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ORIGINAL ARTICLE

Access to novel cancer medicines in Europe: inequities across countries and their drivers

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Background: An increasing number of cancer medicines are being developed and approved. Access to these medicines is important for improving patient outcomes and overall quality of care, yet achieving equitable access across countries in Europe is challenging.

Method: This study reviews inequities in access to novel cancer medicines in countries of the European Union (EU) and European Economic Area (EEA), and neighboring countries, at three critical stages: regulatory approval, reimbursement approval, and use in clinical practice. It also examines reasons contributing to these inequities. The analysis builds on published evidence from a predefined set of international stakeholders.

Results: Inequities vary across the three stages. At the regulatory stage, disparities are minimized within EU/EEA countries due to centralized approval by the European Medicines Agency (EMA), while worse access exists outside this region. Reimbursement of EMA-approved medicines varies significantly, with rates ranging from 0% in Malta to 96% in Germany, and timelines spanning <100 days to nearly 1000 days. Alternative access schemes enable (limited) access before and after regulatory and reimbursement approval, which may change conclusions about access in some countries. Clinical use exhibits a 10-fold difference across countries in some cases, with Central and Eastern Europe consistently lagging. Contributing factors include country-specific prioritization of pharmaceutical companies for regulatory and reimbursement applications, health technology assessment (HTA) processes and criteria, constraints in financial resources for medicines and testing infrastructure, suboptimal care processes, organization, and continuing medical education.

Conclusion: Patient access to novel medicines differs widely across European countries, caused by financial, organizational, administrative, and capacity reasons. Policy harmonization, as seen with mandatory regulatory approval by the EMA and the EU HTA Regulation, has the potential to reduce inequities, but it will not address underlying economic and health care system constraints. Achieving equity will require a balance between innovation, affordability, and sustainability in health care systems.

Key words: cancer medicines, reimbursement decision, drug access, inequity, Europe

INTRODUCTION

The number of newly diagnosed cancer cases in Europe is on the rise.[1] An estimated 4.1 million new cancer cases were diagnosed and 2.0 million people died from cancer in 2022.[2] Improvements in survival have been achieved for many cancer types in the past decades in European countries,[3,4] which have been attributed to advances in early detection, diagnostics, and treatment of cancer.[4,5]

Cancer medicines are, together with surgery and radiotherapy, the main treatment modalities in cancer care, and patient access to effective medicines is crucial to achieve better health outcomes.[6-9] The approval of novel cancer medicines has accelerated in recent decades.[10,11] For instance, the European Medicines Agency (EMA) approved, on average, four new cancer medicines per year in 2001-2011 but 14 new ones in 2021-2024.[1] Moreover, the number of approvals of new indications of previously approved medicines has almost been twice as high as the number of new medicines in 2015-2024.[1]

While the introduction of new cancer medicines holds the potential to improve patient outcomes, health care

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systems face the challenge of providing timely and equitable access to patients. A significant challenge for health care payers with constrained budgets are the prices of new cancer medicines (i.e. monthly/annual costs per treatment), which have been increasing since 2000 (based on list prices).[12,13] This is compounded by the sheer increase in the number of new cancer medicines and the rising number of cancer patients.[14] In Europe, total expenditure on cancer medicines grew from €49 to €126 per capita (inflation-adjusted; based on list prices) between 2014 and 2023.[1]

Another challenge is the lack of robust evidence on the relative effectiveness of new cancer medicines when regulatory bodies or third-party payers make their assessments. For instance, in regulatory approvals of cancer medicines by the EMA from 2017 to 2022, the proportion of single-arm trials underpinning the approval rose from 28.6% to 53.6%.[15] The use of such trials results in additional uncertainty in the comparative benefit of new medicines. In addition, a study of 132 EMA-approved indications in solid tumors in 2015-2020 showed that the median gain in overall survival was 2.8 months.[16] Relying on the European Society for Medical Oncology (ESMO) Magnitude of Clinical Benefit Scale (MCBS), a value framework developed by the ESMO,[17] an analysis of 144 indications used in solid tumors with EMA approval in 2009-2020 found that only 33% had a 'substantial' clinical benefit.[18] Previous studies and reports have indicated vast differences in patient access to novel cancer medicines across European countries.[1,14,19-22] However, definitions of measuring access differ, with most studies only focusing on reimbursement. The aim of this study is to bring together evidence and provide a clear structure in the discussion on patient access. It proposes three critical stages for studying and comparing access across countries—regulatory approval, reimbursement approval, and use in clinical practice. For each stage, it summarizes existing evidence on inequities in access across countries and underlying reasons that may contribute to these inequities.

MATERIAL AND METHODS

Study design and definitions

According to the Organisation for Economic Co-operation and Development (OECD), access to new cancer medicines is a multidimensional concept encompassing availability, affordability, accessibility, acceptability, and quality.[22,23] This study mainly focuses on access at three stages of the lifecycle of a medicine; regulatory approval by the competent authorities (marketing authorization), reimbursement/coverage approval by third-party payers (inclusion in drug formulary/positive list of funded medicines), and actual use (prescription) in clinical practice. In addition, alternative access schemes (e.g. compassionate use, early access programs, off-label use) before and after regulatory and reimbursement approval are briefly described.

Existing evidence on access to new cancer medicines in Europe was reviewed. Reports and studies published by a predefined set of international stakeholders from 2015 until April 2025 were considered; see Supplementary Appendix A, available at https://doi.org/10.1016/j.esmoop.2025.105810. This encompassed professional societies (ESMO), patient organizations (Cancer Patients Europe, Digestive Cancers Europe, Europa Donna, Lung Cancer Europe), multidisciplinary organizations (European Cancer Organisation), research institutes [The Swedish Institute for Health Economics (IHE)], industry associations [European Federation of Pharmaceutical Industries and Associations (EFPIA)], intergovernmental organizations (OECD), and the European Commission. Complimentary information from other studies was used to fill notable gaps.

The definition of cancer medicines and the geographical coverage of Europe in this review follows the definition used in the underlying source. Novel (or new or innovative) medicines are usually defined as those that have been launched anywhere globally within the last 1-15 years and still have market exclusivity. Essential cancer medicines that are on the World Health Organization's Essential Medicines List (WHO EML) are not the focus here. The geographical focus is on countries of the European Union (EU) and European Economic Area (EEA) and neighboring countries.

Data analysis and outcome measures

The metrics to quantify inequities in access across countries come mainly from the underlying source. For regulatory approval, this included the proportion of approved medicines relative to some reference basket, as well as the time until approval. For reimbursement approval, the two main metrics were the proportion of medicines with regulatory approval that are reimbursed and the time from regulatory to reimbursement approval. For use in clinical practice, the measurement is more complicated in the absence of standard units for all cancer medicines such as defined daily dose,[24] but it should preferably capture the extent of use by patients who could potentially benefit.[22] Available metrics encompassed the proportion of patients with a valid prescription who can actually access the prescribed medicine, the value and volume of medicines sold, and the number of patients treated according to clinical guidelines. Lastly, the key reasons underlying inequities across countries in each of the three phases identified in the reviewed material were assessed and synthesized.

RESULTS

Regulatory approval

The authorization of a new medicine by the regulatory agency in a country is the first stage for patient access. The decision to approve is made after an assessment of the evidence on safety, quality, and efficacy provided by the applying pharmaceutical company.

Inequities across countries. There are no inequities in regulatory approval across EU/EEA countries, while all other European countries experience fewer and slower approvals; see Supplementary Appendix B, available at https://doi.org/10.1016/j.esmoop.2025.105810 for details. In the EU/EEA countries, all new cancer medicines are

approved through a mandatory process of centralized marketing authorization by the EMA—with the formal decision taken by the European Commission—since 2004 [Regulation (EC) No 726/2004].[25] In the UK, the Medicines and Healthcare products Regulatory Agency (MHRA) became the responsible body after withdrawal of the country from the EU. Subsequently, several analyses found that the MHRA approved slightly fewer medicines (including nononcology medicines) and almost always approved them later by ∼1-4 months than the EMA in 2021-2023.[26,27] This resembles the situation in Switzerland where several studies showed that Swissmedic approves slightly fewer cancer medicines and with a median delay of ∼3-5 months compared with the EMA.[22,27,28] In less affluent countries, such as Serbia and Türkiye, differences are greater with 29%-41% of EMA-approved medicines in lung cancer not being approved by the respective regulatory bodies.[20,29]

It should also be noted that some patients may have access to new cancer medicines before regulatory approval through alternative access schemes,[30] yet to varying extent across countries. This includes clinical trials [with evidence showing five-fold differences across Europe, typically highest in Northwestern Europe and lowest in Central and Eastern Europe (CEE)[14,31]], compassionate use programs (no evidence available on country differences[32]), early access programs (EAPs; available in many countries, often on a named-patient basis and often with few clinically eligible patients benefiting from them[14]), and off-label use (no evidence available on country differences[22]).

Reasons for inequities. Two main reasons for inequities in regulatory approval across countries have been cited by the OECD.[22] These are companies' launch strategies to apply in the biggest and most lucrative markets first (i.e. the United States followed by the EU/EEA, followed by the UK and Switzerland, and then other countries) and the duration of the regulatory process. The latter is also highlighted by EFPIA.[33] Several studies of cancer medicines found that companies filed applications ∼20 days-2 months later to the EMA than to the United States Food and Drug Administration (FDA), while the median review time was 200 days for the FDA but 426 days for the EMA, which was explained by much greater use of expedited review pathways by the FDA.[28,34]

Reimbursement approval

Decisions to reimburse/cover an authorized medicine and include it in the drug formulary are made by third-party payers (government, sickness funds, health insurances) at the national or even subnational level in European countries.[14] A health technology assessment (HTA) is usually carried out by a competent body to inform the reimbursement decision. Price negotiations between the pharmaceutical company and the third-party payer(s) also typically take place before the decision.

Inequities across countries. Landmark studies by ESMO and an annual report by EFPIA about the reimbursement status of new cancer medicines in Europe show that high-income countries in Northern, Western, and Southern Europe generally reimbursed the greatest proportion of medicines, while less affluent, mostly non-EU countries in CEE reimburse fewer medicines.[19,35,36] The ESMO studies also showed that the disparities are much smaller for older medicines on the WHO EML[19,36]; see Supplementary Appendix B, available at https://doi.org/10.1016/j.esmoop.2025.105810 for details. The latest EFPIA report found that the mean time from EMA approval to local reimbursement was shortest in Germany, with <100 days, and longest in Lithuania, with >900 days.[35] The EU Transparency Directive (Directive 89/105/EEC) sets a maximum of 180 days for countries to make pricing and reimbursement decisions, yet 'clock stops' during which national authorities request and wait for additional information from companies prolong observed timelines.[14] In relation to the findings in the EFPIA report, the European Commission notes that patients in small EU countries or countries with low gross domestic product (GDP) had access to fewer new medicines and had to wait significantly longer to access them[37]; see Figures 1 and 2 for country-level correlations with GDP per capita.

Studies by the OECD that have focused on the reimbursement status of specific indications of cancer medicines generally found a similar pattern of slower reimbursement and a lower reimbursed proportion in CEE countries together with Malta.[14,22] Yet considerable differences exist even across CEE countries with similar GDP per capita, with the reimbursed proportion of EMA-approved indications ranging from 19% in Slovakia to 64% in Czechia and the median time to reimbursement ranging from 27 months in Poland to 37 months in Hungary in one study.[38] Numerous studies with a specific focus on lung cancer echo these findings.[20,29,31,39,40]

Certain nuances in studies on reimbursement are noteworthy, which may change conclusions about access in some countries. Firstly, reimbursement is often not a binary decision, as the eligible patient population might be restricted compared with the scope of regulatory approval or there might be restrictions on physician or provider specializations allowed to prescribe (e.g. only specialized centers).[30] Such restrictions are common in many European countries, although the nature of these restrictions varies by indications and countries, with different impacts on the size of the patient population affected.[14,35,38] Secondly, a reimbursement rate of zero does not mean that no patients have access. EAPs (typically on a named-patient basis) allow access between regulatory approval and reimbursement approval in many European countries, including Malta and Slovakia.[14,41] Thirdly, managed entry agreements with performance-based, conditional reimbursement may restrict the number of patients who have access to the relevant medicines.[30]

Reasons for inequities. Many different reasons have been established to explain differences in reimbursement and the time to reimbursement across European countries. In general, the total time period is shaped by factors and processes that are in control of both the applying company

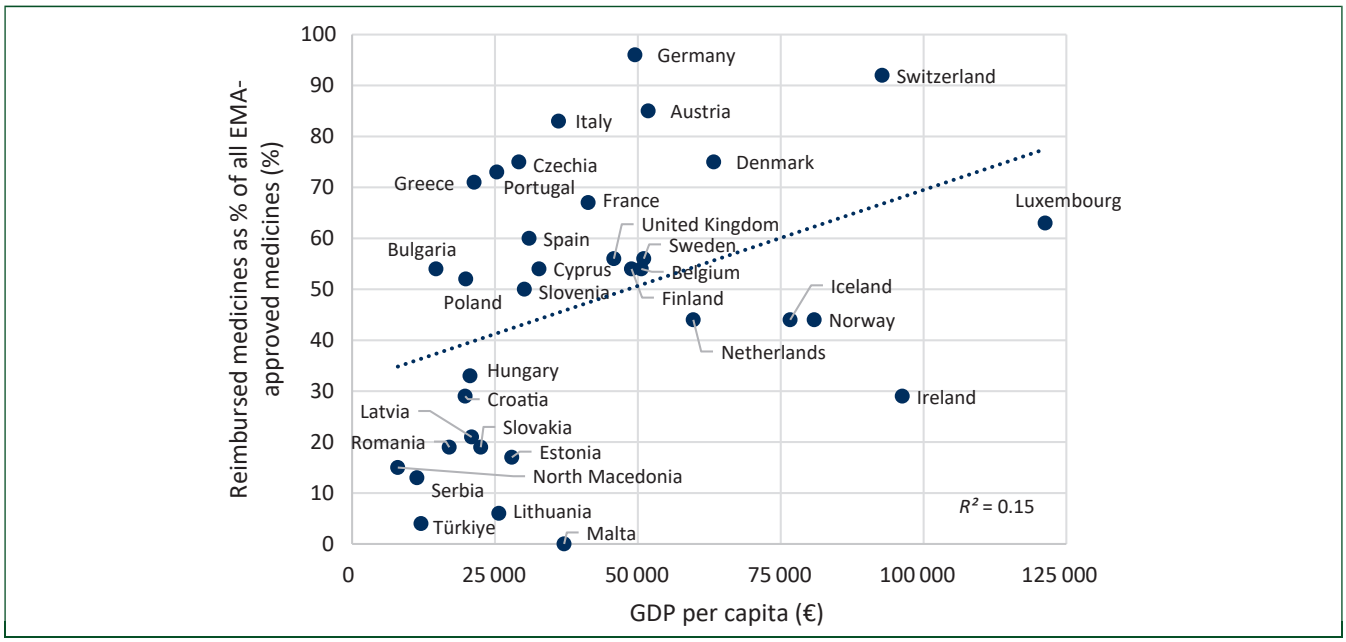

Figure 1. Proportion of EMA-approved cancer medicines with local reimbursement in 2024 compared to countries' GDP per capita in 2023. Every dot represents a country. 'GDP per capita' in euros (€) in 2023 based on data from Eurostat, except for the UK with data from the Office for National Statistics. The 'Reimbursed medicines as % of all EMA-approved medicines' represents the proportion of cancer medicines with EMA approval in 2019-2022 that had reimbursement at the beginning of 2024, based on data from the EFPIA Patients W.A.I.T. Indicator Survey 2023.[35] The reimbursed proportion for the UK refers to England only. All countries appearing in the EFPIA Patients W.A.I.T. Indicator Survey are included except for Bosnia and Herzegovina due to lack of information on GDP per capita from Eurostat. EMA, European Medicines Agency; GDP, gross domestic product.

and the national authorities as noted by the OECD and EFPIA.[22,33] Companies decide on filing a pricing and reimbursement (P&R) application and launch sequences, but their decisions are influenced by the ability to file an application. In some countries, P&R applications can be made before regulatory approval and in others only afterwards or only once a certain number of specified countries have made a positive reimbursement decision (as in Bulgaria and Greece).[14,33] Companies' launch strategies are also driven by external reference pricing systems, which

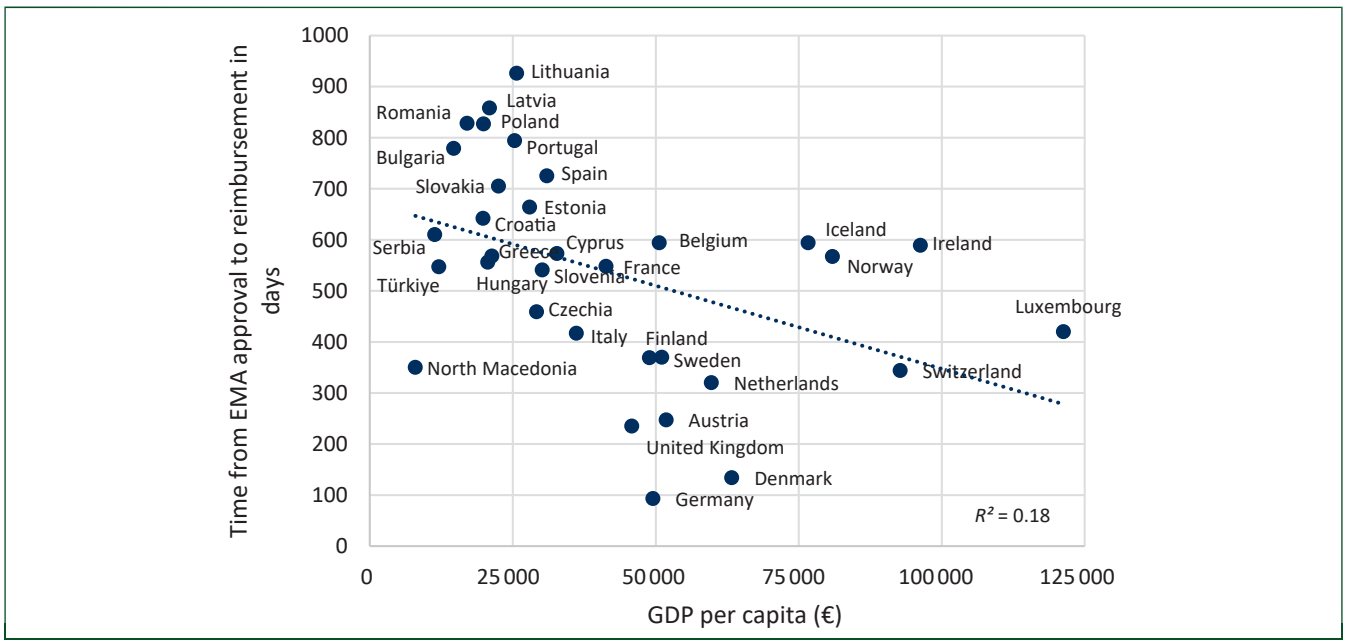

Figure 2. Time from EMA approval to local reimbursement in days for new cancer medicines in 2024 compared with countries' GDP per capita in 2023. Every dot represents a country. 'GDP per capita' in euros (€) in 2023 based on data from Eurostat, except for the UK with data from the Office for National Statistics. The 'Time from EMA approval to reimbursement in days' is based on cancer medicines with EMA approval in 2019-2022 that had been reimbursed until the beginning of 2024, using data from the EFPIA Patients W.A.I.T. Indicator Survey 2023.[35] The time to reimbursement for the UK refers to England only. All countries appearing in the EFPIA Patients W.A.I.T. Indicator Survey are included except for Bosnia and Herzegovina due to lack of information on GDP per capita from Eurostat.
EMA, European Medicines Agency; GDP, gross domestic product.

make it more attractive to launch first in high-price, non-referenced countries and to delay launch in low-price, high-referenced ones.[42,43] The OECD found that companies file applications for cancer medicines earlier in high-income European countries where price expectations and willingness/ability to pay higher prices are greater.[14]

Processing times for P&R applications most often account for the majority of the time between EMA approval to reimbursement approval.[14] The HTA (or value assessment) process to inform the reimbursement decision can differ considerably across countries.[22] This includes misalignment on evidence not only between companies and HTA bodies but also between HTA bodies in assessment criteria, e.g. patient population, comparators, trial design, endpoints, and statistical analysis.[33] Another factor is misalignment between value and price, where prices demanded by companies are higher than the perceived value or affordability of the national bodies, resulting in a need for price negotiations.[33] Even countries with rather similar GDP per capita in CEE may apply varying cost-effectiveness thresholds in the HTA process, which might explain some of the observed inequities.[38] National bodies may also have different preferences for class competition and choice, where the number of products reimbursed in a therapeutic class may be favored or disfavored.[33] From a system perspective, EFPIA also notes that some countries have limited capacity to perform HTA, especially those with more recently established HTA bodies,[33] which is compounded by the increasing number of new medicines and indications.

Third-party payers may anticipate insufficient budget to implement reimbursement decisions.[22,33] Even if the HTA process concludes that a new medicine is cost-effective, its price (which is fairly rigid across countries) in combination with the size of the eligible patient population may exceed budgetary constraints, as health care funding differs widely across European countries.[44]

Use in clinical practice

A positive reimbursement/coverage decision by a third-party payer does not necessarily translate into immediate access for all intended patients across a country. Only when a medicine is prescribed will it be accessible to patients in clinical practice.

Inequities across countries. The latest available numbers on the use of cancer medicines across European countries in costs and volume are from 2023[1]; see Supplementary Appendix B, available at https://doi.org/10.1016/j.esmoop.2025.105810 for details. Spending on cancer medicines (measured in list prices and therefore overestimated) ranged from €31 per capita in Latvia to €195 per capita in Austria, with countries in Western Europe tending to record the highest spending levels, followed by countries in Southern and Northern Europe, and CEE countries spending the least.[1] Sold volumes of newer cancer medicines (most of which with ESMO-MCBS scores of $\geq$3) in 2023 differed most for medicines used in lung and gastrointestinal cancers, multiple myeloma, and immune checkpoint inhibitors with sometimes a seven-fold to 10-fold difference in use across countries.[1,21] Generally, CEE countries recorded lower use than other countries, partly explained by the lack of reimbursement of the medicines and all their indications; see Figure 3 as an example for a correlation of lung cancer medicine use with GDP per capita. For older medicines, such as trastuzumab in breast cancer, smaller differences in volume use were observed albeit still with a tendency to lower use in CEE countries than elsewhere in 2018[21]; see Figure 4 as an example for a correlation of trastuzumab use with GDP per capita.

Medicine shortages might also affect use. Studies by ESMO found that reimbursed medicines were almost always available in Western Europe when prescribed, but less so in CEE, especially in non-EU Eastern European countries.[19,36] This was true both for newer medicines with high ESMO-MCBS scores and medicines on the WHO EML.

An important question is whether medicines have been prescribed according to clinical guidelines. A study of treatment patterns in non-small-cell lung cancer in 12 countries showed that, compared with recommended standards in ESMO guidelines, most countries seemed to treat a lower proportion of patients with cancer medicines than recommended, with Poland and the UK only treating about half of the recommended patient population.[45] Moreover, the type of medicines administered was below the level recommended in ESMO guidelines for both immunotherapy and targeted therapy and above the level for older chemotherapy in all countries.[45]

Reasons for inequities. Several interconnected reasons may explain country differences in the use of new cancer medicines in clinical practice. ESMO emphasizes the cost and affordability of newer medicines as a major factor contributing to inequities.[19] Limited resource allocation to implement reimbursement decisions and ensure availability of reimbursed medicines is another reason cited by EFPIA.[33] The abovementioned restrictions in the reimbursement decision limit the eligible patient population and thereby contribute to country differences.[46] ESMO identified medicine shortages and supply chain problems, especially in Eastern Europe, which might impair the ability to prescribe.[19] Subnational and multitiered decision-making processes, as seen in countries such as Italy and Sweden with regional health care payers, prolong the time to local availability, introduce variation in use, and can even block the use in certain regions.[33,47,48]

Testing infrastructure constraints are another pivotal reason. There is a large variation in the availability of adequate diagnostic facilities across countries, especially for advanced molecular testing required for many new cancer medicines.[49,50] This gap is most evident in CEE, where patients frequently face barriers, including low test order rates and limited reimbursement of tests.[31,49,50] Previous research has identified a paradoxical situation in which third-party payers may decide to reimburse a medicine but not its companion diagnostic.[51] In more than half of OECD countries, the reimbursement of companion

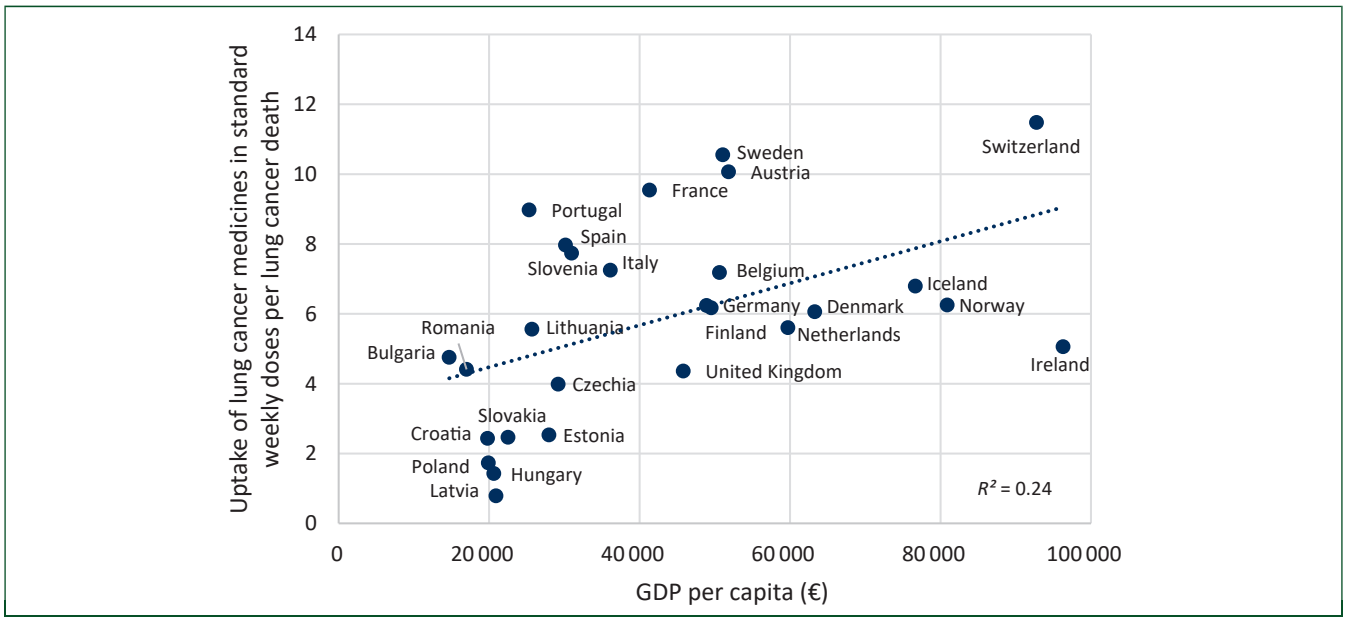

Figure 3. Uptake of targeted lung cancer medicines in standard weekly doses per lung cancer death in 2023 compared to countries' GDP per capita in 2023. Every dot represents a country. 'GDP per capita' in euros (€) in 2023 based on data from Eurostat, except for the UK with data from the Office for National Statistics. The 'Uptake of lung cancer medicines' was defined as sold volumes (in milligrams), standardized by the recommended dose and converted to a weekly equivalent (standard weekly dose), and divided by the number of lung cancer deaths in a country, based on data from Manzano et al. (2025).[1] Lung cancer medicines include alectinib, brigatinib, crizotinib, lorlatinib, osimertinib, selpercatinib, and sotorasib but no immune checkpoint inhibitors. All countries appearing in Manzano et al. (2025) are included.
GDP, gross domestic product.

diagnostics is not automatically coupled with the reimbursement of medicines.[14]

Slow adoption of new cancer medicines is another reason. Despite reimbursement, new medicines may take months or years to be used on a broad scale in all clinics across a country and in all clinically eligible patients.[14,52] Variations in hospital-level resources and practices may explain why university hospitals and comprehensive cancer centers often are early adopters whereas other hospitals are typically slower. A contributing factor is delayed

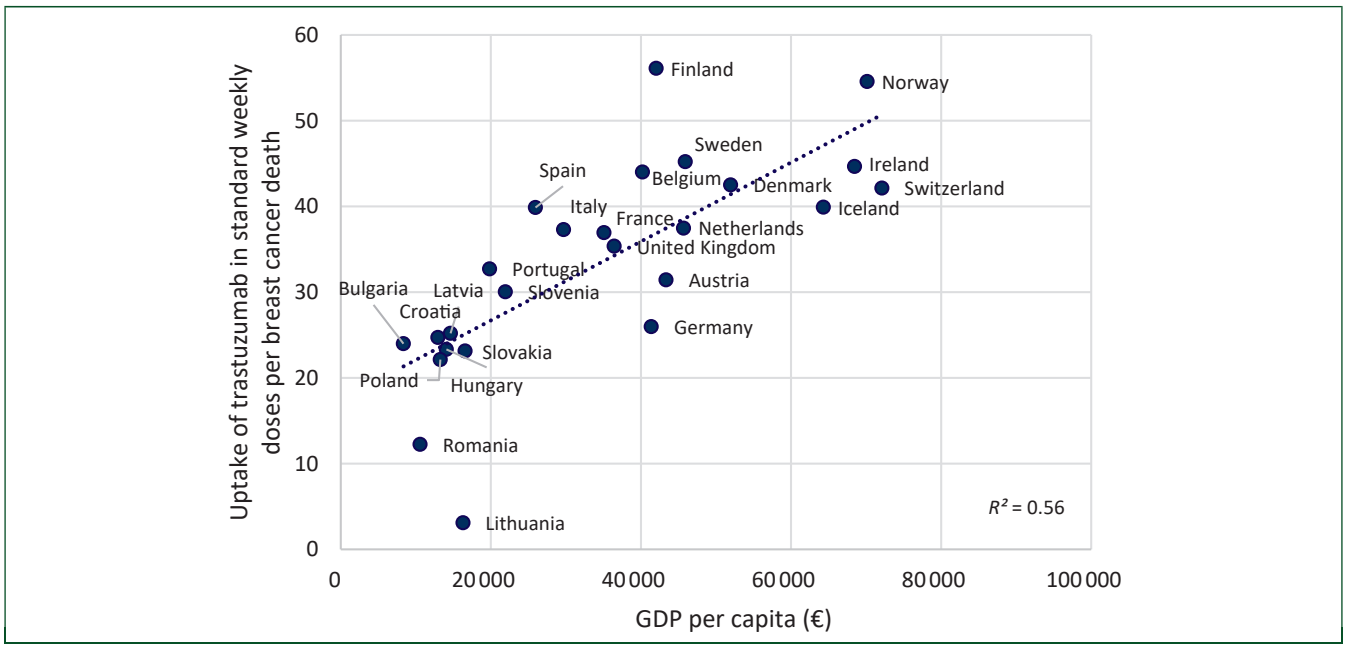

Figure 4. Uptake of trastuzumab in standard weekly doses per breast cancer death in 2018 compared to countries' GDP per capita in 2018. Every dot represents a country. 'GDP per capita' in euros (€) in 2018 based on data from Eurostat, except for the UK with data from the Office for National Statistics. The 'Uptake of trastuzumab' was defined as sold volumes (in milligrams), standardized by the recommended dose and converted to a weekly equivalent (standard weekly dose), and divided by the number of breast cancer deaths in a country, based on data from Hofmarcher et al. (2019).[21] All countries appearing in Hofmarcher et al. (2019) are included, except for Czechia due to incomplete sales data.
GDP, gross domestic product.

inclusion of new medicines in local clinical guidelines and treatment protocols.[14,33] The varying level of continuing medical education of clinical staff is yet another important factor that may contribute to inequities across countries but also across clinics within countries.[14,46]

DISCUSSION

With rising cancer incidence, the urgency for access to new and effective medicines is increasing. Regulatory approval is a necessary but not a sufficient prerequisite for reimbursement approval, which in turn is often a necessary but not a sufficient prerequisite for access in clinical practice. In discussions of access to new medicines it is therefore important to define at which stage in the lifecycle of a medicine and in which way access is measured. Across European countries, equitable access to new cancer medicines remains elusive, except at the regulatory stage in the EU/EEA countries. A diverse list of reasons for inequities has been identified, going beyond the financial dimension and also pointing to organizational, capacity, and administrative aspects. Interestingly, there seems to be broad consensus on most of these reasons across the reviewed reports and studies of the included stakeholders.

The centralized marketing authorization by the EMA has eliminated disparities in regulatory approval within the EU/EEA. However, inequities and worse access persist outside this co-operation, particularly in Serbia, Türkiye, and other Eastern Europe countries. Switzerland and the UK have joined Project Orbis together with other regulatory bodies from high-income countries to accelerate approval,[53] but the limited scope has probably only a marginal impact. In 2024, the UK also launched the International Recognition Procedure to recognize foreign approvals.[54] Encouraging non-EU/EEA countries to follow the EMA's decisions could provide a pathway for regulatory harmonization across a broader region.

Reimbursement inequities are much pronounced, with significant variation in both the reimbursed proportion of EMA-approved medicines and the time to reimbursement. Economic factors, coupled with companies' launch strategies, the complexities of national HTA processes and cost-effectiveness thresholds, and administrative hurdles, contribute to worse access in CEE countries than those in Northern and Western Europe. However, both the OECD and EFPIA note that a 100% reimbursement rate of EMA-approved medicines/indications is neither necessary nor essential from a clinical perspective.[22,33] If several medicines with similar effectiveness are available for a given indication, it is enough to provide one medicine without disadvantaging patients. Indeed, a previous OECD analysis found that country differences in the reimbursement rate are smaller if specific indications with multiple, similar alternatives are considered.[14] Moreover, not all new medicines offer the same or a significant clinical benefit over the existing standard-of-care, which calls for a prioritization of effective medicines, especially in countries with limited resources.[55,56] ESMO launched the MCBS in 2015 to score new indications and to support the HTA process and assist in rationalizing reimbursement decisions.[17] An analysis of 124 EMA approvals in 2011-2020 found that almost half (48%) of the new indications in solid tumors had a non-substantial clinical benefit according to the ESMO-MCBS,[38] meaning that their nonreimbursement may not significantly affect patient outcomes.

Two recent developments might reduce disparities in reimbursement in the coming years. Firstly, in 2022, EFPIA member companies issued a commitment to file P&R applications in all EU countries no later than 2 years after EMA approval, provided that local systems allow it.[57] Secondly, the EU HTA Regulation [Regulation (EU) 2021/2282] came into force in January 2025 and mandates joint clinical assessments of the relative effectiveness of new cancer medicines by the EMA, which therefore offers EU/EEA countries a chance to reduce their workload and complete assessments more quickly. Nevertheless, the impact of these efforts might remain limited without addressing underlying economic and administrative barriers.

The use of new cancer medicines in clinical practice varies greatly across Europe, with CEE countries recording the lowest usage rates, which can have implications for patient outcomes. Factors contributing to these disparities include the costs and affordability of medicines together with underfunded health care budgets, limited diagnostic infrastructure and routines and funding for biomarker testing, delays in integrating new treatments into local guidelines and protocols, and imbalances in continuing medical education. Addressing these barriers requires investment in health care, infrastructure, human resources, and organization. Establishing regional centers of excellence and promoting cross-border collaborations could enhance capacity in resource-constrained countries.

Limitations

This review has several limitations that should be acknowledged. Firstly, the analysis relies heavily on evidence from a set of international stakeholders. While these sources provide valuable insights, their perspectives may be influenced by specific agendas or focus areas, potentially introducing bias.

Secondly, measuring access to cancer medicines is inherently challenging due to the lack of standardized metrics. The use of different methodologies across studies, such as self-reported survey responses from local experts or the use of sales data that is partly estimated, could introduce variability in findings. Moreover, many analyses only focus on a medicine and its first approved indication but not any subsequent indications, which limits the generalizability of the findings. The timeframe for follow-up in many studies is limited, which may underestimate the (time to) reimbursement and use. A differentiation of medicine access along ESMO-MCBS scores would be desirable to measure access according to clinical benefit.

Thirdly, the studies reviewed often rely on aggregated national-level data, which may not fully capture

subnational disparities in access. Local differences in health care infrastructure, resource allocation, and decision-making processes may contribute to inequities in clinical use that are not evident in national averages. The establishment of nationwide clinical cancer registries would help create real-time monitoring systems for treatment uptake and outcomes across all hospitals. Collecting structured real-world data from electronic patient records is the most important basis for establishing real-world evidence on the clinical effectiveness of new cancer medicines. The analysis of treatment patterns, adherence to guidelines, and meeting quality targets could provide valuable insights to guide policy interventions and improve equitable use. At present, there is a fundamental lack of these data in most countries.

Finally, while this review synthesized information on reason for inequities in access, the underlying qualitative insights were not always systematically collected. Future research incorporating qualitative methods would enhance the understanding of barriers to access and guide more targeted interventions. By addressing these limitations, future studies can provide a more comprehensive and nuanced understanding of inequities in access to cancer medicines across Europe.

Conclusion

Achieving equitable access to novel cancer medicines in Europe remains a significant challenge and demands a multifaceted approach. While regulatory approval processes have achieved harmonization within the EU/EEA, stark differences persist in reimbursement and use in clinical practice. Transferring more competences from the national to the European level, as exemplified by the EMA and the recent EU HTA Regulation, could reduce inequities. However, addressing disparities in reimbursement and clinical use requires local solutions tailored to each country's economic and health care system constraints. Policymakers should prioritize medicines with proven clinical value, align reimbursement decisions with available resources, and consider investing more in health care where needed, especially in CEE countries. More data-driven online monitoring systems through clinical cancer registries to track utilization patterns of new medicines—also compared with recommended standards in clinical guidelines—should be established and feed into a permanent quality assurance cycle. This should be complemented by qualitative research to understand deviations from recommended standards and to help design solutions. Ultimately, achieving equity will require a balance between innovation, affordability, and sustainability in health care systems.

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DISCLOSURE

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DECLARATION OF GENERATIVE AI AND AI-ASSISTED TECHNOLOGIES IN THE WRITING PROCESS

During the preparation of this work, the authors used ChatGPT in order to edit the language. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

REFERENCES

1. Manzano A, Svedman C, Hofmarcher T, Wilking N. Comparator Report on Cancer in Europe 2025 — Disease Burden, Costs and Access to Medicines and Molecular Diagnostics. Lund, Sweden: IHE. Available at https://ihe.se/app/uploads/2025/03/IHE-REPORT-2025_2_.pdf. Accessed April 8, 2025.
2. Ferlay J, Ervik M, Lam F, et al. Global Cancer Observatory: Cancer Today (version 1.1). Lyon, France: International Agency for Research on Cancer. Available at https://gco.iarc.fr/today/en. Accessed December 11, 2024.
3. Allemani C, Matsuda T, Di Carlo V, et al. Global surveillance of trends in cancer survival 2000-14 (CONCORD-3): analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. *Lancet*. 2018;391 (10125):1023-1075.

4. De Angelis R, Sant M, Coleman MP, et al. Cancer survival in Europe 1999-2007 by country and age: results of EUROCARE-5—a population-based study. *Lancet Oncol*. 2014;15(1):23-34.
5. OECD. *Cancer Care: Assuring Quality to Improve Survival*. Paris, France: OECD Publishing; 2013.
6. Hofmarcher T, Jönsson B, Wilking N. Access to High-quality Oncology Care Across Europe. Lund, Sweden: IHE. Available at https://ihe.se/app/uploads/2014/03/IHE-Report-2014_2.pdf. Accessed December 23, 2024.
7. Lichtenberg FR. Has Medical innovation reduced cancer mortality? *CESifo Econ Stud*. 2014;60(1):135-177.
8. Lichtenberg FR. The impact of new drug launches on life-years lost in 2015 from 19 types of cancer in 36 countries. *J Demogr Econ*. 2018;84(3):309-354.
9. MacEwan JP, Dennen S, Kee R, Ali F, Shafrin J, Batt K. Changes in mortality associated with cancer drug approvals in the United States from 2000 to 2016. *J Med Econ*. 2020;23(12):1558-1569.
10. Scott EC, Baines AC, Gong Y, et al. Trends in the approval of cancer therapies by the FDA in the twenty-first century. *Nat Rev Drug Discov*. 2023;22(8):625-640.
11. Wu Q, Qian W, Sun X, Jiang S. Small-molecule inhibitors, immune checkpoint inhibitors, and more: FDA-approved novel therapeutic drugs for solid tumors from 1991 to 2021. *J Hematol Oncol*. 2022;15(1):143.
12. Chapman S, Paris V, Lopert R. Challenges in Access to Oncology Medicines: Policies and Practices Across the OECD and the EU. Paris, France: OECD Publishing; 2020.
13. IQVIA Institute for Human Data Science. Global Oncology Trends 2024: Outlook to 2028. Parsippany, NJ: IQVIA. Available at https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/global-oncology-trends-2024. Accessed December 11, 2024.
14. Hofmarcher T, Berchet C, Dedet G. *Access to Oncology Medicines in EU and OECD Countries*. Paris, France: OECD Publishing; 2024.
15. Assi A, Karbanova T, Alghawas L, et al. Surrogate measures and the health technology assessment of cancer drugs in Ireland: a retrospective analysis of EMA cancer drug indication approvals between 2017 and 2022 and recommendations made by the NCPE in Ireland. *Value Health*. 2023;26(12):S334.
16. Falcone R, Lombardi P, Filetti M, et al. Oncologic drugs approval in Europe for solid tumors: overview of the last 6 years. *Cancers (Basel)*. 2022;14(4):889.
17. Cherny NI, Sullivan R, Dafni U, et al. A standardised, generic, validated approach to stratify the magnitude of clinical benefit that can be anticipated from anti-cancer therapies: the European Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS). *Ann Oncol*. 2015;26(8):1547-1573.
18. Grossmann N, Wolf S, Rothschedl E, Wild C. Twelve years of European cancer drug approval-a systematic investigation of the 'magnitude of clinical benefit'. *ESMO Open*. 2021;6(3):100166.
19. Cherny N, Sullivan R, Torode J, Saar M, Eniu A. ESMO European Consortium Study on the availability, out-of-pocket costs and accessibility of antineoplastic medicines in Europe. *Ann Oncol*. 2016;27(8):1423-1443.
20. Cufer T, Ciuleanu TE, Berzinec P, et al. Access to novel drugs for non-small cell lung cancer in Central and Southeastern Europe: a Central European Cooperative Oncology Group Analysis. *Oncologist*. 2020;25(3):e598-e601.
21. Hofmarcher T, Brådvik G, Svedman C, Lindgren P, Jönsson B, Wilking N. Comparator Report on Cancer in Europe 2019 — Disease Burden, Costs and Access to Medicines. Lund, Sweden: IHE. Available at https://ihe.se/app/uploads/2020/10/IHE-Report-2019_7_.pdf. Accessed December 23, 2024.
22. OECD. Addressing Challenges in Access to Oncology Medicines: Analytical Report. Paris, France: OECD Publishing; 2020.
23. Chapman S, Szklanowska A, Lopert R. *Exploring the Feasibility of Monitoring Access to Novel Medicines: A Pilot Study in EU Member States*. Paris, France: OECD Publishing; 2023.
24. Wilking N, Hofmarcher T, Wilking U, Jönsson B. Drug utilization research in the area of cancer drugs. In: Elseviers M, Wettermark B, Almarsdottir AB, et al., editors. *Drug Utilization Research: Methods and Applications*. Chichester, UK: Wiley-Blackwell; 2016. p. 315-327.
25. European Commission. Authorisation Procedures — The Centralised Procedure. Available at https://health.ec.europa.eu/medicinal-products/legal-framework-governing-medicinal-products-human-use-eu/authorisation-procedures-centralised-procedure_en. Accessed December 12, 2024.
26. Dayan M, Hervey T, McCarey M, et al. *The Future for Health After Brexit*. London, UK: Nuffield Trust. Available at https://www.nuffieldtrust.org.uk/research/the-future-for-health-after-brexit. Accessed December 12, 2024.
27. Hofer MP, Criscuolo P, Shah N, Ter Wal ALJ, Barlow J. Regulatory policy and pharmaceutical innovation in the United Kingdom after Brexit: initial insights. *Front Med (Lausanne)*. 2022;9:1011082.
28. Hwang TJ, Kesselheim AS, Tibau A, Lee CC, Vokinger KN. Clinical benefit and expedited approval of cancer drugs in the United States, European Union, Switzerland, Japan, Canada, and Australia. *JCO Oncol Pract*. 2022;18(9):e1522-e15e32.
29. Hofmarcher T, Lindgren P, Wilking N. Cancer Care in Türkiye in a European Context. Lund, Sweden: IHE. Available at https://ihe.se/app/uploads/2022/11/IHE-Report-2022_10_.pdf. Accessed December 23, 2024.
30. Loblova O, Csanadi M, Ozieranski P, Kalo Z, King L, McKee M. Alternative access schemes for pharmaceuticals in Europe: towards an emerging typology. *Health Policy*. 2019;123(7):630-634.
31. Lung Cancer Europe. Disparities and Challenges in Access to Lung Cancer Diagnostics and Treatment Across Europe. Bern, Switzerland: Lung Cancer Europe. Available at https://www.lungcancereurope.eu/wp-content/uploads/2021/12/LuCE-POSITION-PAPER-English-2.pdf. Accessed December 12, 2024.
32. European Medicines Agency. Compassionate Use. Available at https://www.ema.europa.eu/en/human-regulatory-overview/research-development/compassionate-use. Accessed December 13, 2024.
33. European Federation of Pharmaceutical Industries and Associations. The Root causes of Unavailability of Innovative Medicines and Delay in Access: Shortening the Wait. Brussels, Belgium: EFPIA. Available at https://www.efpia.eu/media/xsmfuf4h/root-causes-of-unavailability-and-delay-efpia-cra-2024.pdf. Accessed December 13, 2024.
34. Lythgoe MP, Desai A, Gyawali B, et al. Cancer therapy approval timings, review speed, and publication of pivotal registration trials in the US and Europe, 2010—2019. *JAMA Netw Open*. 2022;5(6):e2216183.
35. Newton M, Stoddart K, Travaglio M, Troein P. EFPIA Patients W.A.I.T. Indicator 2023 Survey. IQVIA. Available at https://efpia.eu/media/vtapbere/efpia-patient-wait-indicator-2024.pdf. Accessed December 11, 2024.
36. Cherny NI, Trapani D, Galotti M, et al. ESMO Global Consortium Study on the availability, out-of-pocket costs, and accessibility of cancer medicines: 2023 update. *Ann Oncol*. 2025;36(3):247-262.
37. European Commission. EU Pharmaceutical Reform: Access to Medicines in All Member States. 2024. Available at https://health.ec.europa.eu/document/download/5d6fb6a0-357f-47c9-8e11-844d17468bc8_en?filename=factsheet_market-launch_en.pdf. Accessed December 22, 2024.
38. Hofmarcher T, Szilagyiova P, Gustafsson A, et al. Access to novel cancer medicines in four countries in Central and Eastern Europe in relation to clinical benefit. *ESMO Open*. 2023;8(4):101593.
39. Baird AM, Villalón D, Aguarón A, et al. Access disparities and challenges in lung cancer diagnostics and treatment — a European perspective. *J Thorac Oncol*. 2021;16(suppl 3):S467-S468.
40. Manxhuka B, Hofmarcher T. Cancer Dashboard for Poland - Lung Cancer. Lund, Sweden: IHE. Available at https://ihe.se/app/uploads/2024/09/IHE_-_Lung-Cancer_Dashboard_Poland_.pdf. Accessed December 21, 2024.
41. Loblova O, Csanadi M, Ozieranski P, Kalo Z, King L, McKee M. Patterns of alternative access: unpacking the Slovak extraordinary drug reimbursement regime 2012-2016. *Health Policy*. 2019;123(8):713-720.
42. Remuzat C, Urbinati D, Mzoughi O, El Hammi E, Belgaied W, Toumi M. Overview of external reference pricing systems in Europe. *J Mark Access Health Policy*. 2015;3:27675.

43. Toumi M, Rémuzat C, Vataire A-L, Urbinati D. External Reference Pricing of Medicinal Products: Simulation Based Considerations for Cross Country Coordination. European Commission. Available at https://health.ec.europa.eu/system/files/2016-11/erp_reimbursement_medicinal_products_en_2.pdf. Accessed December 23, 2024.
44. OECD/European Commission. *Health at a Glance: Europe 2024: State of Health in the EU Cycle*. Paris, France: OECD Publishing; 2024.
45. Hofmarcher T, Lindgren P, Wilking N. Systemic anti-cancer therapy patterns in advanced non-small cell lung cancer in Europe. *J Cancer Policy*. 2022;34:100362.
46. Hofmarcher T, Lindgren P, Wilking N. Diagnosed But Not Treated: How to Improve Patient Access to Advanced NSCLC Treatment in Europe. Lund, Sweden: IHE. Available at https://ihe.se/app/uploads/2022/02/IHE-Report-2022_2_.pdf. Accessed December 27, 2024.
47. Pousette A, Hofmarcher T. Cancer Dashboard for Italy — Access to Cancer Medicines. Lund, Sweden: IHE. Available at https://ihe.se/app/uploads/2024/11/IHE-Cancer-Dashboard_Italy_.pdf. Accessed December 25, 2024.
48. Hofmarcher T, Brådvik G, Lindgren P, Jönsson B, Wilking N. Comparator Report on Cancer in the Nordic Countries — Disease Burden, *Costs and Access to Medicines*. Lund, Sweden: IHE. Available at https://ihe.se/app/uploads/2019/05/IHE-Report-2019_2b_.pdf. Accessed April 8, 2025.
49. Bayle A, Bonastre J, Chaltiel D, et al. ESMO study on the availability and accessibility of biomolecular technologies in oncology in Europe. *Ann Oncol*. 2023;34(10):934. 845.
50. Normanno N, Apostolidis K, Wolf AJ, et al. Access and quality of biomarker testing for precision oncology in Europe. *Eur J Cancer*. 2022;176:70-77.
51. Mateo J, Steuten L, Aftimos PE, et al. Delivering precision oncology to patients with cancer. *Nat Med*. 2022;28(4):658-665.
52. Vintura. Every Day Counts — Improving Time to Patient Access to Innovative Oncology Therapies in Europe. Utrecht, Netherlands: Vintura. Available at https://www.vintura.com/wp-content/uploads/2020/08/White-paper-every-day-counts-improving-time-to-patient-access-to-innovative-oncology-therapies-in-europe_from-EFPIA_and_Vintura.pdf. Accessed December 24, 2024.
53. US Food and Drug Administration. Project Orbis. Available at https://www.fda.gov/about-fda/oncology-center-excellence/project-orbis. Accessed December 27, 2024.
54. Medicines and Healthcare Products Regulatory Agency. International Recognition Procedure. Available at https://www.gov.uk/government/publications/international-recognition-procedure/international-recognition-procedure. Accessed December 27, 2024.
55. Godman B, Hill A, Simoens S, et al. Potential approaches for the pricing of cancer medicines across Europe to enhance the sustainability of healthcare systems and the implications. *Expert Rev Pharmacoecon Outcomes Res*. 2021;21(4):527-540.
56. World Health Organization. Technical Report: Pricing of Cancer Medicines and Its Impacts: A Comprehensive Technical Report for the World Health Assembly Resolution 70.12: Operative Paragraph 2.9 on Pricing Approaches and Their Impacts on Availability and Affordability of Medicines for the Prevention and Treatment of Cancer. Geneva, Switzerland: WHO. Available at https://iris.who.int/handle/10665/277190. Accessed December 27, 2024.
57. European Federation of Pharmaceutical Industries and Associations. Addressing Patient Access Inequalities in Europe. Brussels, Belgium: EFPIA. Available at https://www.efpia.eu/media/677156/addressing-patient-access-inequalities-in-europe.pdf. Accessed December 27, 2024.