier to PRO data being acceptable.[153]	The HAS Doctrine states that rigorous demonstration of QoL benefits may increase the clinical added value given to a product, limiting the scope of the assessment to pure clinical efficacy.[153]
Germany	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (IQWiG)	Patients[151]	Health-related QoL data is integral and ranked equally important to morbidity data.[134]	PROs are used as sources of additional evidence for the deliberative process[154] and PRO data can result in added benefit based on patient-relevant endpoints such as morbidity and Health-related QoL.[134]
Italy	Agenzia Italiana del Farmaco (AIFA)	Preferred source not specified[151]	Guidance does not include the role of patients in their assessment processes in any detail.[151]	No evidence found.

Japan 	Center For Outcomes Research And Economic Evaluation For Health (C2H)	Public[147]	EQ-5D-5L is formally included in guidelines for cost-utility analysis[147] and quantitative PROs are used in the assessment of costs and benefits.[147]	No evidence found.
Singapore 	Agency for Care Effectiveness (ACE)	Public[155]	There is a preference for using generic systems for utility scoring like EQ-5D, but disease-specific measures for health-related QoL can be presented as supplementary analyses.[155]	No evidence found.
South Korea 	Health Insurance Review and Assessment Service (HIRA)	No evidence found.	No evidence found.	There are examples of EQ-5D-5L and other instruments being used, but there are no specific recommendations.[147]
Sweden 	Dental and Pharmaceutical Benefits Agency (TLV)	Patients or public[151]	PRO evidence is provided through quantitative studies and is used in the assessment of costs and benefits.[147] Specific instruments were not discussed, however, the process does not primarily rely on the QALY.[151]	There is a flexible and pragmatic approach in how it accepts various forms of patient evidence.[151] There are examples of EQ-5D-5L, and other instruments being used, but no tool is included specifically in the guidelines.[147]

* Public – data is collected from the general population. I.e., members of the public are asked to hypothetically think about what it would be like to be in different health states.[156]

** Patient – data collected from real patients about being in different health states. While this process might be somewhat hypothetical, patients will generally have a better idea of what being in that health state is really like.[156]

2.3. Economic value

2.3.1. What is economic value?

Economic value is the consideration of value for money, including measurement of direct and indirect costs to the healthcare system, individuals and society.[41,157]

2.3.2. What should we value?

Economic value is a function of cost and benefit. These benefits may include years of survival, QoL, or other metrics that matter to patients, clinicians, health systems, and policymakers.

Costs can include:

- **Health system costs**
  - **Direct costs of healthcare**, for instance, costs of drug acquisition, diagnostic tests, administration, and management of adverse events.[158]
  - **Indirect cost to the health system** such as changes in healthcare resource utilization, including expenses from hospitalization and outpatient visits.[3,159]
- **Patient and caregiver costs**
  - **Rate of individual employment and productivity** is impacted by the ability of people living with cancer to maintain full-time work. Cancer can affect personal performance, working hours, and job-retention, and consequently impact national income, productivity, and employment rates.[160] Caregivers also experience these costs.[160]
  - **Out-of-pocket (OOP) costs** include patient medical expenses like treatment and medications.[160] Cancer care is often associated with high OOP costs, estimated as average proportion of income spent as non-reimbursable costs.[161]
  - **Non-medical expenses** including travel for treatment, home care, lodging, nutrition, and childcare costs are paid for by family members, caregivers, and patients.[160]
- **Societal costs**
  - **Societal impact costs** help assess the wider societal costs that fall outside the healthcare system.[162] These societal costs might be productivity costs to society from people with cancer or caregivers unable to work, and costs to other government sectors.[162] Please see Case Study 1 for more information on measuring productivity.
  - **Scientific spillover** reflects that technological breakthroughs can potentially have scientific spillover benefits that enable advances beyond the current product or indication.[41]
  - **Insurance value** reflects the benefit of being protected from the physical and financial burden of illness due to the availability of a new medicine.[163] While it can be difficult to quantify and there is no consensus on how to capture this component,[41] it is nevertheless important to understand and value.[41]
  - **Real option value** reflects the benefit when treatments extend the lives and wellbeing of people with cancer, so they can benefit from future treatment options.[112] Although it may be difficult to quantify the cost-benefit, requiring a more qualitative approach.[41]

"Health systems are operating under difficult financial circumstances, especially in LMICs. But economic evaluation frameworks tend to focus on direct costs, and under-value longer-term and indirect cost savings that may be seen elsewhere in the system or society. This means the full economic value of medicines is not captured – potentially impacting patient access to innovative therapies."

Stephen Stefani, MD, MBA
Head of Health Technology Assessment, UNIMED, Brazil



It is important to recognize that health system decision-making often focuses on finite, short-term budgets, rather than longer-term funding allocations. This means costs need to be managed, but also that there is an opportunity for longer-term return on investment and cost savings from introducing effective interventions. This will be important for LMICs, where limited resources and constrained healthcare budgets mean the high upfront costs associated with innovative treatments may not be affordable.[164]

Case study 1
Importance of measuring improved productivity

Assessing productivity may help capture the broader socioeconomic effect of cancer medicines.[112] The global economic burden of cancer is significant, marked by rising healthcare costs and lost productivity driven by morbidity and premature death from cancer.[165]

For example:

- In the US in 2017, the estimated cancer healthcare spending was US$161.2 billion, and productivity losses from morbidity and premature mortality were reported to be US$30.3 billion and US$150.7 billion, respectively.[165]
- The total burden of cancer in the European Union was estimated to be EUR141.8 billion, which includes healthcare spending of EUR57.3 billion, productivity losses due to morbidity of EUR10.6 billion and premature death of EUR47.9 billion, and informal care costs of EUR26.1 billion.[165]
- Productivity losses due to premature deaths from cancer were estimated to be US$30 billion in China, US$7.2 billion in India, US$5 billion in Brazil, and US$2 billion in South Africa.[165]

2.3.3.
How do we measure what we value?

Economic value measurements in the past have not captured wider economic benefits and the patient experience. The quality-adjusted life year (QALY) has served as a fundamental component of cost-effectiveness analyses of treatments for decades.[166] However, QALYs have their limitations and are sometimes insufficient in capturing the full value for people living with cancer and society.[167,168] Therefore, other methods of economic evaluation are needed to supplement the QALY. For more information on QALYs refer to Box 1.

HTAs and payers have not always had other methodologies and metrics to reliably measure broader value components when making decisions.[169] There are novel approaches which may provide a more nuanced vision of economic value, but standardized methodologies are needed to support their consistent utilization by HTAs and payers.[169,170] Techniques to assess economic value beyond the QALY are outlined below:

- **Generalized Risk-Adjusted Cost-Effectiveness (GRACE)** is a modification of the standard cost-effectiveness analysis.[171] It uses the idea that individuals are willing to trade fewer years of survival for improvements in QoL as they near the end of life.[172] This method helps to capture the value of improving QoL for people with disabilities or those with severe diseases like cancer and may help align HTA practices with what matters most to patients.[172]
- **Multiple Criteria Decision Analysis (MCDA)** has emerged as an alternative or complementary framework with the aim of addressing the limitations of traditional economic evaluation approaches.[173] Aspects such as patient needs, equality and other ethical or social values are incorporated into decision-making about economic value.[174,175] This method is useful to improve the quality of decision-making where decisions are complex and involve trade-offs.[176]
- **Equal Value of Life Years Gained (evLYG)** measures health-related QoL equally for everyone. For instance, a treatment that extends the life of a person with cancer by one year is valued equally to a treatment that adds a year to the life of a healthier person. This may help to eliminate the risk of undervaluing life-extension for people with disabilities or long-term health conditions and reduce risk of discrimination.[166]
- **Health Years in Total (HYT)** separates life expectancy and QoL changes on an additive scale. HYT addresses the discrimination concerns of the QALY and better captures the QoL gains during an added year of life, in comparison to equal value of life (EVL).[177] The modified QALYs are calculated over a timeframe corresponding to the maximum survival of any given alternative treatment.[178]

Box 1:
Quality-Adjusted Life Year (QALY)

The QALY, a traditional economic evaluation method, has served as a fundamental component of cost-effectiveness analyses of treatments around the world for many years.[166,179] It is used to understand the value of an intervention in terms of how it impacts both the quality and quantity of life lived.[41,167]

However, QALYs are insufficient in capturing full value for people living with cancer and society.[167] The QALY does not consider the psychological and emotional dimensions of living with cancer and other health conditions.[41] It also does not look at the broader social implications of treatment, such as the improved wellbeing of caregivers and loved ones.[180] Furthermore, OS is required for the estimation of QALYs,[167] but it is impractical to expect mature OS data for reimbursement decisions in the early-stage cancer setting.[62] Discrimination concerns have also been raised with many groups contending that the QALY is biased against older adults and people living with disabilities.[166] It is argued that the QALY assigns a person living with disability a lower value of a year of life than a person considered to have optimal health. For this reason, in the USA, the Affordable Care Act banned Medicare from using QALYs for use in payer cost-effectiveness analyses, so alternative or complementary solutions are needed, especially if similar legislation is passed in other countries.[181]

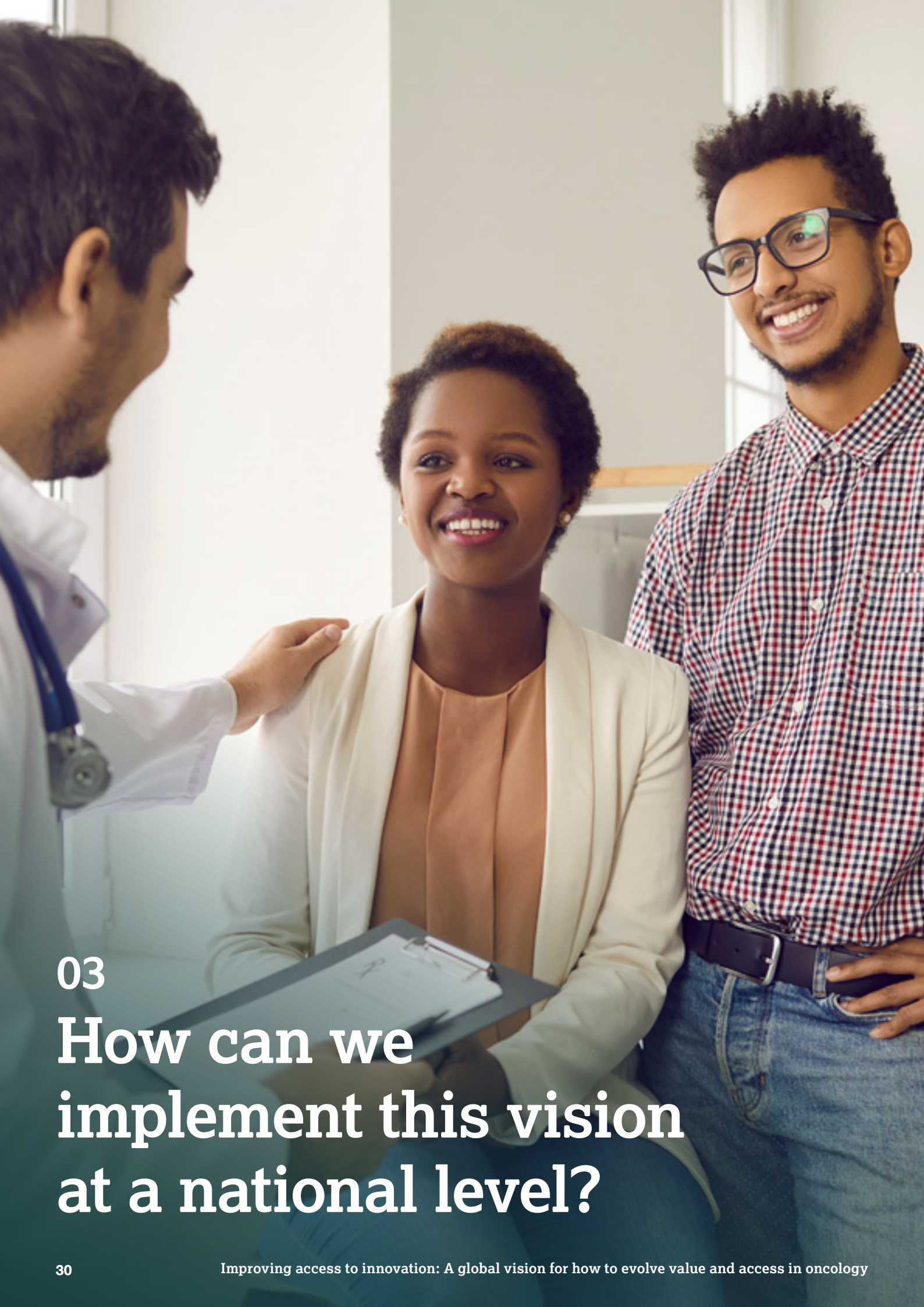
The QALY can provide useful information for decision-making, but it should be used in combination with other measures of health benefit to mitigate its limitations and ensure that what matters most to people living with cancer and society more broadly are reflected in decision-making.

2.3.4.
How do we use these metrics currently in HTA frameworks?

The current HTA frameworks may focus more on direct costs and do not always capture the full economic value of medicines.[41,182] For instance, several countries' payers limit their assessment to the cost impact on the healthcare system.[183] The UK only considers indirect economic costs as additional qualitative information.[184] Where countries apply a narrow scope in their cost-effectiveness analysis to inform HTA decisions, patient access to innovative cancer medicines can be impacted.[185] Scientific spillover is another value component that looks beyond direct costs, and it is observed by PBAC in Australia.[186]

Current frameworks particularly undervalue longer-term cost savings. This short-term focus and siloed budgets often ignore broader economic benefits, like the savings from more people staying employed and paying taxes, as well as reduced healthcare resource utilization. For instance, recent research in Australia found a AUD$3.17 billion return on investment over 5 years in societal benefit of new technologies, therapies, and services that extend the prognosis and HRQoL of people with non-curative cancers.[187] For every AUD$1 invested in cancer treatments, there is AUD$3.06 of social and economic value created.[188]





03
How can we implement this vision at a national level?

The following section outlines key recommendations to turn this vision of value into a reality. It is important to acknowledge the differences in healthcare system maturity, resources, and access to essential and innovative oncology medicines around the globe.[30]

All countries need to re-consider how value is assessed and better reflect what matters most to people living with cancer and their families. The recommendations offer a path to evolving value assessment in healthcare systems through collaborative efforts from stakeholders across the entire oncology ecosystem. They endeavour to make effective cancer treatments universally available, not just to those who can afford them. Some recommendations may be more applicable to HICs than LMICs, but there are specific recommendations for LMICs to work towards these shared goals.

3.1.
We need to refocus HTA and payer decisions on the needs of people living with cancer and caregivers

"HTAs and payers need to fully embrace the holistic needs of the patients and caregivers. But the situation of caregivers is an often underestimated social and public health problem. Better consideration for caregivers could not only improve their quality of life, but also help to ensure continuity of care for patients who depend on them."

Alexandre Brutti
Patient Advocate, Active Member, Mon Réseau Cancer du Poumon; Treasurer, Lung Cancer Europe, France

ACTION

PAGs and caregiver groups need to be supported to proactively engage in HTA and payer decision-making processes.

This will ensure that the perspectives of people living with cancer and caregivers are not only heard, but form an integral part of decision-making.[188,189] Relationships and collaboration could include participating in consultations, contributing patient experiences during evaluations and aiding the development and validation of assessment criteria. **Case Study 2** outlines how different HTAs involve caregiver insights – underscoring the value of direct engagement.

Building these relationships may involve considerable time and rely on support from PAG networks.[190] However, other stakeholders – including academia, pharmaceutical developers, HTAs, and payers – can facilitate improved patient involvement via educational initiatives and partnerships. **Case Studies 3 and 4** outline different initiatives to support patient involvement in assessing value.

Case study 2
Caregiver engagement in HTA processes

Despite their clear value, caregiver insights are included in only a minority of HTA submissions and there is significant variation in what types of data and insights are considered across countries and disease areas.[114]

For example:

- The US Institute for Clinical and Economic Review (ICER) appraisal committees discuss and vote on the impact on caregivers and families through a deliberative approach.[191]
- The German Institute for Quality and Efficiency in Health Care (IQWiG) permits qualitative research methods to understand the experiences of family members.[192]
- The National Institute for Health and Care Excellence (NICE) in the UK requires evidence to demonstrate that the health condition is associated with a substantial effect on caregiver's health related QoL and how the technology under assessments affects caregivers.[159]
- The Swedish Agency for Health Technology Assessment and Assessment of Social Services (SBU) describes how costs and effects are distributed among different stakeholders.[144]

Case study 3
The EUPATI toolbox to train patients

The European Patients' Academy on Therapeutic Innovation (EUPATI) are a non-profit, public-private partnership based in the Netherlands. The group aims to better educate patients and patient representatives, enabling them to contribute to medical research and development.[193] A key offering is their Patient Expert Training Programme, which offers extensive education, training and guidance on aspects such as how patients can be involved in HTA processes.[194] Their resources - the 'toolbox' - have been accessed by more than 6 million users in less than 4 years.[195]

Case study 4
Patient-centered principles for engagement with the Centers for Medicare & Medicaid Services

Cancer Support Community came together with the US patient advocacy community to align on patient-centered principles of engagement and inform a definition of clinical benefit for patients and caregivers that can be used with the Centers for Medicare & Medicaid Services (CMS). This includes calls for improved education for the patient community and infrastructure to facilitate meaningful feedback that prioritizes patient definitions of value. It also considered how best to activate un-engaged and under-served populations to avoid exacerbating existing health equity challenges.[196]



ACTION

HTAs and payers need to actively invite PAGs and caregivers to consistently incorporate their insights and inform the decision-making process.

All HTAs and payers should have structured processes for qualitative patient, PAG and caregiver input, such as regular public consultations and representation on decision-making committees and advisory panels across the entire decision-making lifecycle.[197] However, it is important that input from diverse populations is captured, otherwise the insights that inform decision-making will only reflect certain populations and exacerbate health inequities. To facilitate engagement among patients or caregivers who lack awareness of HTA processes,[198] lay summaries of all relevant HTA documents should be publicly available.[199,200]

Additionally, PROs should be systematically collected, analyzed, and included by HTAs and payers decision-making frameworks with a clear indication of the weight given to patient, PAG, and caregiver input. This will ensure that decisions also reflect quantitative aspects of patient and caregiver experiences, treatment satisfaction, and QoL. PROs chosen should be consensus-driven and based on the most up-to-date international standards and consensus. It will also be valuable to understand the impact of decisions by collecting PROs and other types of insights as experience with a newly approved treatment matures.

ACTION

The clinical, research, PAG, and health economics communities need to co-develop international standards and consensus on PROs.

International standards and consensus will ensure PROs are fit for purpose, are in line with emerging treatments, address the many barriers to use and improve consistency of definitions, measurements, and interpretations across different healthcare systems.[201,202] Any international standards and consensus should be stratified by the level of resources needed and include diverse participation, including practitioners and patients from LMICs, to ensure they are truly representative of different economic, social and cultural values.

These standards will also improve usability for patients, improve administration by researchers, and enhance the quality and completeness of the data collected.[133,201,203,204] Each of these steps will help to increase the generalizability and applicability of research findings. **Case Studies 5 and 6** outline important initiatives to improve data collection and utilization.

Case study 5

Reviewing PRO methodologies in Canada

The Centre for Advancing Health Outcomes in Canada is working to update PRO measures and the methodologies behind them.[205,206] In particular, they test different PRO tools with the aim of creating standardized statistical models to, in time, make PROs both reliable and comparable for use in HTA decision-making frameworks.

Case study 6

EAU's UroEvidenceHub data innovation program

The European Association of Urology's (EAU) UroEvidenceHub is a new data innovation program, aiming to become a hub for urologists seeking high-quality personalized care guided by the right evidence and patient preferences. It brings together experts in urology, real-world evidence generation, artificial intelligence in healthcare, epidemiology, data science, and guideline development. This will help to accelerate research into prevention, treatment, rehabilitation, and QoL of patients with urological disease.[207]





ACTION

Health economists in collaboration with other stakeholders need to find consensus on, and develop new metrics for, wider values that complement the QALY.

A potential complementary measure to the QALY should be identified to directly address the documented limitations of the metric.[166,168,167] There are many metrics on the horizon (Section 2.3.3) that could be taken forward, or new metrics and ways of evaluating may also come to the fore that the health economics community should be open to considering. Metrics to understand wider value measures such as the value of hope, value of choice, insurance value and real option value also need to be developed, validated, and rolled out.

Facilitating action in LMICs

- National and regional PAGs should seek support from international PAG networks operating in the same or similar disease areas by sharing best practices, expertise or even resources (e.g. personnel and funds). They can use this knowledge to develop a best-in-class system, identifying and pre-emptively avoiding challenges that other HTAs have faced in the past.
- Where they exist, HTAs and payers should take a more active role in sourcing patient experiences. Where possible they should seek support from HTAs in other countries to learn about and facilitate PAG participation.
- National and regional members of the clinical, research and PAG communities should work together to adapt current and future standards for PROs, so insights from people with cancer in LMICs are collected and available to support decision-making.

3.2.
We need appropriate infrastructure to support assessment, reimbursement, and reassessment of innovative oncology therapies

ACTION
Policymakers need to create appropriate legislative and governance frameworks for innovative contracting mechanisms.

Innovative contracting models or managed entry agreements (MEAs) focus on high-value products and/or disease areas with considerable unmet needs.[208] These models include value-based pricing agreements, performance-based agreements, outcomes-based agreements, financial agreements and early access schemes. Such models can be used to protect payers against the uncertainty of the impact of a specific therapy, maximize therapeutic use or limit their budget impact whilst ensuring patient access to new medicines and further collection of data.[208,209,210] This supports sharing of risks across all stakeholders.[208] Innovative models can also support access in less well-resourced countries which might struggle to fund a new drug outright.[211]

Frameworks for these models need to be:[208,212,213,214]

- » transparent in how they prioritize medicines for expedited review and/or qualified entry requirements;
- » transparent in how they assess medicines, particularly in circumstances where health system infrastructure may not allow for accurate or timely data collection;
- » equitable and in the best interests of the patient and healthcare systems; and
- » tackle costs and bureaucracy associated with these agreements.

As these innovative contracting models can be burdensome and require specific infrastructure to monitor outcomes in the longer-term, they have been mostly rolled out in high-income settings. These models have become established in several countries including Italy, the United Kingdom, France, and Australia.[215] Other countries such as New Zealand, Belgium, Poland, and Hungary are beginning to pilot and use these types of agreements.[215] **Case Study 7** outlines how these contracting models work in practice.

However, there is limited evidence on the use of these more complex agreements by LMICs.[216] Financial schemes may be more common as they are less complex to implement than performance-based schemes.[216]

> *"Innovative contracting models can be used to support patient access to new medicines while further data is collected to help payers manage uncertainty and limit their budget impact. But we must remember that reimbursement of medicines does not guarantee patient access as this relies on health systems being ready to adopt them."*
>
> **Robert Bick**
> Co-Lead, CanCertainty Coalition, Canada

Case study 7

Examples of MEAs and other types of innovative contracting models and early access schemes underway

- The UK's Early Access to Medicines Scheme (EAMS), run by the Medicines and Healthcare Products Regulatory Agency (MHRA), aims to give patients with life-threatening or seriously debilitating conditions access to medicines that do not yet have a marketing authorization when there is a clear unmet medical need.[217]
- The UK's Cancer Drug Fund's (CDF) and Innovative Medicines Fund (IMF) fast-track promising treatments whilst allowing more data to be collected.[218] This enables NICE to determine whether the medicine is affordable and effective, and provides the evidence for a long-term decision to be made on patient access to the therapy. Clear principles guide the use of the ringfenced £680 million funding.[218]
- The Haute Autorité de Santé (HAS) in France has an early access program which allows patients who have reached a therapeutic barrier to access medicinal products that are not authorized in a specific therapeutic indication on an exceptional and temporary basis. In the first ten months of this program, 80% of applications were approved for early authorization.[219]
- The Japanese Pharmaceutical and Medical Devices Agency (PMDA) has been trialing an accelerated approval program for innovative drugs and medical devices since 2015.[220] The program allows manufacturers to gain early approval for their products if they achieve reasonable standards of safety and effective use of novel endpoints in exploratory trials.[220] Measures to expedite access include prioritized consultation, substantial pre-application consultation, expedited review, the assignment of a PMDA concierge, and an extended re-examination period.[221]
- The Italian Medicines Agency (AIFA) has set up financial agreements where payers share the post-marketing budget impact of new drugs with pharmaceutical developers. Outcomes-based agreements link payers' commitment to actual impact of drugs on health.[222]



ACTION

Pharmaceutical developers should commit to undertaking and facilitating data collection to support innovative contracting mechanisms.

The success of innovative contracting mechanisms rely on the continuous collection and analysis of data to assess the real-world effectiveness of therapies. For example, patient registries and post-marketing surveillance can inform ongoing reimbursement decisions and ensure that MEAs are based on accurate and up-to-date information. However, these can be costly to set up and pharmaceutical developers will be much more likely to invest in this undertaking if they can reasonably predict their product's eligibility for an MEA as early as possible and the data needed to inform reimbursement or reassessment. Timely clarity on MEA criteria and other incentives encourages investment in this space, while uncertainty in MEA frameworks may deter it.[214,213]

Most HTAs tend to be cautious of sharing criteria of consideration for an innovative contracting mechanism and prefer to focus on a case-by-case evaluation. Denmark is one of the only systems to have a published white paper laying out their framework for value-based agreements **(Case Study 8).**

Case study 8

Denmark's framework for value-based agreements

In Denmark, the Knowledge Centre for Life Science has published one of the few government guidance publications on alternative agreement models in the pharmaceutical sector. The report, "Health Data as the Foundation for Effect-Based Agreements", focuses on agreement models developed by the OECD.[223] The Danish central procurement agency for medicines and medical devices (Amgros) has chosen to adopt this framework in its work.[223] Amgros is a procurement service working across the Danish regions to secure medicines and negotiate price for public hospitals.[224]

ACTION

Payers and pharmaceutical developers need appropriate value-based infrastructure to enable the calculation and processing of specific payments or rebates.

Every system should have a reliable process for calculation and payment of invoices or rebates, while also maintaining the confidentiality of net prices.[225] For instance, outcomes-based contracts, which link the payment for a drug to the clinical outcomes it achieves, require tracking and data analysis systems to monitor patient outcomes.[213]

If pre-agreed outcomes are exceeded, additional payments may be required. But if they are not met, pharmaceutical developers may face price reductions or provide rebates back to the payer.[214] Confidentiality is therefore a critical concern for pharmaceutical developers and payers alike. Italy has developed an interesting model to tackle this challenge **(Case Study 9).**

Case study 9

Italian Medicines Agency and evaluation in real-world settings

For over a decade, the Italian Medicines Agency's (AIFA) has been an international pioneer of performance evaluation in real-world settings. They have drug-monitoring registries for continued evaluation of patient eligibility, utilization in clinical practice, and other additional information that may have been unavailable during the first evaluation stage.[226] This robust data infrastructure may facilitate the objective calculation of value, and any payments or rebates required as part of a MEA.

ACTION

Health system decision-makers need to invest in capacity and infrastructure to ensure timely adoption of effective treatments once approved and reimbursed.

Regulatory approval of a new therapy does not guarantee that patients in need can access the treatment; integrating these treatments into clinical practice requires a context-specific learning curve for the healthcare system and their clinicians. Dependent on the complexity of the approved therapy, significant investment in the healthcare team, healthcare facilities, supply chain, and health data infrastructure may be necessary.[227] Health system leaders need to make these investments and engage with various stakeholders, including with professional societies. Pharmaceutical developers, PAGs, caregivers, and the clinical community need to support the uptake of innovative medicines through a variety of pathways including educational initiatives.

Facilitating action in LMICs

- Countries with experience with innovative contracting models should share best practices so that LMICs can learn about the challenges, minimum requirements and potential best practices to introduce these models in the future.
- Initial roll-out of smaller pilot schemes could allow LMIC payers to trial new medicines at a smaller investment rate and scale up successful schemes once the value of investment has been demonstrated.
- National and regional policymakers, scientific agencies, pharmaceutical developers, and the wider scientific community should look to develop interoperable data collection infrastructure for long-term data collection and analysis.
- Pharmaceutical developers should actively support access in LMICs and offer pricing flexibility or logistical support for medicine distribution.



3.3.
We need to advance science policy and collaboration among government entities

ACTION

Policymakers, scientific agencies, pharmaceutical developers, and the wider scientific community need new mechanisms to bridge the gap between the science of innovative therapies and their application within health systems.

Policy must be designed with a focus on prioritizing innovation and translating scientific breakthroughs into clinical practice. This process requires new mechanisms and collaborative approaches.[228] This could include the creation of dedicated translational research units, public private partnerships, adaptive regulatory frameworks and other incentive structures to encourage the development and adoption of new cancer treatments. **Case Study 10** outlines an initiative to close the gap.

In a time of precision oncology, leading clinical research centers in HICs should collaborate with LMICs to ensure that the safety, efficacy and effectiveness of new therapies is tested in broader populations to reduce bias in research. This may not only support access for people in LMICs, but also support building foundational research infrastructure that can leave a lasting positive impact on local healthcare systems.

"Global collaboration offers the chance to bridge the gap between the science of innovative therapies and their application in health systems. Collaboration is key for LMICs where solutions – such as using HTA processes and assessments by more established HTA agencies – are helping to address equity challenges."

Ravindran Kanesvaran, MD, FAMS (Singapore), MRCP (UK)
Chairman, Division of Medical Oncology, National Cancer Centre Singapore, Singapore

Case study 10

Collaborations to translate the latest research and innovation into everyday patient care

The Innovative Medicines Initiative (IMI) is a joint undertaking between the European Union and the European Federation of Pharmaceutical Industries and Associations, designed to facilitate collaboration between key stakeholders, including universities, pharmaceutical developers, and other public and private partners. This initiative has been instrumental in aligning scientific research with regulatory and healthcare policies, thereby streamlining the path from laboratory to patient.[229] The IMI's CANCER-ID initiative successfully led to the development and validation of a range of methods for conducting liquid biopsy for tracing cancerous tumour cells and DNA fragments in the bloodstream.[230]

ACTION

HTAs, payers, regulators, and pharmaceutical developers need to align more closely on the evidence they accept.

Regulatory bodies such as the European Medicines Agency (EMA) and FDA conduct rigorous evaluations of new therapies to ensure they meet safety and efficacy standards to support marketing authorization. HTA agencies utilize comparative effectiveness and cost-effectiveness frameworks to support reimbursement.[83] Regulators may approve medicines based on various oncology endpoints, while payers often seek more evidence on added clinical value, ethics, cost, and QoL to inform reimbursement.[83,91]

More needs to be done to support HTA agencies and payers with evidence – including real-world evidence – that can be utilized in assessments and reimbursement decisions. While HTAs and payers cannot rely solely on regulatory clinical analysis given their differing remits, there may be the opportunity to reduce unnecessary duplication and focus limited HTA agency resources on generating insights that complement and enhance the regulatory analysis. Work to reduce duplication and to improve alignment between regulatory and HTA requirements is already underway in certain countries,[231] but more needs to be done.

ACTION

HTAs and regulators around the world need to improve global collaboration and coordination.

New mechanisms to facilitate global sharing of data, methodologies, expertise, and best practices would allow HTAs to focus on assessing value at a national level and do so more consistently and robustly.[232] While assessment methods and goals vary across different HTAs and payers, further collaboration and information sharing would ensure all countries use the most up-to-date evaluation methods and standardize the basis for evidence-based decisions worldwide. Global collaboration of HTAs would be particularly beneficial in LMICs. Many of these countries face significant infrastructure challenges such as limited regulator investment or capacity, which make it more difficult for them to assess new therapies or adopt innovative contracting methods.[233] The use of third-party assessments, AI, and other technologies could play a pivotal role in the future in this regard **(Case Study 11,12 and 13).**

Case study 11

The use of AI and technology in Thailand

The Health Intervention and Technology Assessment Program (HITAP) in Thailand provides assessment guidance and support to other countries in the region, demonstrating the potential for shared learning and capacity building in HTA.[234] It leverages technology, such as AI-driven data analysis, to streamline HTA processes. This has the potential to enable more rapid and informed decision-making that can benefit health systems with lower resources.[234]

Case study 12

HICs conducting assessments on behalf of other countries

LMICs which do not have established HTAs frequently use other countries' HTA processes. A 2016 study found that Ethiopia, Jordan, and Kenya used HTAs from other countries some of the time, and Rwanda reported frequent use of foreign HTAs.[235] South Africa and Vietnam reported using published HTAs only from HICs.[235] In the absence of local cost-effectiveness analyses, overseas assessments – primarily from NICE (UK) and PBAC (Australia) – were used to inform decisions in Singapore.[236]

This culture of knowledge sharing across systems protects countries without capacity for assessment from being left behind in medical advancement, and also supports greater consistency in international practices.

Case study 13
International collaboration and comparisons

» Starting from January 2025, Europe's Joint Clinical Assessment (JCA) will provide guidance on endpoint use and evidence requirements across EU Member States. The European Commission's intent is that this initiative will streamline processes for both national HTAs and pharmaceutical developers.[237,238]

» Project Orbis, initiated by the US's FDA Oncology Center of Excellence in 2019, provides a framework for concurrent submission and review of oncology products among international partners that may allow patients with cancer to receive earlier access to products in other countries where there may be significant delays in regulatory submissions. Partnering regulators are from Australia, Brazil, Canada, Israel, Singapore, Switzerland, and the UK. Since its inception, Project Orbis has received many oncology marketing applications and led to the approval of numerous oncology drugs for patients across the world.[12]

» A group of HTA agencies from across the UK, Canada, Australia, and New Zealand was established in 2021 to improve international collaboration. For 2023 and 2024, their priorities include improving work sharing to support HTA decision making and increase HTA agency capacity; considering methodological guidance; and a new joint science advice procedure on the use of surrogate outcomes when analysing cost-effectiveness.[239]



Facilitating action in LMICs

» National and regional policymakers, scientific agencies, pharmaceutical developers, and the wider scientific community should facilitate greater access to clinical trials in their countries.

» International collaborations should include LMIC HTAs and payers or at least share information with them so they can benefit from shared knowledge.

» Payers in LMICs should proactively use oversees assessments from well-established HTA agencies to inform decision-making. However, they should not rely solely on these, as their decisions should also be informed by local population needs and culture

3.4.
We need to use data to mitigate uncertainty and inform reimbursement and pricing decisions

"HTA and payers deal with significant uncertainty when reimbursing innovative oncology therapies – especially in the early-stage setting, where OS may not always be available. Beyond utilizing other endpoints in assessments where appropriate, the collection of reliable, robust real-world evidence will be paramount in addressing uncertainty, but more needs to be done to standardize and build trust in its use."

Oriana Ciani, PhD
Associate Professor of Practice in the Public Management, Policy, Health Economics, and HTA Area, SDA Bocconi School of Management, Centre for Research on Health and Social Care Management (CERGAS), Italy

ACTION

Payers and pharmaceutical developers need to develop a reliable data generation model to inform contract development, agreement and implementation.

Ensuring the integrity, validity, and robustness of data is important, as it directly influences value assessments, contracting, financial agreements, healthcare outcomes, and ultimately the overall sustainability of healthcare systems.

As the amount of real-world evidence sources has grown over the past decade, there is increasing pressure for a standardization framework to guarantee the quality of findings.[240] Just as standardization frameworks have been used to improve usability, consistency, and comparability in cancer surveillance[241] **(Case Study 14),** a similar framework is needed for data on oncology treatments.

Case study 14
The Bray and Parkin framework for cancer surveillance

The Bray and Parkin registry and data quality framework, applied globally, ensures high-quality cancer data through four key principles:

- **Completeness**: the extent to which all cancer cases occurring in the population are included in a registry.
- **Comparability**: the extent to which statistics generated for different populations, different sources and data points over time can be compared.
- **Timeliness**: the speed at which a registry can abstract and report data.
- **Validity**: the proportion of cases in a dataset with a given characteristic that truly has that attribute.

This framework has been applied across numerous cancer registries worldwide, and the US National Cancer Database has demonstrated high quality across all four of the above domains.[241]

ACTION

Public and private investments are needed to build data collection capabilities

Investments should focus on developing a robust data ecosystem, including advanced data analytics tools, interoperable electronic health record (EHR) systems, patient registries, biobanks, and secure data-sharing platforms to gain insights into real-world patient outcomes and treatment efficacy.[242,243] By pooling resources and expertise, public and private entities can create a data ecosystem that not only facilitates the gathering of high-quality data, but also ensures its meaningful analysis and application in improving healthcare outcomes and informing health policy.[244]

Numerous ongoing initiatives highlight the benefits of investing in data infrastructure, which can enhance HTA processes and patient care over the long term – one of which is the UK Biobank **(Case Study 15).**

Case study 15

UK Biobank to support genetics research

UK Biobank is a large-scale biomedical database and research resource containing de-identified genetic, lifestyle, health, and biological information from half a million people from the UK.[243] This has become an indispensable resource for research at a global level, enabling a deeper understanding of the determinants of diseases and allowing data to be reliably sourced from different contributors.[245]

The biobank's work has already been used to support obesity genetics research with a focus on developing preventative treatments.[246] Similar advances are expected in oncology.[243]



ACTION

HTA agencies, the research community and pharmaceutical developers need to improve confidence in the use of real-world data.

To improve the use of real-world data and address uncertainty, international standards for data collection, analysis, and reporting must be established. This would address the current discrepancies in data standards and assessment methods which contribute to today's fragmented and inconsistent healthcare policies.[247] A collaborative data environment based on trusted methodologies will allow all parties to reduce uncertainty and HTAs improve the credibility of their ongoing evaluations.

Facilitating action in LMICs

» Members of the national and regional clinical and research community should utilize internationally standardized datasets and contribute to international and regional databases where possible.

» Health systems across the globe can take steps to support real-world data collection by broadening use of EHRs.

» Pharmaceutical developers should continue to have flexibility on pricing so that LMICs are not expected to reimburse at the same rates as HICs.



3.5.
We need to secure alignment on clinical value with clear, timely guideline updates and communication



"Medical societies have an important role in guiding regulatory, HTA and payer decision-making processes, but clinical guidelines are not updated regularly enough. Guidelines need to be promptly revised to provide clear recommendations on emerging therapies and different endpoints best suited to different cancer types, stages, and treatment settings. It is also important to ensure guidelines reflect what matters most to people living with cancer and caregivers."

Javier Cortes, MD
Founding Partner, Medica Scientia Innovation Research (MedSIR); Head, International Breast Cancer Centre (IBCC), Spain



ACTION

Medical societies and PAGs need to collaborate and align on the clinical value of different endpoints and publish guidance on their use for different types and stages of cancer.

Recommendations from medical societies often guide regulators, payers, and HTA bodies in their decision-making processes. It is therefore essential that their guidance and guidelines reflect best practices and recommendations on different endpoints best suited to understanding value within different cancer types, stages, and treatment settings. The endpoints recommended should also reflect the expected trajectory of the disease, and the specific goals of treatment at different stages, whether curative intent, life-prolonging, or palliative.[39]

However, different medical societies may propose conflicting recommendations based on differing priorities or interpretations of evidence. This can introduce uncertainty for decision-makers and potentially undermine the perceived validity of medical society findings. By collaborating, medical societies can present a more unified front, lending credence to their shared recommendations and reducing uncertainties for decision-makers. PAGs also have a role to play in building consensus and co-developing strategies for validating different endpoints in collaboration with other stakeholders.[248] **Case Studies 16, 17, and 18** outline some examples of collaboration and nuance across different guidelines.

Case study 16

Collaboration and alignment between medical societies

Two of the largest international oncology societies – the European Society for Medical Oncology (ESMO) and the American Society of Clinical Oncology (ASCO) – have both published recommendations on the use of PFS as an endpoint in cancer trials, advocating for standardized definitions and reporting practices.[40,249] With both of these high-profile organizations in public alignment on the subject, their recommendations are far more likely to be implemented across a range of health systems – supporting greater international consistency on the use of PFS as an endpoint.

Case study 17

Tailoring the use of endpoints to different settings in prostate cancer

Guidelines from the American Urological Association (AUA), Society of Urological Oncology (SUO), and the American Society for Radiation Oncology (ASTRO) on clinically localized prostate cancer considered various endpoints to demonstrate improved patient survival including OS, cancer-specific survival (CSS), and metastasis-free survival (MFS).

Uniquely, the guidelines considered different metrics based on what is feasible in different settings. Biochemical recurrence-free survival (BRFS) and MFS were considered in localized prostate cancer where mortality was not related to the specific cancer being treated.[250,251,252]

Case study 18

Advocacy group's role in supporting validation of ctDNA as an early endpoint

Friends of Cancer Research (FOCR), an advocacy organization in the US, is making efforts to validate ctDNA as an early endpoint for accelerated drug approval in solid tumours. In 2022, they issued an evidentiary roadmap which provided a strategy for generating the data needed to support the use of ctDNA as a drug development tool in regulatory decision-making. FOCR assembled a multi-stakeholder working group comprised of pharmaceutical developers, diagnostic labs, government health officials, patient advocates, and academic researchers to develop the strategy.[248]

ACTION

Medical societies and the scientific community need to regularly update guidelines with input from PAGs and pharmaceutical developers to ensure they remain up to date to the latest innovations.

Clinical guidelines are slowly updated, focusing on OS and not fully considering alternative endpoints more suited to early-stage medicines, new treatments, and other innovations on the horizon.[3,85] Medical societies need to promptly revise guidelines to incorporate emerging therapies and include alternative endpoints as ways to strengthen, not replace, existing evidence.

Similarly, it is essential to integrate a diverse range of perspectives when developing clinical guidelines, particularly the inclusion of patients and caregivers. This can ultimately lead to more comprehensive and patient-centered recommendations.[253] Cross-stakeholder partnerships offer opportunities for medical societies to contextualize their guidance with patient perspectives and integrate aspects of public need, resourcing, and logistics.

Facilitating action in LMICs

» International medical societies and the scientific community should consider how to prioritize their recommendations and guidelines to ensure that their work is easily accessible and usable for LMICs.

» National and regional PAGs, medical societies and members of the scientific community should develop their own consensus positions and resources to support regulatory decision-making and priority-setting in LMICs.

3.6.
We need to incorporate broader perspectives and measures of economic value

"The economic value of innovation in oncology is more than the impact on health sector costs and the impact on patients' length and quality of life. Those are central, of course, but improved patient, caregiver, and family wellbeing by reducing uncertainty, by providing hope through continued scientific advances, and by enhancing productivity in the workplace and at home are also important."

Lou P. Garrison, Jr., PhD
Professor Emeritus, The Comparative Health Outcomes, Policy, and Economics (CHOICE) Institute, University of Washington, USA

ACTION

Payers and HTAs need to proactively communicate and ensure a balance of consistency and flexibility in the evidence they accept.

Payers and HTAs need to continue to proactively communicate with pharmaceutical developers and the clinical, scientific, and patient communities about the criteria and evidence that they accept across all of their decision-making processes.[254] However, these bodies must evolve their evidence requirements to accommodate new types of data and methodologies and communicate these changes to all relevant stakeholders.[254] Consistency between bodies, countries, and across different types of value assessments will streamline the approval process, reduce ambiguity, and foster a more efficient pathway to market for innovative therapies.[255,256]

The balance between flexibility and predictability in data requirements is another critical factor. Different countries exhibit varying levels of flexibility in their HTA processes. For instance, Germany offers clear guidance but with limited flexibility, whereas the UK has greater flexibility but also unpredictability in the data it accepts, which is quantified through sensitivity analysis before making a recommendation.[257] This flexibility can be beneficial in terms of time to access, but it also presents challenges in maintaining consistency – a balance will be important to achieve.

ACTION

Payers and HTAs need to introduce longer-term analyses and include indirect economic impact of medicines, particularly for early-stage disease.

HTAs and payers need to look beyond the direct impact of a therapy and consider all aspects of clinical, wellbeing, QoL, and economic value in order to approve and fund approaches that contribute most efficiently and effectively to patients, the overall health system, and wider societal goals.[3,258,259] In the case of early-stage cancers, the imperative to look beyond immediate clinical value is even greater.

By looking beyond their budget 'silos' and adopting a more comprehensive, long-term vision of value, healthcare decision-makers can make informed choices that make the best use of increasingly tight healthcare budgets, ensure more equitable allocation of resources and remain flexible to changes and innovation.[258,259] This may lead to substantial societal and economic gains over time. This way of thinking has yet to be applied widely, however, examples do exist **(Case Study 19).**

Case study 19

Integrating societal analysis in HTA decisions in Canada

As of 2024, Canada's Drug Agency (CDA) is trialing the inclusion of societal perspectives within their economic evaluations of certain new therapies in their 'complex review process'.[260] These are typically cell and gene therapies, first-in-class therapies, therapies reviewed via Health Canada's expedited pathways, and drugs that have an undefined place in therapy.[162]

From October 2024, all applications must include an evaluation of societal costs such as patient time off for treatment, productivity losses, and cross-sector government expenses. After this date, any applications which do not have these societal perspectives included will need to justify why they are not included.[162]

This pilot is in line with other Canadian health technology assessment bodies, for example:

- The Institut National d'Excellence en Santé et en Services Sociaux (INESSS) requires manufacturers to submit both the healthcare payer and societal perspectives.[162]
- The Public Health Agency of Canada also uses healthcare payer and societal cost reference cases when the National Advisory Committee on Immunization (NACI) evaluates vaccines and vaccination programs.[162]



ACTION

HTA should prioritize innovative treatments, including for cancers with high unmet need, for expedited review.

HTA agencies face challenges due to high volumes of therapies for assessment and limited resources.[261,262] It can therefore be difficult to make decisions about the order in which to review submissions to deliver the most value to people living with cancer.[262] To address this, HTAs should adopt accelerated access models to fast-track evaluations and allow earlier access based on preliminary data, with ongoing effectiveness and safety monitoring and periodic updates to HTA guidance.[220]

This can also reduce uncertainty for pharmaceutical developers,[263] and maintain important momentum of innovation at a health system level. This approach is becoming more widespread **(Case Study 20).**

Case study 20

Prioritizing assessment of innovative treatments in China

China has priority review and approval measures to encourage pharmaceutical innovation.[220] To qualify for an expedited review over the standard approval pathway which has a 200-day review timeline, submissions must fulfill certain criteria:[264]

- Priority approval pathway taking 70-130 days:
  - Therapies with urgent clinical shortages and are used to prevent and treat major infectious diseases, rare diseases and other significant conditions.
  - Drugs included in the breakthrough drug procedure.
  - Drugs that meet the conditional approval criteria.
  - New types and new dosage forms of pediatric drugs.
  - Vaccines for disease prevention and control.
  - Drugs that meet other unspecified priority approval situations.
- Breakthrough therapeutic drug pathway taking 130 days:
  - Therapies used to prevent and treat diseases that are severely life-threatening, or which affect HRQoL, and for which there is no current effective prevention or treatment with significant clinical benefits.

In reality, approval times are often longer than these guidelines. However, regardless, the number of therapies being assessed via priority review pathways has increased dramatically in recent years: from 7 in 2016 to 82 in 2018.[264]





Facilitating action in LMICs

- LMICs should manage limited regulatory and HTA agency capacity by prioritizing review and assessment of medicines with the greatest unmet need.
- LMIC payers should carefully consider broader economic costs, such as GDP costs of health-related productivity loss, in order to prioritize medicines with greatest potential impact in their countries.



Conclusion

The current trajectory of oncology care necessitates a re-evaluation of value assessment frameworks to support optimal global innovation in oncology and to ensure timely access to effective treatments and equitable care. With the global cancer burden set to rise significantly, it is imperative to evolve these frameworks to better capture the full spectrum of potential benefits provided by innovative therapies, encompassing clinical value; quality of life and wellbeing value; and economic value. This evolution should be accompanied by a transfer of knowledge from the early adopters to the LMICs that bear a higher cancer burden and cannot yet ensure access to essential cancer medicines.[30,8]

The economic and human impact of cancer is substantial and requires global action to develop effective cancer treatments that are available and accessible to all. While HICs are equipped to bear the costs of assessing and distributing new medicines at a national level, LMICs experience significant disparities in patient outcomes and significant economic burdens.[24] There is urgent need to foster global equity in cancer care. To achieve this, a concerted international effort across the various sectors of society must be made to ensure that effective cancer treatments are accessible to all patients in need, regardless of geographic location or economic status.

To realize the potential of scientific advances in oncology, policy solutions must focus on collaborative, multistakeholder policy interventions. HTA and payer decisions should be refocused on the needs of people living with cancer and caregivers, so that treatment options can better cater to their needs. Access to innovative medicines can be improved through the development of appropriate infrastructure to support assessment and reimbursement, while such innovations can be further encouraged through advancements in science policy and collaboration among government entities. Innovative contracting mechanisms, such as MEAs, can facilitate access to high-value treatments while managing budgetary constraints and collecting further data. Any uncertainties in assessment or pricing decisions could be largely mitigated through widely recognized best practices in data collection and usage. Alignment on clinical value could also be secured through clear, timely guideline updates and communication – ensuring consistency metrics across systems. Finally, we need to incorporate broader perspectives and measures of economic value beyond direct healthcare costs to include indirect impacts, such as productivity losses and societal costs.

By implementing these changes, we can work to improve access to innovative cancer medicines – leading to better coordination and efficiency across global health systems and critically helping people with cancer receive the optimal care they need.

Glossary

Adjuvant therapies

Additional cancer treatment given after the primary treatment to lower the risk that the cancer will come back. Adjuvant therapy may include chemotherapy, radiation therapy, hormone therapy, targeted therapy or biological therapy.[265]

Administration

The act of giving a treatment, such as a drug, to a patient. It can also refer to the way it is given, the dose or how often it is given.[266]

Cancer stage or staging

A system that is used to describe the extent of cancer in the body. Staging is usually based on the size of the tumor and whether the cancer has spread from where it started to nearby areas, lymph nodes or other parts of the body.[267]

Cancer type

Cancer is not one disease but rather a cohort of related diseases. Solid and blood cancers require a range of treatments with different goals and outcomes, and therefore relevant trial endpoints also vary.[268]

Circulating Tumour DNA (ctDNA)

DNA from cancer cells that is found in the bloodstream, which can be used as a biomarker to detect cancer presence or response to treatment.[76]

Clinical benefit

A positive effect of a therapeutic intervention, for example, slowing or curing disease, and improving QoL.[269]

CRISPR

A gene editing tool used to change or "edit" pieces of a cell's DNA.[270] It has many applications including for treating diseases.

Disease-Free Survival (DFS)

The length of time after primary treatment for cancer ends that the patient survives without any signs or symptoms of that cancer.[65]

Direct costs

Costs that are directly attributable to patient care. Examples include resources used in treatment, hospitalization and rehabilitation.[271]

Efficacy

The ability of an intervention (for example, a drug or surgery) to produce the desired beneficial effect.[272]

Event-Free Survival (EFS)

The length of time after primary treatment for cancer that the patient remains free of certain complications or events that the treatment was intended to prevent or delay.[66]

Health Technology Assessment (HTA)

A multidisciplinary process that summarizes information about the medical, social, economic, and ethical issues related to the use of a health technology in a systematic, transparent, unbiased, and robust manner.[80] This information can be used by decision-makers to support health policy decisions.

Healthcare system resources

Includes financial (health spending) and human resources. Health spending includes outpatient care, hospital care, long-term care, pharmaceuticals, and other medical goods, among other services.[273]

High-income country

Nations with a gross national income (GNI) per capita above $14,005 in 2023.[274]

Indication

Use of a therapy for treating a specific disease such as a specific type of cancer at a specific stage.[275]

Low- and middle-income country

Nations with a gross national income (GNI) per capita below certain thresholds defined by the World Bank. Low-income countries have a GNI per capita of $1,145 or less and lower middle-income countries are between $1,146 and $4,515 in 2023.[274]

Managed entry agreements

Contracts between a payer and pharmaceutical developer that can be used to mitigate the uncertainty regarding a medicine's relative effectiveness, cost-effectiveness, or budget impact.[225]

Minimal Residual Disease (MRD)

The number of cancer cells that remain in the body during or after treatment, which can be an indicator of the effectiveness of the treatment and the likelihood of relapse.[276]

Overall Survival (OS)

The length of time from either the date of diagnosis or the start of treatment for a disease that patients diagnosed are still alive. This measure is used in clinical trials to assess the effectiveness of a cancer treatment.[57]

Pathologic Complete Response (pCR)

A measure used in cancer treatment trials to assess the absence of detectable cancer cells in tissue samples after treatment.[70]

Patient-reported outcomes (PRO)

Measures that directly capture a patient's perspective on their health without interpretation by a clinician or anyone else. These can measure the impact of disease, or the functional status associated with treatment.[115]

Progression-Free Survival (PFS)

The length of time during and after cancer treatment that a person lives with the disease, but it does not get worse.[67]

Quality-Adjusted Life Year (QALY)

A measure used to assess the value of medical interventions in terms of their impact on both the quality and quantity of life lived.[166]

Quality of Life (QoL)

A concept that measures the impact of a disease and its treatment on an individual's wellbeing and ability to perform the activities of daily life.[97]

Relapse-Free Survival (RFS)

The length of time after primary treatment for cancer that the patient remains free from relapse.[277]



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