

## European Groundshot—addressing Europe’s cancer research challenges: a *Lancet Oncology* Commission



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Cancer research is a crucial pillar for countries to deliver more affordable, higher quality, and more equitable cancer care. Patients treated in research-active hospitals have better outcomes than patients who are not treated in these settings. However, cancer in Europe is at a crossroads. Cancer was already a leading cause of premature death before the COVID-19 pandemic, and the disastrous effects of the pandemic on early diagnosis and treatment will probably set back cancer outcomes in Europe by almost a decade. Recognising the pivotal importance of research not just to mitigate the pandemic today, but to build better European cancer services and systems for patients tomorrow, the *Lancet Oncology* European Groundshot Commission on cancer research brings together a wide range of experts, together with detailed new data on cancer research activity across Europe during the past 12 years. We have deployed this knowledge to help inform Europe’s Beating Cancer Plan and the EU Cancer Mission, and to set out an evidence-driven, patient-centred cancer research roadmap for Europe. The high-resolution cancer research data we have generated show current activities, captured through different metrics, including by region, disease burden, research domain, and effect on outcomes. We have also included granular data on research collaboration, gender of researchers, and research funding. The inclusion of granular data has facilitated the identification of areas that are perhaps overemphasised in current cancer research in Europe, while also highlighting domains that are underserved. Our detailed data emphasise the need for more information-driven and data-driven cancer research strategies and planning going forward. A particular focus must be on central and eastern Europe, because our findings emphasise the widening gap in cancer research activity, and capacity and outcomes, compared with the rest of Europe. Citizens and patients, no matter where they are, must benefit from advances in cancer research. This Commission also highlights that the narrow focus on discovery science and biopharmaceutical research in Europe needs to be widened to include such areas as prevention and early diagnosis; treatment modalities such as radiotherapy and surgery; and a larger concentration on developing a research and innovation strategy for the 20 million Europeans living beyond a cancer diagnosis. Our data highlight the important role of comprehensive cancer centres in driving the European cancer research agenda. Crucial to a functioning cancer research strategy and its translation into patient benefit is the need for a greater emphasis on health policy and systems research, including implementation science, so that the innovative technological outputs from cancer research have a clear pathway to delivery. This European cancer research Commission has identified 12 key recommendations within a call to action to reimagine cancer research and its implementation in Europe. We hope this call to action will help to achieve our ambitious 70:35 target: 70% average survival for all European cancer patients by 2035.

### Introduction

A crucial inflection point for cancer research in Europe has been reached. The challenge for cancer research in Europe is unequivocal: how best can research play a transformative role in promoting more effective prevention; facilitating earlier diagnosis; delivering better, safer, and potentially more affordable treatments; and ensuring enhanced quality of life for current patients and those living beyond cancer? Furthermore, how can this challenge be addressed through the prism of the substantial impact of the COVID-19 pandemic and other externalities (eg, Brexit, the Russian invasion of Ukraine, or the economic recession)?

The need for accurate, timely, granular data that capture the current landscape of research activity and highlight the gaps that need to be addressed is crucial

to inform a person-centred ambitious cancer research agenda for Europe. Too often, opinion, even expert opinion, has trumped data in the genesis and implementation of cancer research policies. In this *Lancet Oncology* European Groundshot Commission on cancer research, we have first focused on generating data to provide an overview of the current European cancer research landscape, highlighting its strengths and capturing its weakness, contrasting areas that have perhaps received an overemphasis of effort with those that have been underserved. Analysing these data and deploying the resulting evidence underpins a series of recommendations and a call to action, which, if acted upon, will help nurture a cancer research culture that delivers pragmatic, patient-focused solutions for Europe.

### Lancet Oncol 2022

Published Online  
November 15, 2022  
[https://doi.org/10.1016/S1470-2045\(22\)00540-X](https://doi.org/10.1016/S1470-2045(22)00540-X)

See Online/Comment  
[https://doi.org/10.1016/S1470-2045\(22\)00651-9](https://doi.org/10.1016/S1470-2045(22)00651-9),  
[https://doi.org/10.1016/S1470-2045\(22\)00653-2](https://doi.org/10.1016/S1470-2045(22)00653-2),  
and [https://doi.org/10.1016/S1470-2045\(22\)00641-6](https://doi.org/10.1016/S1470-2045(22)00641-6)

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of population-based cancer registries have been crucial in a data-driven approach to understanding cancer and enhancing cancer outcomes.

One unintended consequence of the COVID-19 pandemic, with rapid repurposing of health services and introduction of national lockdowns, has been the adverse effects that these measures and their continuing legacy have had on cancer services, on cancer research, and most importantly on patients with cancer.<sup>1-4</sup> To emphasise the scale of this problem, we estimate that about 1 million cancer diagnoses might have been missed across Europe during the COVID-19 pandemic.<sup>5</sup> There is emerging evidence that a higher proportion of patients are diagnosed with later cancer stages compared with pre-pandemic rates as a result of substantial delays in cancer diagnosis and treatment. This cancer stage shift will continue to stress European cancer systems for years to come.<sup>6</sup> These issues will ultimately compromise survival and contribute to inferior quality of life for many European patients with cancer. COVID-19 has regrettably exposed the poor resilience in current cancer health systems that will prompt a cancer epidemic over the next decade if not addressed urgently.<sup>7</sup>

Much of the success achieved in improving cancer outcomes over the past two decades in Europe could be reversed by the impact of the pandemic.<sup>8</sup> Crucially, in the context of this *Lancet Oncology* Commission, there has been an unsettlingly negative effect of the COVID-19 pandemic on cancer research, with substantial reductions in cancer clinical trial activity, disruption to discovery cancer research, and major reductions in cancer research funding.<sup>9</sup>

Against this backdrop, this *Lancet Oncology* Commission provides crucial evidence on the current landscape of cancer research across Europe, exposes the key gaps in research, and demands a reprioritisation of European cancer research agendas over the next decade. We focus on the gaps and inequalities in cancer research that would create a more effective cancer research ecosystem if addressed. If these gaps and inequalities were addressed, cancer research and its implementation across Europe could be reimaged. Simply continuing to dedicate resource and effort to a narrow research agenda is no longer desirable or viable: we must follow the data and act on what they reveal.

## Section 1: examples of cancer research domains with particular strength in Europe

There are many research domains in which Europe can be categorised as world leading. The European continent (not just the European Union [EU]) is a global leader in cancer discovery science. Strengths are evident in molecular, cellular, and structural cancer biology; modelling; diagnostics and early detection; new medical technologies and personalised treatments; precision oncology; vaccines, immunotherapies, and drug-antibody conjugates; and paradigmatic shifts in neoadjuvant therapy, especially for immunotherapy. European cancer epidemiology research and deployment

### Cancer registries

More than 180 cancer registries are in operation across Europe in more than 30 countries, coordinated by the European Network of Cancer Registries. In most countries, cancer registration covers the entire national population and is a statutory requirement. Cancer registries provide a comprehensive picture of Europe's cancer burden, but problems in accessing the data can make it difficult for researchers to produce reliable data-driven analyses in a timely fashion. The COVID-19 pandemic has shown that governments can ensure rapid access to data when they perceive a pressing need. The European Centre for Disease Control<sup>10</sup> was able to produce daily updates of the number of people who had COVID-19 and the number of COVID-19-related deaths within 2–3 days of their occurrence. We should have similar timely cancer data to inform our research and care agendas. Population-based cancer registries represent key enabling infrastructure to help define cancer inequalities, evaluate the effect of cancer-prevention research strategies, and determine the effectiveness of national health-care systems in providing the best care for patients with cancer, regardless of their socioeconomic status.

There is a strong public health case for ensuring that high-quality data on cancer in all European countries are as up to date as possible, and that these data are made available for research in compliance with national laws and the EU General Data Protection Regulation (GDPR),<sup>11</sup> without unnecessary constraints. GDPR is not sufficiently well understood and in some countries its interpretation can be restrictive for research. We need a pragmatic approach to ensure protection of the individual's rights while also making data available for bona-fide research. Without access to data, the ability to address the challenges of the COVID-19 pandemic would have been severely compromised.<sup>5</sup>

### Cancer model systems

The discovery and development of organoids as a model system to elucidate crucial drivers of cancer has allowed for the precise definition of distinct mechanisms of tumour-cell killing and has helped to determine emerging drug resistance.<sup>12</sup> Creation of so-called living biobanks for multiple tumour types provides an excellent platform for driving cancer research and innovation.<sup>12,13</sup> Appropriate and well characterised model systems have been important drivers in the rapid development of drug-sensitivity screening models, with predictive value in multiple tumour types, underpinning innovative precision oncology and immunotherapy research.<sup>12,14,15</sup>

In parallel, the creation and deployment of a variety of animal model systems that recapitulate the tumour biology

of multiple cancer types has facilitated the evaluation of innovative treatment modalities at the preclinical stage. Europe has shown strengths and pursued innovation in animal models, particularly for genetically engineered mouse models and patient-derived xenografts.<sup>16</sup> The importance of animal model systems and their relevance to cancer is supported by the UK's Medical Research Council. In 2022, the Medical Research Council announced a multimillion investment in a National Mouse Genetics Network, with cancer as a key cluster.<sup>17</sup>

### Early-detection research

The NELSON randomised lung cancer screening study has been pivotal because of the convincing early detection rates achieved and their impact on lung cancer survival.<sup>18</sup> New European-driven developments in ultra-thin rapid next-generation CT-scanning and artificial intelligence-enhanced early detection (and prediction) will further empower robust early detection, enhanced by robotic read-out systems and machine learning approaches that provide increasing precision and speed in early cancer detection. Although this approach will require investment, it will subsequently be accompanied by a lowering of costs, driving the dual imperative of saving people's lives while delivering value-based care.<sup>19</sup>

### Cancer diagnostics and precision oncology

There has been a notable push in Europe to embrace new medical technologies, which involves developing and deploying innovative tools to enhance cancer diagnosis and treatment. Cancer biomarkers and genomic testing are key enablers to unlock the promise of precision oncology. A robust cancer biomarker infrastructure must be embedded across health systems, to ensure their deployment as innovation drivers across Europe. Cancer biomarkers must also be considered in the context of the EU In-Vitro Diagnostics Regulation, which might still pose some challenges.<sup>20</sup> Embedding cancer biomarkers within real-world oncology delivery and providing genomic testing across Europe, while ensuring that inequity gaps for patients are narrowed and not widened, must be the goal.<sup>21</sup> Importantly, patients with cancer must be at the centre of this biomarker-driven precision oncology research agenda, with research into value-based care informing appropriate biomarker use.

If deployed appropriately, cancer biomarkers can reduce costs by ensuring the right treatment, for the right patient, at the right dose, at the right time. Using cancer biomarkers can avoid specific cancer treatment sequelae for patients who gain no therapeutic benefit from these treatments. The health economic analyses we conducted between 2020 and 2022 have underlined the potential for cancer biomarkers to deliver value for money.<sup>22-24</sup> However, we also found a paucity of studies that used detailed health economic analysis to inform the feasibility of incorporating cancer biomarkers or genomic testing into the clinic, highlighting the need for wider

deployment of health economic evaluation to inform value-based care. Precision diagnostics can also help target interventions to the most important areas of disease.<sup>25</sup>

### Radiation oncology

Europe's radiotherapy research agenda is highly focused on precision radiation therapy development. For example, new-generation MRI-guided radiotherapy,<sup>26</sup> adaptive radiotherapy, or FLASH radiotherapy<sup>27</sup> systems search for the optimal balance between treatment toxicity and tumour control. This continuous search for better-tolerated radiotherapy not only allows for them to be integrated in combination with new drugs, but has also facilitated hypofractionated delivery, which has become the standard-of-care in breast cancer and prostate cancer thanks to large randomised European clinical trials.<sup>28</sup> Research into radiotherapy has also allowed for the expansion of this treatment to new patient populations, such as in the radical approach to oligometastatic disease with stereotactic body radiotherapy.<sup>29</sup> Shortening radiotherapy delivery through hypofractionation using unique radiobiological profiles of different tumour types has profoundly enhanced radiotherapy delivery, with a positive effect on cancer burden for patients and society. Europe's commitment to practice-changing randomised controlled trials<sup>30</sup> has enabled radiotherapy to be reactive to the effects of the COVID-19 pandemic, facilitating changes in practice-of-care to enable the continuation of services during the pandemic and the subsequent management of the cancer backlog.

### Vaccine development

Overall, there are substantial strengths in cancer vaccine expertise across Europe. Successful development of the preventive human papillomavirus (HPV) vaccine and its implementation to protect women and girls from cervical cancer, and its implementation within the past 5 years to protect both sexes from HPV-driven cancers, such as oropharyngeal and anal cancers, had its origins in the pioneering research of 2008 Nobel Prize winner Harald zur Hausen. Furthermore, Europe has been at the forefront of the development of COVID-19 vaccines, deploying mRNA personalised vaccine approaches for vaccination strategies in solid tumours.<sup>31</sup>

### Tumour immunology and immunotherapy

Tumour immunology and immunotherapy are examples of recognised research strengths in Europe. The early work on anti-PD1 drugs (eg, nivolumab and pembrolizumab) is both a seminal development and an exemplar of European research strength.<sup>32</sup> Recognition of the importance of immunogenic cell death has been pivotal, particularly for classifying chemotherapeutic drugs and enhancing combination strategies.<sup>33</sup> Europe is also a global leader in determining the role of the microbiome on cancer treatment efficacy, particularly in treatments

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For the European Network of Cancer Registries see <https://enr.eu>

For the Incisive project see <https://incisive-project.eu/>

that use immune checkpoint inhibitors.<sup>34–37</sup> Discovery science has informed clinical trials, allowing the use of microbiome-management approaches to optimise anti-tumour responses.<sup>38</sup> Characterising the immune component of the tumour microenvironment has been crucial in developing tumour immunoscores,<sup>39</sup> which involves detailing immune-enhancing and immunosuppressive components that are fundamental to our understanding of the immune environment. Manipulation of the immune system and the tumour microenvironment are important targets in cancer therapy development.<sup>40</sup>

Immunotherapy is currently undergoing its next revolution. Translating discovery science in advanced disease in melanoma and its rollout in multiple tumour types was the first paradigm shift. This rollout was rapidly followed by the development of adjuvant therapy approaches, initially in patients with stage 3 melanoma.<sup>41</sup> This neoadjuvant immunotherapy framework is achieving highly substantial reductions in clinical relapses, more cures, shorter treatment cycles, and less surgery.<sup>42</sup> Neoadjuvant immunotherapy has been deployed effectively to avoid rectal cancer surgery in almost all patients,<sup>43</sup> with promising results for head and neck cancer,<sup>44</sup> bladder cancer,<sup>45</sup> and locally advanced lung cancer.<sup>46</sup>

## Section 2: challenges for cancer research in Europe

Although we have reflected on some examples of pre-existing research excellence and front-line innovation in Europe, there are several substantial research challenges that must also be considered and addressed. The focus of this *Lancet Oncology* European Groundshot Commission on cancer research is to identify and codify these challenges and use the evidence generated to propose a broader, more person-centred, data-informed cancer research agenda for all of Europe, not just the current 27 EU member states (EU27). Cancer prevention research, for example, has not had the attention (or the funding) it deserves, given its potential role in cancer control.<sup>47</sup> Screening recommendations from 2003 have not been fully implemented, which emphasises the dearth of national implementation science programmes to address this deficit.

Similarly, our ability to convert research discovery into therapeutic innovation is compromised by regulatory, implementation, and scale-up challenges.<sup>48</sup> More support is required for both academic-led clinical trials and real-world evidence studies. Health services research and implementation science are crucial to ensuring the translation of research into clinical practice, but research focus and funding for these two important areas has been woefully scarce. Overall, the insufficient support for this research is curtailing our ability to deliver new diagnostics and therapeutics that can be sustainably and equitably embedded across European health systems. Crucially, despite the 20 million European citizens living with and beyond cancer,<sup>49</sup> a distinct lack of focus on developing research programmes that address the

physical, psychosocial, and financial needs of cancer survivors remains.

From an infrastructure perspective, substantial gaps exist. We must occupy the vanguard of the digital health revolution, ensuring well structured data warehouses, databanks, and computer-based systems to support rapid deployment of machine learning and accelerated analytical approaches. Europe does have world-leading excellence in data science, including the pioneering work of the European Bioinformatics Institute and Health Data Research UK, but what is needed is the creation of highly curated datasets that are linked across Europe to enable national evaluation of practice, policy, and performance. Federated data approaches should also be encouraged.

We need to facilitate precise analysis of the impact of new cancer technologies on health systems, analysis of the real-world impact of new treatments, and analysis of new prevention and lifestyle adaptation strategies. These developments are currently hampered by Europe's fragmented system of health informatics. However, a great advantage that we must build on is that research policies are defined and research funding is allocated both at a national and European scale, providing an opportunity to break down traditional silos and enhance the value of cancer research and its translation across Europe. These opportunities are particularly relevant, as already highlighted by Europe's Beating Cancer Plan, the EU Cancer Mission, and Horizon Europe's research funding programmes. Crucial to this effort is the need for the bioinformatic, statistical, and advanced data analytics skills and frameworks to drive a digital health agenda that places substantial emphasis on data and its deployment to underpin cancer research and its real-world translation for the benefit of human health and wellbeing. With the push for federated datasets and the ongoing development of the European Health Data Space, Europe is ideally positioned to be a world leader in cancer health data science and its application.

Another important gap in European cancer research is the poor quality of real-world studies,<sup>50</sup> which reinforces the need for better data strategies and systems for post-marketing studies. Through more data-empowered, morpho-molecular analyses, which are then coupled with clinical information, the unique nature of every patient with cancer is being understood. Consequently, the classical research paradigm will undoubtedly shift, in the near future, to an agenda that is focused on collecting and analysing real-world data from all oncology patients.<sup>51,52</sup> In this context, new financing models, such as coverage linked with evidence development, could aid the generation of both clinical and economic evidence to support formal reimbursement schemes in a real-world setting.<sup>53</sup>

## Section 3: cancer research in Europe—the political opportunity

In many European countries, cancer is the leading cause of premature morbidity and mortality, and a major

For the European Bioinformatics Institute see <https://www.ebi.ac.uk>

For Health Data Research UK see <https://www.hdr.uk.ac.uk>

For more on EU efforts see [https://european-union.europa.eu/index\\_en](https://european-union.europa.eu/index_en)



economic burden for citizens and societies. The human and financial costs of cancer to Europe and its citizens will only continue to grow. Although Europe provides some of the best cancer care in the world and conducts high-quality, globally recognised cancer research, there are notable disparities in access to, and delivery of, optimal cancer control. Furthermore, there is a need to ensure that cancer research and innovation address these disparities to reduce inequalities between and within European countries. European cancer research strengths are currently unevenly distributed and do not necessarily align with the cancer priorities of individual European countries, which is an issue that we explore in more detail in this Commission.

Despite these challenges, there have been some encouraging developments in the current European cancer control and research landscapes. Crucially, Ursula von der Leyen, President of the European Commission, has championed the need for a clearer strategic focus on health, exemplified by her call for a stronger European Health Union. Previous incumbents of her office have shied away from this strategic focus, suggesting instead that health is a national competency. Variations in survival, however, suggest that relying on national competency alone is not in the best interests of European citizens. The COVID-19 pandemic has shown that collaborative vaccine development; the rapid delivery of effective vaccines to European citizens; and collaboration between countries, jurisdictions, and sectors is absolutely essential.

This reorientation of the narrative (ie, prioritising the enhancement of our cancer health and wellbeing as part of a pan-European effort) was reinforced by the conclusions of the Conference on the Future of Europe in 2022, calling for more pan-European cooperation in health care and research (appendix p 4).<sup>54</sup> A stronger European Health Union beyond the political boundaries of the EU27, with an emphasis on greater health resilience and integrated research, a health in all policies approach, and a data-informed, citizen-focused, research-driven agenda (eg, the research agenda that we are proposing) are urgently required to address the challenges that cancer poses. Putting patient-focused and citizen-focused (and approved) research at the heart of a pan-European cancer strategy will be an important driver of enhanced health outcomes.

The president of the European Commission tasked Stella Kyriakides, the Health and Food Safety Commissioner, with developing an ambitious plan for cancer, emphasising the importance of tackling this devastating disease. In 2020, cancer was diagnosed in 2.7 million citizens and led to more than 1.3 million deaths in the EU.<sup>55</sup> Following a period of development and a degree of consultation, Europe's overarching Beating Cancer Plan was launched by Kyriakides on the eve of World Cancer Day in 2021. This plan has four key pillars: prevention; early detection; diagnosis and treatment; and quality-of-life. Progress within these four

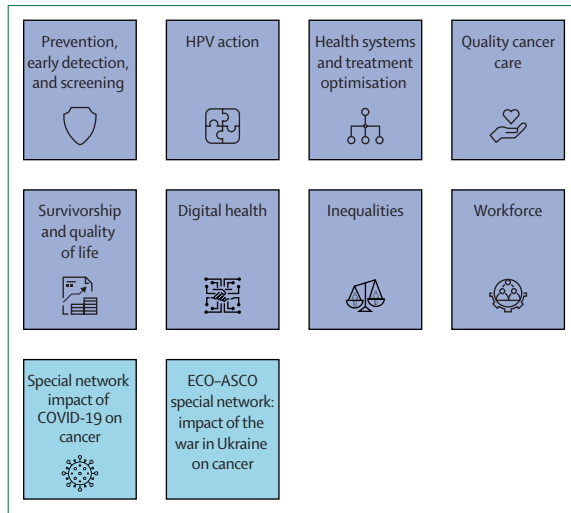
pillars will be achieved through implementation of ten key Flagship Initiatives (appendix p 5), and a series of accompanying supporting actions. On Feb 16, 2022, the European Parliament ratified Europe's Beating Cancer Plan, which was the first time that Europe developed a consolidated approach to address this deadly disease that is overtaking cardiovascular disease as the most common cause of premature death in Europe.

From a research perspective, and thus of crucial importance to this Commission, cancer was also selected as one of the EU's five research missions, emphasising the importance placed on cancer research as integral to national cancer control planning. Evidence generated by authors of this Commission and by others indicates that patients treated in research-active hospitals have substantially better outcomes than patients who are not treated in these settings.<sup>56</sup> *Conquering cancer: mission possible*, the interim report of the Cancer Mission Board was published in September, 2020.<sup>57</sup> A number of key research themes, which were supported by a series of activities, were identified in this report, echoing the pillars of Europe's Beating Cancer Plan: understanding of cancer; prevention and early detection, diagnosis and treatment, and quality of life for patients and their families (appendix p 6). Additionally, the Cancer Mission Board supports a set of guiding principles (appendix p 7). The efforts by the Cancer Mission Board are noble ambitions, but they must be underpinned by an appropriate evidence base, as we have sought to do in this Commission.

Politically, as Europe's Beating Cancer Plan and the Cancer Mission were being developed and shared with the cancer community, a focus on cancer also emerged within the European Parliament. The European Beating Cancer Committee hearings received substantial evidence submissions from stakeholders across the cancer community. The establishment of a new cross-party European Parliament Challenge Cancer Intergroup, with a secretariat provided by the European Cancer Patient Coalition (ECPC), which is Europe's largest umbrella advocacy organisation for patients with cancer, provides a complementary voice to the already existing Members of the European Parliament Against Cancer. These two cross-party European Parliamentary groups emphasise the commitment of Members of the European Parliament to cancer issues. Political support is key in driving a cancer research agenda as Europe navigates turbulent economic, social, and political circumstances in the context of the COVID-19 pandemic, the Russian invasion of Ukraine, and economic contractions.

The aims and specific objectives of Europe's Beating Cancer Plan and, in particular, the Cancer Mission echo the US Cancer Moonshot,<sup>58</sup> with its aspiration to accelerate efforts to prevent, diagnose and treat cancer and, perhaps more controversially, its aspiration to achieve a decade of progress in just 5 years. The aspirations of the US Cancer Moonshot were articulated in a 2017 *Lancet Oncology* Commission on future cancer research priorities in the

See Online for appendix



**Figure 1: The ECO's ten Focused Topic Networks<sup>62</sup>**  
 ASCO=American Society of Clinical Oncology, ECO=European Cancer Organisation. HPV=human papillomavirus.

USA.<sup>59</sup> On Feb 3, 2022, US President Joe Biden announced the reignition of the Moonshot (ie, Cancer Moonshot 2.0), with an aim to reduce cancer deaths by 50% in the next 25 years.<sup>60</sup> But does Europe really need another Cancer Moonshot? In developing the *Lancet Oncology* European Groundshot Commission on cancer research,<sup>61</sup> we argue that a more citizen-focused and patient-focused and less techno-centric cancer research approach is more appropriate to the challenges that cancer poses for Europe. Cancer research prioritisation for Europe must reflect what is happening on the ground, empowering a more holistic, person-focused cancer research agenda and informing cancer research priorities and their implementation across all of Europe.

This Commission is supported by a substantial number of new analyses, uncovering novel insights, combined with evidence generated by authors of the Commission. Crucially, this cancer-research analysis has been enhanced with substantial input from members of the Focused Topic Networks<sup>62</sup> of the European Cancer Organisation (ECO). ECO is the largest multiprofessional cancer organisation in Europe, bringing together more than 40 European health and care professional societies and 22 cancer patient advocacy groups to provide the authoritative, united policy voice of the European cancer community. Initially, ECO established eight Focused Topic Networks in areas of strategic relevance: prevention, early detection, and screening; HPV action; health systems and treatment optimisation; quality cancer care; digital health; workforce; survivorship and quality of life; and inequalities.<sup>62</sup> The COVID-19 pandemic prompted ECO to establish a special Focused Topic Network on the impact of COVID-19 on cancer<sup>63</sup> and in response to the Russian invasion of Ukraine, ECO joined with the American Society of Clinical Oncology (ASCO) to form an ECO-ASCO special network on the impact of the war in Ukraine on cancer.<sup>64</sup> The ten

focused topic networks which have inputted to this Commission are highlighted in figure 1.

Additionally, there have been major contributions through specific partnerships with pan-European organisations including ECPC; the International Agency for Research on Cancer (IARC); the European Academy of Cancer Sciences (EACS), a pan-European body which convenes clinicians and scientists to provide evidence-based advice to underpin cancer policy in Europe; the Organisation of European Cancer Institutes (OECI), a cancer research network that promotes greater cooperation among European cancer centres and institutes; and the International Cancer Research Partnership (ICRP), a unique alliance of more than 150 cancer research organisations that maintains the only public repository of publicly funded cancer research globally.

A considerable challenge for Europe, both for the Beating Cancer Plan and the Cancer Mission, is the inequalities that persist in many aspects of cancer health systems and services, including screening, diagnosis, treatment, and supportive care, particularly in central and eastern European countries. Illuminating such inequalities within national cancer research agendas is pivotal for developing new policies that deliver better patient outcomes.

#### Section 4: a person-centred European cancer research agenda

This Commission on cancer research is also informed by several patient-enabled initiatives driven by the European cancer community. A project by the European Cancer Concord, a pan-European collaborative group of patients and health professionals, gathered and analysed comprehensive data from across Europe, facilitating characterisation of Europe's key cancer inequalities.<sup>65</sup> This led to development of the European Cancer Patient's Bill of Rights<sup>66</sup> (appendix p 8), launched with cross-political party support in the European Parliament on World Cancer Day, 2014. The Bill of Rights, cocreated by patients and health professionals, was developed as a catalyst for change and an empowerment tool for patients with cancer across Europe. The second of its three components was a commitment to optimal cancer care, underpinned by research and innovation (appendix p 8). The Bill of Rights and its implementation across Europe received the prestigious 2018 European Health Award at the European Health Forum that took place in Gastein, Austria.<sup>67</sup>

Congruent with the development of the Bill of Rights was the launch of the Europe of Disparities in Cancer initiative (appendix p 9),<sup>68</sup> which is led by ECPC, with input from European health professionals. This initiative forms the bedrock of ECPC's cancer inequalities agenda. An important evidence-informed output in the context of this *Lancet Oncology* Commission is the policy paper on tackling social determinants in cancer prevention, cancer

research, and cancer control in Europe,<sup>69</sup> published through CanCon, the EU Joint Action on Cancer Control. The Workgroup of European Cancer Patient Advocacy Networks (WECAN) have contributed substantially to the shaping of Europe's Beating Cancer Plan.

### Section 5: the 70:35 vision for cancer control and research in Europe

These initiatives, with their citizen-driven and patient-driven focus on addressing cancer inequalities, have been instrumental in developing an overarching new vision for cancer research and control in Europe (the 70:35 vision). The 70:35 vision was cocreated with multiple stakeholders through consultation and data-enabled research, evaluating different scenarios, which, if realised, would help reduce lives lost due to cancer. This analysis culminated in a proposed target of an average of 70% 10-year survival for patients treated for cancer in Europe by 2035.<sup>70</sup> Research and innovation form a crucial pillar to support the delivery of this 70:35 vision (appendix p 10).

In this Commission, we have collected and analysed high-resolution data on cancer research activity and its funding in Europe, with a particular emphasis on central and eastern European countries. This high-quality evidence provides the narrative for current cancer research being performed in Europe and informs our 12 recommendations framed within our call to action that address the challenges that European citizens face in their daily lives, including a burgeoning divide between eastern and western Europe in cancer research.

### Section 6: methods

#### Definitions of Europe

The definition of Europe used in this Commission is shown in the appendix (p 11). In summary, we are defining Europe geographically (EUR), namely, as the EU27 plus 17 other countries that are not members of the EU.

#### European cancer outcomes

##### *Determining inequalities in cancer survival*

Data from population-based cancer registries across Europe provide comprehensive evidence that facilitates an estimation of survival for patients with cancer. These data are an important metric for the overall effectiveness of a national or regional country or region's health system in managing cancer, from early diagnosis through to treatment delivery and final outcome.<sup>71</sup> For this *Lancet Oncology* Commission, survival estimates were provided by the third cycle of the CONCORD programme,<sup>72</sup> which analysed individual records for 37·5 million patients diagnosed with one of 18 common cancers between 2010 and 2014 worldwide, including more than 15 million patients with cancer diagnosed in Europe. This timeframe was chosen because it includes the most recent internationally comparable estimates of

population-based survival worldwide. Data for more than 15 million patients with cancer were provided by 157 population-based cancer registries in 31 European countries, 22 of which provided data with national coverage. We estimated 5-year net survival: the cumulative probability of surviving up to 5 years after a diagnosis of cancer and correcting for other causes of death (ie, background mortality).<sup>73,74</sup> Survival estimates were age-standardised using the International Cancer Survival Standard weights for adults<sup>75</sup> and children.<sup>76</sup>

##### *Determining inequalities in cancer mortality*

Official death certification data for 22 anatomical cancer sites and estimates of resident populations for European countries, based on official censuses, were extracted from the WHO database.<sup>77</sup> All cancer deaths were recoded according to the tenth revision of the International Classification of Diseases.<sup>78</sup> Age-specific rates for quinquennia of age (from 0–4 years of age to over 85 years of age) were computed. Age-standardised mortality rates per 100000 person years, based on the world standard population, were obtained for each calendar year (1985–2016) and sex. These rates were also obtained for central, eastern, and western European regions. The number of avoidable deaths in 2016 in central and eastern European countries was estimated by applying the age-specific and sex-specific western European rates to the corresponding central and eastern European populations. Similarly, avoided deaths from all cancers combined between 1991 and 2016 were estimated by applying the 1990 peak age-specific mortality rate to the population of the successive calendar periods and comparing the resulting numbers of deaths with the observed ones.

#### European cancer research landscape

##### *Bibliometric analysis of European cancer research outputs*

Cancer research papers (articles and reviews) were identified in the Clarivate Core Collection Web of Science database through a complex filter with the names of 396 specialist oncology journals and 384 title words and phrases that have been previously described.<sup>79</sup> The filter was calibrated and had a precision value of 0·95 and a recall value of 0·98. Additionally, we identified biomedical research papers with a second filter, containing a list of 172 address words and contractions in oncology, which had a precision value of 0·91 and a recall value of 0·91. The number of papers in each subject area, year-by-year, from the world (ie, other regions that are not in Europe), the 44 European region countries as a group (appendix p 12), and from each European country individually were extracted to underpin our landscape mapping analysis.

Sets of papers were further analysed with a series of subfilters based on title words and on the names of specialist journals. Identified papers captured cancer research outputs across 14 research domains (chemotherapy, clinical trials, diagnosis, epidemiology, genetics,

For WECAN see <https://wecanadvocate.eu>

paediatrics, palliative care, pathology, prognosis, quality of life, radiotherapy, screening, surgery, targeted therapy; for abbreviations see appendix p 13). Using these subfilters, papers relating to 17 anatomical cancer sites were also identified (appendix p 13). For each of these 31 subject areas, annotated with tetragraph and trigraph codes, we determined the numbers of papers from each of the 44 European region countries in the 12-year period (2009–2020), and from the whole European region. These data allowed for the comparison of the amount of research done on each anatomical site with the relevant disease burden (in disability-adjusted life years [DALYs]) for the whole European region. These data also provided the potential to determine which European countries had tailored their cancer research portfolio to take proportional account of the cancer burden distribution between anatomical sites.

We also compared the cancer research outputs of individual countries, and groups of countries, with their gross domestic products (GDP) in 2015. Data were taken from those provided by The World Bank.

#### Patterns of international cooperation

Europe-wide activities have already stimulated much coauthorship in cancer research within the region, and not just between the 27 member states. We sought to determine the pattern of international collaboration for the ten countries with the largest output of cancer research papers (at least 18 000 papers published over the 12-year study period). For each country we compared the numbers of paper published in cooperation with other named countries. For example, of 42 812 German papers with international collaboration, from a total output from Germany of 118 719 papers, Sweden contributed to 3899 (3·28%) papers, whereas South Korea contributed to 1125 (0·95%) papers. Of 1196 119 cancer papers that did not have a German author, from a total of

1491804 national contributions, Sweden contributed to 17 653 (1·18%) papers, whereas South Korea contributed to 54 180 (3·63%). Therefore, Sweden was a preferred partner of Germany by a factor of 2·84 (3·28/1·18), but South Korea was a non-preferred partner of Germany, because it had a factor of 0·25 (0·95/3·63).

#### Actual citation impact

Citation counts for each paper (2009–20), year by year, were downloaded from Web of Science. 5-year citation counts (ie, actual citation impact [ACI]), beginning in the publication year, were calculated. A 5-year window was used as a compromise between the need for immediacy (ie, citations for recent papers) and stability (ie, inclusion of the peak year for citations, usually the second or third year after publication).

#### Cancer research activity by gender

Gender of authors was captured through Gender API, which has been used in a previous study.<sup>80</sup> This online tool determines the gender of a first name using a database of 4 million names across Europe, categorising them into regional-level or country-level coding. Gender of project principal investigators was determined using Gender API, ORCID, and internet searches when first names were not provided.

### European cancer research in comprehensive cancer centres

#### Driving the research agenda

Comprehensive cancer centres (panel 1)<sup>81</sup> and comprehensive cancer infrastructures have a key role to play in European cancer research and care agendas. The EU's Cancer Mission Board has recommended the establishment of "a network of comprehensive cancer infrastructures within and across all EU member states to improve the quality of research and care".<sup>82</sup> Additionally, comprehensive cancer infrastructures need to be underpinned by quality standards and accreditation processes, for both cancer research and cancer care. The aspirations espoused in the EU Cancer Mission are complemented by the fifth Flagship Initiative of Europe's Beating Cancer Plan (appendix p 14).<sup>83</sup> Allied to these statements, the Porto Declaration of May 5, 2021 indicates that an enhancement of the European cancer research infrastructure, with better connection of comprehensive cancer centres, could help enable "a ten-year cancer-specific survival for 75% of patients diagnosed in EU member states with a well-developed health-care system",<sup>84</sup> echoing our 70:35 vision.

#### Comprehensive cancer centres as research hubs and research drivers

51 comprehensive cancer centres and large clinical centres in 19 European member states have been accredited by OECI to date (appendix p 15). There are 12 centres in Italy and eight in France, but in

For the Gender API tool see <https://gender-api.com>

For GDP data from The World Bank see <https://data.worldbank.org/indicator/NY.GDP.MKTP.KD>

#### Panel 1: Definition of a comprehensive cancer centre, according to the Organisation of European Cancer Institutes and the European Cancer Organisation<sup>81</sup>

A comprehensive cancer centre is an organisational entity with a clear central governance spanning cancer care, research, and education (generally in one geographical location), including (1) a direct provision of an extensive range of high-quality cancer diagnostics and care covering at least all the major cancers; (2) a high level of infrastructure, expertise, and innovation in cancer research, especially in translational and clinical research (including early clinical trial units), but also in many cases including basic science and discovery science; (3) a university partnership as part of the centre, or strong links with universities and research institutes; and (4) extensive international networking in research and clinical trials, and educational programmes for clinicians, researchers, and patients



ten countries there is only a single accredited centre. Mapping of existing structures for translational, clinical, and outcomes research shows that comprehensive cancer centres and large clinical centres are key drivers of research (the first 40 centres accredited by OECI produce approximately 12 400 peer-reviewed papers annually).<sup>81</sup> Additionally, within the German Cancer Aid and German Cancer Society accreditation programmes, there are 14 designated *Oncologische Spitzenzentren*, each with a high degree of cancer research.<sup>85</sup> Furthermore, EACS has developed a Designation of Research Excellence for comprehensive cancer centres, which has to date designated two centres.<sup>86</sup> Disease-specific accreditation programmes are also available from professional organisations: breast (European Society of Breast Cancer Specialists),<sup>87</sup> neuroendocrine (European Neuroendocrine Tumour Society),<sup>88</sup> and prostate (European Association of Urology),<sup>89</sup> whereas the European Society of Medical Oncology leads an accreditation programme in palliative care.<sup>90</sup>

Several European networks of comprehensive cancer centres have been formed to address specific research areas and their translation. These include Cancer Prevention Europe, bringing together ten major centres with a focus on cancer prevention;<sup>91</sup> Cancer Core Europe, linking seven comprehensive cancer centres to help drive a precision oncology agenda, with a particular focus on early-phase clinical trials;<sup>92</sup> and the European Organisation for Research and Treatment of Cancer, aligning multiple stakeholders for delivery of high-quality translational and clinical trial research.<sup>93</sup>

#### *Bibliometric analysis of research outputs for the Organisation of European Cancer Institute (OECI) centres*

Our filter was applied to Web of Science, and the numbers of papers published, year by year, were determined for the world (excluding Europe), the EU27 plus Iceland, Norway, Switzerland, Türkiye, and the UK (EUR32), and for the group of 19 European countries (EUR19) with one or more OECI-accredited centres. The countries that made up the EUR19 were Belgium, Czech Republic, Denmark, Estonia, Finland, France, Hungary, Ireland, Italy, Lithuania, the Netherlands, Norway, Portugal, Romania, Spain, Slovenia, Sweden, Türkiye, and the UK. The 51 OECI cancer centres are listed in the appendix (p 15). Data from 51 OECI-accredited centres were grouped according to the country groups in which the centres are located (the UK and Ireland; Iberia [Portugal and Spain]; BeNe [Belgium and The Netherlands]; central and eastern Europe [Hungary, Czech Republic, Romania, Slovenia, Türkiye, Lithuania, and Estonia]; the Nordic countries [Denmark, Finland, Norway, and Sweden]; and France and Italy). These country groups were chosen so as not to identify results with any specific OECI-accredited centre. To determine the amount of collaboration, sums of the outputs of the individual countries or centres in the

three groups (the world [excluding Europe], the EU27, and the EUR19) were compared with totals for each group. We also applied sub-field filters to each of the four groups (the world [excluding Europe], the EU27, the EUR19, and all OECI-accredited centres) that identified papers in different research domains and different anatomical sites (appendix p 16). These filters mainly consisted of lists of title words and, for some sub-fields, journal name-strings. The filters were combined into a series of search statements that could be applied directly to Web of Science, in combination with cancer research and appropriate geographical filters.

#### *Measuring clinical trial output in comprehensive cancer centres and other cancer centres*

Data on clinical trial outputs of OECI-accredited centres were collected between 2015 and 2020 as part of regular accreditation processes, and validated through peer review. OECI distinguishes between comprehensive cancer centres, which meet the definitions listed in panel 1 and the designation criteria of the OECI,<sup>94</sup> and other centres, which are designated as cancer centres.

When relating the clinical trial outputs to the financial inputs, the research and oncology budgets of each OECI centre were adjusted upwards or downwards according to the relative purchasing power parity of the euro in that country. Purchasing power parity rates published annually by the OECD<sup>95</sup> were used, according to the relevant year of collection of the budget data at each centre.

#### **Cancer research funding in Europe**

##### *Public sector and governmental funding for cancer research in Europe*

The Cancer Mission, Europe's Beating Cancer Plan, the EU for Health Programme, Horizon Europe, and other programmes all provide important opportunities for research funding at the supra-regional scale. However, it is important to learn from previous funding activities and align future resources to disease and research domains where they are most needed, heeding our analysis on the European cancer research landscape. National funding agencies should also align their funding schemes to the relevant research priorities in the given country.

Collaboration, including strategic partnerships between research funding organisations, is becoming increasingly important internationally, allowing coordination of investment in common identified priority areas, reducing duplication, and fast-tracking better outcomes. The International Cancer Research Partnership (ICRP) is an alliance that currently includes more than 150 cancer research organisations from the USA, Canada, Europe, Japan, South Africa, and Australia. ICRP maintains the only public source, worldwide, of current and past grants, totalling more than US\$100 billion in cancer research funding since 2000. ICRP member organisations submit project-level data for their research portfolios to the

For the ICRP database see [https://www.icrpartnership.org/db\\_search](https://www.icrpartnership.org/db_search)

ICRP database, including the name of the principal investigator, host institution, city, country, funding organisation, project title, abstract, start date, end date, and total funding amount. Each project is assigned to one or more cancer anatomical sites and research domains. The research domain classification (CSO) includes 34 codes, grouped into six categories (biology [CSO1]; aetiology [CSO2]; prevention [CSO3]; early diagnosis and prognosis [CSO4]; treatment and survivorship [CSO5]; and cancer control [CSO6]). All fields, except funding amount, are visible on the ICRP public website. Funding amount is visible to partners who contribute data. It is estimated that ICRP captures over 60% of global cancer research funding.

### Cancer research funding

Projects supporting principal investigators in European countries (appendix pp 17–18) between 2010 and 2019 (inclusive) were extracted from the ICRP database (n=20761; total value €10·8 billion) or provided in Excel by partner organisations whose historic data were not yet included in the database due to GDPR or other constraints. To complement ICRP data, Framework Programme 7 (FP7) and Horizon 2020 (H2020) projects active between 2010 and 2019 (inclusive) and relevant to cancer research (keyword search using terms: cancer; oncol\*; malign\*; tumor\* or tumour\*; \*oma; melanom\*; and leuk\*) were extracted from the EU CORDIS database (n=3212; total value €5·4 billion and only project funding to partners in European countries was included) and projects funded by the Swedish Research Council between 2016 and 2019 were extracted from World Report (n=471; total value €0·5 billion). Other cancer-relevant projects from World Report were already included in the ICRP database. For non-ICRP data, a manual review of projects with low numbers of keywords was done to exclude projects without a specific focus on cancer research. Non-ICRP projects were coded by ICRP to one or more Common Scientific Outline research domains and cancer anatomical sites.

A list of funding organisations whose data were included in the analysis is shown in the appendix (pp 17–18). Projects whose funding data were not in euros (eg, CA\$, US\$, £, and kr) were converted to euros using the 2019 average annual exchange rate, to avoid trends solely due to currency fluctuations. Analyses represent the full value of the projects active in the relevant timeframe. To complement the detailed analyses based on aggregated project-level data, estimates of overall cancer research funding by other European cancer research funding organisations, for which project details were not found in the public domain, were sourced from internet searches for annual reports, using as a starting point the IARC list of global cancer research funders.<sup>96</sup> This approach was limited to data that were available in the public domain. For biomedical research funders, it was not always possible

to identify spend that was specifically dedicated or relevant to cancer. A further limitation in capturing overall cancer research expenditure was that details of funding from pharmaceutical companies were generally not available in the public domain.

### Cancer research funding for prevention

Analysis of cancer research funding for prevention builds on a previous mapping exercise using bibliometric data as the initial basis for creating a comprehensive database on all cancer research funding entities.<sup>96</sup> The database was updated to include the years 2019–2021, bringing the total number of cancer research funders identified in the world to 4998 and in Europe to 1477. A methodology based on a keyword analysis (appendix p 19) of all cancer research papers in the Web of Science from 2008 to 2021 was developed with cancer researchers to extract prevention research publications. A so-called bottom-up approach was applied: funding acknowledgments were used to identify funders active in prevention research and assess current trends. For the purpose of this Commission, the following three areas were included: aetiology; primary prevention; and early detection, diagnosis, and prognosis. Tertiary prevention was excluded.

## Section 7: results

### Mapping European cancer outcomes

#### *Inequalities in survival between European countries*

Our overall findings indicated that survival varied substantially between European countries and regions (appendix pp 20–27). For several countries in northern Europe (Finland, Iceland, Norway, and Sweden) and western Europe (Belgium, Germany, and Switzerland), age-standardised 5-year net survival for patients diagnosed during 2010–2014 was the highest in Europe for many of the cancers evaluated. In contrast, survival was lowest in most of the central and eastern European countries evaluated (Bulgaria, Poland, Romania, and Slovakia). However, in some southern and eastern European countries, 5-year survival for liver, lung, and pancreatic cancer was similar to, or higher than, the 5-year survival in northern European countries. Denmark is closing the survival gap with its Nordic neighbours.<sup>97,98</sup> For patients diagnosed between 2010 and 2014, 5-year survival in Denmark was among the highest in Europe for cancers of the rectum, breast, cervix, and brain, and for melanoma and lymphoid malignancies. In the UK, which like Denmark has also exhibited lower survival for patients diagnosed between 1995 and 2007 (EUROCARE; International Cancer Benchmarking Partnership),<sup>97,98</sup> 5-year net survival from the CONCORD programme for patients diagnosed between 2010 and 2014 with cancers of the stomach, pancreas, lung, ovary, and brain was similar to the 5-year net survival seen in some central and eastern European countries. 5-year survival in the UK was high in the European range only for melanoma. Europe-wide differences in survival were particularly marked for

For the EU CORDIS database see <https://cordis.europa.eu/>

For World Report see <https://worldreport.nih.gov/>

For exchange rates see <https://www.exchangerates.org.uk/>

For EUROCARE see <https://www.eurocare.org/>

cancers of the oesophagus, stomach, and rectum, and for melanoma and lymphoid malignancies, particularly for patients diagnosed between 2010 and 2014.

#### *Regional variation in survival within European countries*

For a substantial proportion of cancers, 5-year net survival also varied widely within countries (appendix pp 28–31). 5-year survival increased steadily for many cancers between 2000 and 2004, and between 2010 and 2014, particularly for colon cancers, rectal cancers, and lymphoid malignancies. For some cancers (eg, oesophageal, liver, pancreatic, and lung), age-standardised 5-year net survival remains below 20%.

#### *Inequalities in cancer mortality across Europe*

Cancer mortality has shown substantial variation across different European countries. The highest mortality rates, particularly for men, have been recorded in eastern Europe, with a greater than two-fold difference in total cancer mortality between the highest (>250 per 100 000 in men in Hungary) and the lowest (about 110 per 100 000 in men in most Nordic countries and in Switzerland).<sup>99,100</sup> A substantial proportion of the higher cancer mortality in eastern Europe is due to lifestyle factors (eg, use of tobacco, consumption of alcohol, and dietary choices).<sup>101</sup> However, part of the inequalities in cancer mortality in some European countries reflects inadequate cancer management.<sup>102</sup>

Previously, we used cancer registration data from EUROCARE-5 and a modelling approach using different survival scenarios to estimate the number of avoidable cancer deaths in Europe, on the basis of survival estimates across European countries. We found that, if 5-year cancer survival in EU countries where survival is currently low (mainly in eastern Europe) could be raised to the median rate of survival of all European countries, then about 50 000 additional deaths from cancer would be avoided each year.<sup>103</sup> If cancer survival in all European countries could be raised further to the level of the 75th percentile, then more than 100 000 deaths from cancer would be avoided annually. These data were the crucial evidence that informed the 70:35 vision (ie, 70% average survival for at least 10 years across Europe by 2035).<sup>70</sup> Here, we update these data analyses, with additional analyses specifically comparing western and eastern European countries to inform the recommendations in this Commission in relation to building research capacity and capability to help improve outcomes in all European countries.

#### *Persisting differences in cancer mortality between eastern and western Europe*

When central and eastern European countries gained access to the EU in 2004, large differences were evident for total mortality and cancer mortality in particular. Using the most up-to-date available data, we now investigate whether such a gap in cancer mortality has closed over the past 10 years and estimate the potential number of

avoidable cancer deaths, assuming that such a gap would be closed.

We present age-standardised mortality rates from cancer sites per 100 000 person-years in western Europe and central and eastern Europe in 2010 and in 2016, together with number of deaths observed in 2016 and the percentage change between the two rates (table 1). From 2010 to 2016, in men, mortality rates for all cancers combined declined from 131.51 per 100 000 population to 122.23 per 100 000 (–7.1%) in western European countries, and from 176.98 per 100 000 to 168.17 per 100 000 (–5%) in central and eastern European countries, which means there was a persisting 38.6% excess mortality rate (as calculated from age-standardised rates) in central and eastern Europe compared with western Europe. Corresponding rates in women declined from 80.74 per 100 000 to 77.97 per 100 000 (–3.4%) in western Europe, and from 95.93 per 100 000 to 94.74 per 100 000 (–1.2%) in central and eastern Europe, which means there was a 21.5% excess mortality rate (as calculated from age-standardised rates) in central and eastern Europe compared with western Europe.

In western Europe, mortality rates for men declined in most cancer sites from 2010 to 2016 (eg, Hodgkin lymphoma [–22.9%], and laryngeal [–17.3%], testicular [–16.7%], and stomach [–16.0%] cancer). Unfavourable patterns with documented rises in mortality were seen for pancreatic (+3.3%) and renal (+4.2%) cancer. Overall declines in mortality rates were smaller in women (–3.4%), due to persisting rises in tobacco-related cancers. For women, major decreases were observed in mortality from Hodgkin lymphoma (–39.1%), and thyroid (–16.7%) and stomach (–15.3%) cancer. Unfavourable trends were detected in lung (+6.2%), laryngeal (+5.3%), pancreatic (+5.0%), oral cavity and pharyngeal (+3.7%), and liver (+3.0%) cancer. The highest mortality rates for women in 2016 were for breast (14.37 per 100 000 people), lung (13.97 per 100 000), and colorectal (8.87 per 100 000) cancer. For men the highest mortality rates were for lung (30.81 per 100 000), colorectal (14.43 per 100 000), and prostate (10.15 per 100 000) cancer.

In central and eastern European countries, greater variability was observed in both rates and trends. In men, major declines in mortality rates from 2010 to 2016 were observed for Hodgkin lymphoma (–22.9%) and stomach cancer (–19.5%). Unfavourable patterns of mortality were registered for skin cancer (+13.7%), multiple myeloma (+7.8%), non-Hodgkin lymphoma (+7.5%), liver cancer (+6.1%), testicular cancer (+5.5%), bladder cancer (+3.5%), and prostate cancer (+1.3%). Similarly, in women, major declines in mortality rates from 2010 to 2016 were observed in Hodgkin lymphoma (–20.7%) and stomach cancer (–18.5%). Increased mortality was registered for lung (+17.7%), bladder (+17.2%), oral cavity and pharyngeal (+14.4%), pancreatic (+7.5%), oesophageal (+6.6%) cancer, for multiple myeloma (+6.2%), and for liver (+6.1%), skin (+4.0%), and breast

	Central and eastern Europe																	
	Western Europe						Men						Women					
	Mortality rate in 2010	Mortality rate in 2016	Number of deaths in 2016	Percentage change in mortality	Mortality rate in 2010	Mortality rate in 2016	Number of deaths in 2016	Percentage change in mortality	Mortality rate in 2010	Mortality rate in 2016	Number of deaths in 2016	Percentage change in mortality	Mortality rate in 2010	Mortality rate in 2016	Number of deaths in 2016	Percentage change in mortality		
Oral cavity and pharynx	4.31	4.11	16 443	-4.6%	1.09	1.13	6195	+3.7%	8.87	8.49	7507	-4.3%	1.32	1.51	1858	+14.4%		
Oesophagus	4.89	4.58	20 194	-6.3%	1.14	1.11	6867	-2.6%	4.31	4.00	3691	-7.2%	0.61	0.65	866	+6.6%		
Stomach	6.14	5.16	25 119	-16.0%	2.94	2.49	16 351	-15.3%	12.60	10.14	10 168	-19.5%	5.02	4.09	5951	-18.5%		
Large intestine (colon and rectum)	15.99	14.43	73 870	-9.8%	9.57	8.87	62 676	-7.3%	22.45	21.72	22 561	-1.9%	11.72	11.24	17 228	-4.1%		
Gallbladder and bile ducts	1.07	1.09	5681	+1.9%	1.15	1.06	7530	-7.8%	1.69	1.75	1809	+3.6%	2.26	1.86	2862	-17.7%		
Liver (specified as primary)	4.92	4.82	22 064	-2.0%	1.66	1.71	10 728	+3.0%	2.96	3.14	3028	+6.1%	1.15	1.22	1742	+6.1%		
Pancreas	7.54	7.79	36 533	+3.3%	5.35	5.62	36 602	+5.0%	9.00	8.72	8538	-3.1%	5.31	5.71	8339	+7.5%		
Larynx	1.85	1.53	6871	-17.3%	0.19	0.20	1028	+5.3%	5.05	4.56	4259	-9.7%	0.36	0.35	429	-2.8%		
Lung	35.20	30.81	143 295	-12.5%	13.16	13.97	73 579	+6.2%	51.88	47.12	45 771	-9.2%	12.94	15.23	19 206	+17.7%		
Skin (including melanoma)	2.41	2.35	11 297	-2.5%	1.42	1.29	7915	-9.2%	2.91	3.31	3334	+13.7%	1.74	1.81	2832	+4.0%		
Breast	..	..	..	..	15.65	14.37	78 050	-8.2%	..	..	..	..	15.25	15.65	19 907	+2.6%		
Uterus (cervix and corpus)	..	..	..	..	3.93	3.88	20 849	-1.3%	..	..	..	..	9.03	8.49	10 082	-6.0%		
Ovary	..	..	..	..	4.94	4.44	24 066	-10.1%	..	..	..	..	6.08	5.94	7173	-2.3%		
Prostate	11.50	10.15	63 927	-11.7%	..	..	..	..	12.56	12.72	14 805	+1.3%	..	..	..	..		
Testis	0.24	0.20	537	-16.7%	..	..	..	..	0.55	0.58	385	+5.5%	..	..	..	..		
Bladder	4.94	4.47	25 957	-9.5%	1.17	1.13	9194	-3.4%	6.60	6.83	7504	+3.5%	1.22	1.43	2418	+17.2%		
Kidney and other urinary sites	4.29	4.47	22 307	4.2%	1.71	1.72	11 744	+0.6%	5.22	5.17	5109	-1.0%	2.06	1.98	2994	-3.9%		
Thyroid	0.28	0.25	1231	-10.7%	0.30	0.25	1767	-16.7%	0.33	0.33	324	+0.0%	0.40	0.37	564	-7.5%		
Hodgkin lymphoma	0.35	0.27	1118	-22.9%	0.23	0.14	801	-39.1%	0.48	0.37	295	-22.9%	0.29	0.23	251	-20.7%		
Non-Hodgkin lymphoma	3.52	3.30	16 524	-6.3%	2.08	1.94	13 690	-6.7%	2.92	3.11	2973	+6.5%	1.82	1.81	2543	-0.5%		
Multiple myeloma	2.07	1.94	10 313	-6.3%	1.37	1.23	8988	-10.2%	1.53	1.65	1685	7.8%	1.12	1.19	1787	+6.2%		
Leukemia	4.37	4.12	20 422	-5.7%	2.69	2.48	15 944	-7.8%	4.94	4.53	4408	-8.3%	2.96	2.89	3817	-2.4%		
All cancers (malignant and benign)	131.51	122.23	59 6181	-7.1%	80.74	77.97	464 672	-3.4%	176.98	168.17	166 544	-5.0%	95.93	94.79	127 317	-1.2%		

Empty cells are due to sex-specific sites. Rates are age adjusted (world standard) per 100 000 population.

**Table 1. Overall age-standardised (world population) mortality rates for 22 specific cancers and for all cancers combined per 100 000 men and women in 2010 and in 2016, the number of deaths in 2016, and the percentage change in mortality between 2010 and 2016 in western Europe compared with central and eastern Europe**



(+2.6%) cancer. In central and eastern Europe the highest rates were for lung (42.12 per 100 000), colorectal (21.72 per 100 000), and prostate (12.56 per 100 000) cancer in men; and for breast (15.56 per 100 000), lung (15.23 per 100 000) and colorectal (11.23 per 100 000) cancer in women.

In table 2, we indicate predicted avoidable deaths from major cancer sites in 2016 in central and eastern European countries, assuming they had the same mortality rates as western European countries. 55 239 deaths (40 804 men and 14 435 women) would have been avoided in central and eastern European countries in 2016. Estimated avoided deaths from total cancer mortality in men and women from western countries and central and eastern European countries between 1991 and 2016, applying the peak age-specific mortality rates in 1990 as constant, are shown in figure 2. In western European countries, we estimate a total of approximately 5 million avoided cancer deaths (over 3 million men and almost 2 million women), whereas we predicted only 62 000 avoided cancer deaths (approximately 52 500 men and 9700 women) in central and eastern European countries. A total of approximately 55 000 deaths would have been avoided in central and eastern European countries in 2016 if they had exhibited the same mortality rates as in the western European region.

For 2016, our current data indicate that the major differences between the two regions were observed in men for lung (30.81 per 100 000 men in western European countries vs 47.12 per 100 000 men in central and eastern European countries), colorectal (14.43 per 100 000 vs 21.72 per 100 000), and oral cavity and pharyngeal (4.11 per 100 000 vs 8.49 per 100 000; table 1) cancer. Major differences between mortality rates in women were for stomach (2.49 per 100 000 women in western European countries vs 4.09 per 100 000 women in central and eastern European countries), colorectal (8.87 per 100 000 vs 11.24 per 100 000), and uterine (3.88 per 100 000 vs 8.49 per 100 000; table 1) cancer. Between 2000 and 2004, total cancer mortality rates were 194.46 per 100 000 in central and eastern European countries versus 155.38 per 100 000 in western European countries (25.2% difference) in men, and 103.94 per 100 000 in western European countries versus 103.80 in eastern European countries in women.<sup>102</sup>

### Mapping the European cancer research landscape

In seeking to frame public policy for European cancer research, its prioritisation, and its funding at national and supra-national (European Commission) levels, objective analysis is crucial to provide strategic evidence to help inform political discourse on the relevance, prioritisation, and implementation of research. Scientometrics (the analysis of scientific outputs) provides a well validated tool to underpin both evidenced-based requirements analysis and criterion-based benchmarking

	Men	Women
Oral cavity and pharynx	3693	327
Stomach	4867	2081
Large intestine (colon and rectum)	7296	2620
Gallbladder and bile ducts	641	1080
Larynx	2740	170
Lung	14 528	470
Skin (including melanoma)	978	988
Breast	..	901
Uterus (cervix and corpus)	..	4913
Ovary	..	1139
Prostate	2790	..
Testis	247	..
Bladder	2443	339
Kidney and other urinary sites	443	205
Thyroid	65	147
Hodgkin lymphoma	50	58
Leukaemia	236	68
All cancers (malignant and benign)	40 804	14 435

Number of deaths from selected major cancers, in men and women, that would not have occurred if mortality rates had been the same as those in western Europe. Some cancer sites have not been included in this table due to their low, and therefore unstable, numbers.

Table 2: Avoidable deaths in central and eastern Europe in 2016

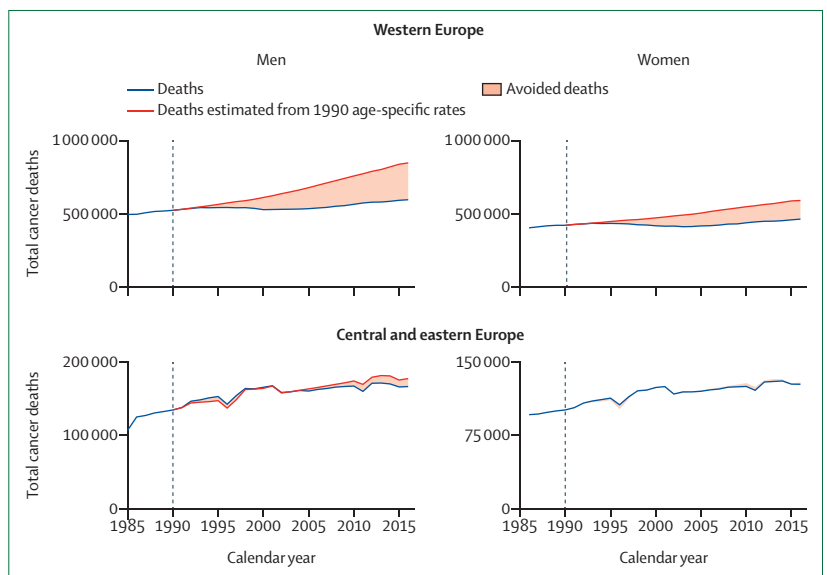
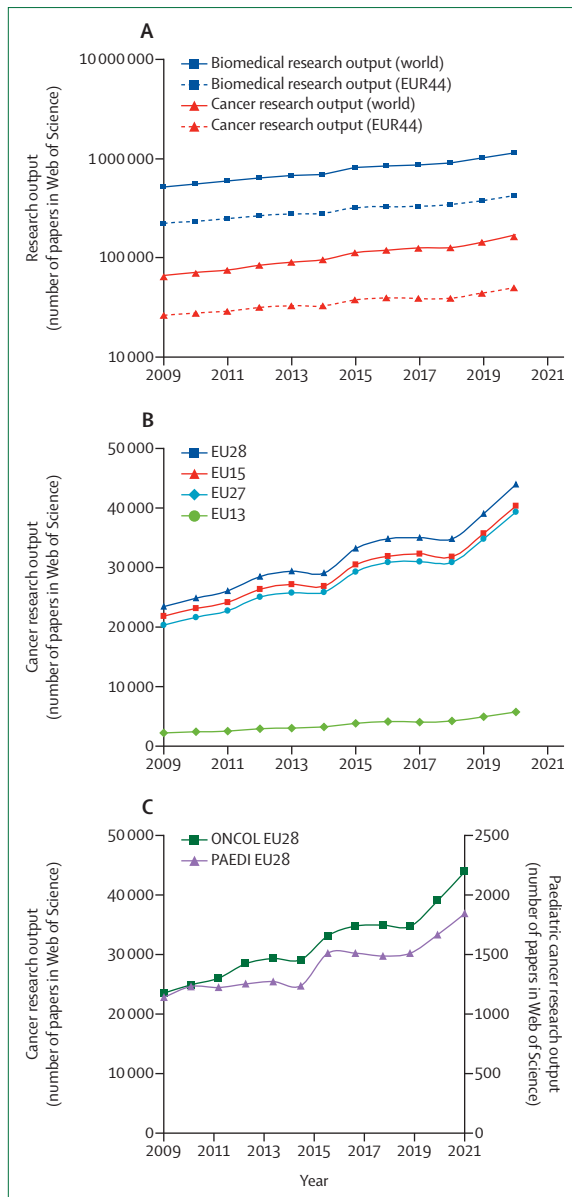


Figure 2: Estimated avoided total cancer deaths from 1991 to 2016, applying the peak age-specific mortality rates in 1990 as constant, in western Europe and central and eastern Europe, in men and women

for European cancer research.<sup>104</sup> We used scientometrics to define the landscape of cancer research activity across Europe between 2009 and 2020, and used this granular data to frame an evidence-based consideration of how best to ensure that the optimal cancer research is enacted within the Cancer Mission and to ensure that it robustly informs Europe's Beating Cancer Plan.



**Figure 3: Outputs of biomedical research papers and cancer research papers from groups of European countries and the world**

(A) Outputs of total biomedical research papers and of total cancer research papers from the world (excluding Europe) and from the EUR44 in the Web of Science between 2009 and 2020. (B) Outputs of cancer research papers (total cancer research papers published) from four groups of European countries in the Web of Science between 2009 and 2020. EU13=member states that joined the EU in 2004 and after. EU15=countries in the EU before 2004. EU27=EU after 2021. EU28=EU up until 2020. EUR44=all the countries in the entire European region. (C) Paediatric cancer research outputs from the EU28 member states (PAEDI), compared with all cancer research paper output from the EU28 member states between 2009 and 2020 (ONCOL).

**Cancer research activity by European region**

In the 12 years (2009–20) leading up to the start of the COVID-19 pandemic, the European region published 3 630 929 (39.4%) of 9 244 900 total worldwide biomedical research papers, but only 426 869 (33.8%) of 1 259 643 total

worldwide cancer research papers (figure 3A). Europe’s output of cancer research papers also grew more slowly (5.1% year) than the research output of the world, excluding Europe (8.1% per year; figure 3A). This difference in output suggests that, despite substantial investment, total cancer research productivity in Europe has been contracting.<sup>79</sup> The reasons for this decline in total cancer research productivity is clarified by a subanalysis of the outputs by high-income European countries that were part of the EU before 2004 (EU15) and the newer 13 countries that joined the EU after 2004 (EU13). Our findings show that, although the high-income EU15 countries have collectively enjoyed a doubling of cancer research activity during the study period, the central and eastern European EU13 countries have seen little improvements (figure 3B). These data suggest that the actions started under EU Research Commissioner Philippe Busquin’s European Research Area and accelerated from the Sixth Framework Programme of Research onward have not succeeded in delivering the trans-European cancer research equity and equality that was part of their intended effect.<sup>105</sup> Therefore, there must be a renewed effort, through a combination of research capacity-building, directed funding, and twinning approaches to enhance cancer research activity, its quality, and its translation in central and eastern European countries.

**Cancer research activity in central and eastern Europe**

Other work that we have completed on mapping cancer research in newer EU13 central and eastern European countries suggests that some countries have an output of research that follows the normal trend (eg, Poland).<sup>106,107</sup> However, the COVID-19 pandemic negatively impacted cancer research activity and funding in Europe (particularly from charity and non-governmental organisation sectors), and both COVID-19 and the war in Ukraine will probably have major negative effects on research funding for cancer in the foreseeable future.<sup>108</sup> Beyond just the capacity to retain an active research community due to these externalities, the low research activity of the EU13 that we highlight (figure 3B) will probably have a direct effect on population cancer outcomes in these countries for many years to come.

**Cancer research activity and Brexit**

In addition to the COVID-19 pandemic and the war in Ukraine, the effect of Brexit and the EU’s contraction to EU27 on cancer research activity, which we have previously articulated,<sup>109</sup> has already been detrimental and will continue to negatively affect European cancer research outputs.<sup>110</sup> In addition to these data, which starkly delineated the detrimental effects of Brexit on cancer research and the cancer research workforce, the work that we present in this Commission highlights the substantial gap in outputs when we compare the research activity of the EU28 (UK included) with the activity of the EU27 (UK not included; figure 3B). The

gap is sizeable, reflecting the fact that the UK is an important player in European cancer research. As such, and based on our data, the UK's strong research outputs are unlikely to be compensated for by increased research activity, either collectively or individually within the other EU27 member states.

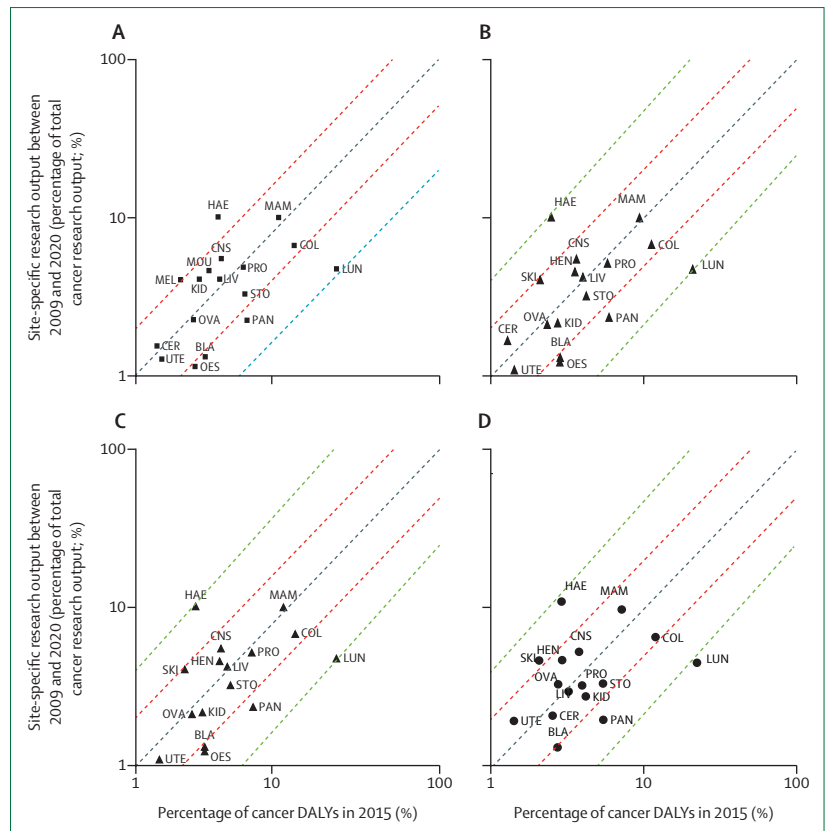
*Paediatric cancer research activity*

Specific domains, such as paediatric oncology research outputs (figure 3C), are broadly in parallel with overall oncology outputs; however, previous analysis has shown that non-commercial domains, such as European childhood cancer research networks, have potentially fragile funding models.<sup>111</sup> This fact lends support to the specific request for a paediatric cancer research uplift, as proposed by the International Society of Paediatric Oncology<sup>112</sup> and supported by this study. Our analysis (figure 3C) shows how different domains in adult versus paediatric cancers (for both solid and haemato-oncology tumours) are balanced across Europe's portfolio, building on our previous work with The European Society for Paediatric Oncology, the 2020 *Lancet Oncology* Commission on sustainable care for children with cancer,<sup>113</sup> and the 2013 *Lancet Oncology* Series on improving cancer care for children and young adults.<sup>114</sup> Paediatric oncology is thus rightly embedded as a recognised domain for research prioritisation within the Cancer Mission.

*Cancer research activity by collaboration*

When it comes to a choice of countries with whom to collaborate, European countries tend to be governed by traditional ties (ie, language, cultural background, and geographical proximity). Within Europe, strong cancer research linkages were detected between most pairs of countries, whereas European interactions with countries in east Asia, for example, were much weaker in comparison. The appendix shows the countries that were preferentially chosen as partners by the ten European region countries (Switzerland, Sweden, Netherlands, Spain, France, the UK, Germany, Italy, Poland, Australia, and Canada; appendix p 32). Iran was non-preferred as a partner by all ten European region countries except Türkiye, and Türkiye was non-preferred as a partner by all nine European countries. By contrast, Switzerland was a preferred partner by all the other nine countries, especially by Germany, Italy, and France, who share common languages with Switzerland. The UK was well represented in the research portfolio of its European partners, and it also favoured them, especially Sweden, the Netherlands, and Austria. Perhaps surprisingly, the USA is a non-preferred country for European countries, particularly compared with Canada and with Brazil.

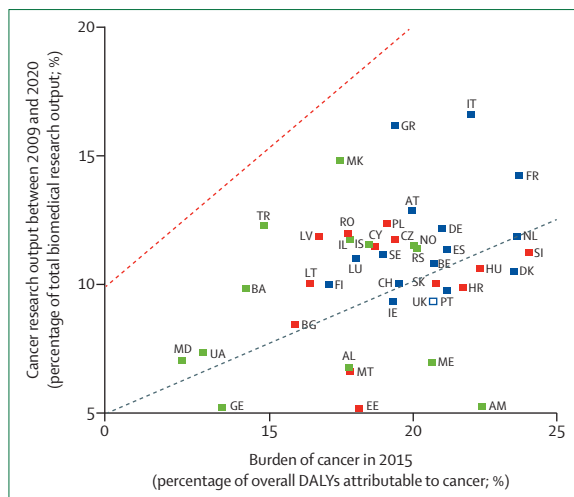
Europe has seen a range of strategic collaborative initiatives, some of which have yielded substantial results. One initiative, the Ireland–Northern Ireland–US National Cancer Institute Cancer Consortium,<sup>115</sup> led to a doubling of joint cancer research outputs from Northern Ireland



**Figure 4: Research outputs of different European country groups on individual anatomical sites between 2009 and 2020 compared with the percentage burden of these cancers in 2015**  
 Research output is site-specific cancer research published by country group between 2009 and 2020 as a percentage of total cancer research papers published by country group between 2009 and 2020. Burden of site-specific cancers is shown as WHO data on DALYs in 2015. Grey dashed lines represent equality between research output (percentage of all cancer research) and disease burden in DALYs (percentage of that from all cancers). Red dashed lines represent where research would be twice or half the burden. Green dashed lines (light blue in figure 4A) represent where research would be five-times (HAE) and one-fifth (LUN) the burden. (A) Research output of entire European region (44 countries). (B) Research output of EU countries (28 member states, including the UK). (C) Research output of countries that were part of the EU in 2003 (15 countries, before enlargement of EU). (D) Research output of member states that acceded in 2004 or after (13 countries).<sup>117</sup> BLA=bladder. CER=cervix. CNS=brain. COL=colorectal. DALYs=disability-adjusted life years. HAE=haematological. KID=kidney. LIV=liver. LUN=lung. MAM=breast. MOU=head and neck (oral). OES=oesophagus. OVA=ovary. PAN=pancreas. PRO=prostate. SKI=melanoma. STO=stomach. UTF=uterus.

and Ireland, a substantial increase in field-weighted citation, and a series of joint research activities between cancer researchers in Ireland and Northern Ireland and their US counterparts. These research activities have delivered notable benefit to cancer systems and patients with cancer in Ireland over a period of more than 20 years, and these activities serve as a model for future cross-jurisdictional collaborative strategic approaches.<sup>115</sup>

The UK–USA axis on cancer research, established in 2021, represents another important development.<sup>116</sup> However, for both the UK and USA, the overall commitment to global cancer research remains very poor (<4.0% of overall research activity).<sup>116</sup> In a similar way, Europe's commitment to collaborate with low-income and middle-income countries in cancer research is also disappointingly low.<sup>116</sup> Only 3.9% to less than 0.5% of



**Figure 5: Output of cancer research (total cancer research papers published) as a percentage of all biomedical research for countries in the European region between 2009 and 2020 compared with the percentage of overall disease burden attributable to cancer in each country in 2015**

Burden of cancer is the percentage of overall disease burden attributable to cancer (WHO data on DALYs in 2015).<sup>117</sup> The red dashed line represents outputs equal to cancer disease burden, as a percentage. Blue squares represent EU member states before 2004. Red squares represent EU member states acceding in 2004 and later. Green squares represent non-EU countries. The blue hollow square represents the UK, a former EU member state (UK). AL=Albania. AM=Armenia. AT=Austria. BA=Bosnia and Herzegovina. BE=Belgium. BG=Bulgaria. CH=Switzerland. CY=Cyprus. CZ=Czech Republic. DE=Germany. DK=Denmark. DALYs=disability-adjusted life years. EE=Estonia. ES=Spain. FI=Finland. FO=Faroe Islands. FR=France. GE=Georgia. GR=Greece. HR=Croatia. HU=Hungary. IE=Ireland. IL=Israel. IS=Iceland. IT=Italy. LI=Liechtenstein. LT=Lithuania. LU=Luxembourg. LV=Latvia. MD=Moldova. MK=North Macedonia. MN=Montenegro. MT=Malta. NL=Netherlands. NO=Norway. PL=Poland. PT=Portugal. RO=Romania. RS=Serbia. SE=Sweden. SI=Slovenia. SK=Slovakia. TR=Türkiye. UA=Ukraine. UK=United Kingdom.

Europe’s research is coauthored with researchers from low-income and middle-income countries. Thus, despite Europe’s substantial expenditure on cancer research, its overall support of global cancer research has been extraordinarily poor, as has that of the USA.<sup>116</sup>

**Cancer research activity by disease burden**

Another important policy question that we have posed is to what extent does European cancer research reflect both the burden of site-specific cancers and DALYs lost to cancer, both in Europe overall and within individual countries and regions. For some site-specific cancers, our data indicate that the research activity is commensurate with their burden across Europe, with some sites (eg, haemato-oncology) even having higher amounts of research activity than would be expected. However, major cancer anatomical sites (eg, lung, colorectal, hepatobiliary, and upper gastrointestinal) are severely under-researched, irrespective of European region, when compared with their relative disease burdens (figure 4).<sup>117</sup> Remarkably, patterns for anatomical site-specific research are similar for all groupings of European countries. For some under-researched anatomical cancer sites, the

amount of research could be as little as a fifth of what would be proportionate (eg, lung cancer is responsible for 20% of DALYs, but only 4% of European oncology research is committed to lung cancer).

We have also conducted a more detailed analysis of the relative commitment of each European country to cancer research within major site-specific anatomical domains. These measures of relative commitment of a given country to cancer research are shown in the appendix (pp 33–34). This in-depth analysis shows that relative strengths, and more importantly, weaknesses, are not a result of gaps in one or two countries’ research activities, but rather reflect pan-European deficits. Addressing such research deficits requires high-resolution strategic insight to understand potential causes and to inform tangible solutions.<sup>118</sup> Such strategic misalignment is further reflected when we evaluate cancer research performance in individual European countries using overall cancer burden (as measured by DALYs). Although some countries have clearly developed national strategies that drive proportional amounts of cancer research aligned to the countries’ disease burden, where there are robust researchable questions as judged by researchers and funders, many countries have not, particularly central and eastern European countries, but also the UK, Portugal, and Ireland are notable high-income countries adding to this deficit in research proportionality (figure 5).

**Cancer research activity by gross domestic product**

Broadly speaking, the rate of cancer research outputs across Europe follows the country’s wealth ( $r^2=0.94$ ; appendix p 35), with four nations—UK, Italy, France, and Germany—collectively dominating (table 3). A combination of huge national investment and collaborations between comprehensive cancer centres in these countries have acted as potent drivers of research activity.<sup>119</sup> Despite the overall strength of these so-called top four countries, many other countries and groupings within Europe also deliver highly cited cancer research (appendix p 36). However, the impact of the low volumes of research being produced by the EU13 (ie, mainly central and eastern European countries) remains poor.

**Cancer research activity by research domain**

For the five largest cancer research domains (genetics, prognosis, surgery, systemic treatment, and pathology), there is a fairly even distribution of research between leading high-income European countries (table 4; appendix p 37). However, surgery continually lags behind other modalities in research effort overall. In epidemiology, another cancer research domain, the four Scandinavian countries, followed by the Netherlands and Greece, have a high relative commitment. Iceland is even more committed to epidemiology than these countries. In clinical research, including clinical trials, Belgium and Switzerland show the highest relative commitment. In palliative care, Norway, Ireland, and the Netherlands show the highest



	GDP of country or country group in 2015*	Number of papers published†	Number of papers published per 2015 GDP	Percentage of world cancer research output	All OECI	Percentage of total number of papers published in country or country group
Italy	1627	73 550	45.2	6.01%	24 375	33.1%
Ireland and UK	2808	73 224	26.1	5.98%	25 233	34.5%
France	2160	52 148	24.1	4.26%	17 894	34.3%
Belgium and the Netherlands	1076	46 474	43.2	3.80%	18 067	38.9%
Central and eastern Europe	1169	43 359	37.1	3.54%	6 428	14.8%
Portugal and Spain	1243	43 060	34.6	3.52%	7 983	18.5%
Nordic countries	1264	42 551	33.7	3.48%	21 521	50.6%
EUR19	11 348	301 854	26.6	24.6%	79 544	26.4%

All OECI refers to the outputs of all the OECI centres in which the papers have an address in the given country or country group. Central and eastern European countries included are Hungary, Czech Republic, Romania, Slovenia, Türkiye, Lithuania, and Estonia. The Nordic countries included are Norway, Sweden, Denmark, and Finland. The EUR19 includes all European countries with one or more OECI-accredited centres. Countries and groups are ranked by the percentage of world cancer research papers. GDP=gross domestic product. OECI=Organisation of European Cancer Institutes. \*GDP is in billion Euros.<sup>117</sup> †There were 72 512 overlapping papers between country groups (24.0% overlap).

**Table 3: The cancer research outputs (number of papers published) in 2012–21 of countries or country groups and the total OECI outputs within each country or group**

	Papers published between 2012 and 2021				Percentage of all cancer research papers published in each group				Relative contribution of OECI-accredited centres*
	World	EUR32	EUR19	OECI-accredited centres	World	EUR32	EUR19	OECI-accredited centres	
Discovery science and genetics	231 878	65 807	50 684	15 225	19.0%	17.0%	16.8%	19.2%	1.14
Biomarkers	178 687	54 756	43 333	13 390	14.6%	14.1%	14.4%	16.8%	1.17
Epidemiology	145 846	45 863	37 831	11 964	11.9%	11.8%	12.6%	15.1%	1.20
Surgery	139 851	44 644	35 098	8 202	11.4%	11.5%	11.7%	10.3%	0.89
Chemotherapy	134 263	39 530	31 391	8 769	11.0%	10.2%	10.4%	11.0%	1.06
Pathology	110 035	38 054	29 532	7 423	9.0%	9.8%	9.8%	9.3%	0.95
Diagnosis	74 670	26 402	20 486	5 157	6.1%	6.8%	6.8%	6.5%	0.95
Radiotherapy	69 546	25 505	17 632	5 496	5.7%	6.6%	5.9%	6.9%	1.18
Targeted therapy	53 565	19 262	15 509	5 303	4.4%	5.0%	5.1%	6.7%	1.30
Paediatrics	52 860	17 506	13 980	3 681	4.3%	4.5%	4.6%	4.6%	1.00
Clinical trials	34 102	13 462	11 365	4 769	2.8%	3.5%	3.8%	6.0%	1.59
Quality-of-life	30 006	12 388	9 743	1 866	2.5%	3.2%	3.2%	2.3%	0.73
Screening	24 463	8 610	7 142	2 030	2.0%	2.2%	2.4%	2.6%	1.08
Palliative care	20 535	7 645	5 844	1 540	1.7%	2.0%	1.9%	1.9%	1.00
Total cancer research papers published	1 223 049	387 125	301 239	79 471	..	..	..	..	..

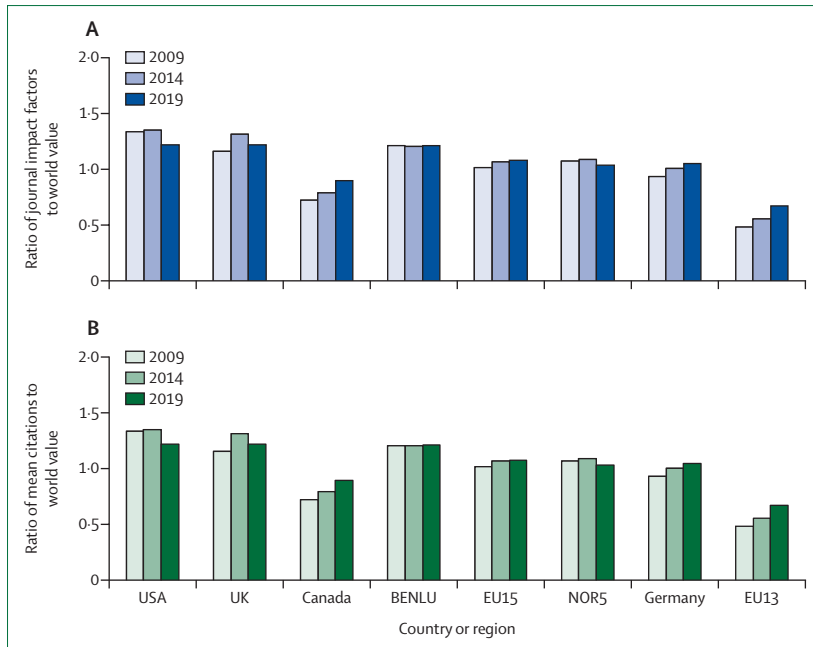
The EUR32 includes the 27 members of the EU plus Switzerland, Norway, Türkiye, Iceland, and the UK. The EUR19 includes the 19 European countries with one or more OECI-accredited centres. OECI=Organisation of European Cancer Institutes. \*Value indicates in which domains the OECI-accredited centres are making the largest contribution, relative to that of the countries in which they are located (ie, the percentages of total research that the OECI-accredited centres have contributed divided by percentage of total research that the EUR19 have contributed).

**Table 4: Outputs of cancer research papers between 2012 and 2021 in 14 research domains from the world, the EUR32 countries, the EUR19 countries, and the 51 OECI-accredited centres**

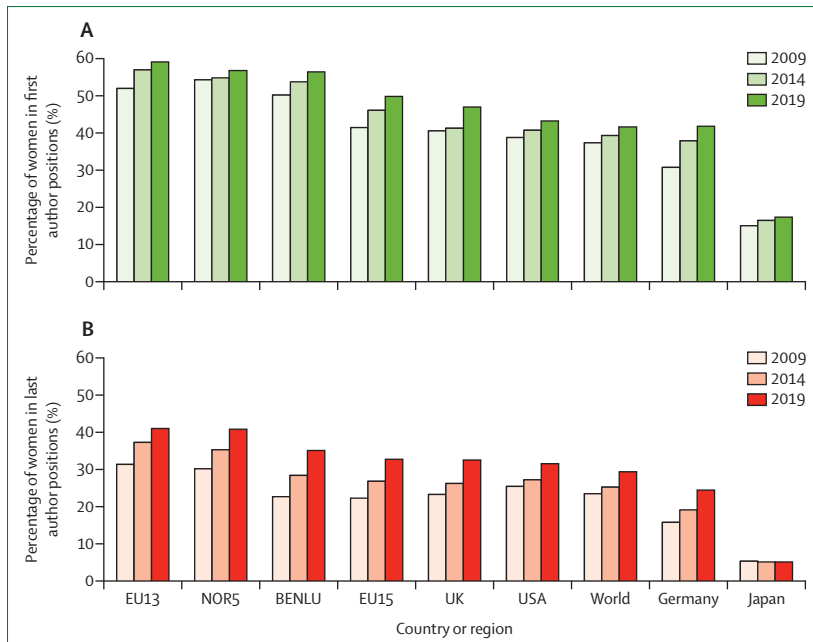
relative commitment, and could perhaps assist the Czech Republic, Spain, Italy, and Greece. Ireland's strength could reflect the All Ireland Institute of Hospice and Palliative Care, a product of the Ireland–Northern Ireland–US National Cancer Institute Cancer Consortium.<sup>115</sup>

*The impact of European cancer research*

The impact of cancer research from some European countries (eg, the Netherlands, Germany, and the UK), as measured by actual citation impact, has been consistently on par with the impact of cancer research in the USA



**Figure 6: Mean 5-year journal impact factors and mean citations for cancer research papers published by authors from nine countries or world regions, relative to world means, in 2009, 2014, and 2019**  
 (A) Ratio expresses mean journal impact factors, relative to world means, published by authors from nine countries or world regions in 2009, 2014, and 2019. (B) Ratio expresses mean citations for cancer research papers, relative to world means, published by authors from nine countries or world regions in 2009, 2014, and 2019. BENLU=Belgium, the Netherlands, and Luxembourg. EU15=EU member states up until 2003. EU13=accession member states in 2004 and after. NOR5=five Nordic countries (Denmark, Sweden, Norway, Finland, and Iceland).



**Figure 7: Percentage of women in first and last author positions for nine countries or regions in cancer research in 2009, 2014, and 2019**  
 (A) Percentage of women in first author positions in 2009, 2014, and 2019 for nine countries or world regions. (B) Percentage of women in last (expected to be senior) author positions in 2009, 2014, and 2019 for nine countries or regions. Japan is included in the comparison to reflect very low involvement of women in research. BENLU=Belgium, the Netherlands, and Luxembourg. EU15=EU member states up until 2003. EU13=accession member states in 2004 and after. NOR5=five Nordic countries (Denmark, Sweden, Norway, Finland, and Iceland).

(figure 6). The most unexpected finding, however, is that the EU13 have a low research impact in addition to low research volumes, again reflecting the uneven progress in building cancer research capacity and capability across Europe. Furthermore, the global expansion of cancer research means that Europe cannot take for granted that its research will continue to be high impact.

**Cancer research activity by gender**

In this section of the Commission, we address a very important research policy topic that has arisen in the past decade, the question of gender equality (or more precisely the absence of gender equality) within research, focusing on cancer research. Although we show that all European countries have improved over time, now performing at or above the world average for gender equality in cancer research outputs, the EU13 and research groups in Nordic countries, and Belgium, the Netherlands, and Luxembourg have done the most to promote women, with the highest numbers of women in both first author and last (senior) author positions (figure 7). Although the overall average for women in first author positions in cancer research papers is approaching 50%, women in last (senior) author positions still only make up a third of all authors for those European countries contributing the most cancer research outputs (figure 7B). In Germany, recognised for its substantial contribution to European cancer research, the number of women in senior author positions is disappointingly low (less than 25% of senior authors are women), Switzerland, Czech Republic, Greece, and Austria also have less than 25% of senior female authors of cancer research publications, emphasising the gender inequality problem.

The gender of principal investigators in Europe was also determined for 22 291 projects in the ICRP database for which investigators' first names could be identified. 65% of principal investigators were men, whereas only 35% of principal investigators were women, similar to the gender inequality results of the analysis of senior authors.

**Comprehensive cancer centres and comprehensive cancer infrastructures**

*Capturing the research activity of OEIC centres*

Outputs of papers for each of the four groups (the world, EUR32 [the 27 EU member states plus Switzerland, Norway, Türkiye, Iceland, and the UK], EUR19, and the OEIC), year-by-year, are presented in table 3. European research output has grown more slowly than that of the world, reflecting the rapid increase in papers from China. However, growth in outputs for the 51 OEIC-accredited centres as a grouping has increased slightly faster than the world, now accounting for 6.6% of world output (up from 6.3% in 2012), and an increasing share of the output of the 19 European countries in which they are located (28.0% in 2021, up from 22.2% in 2012).

Overall, OEIC-accredited centres accounted for over a quarter of the total research output for the top

	Papers published between 2012 and 2021				Percentage of all cancer research papers published in each group				Relative contribution of OECI-accredited centres*
	World	EUR32	EUR19	OECI	World	EUR32	EUR19	OECI	
Breast	118 276	38 362	31 009	9974	9.7%	9.9%	10.3%	12.5%	1.22
Blood	99 597	37 410	29 387	7849	8.1%	9.7%	9.8%	9.9%	1.01
Lung	76 771	19 154	15 122	4538	6.3%	4.9%	5.0%	5.7%	1.14
Colorectal	75 529	25 852	20 834	5234	6.2%	6.7%	6.9%	6.6%	0.95
Liver	74 127	16 192	12 389	2855	6.1%	4.2%	4.1%	3.6%	0.87
CNS	66 832	21 647	15 643	3540	5.5%	5.6%	5.2%	4.5%	0.86
Head and neck	58 578	17 868	13 811	3706	4.8%	4.6%	4.6%	4.7%	1.02
Stomach	56 856	12 597	9857	2402	4.6%	3.3%	3.3%	3.0%	0.92
Prostate	50 940	19 496	15 366	4283	4.2%	5.0%	5.1%	5.4%	1.06
Skin	37 716	16 659	11 635	3439	3.1%	4.3%	3.9%	4.3%	1.12
Pancreas	31 504	9244	6835	1730	2.6%	2.4%	2.3%	2.2%	0.96
Kidney	26 936	8397	6495	1630	2.2%	2.2%	2.2%	2.1%	0.95
Cervix	22 715	5829	4772	1202	1.9%	1.5%	1.6%	1.5%	0.95
Oesophagus	19 770	4425	3496	1168	1.6%	1.1%	1.2%	1.5%	1.27
Total cancer research papers	1 223 220	387 188	301 275	79 479	..	..	..	..	..

The EUR32 includes the 27 members of the EU plus Switzerland, Norway, Türkiye, Iceland, and the UK. The EUR19 includes the 19 European countries with one or more OECI-accredited centres. OECI=Organisation of European Cancer Institutes. \*Value indicates in which anatomical sites the OECI-accredited centres are making the largest contribution, relative to that of the countries in which they are located (ie, the percentages of total research that the OECI-accredited centres have contributed divided by percentage of total research that the EUR19 have contributed).

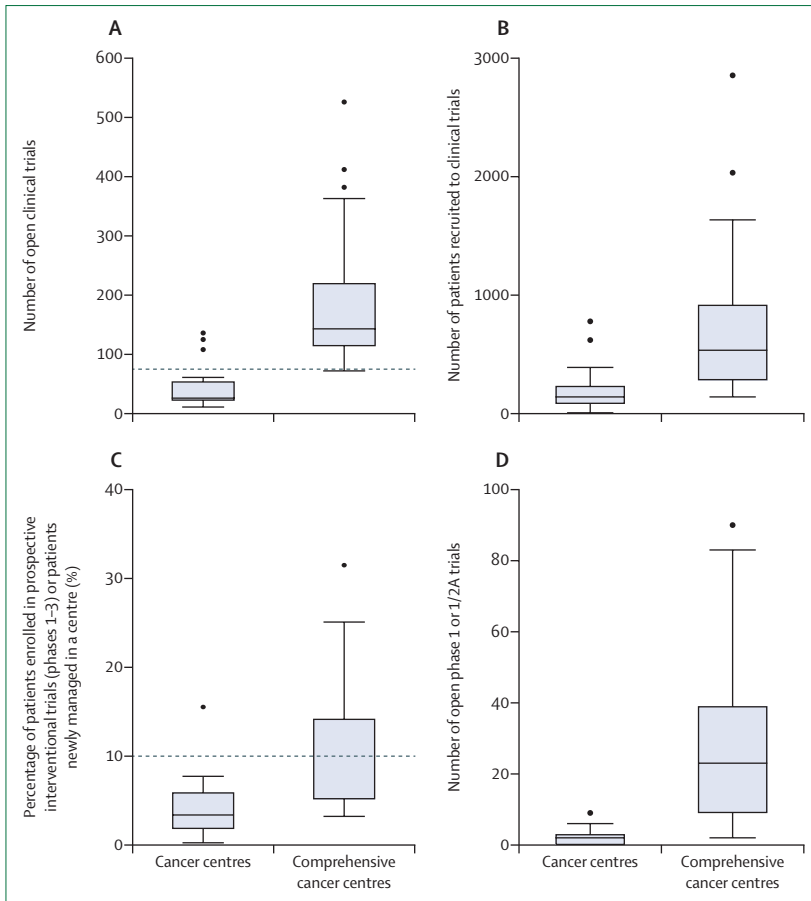
**Table 5: Outputs of cancer research papers between 2012 and 2021 on 14 anatomical sites from the world, the EUR32 countries, the EUR19 countries, and the 51 OECI-accredited centres**

19 European countries (table 3), but this varied greatly, with Nordic countries at 50% and central and eastern European countries at less than 15%. The sum of the outputs of the 51 OECI-accredited centres exceeded the total of EUR19 by 41957 (52.7%) compared with the overlapping authorship of total papers published in the country groups (24.0%), suggesting that membership of the OECI accreditation programme correlates to more collaboration between centres than is the case between individual EU countries.

By research domain for OECI-accredited centres (table 4), OECI-accredited centres contribute relatively the most to clinical trials, followed by targeted therapy, epidemiology, and radiotherapy. However, the centres collectively do relatively little research on quality of life. The quality of life research domain, together with screening and palliative care, is neglected. The departures from unity of the ratios of the relative commitment of the OECI centres to research on different anatomical sites to those of the EUR19 countries are less than for the research domains (table 5). The ratios show a welcome focus of the centres on oesophageal (+27%) and lung (+14%) cancers, which are often relatively neglected in Europe. The greater focus of OECI-accredited centres on breast and skin cancers compared with the world reflects the greater burden associated with these cancers in Europe.

A key question in cancer research is the value of comprehensiveness, or concentration of resources, versus more distributed research networks. Our data indicate a faster growth in cancer research outputs over the last 9 years from larger centres (ie, large enough to be accredited by the OECI), which tend to be those who elected to go for OECI certification and have been accredited. OECI-accredited centres had a 100% growth of relevant cancer research publications from 2012–21, compared with a 59% growth in the EUR32 group (tables 4, 5; figure 8). As a result, the proportion of cancer research papers from OECI-accredited centres within the EUR19 group rose from 22.2% to 28.0%. Larger comprehensive cancer centres, often supported by a targeted-enabling central budget, can galvanise the full resources of universities and institutes, spurring collaborations between physical sciences, mathematics, engineering, and biosciences, increasing the reach of the research. OECI has seen a growth in the number of university hospitals establishing formal comprehensive cancer centres with a central governance, bringing together high-quality clinical care, clinical research, translational research, and in many cases, discovery science.<sup>120</sup>

Geographical differences within the EUR19 were also observed (table 3). However, the number of papers per annual GDP in the two countries (France and Italy) and the four country groups (table 4) show a remarkable



**Figure 8: Data collected between 2015 and 2020 on clinical trials and patient enrolment at OECI-designated cancer centres and OECI-designated comprehensive cancer centres**  
 (A) The annual number of clinical trials open to recruitment at cancer centres and comprehensive cancer centres. Data are from 17 cancer centres and 31 comprehensive cancer centres. The median number of open clinical trials at cancer centres was 26, and the median number at comprehensive cancer centres was 143. The dashed line shows the guide minimum for OECI-designated comprehensive cancer centres (ie, 75 open trials). (B) The annual number of patients recruited at cancer centres and comprehensive cancer centres. Data are from 17 cancer centres and 31 comprehensive cancer centres. The median number of patients at cancer centres was 138, and the median number at comprehensive cancer centres was 534. (C) The percentage of patients enrolled in prospective interventional trials (phases 1–3) or patients newly managed in a centre. Data are from 17 cancer centres and 31 comprehensive cancer centres. The median percentage of these patients at cancer centres was 3.4%, and the median percentage at comprehensive cancer centres was 10.0%. The dashed line shows the guide minimum for OECI-designated comprehensive cancer centres of newly managed patients enrolled in prospective interventional trials (ie, 10%). (D) The number of open phase 1 or 1/2A trials at the centres. Data are from 16 cancer centres and 20 comprehensive cancer centres. The median number of open phase 1 or 1/2A trials at cancer centres was two, and the median number of these trials at comprehensive cancer centres was 23. OECI=Organisation of European Cancer Institutes.

congruence, ranging from 24.1 papers per billion euros GDP in France to 45.2 papers per billion euros GDP in Italy, albeit that the euro purchasing power in those countries and country groups has not been adjusted for.

Networking between centres is vital to cancer research; it is now universally acknowledged that key scientific challenges cannot effectively be tackled by cancer centres or institutes acting alone. These collaborations involve investigators in multiple locations with a team science mindset.

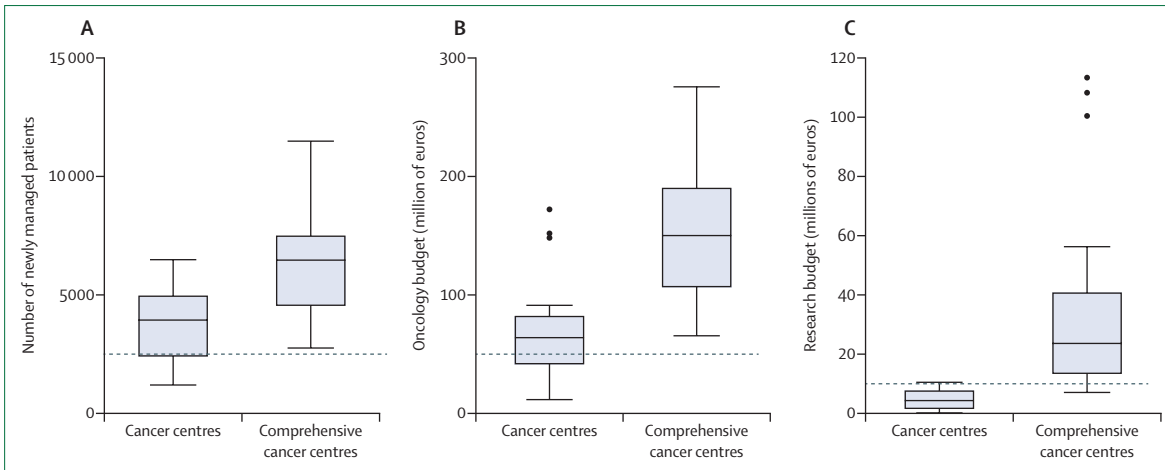
*Clinical research in comprehensive cancer centres*

Critical mass and integration are also important for maintaining a throughput of high-quality clinical trials, focusing on investigator-led studies. Not only are numbers of eligible patients within the network vital, but time for academic clinicians is also protected, and they are supported by a team of research nurses, study coordinators, and other professionals. These resources are generally more available in larger comprehensive cancer centres, which is confirmed in our findings (table 4). Our findings show that a higher preponderance of OECI-certified comprehensive cancer centres corresponds to a higher output of clinical trials (phases 1 to 3) by the EUR32 and EUR19 country groups for targeted therapies including immuno-oncology, genetics and discovery science, radiotherapy, and epidemiology. One surprise is the lower ratio of surgical studies compared with other domains, which could be from university hospitals that have not yet formed into comprehensive cancer centres or that are part of the OECI network.

Regarding clinical trials overall (figures 8A, 8B), in 48 OECI-accredited centres, the number of open clinical trials and patients recruited is presented in two designated groups: OECI comprehensive cancer centres and OECI cancer centres. In the 31 comprehensive cancer centres, there is a large throughput of prospective interventional clinical trials, recruiting substantial numbers of patients, with a median of 534 patients annually. This is 3.8 times greater than their cancer centre counterpart, even without addition of observational or biomarker-driven studies. Comprehensive cancer centres enrolled around 10.0% of new patients to prospective interventional trials, compared with 3.4% in cancer centres (figure 8C). Phase 1 and 1/2a trials are especially concentrated in large comprehensive cancer centres (figure 8D), because they have the critical mass of expertise and patients to conduct such studies. The median comprehensive cancer centre conducted 23 early-phase studies, compared with the a median of 2 early-phase studies for cancer centres. The very largest comprehensive cancer centres have approximately 100 open phase 1/2a studies at any one time.

Research budgets of comprehensive cancer centres and cancer centres, adjusted by purchasing power parity in the country where the centre is located, are commensurate with the volume and spread of clinical research in the two groups, with median annual research budget of comprehensive cancer centres (€26.3 million) five times greater than the median annual research budget of cancer centres (€4.6 million; figure 9C). However, some quite large cancer centres in Europe devote comparatively few financial resources to research compared with comprehensive cancer centres, with concomitantly lower clinical research outputs than comprehensive cancer centres (figures 9A, 9B).



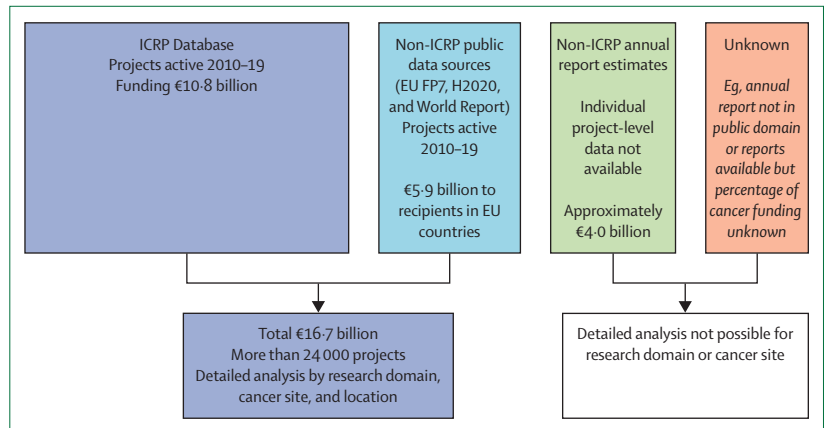


**Figure 9:** Data collected between 2015 and 2020 on patients and budgets at OECI-designated cancer centres and OECI-designated comprehensive cancer centres (A) The annual number of patients newly managed in cancer centres and comprehensive cancer centres. Data are from 18 cancer centres and 31 comprehensive cancer centres. The median number of newly managed patients at cancer centres was 3936, and the median number of patients at comprehensive cancer centres was 6466. The dashed line shows the guide minimum of newly managed patients for OECI-designated comprehensive centres (ie, 2500 patients). (B) The annual oncology care budget of cancer centres and comprehensive cancer centres, adjusted by the purchasing power parity of the euro. The median annual oncology care budget of cancer centres was €64 million, and the median budget at comprehensive cancer centres was €150 million. The dashed line shows the OECI guide minimum for oncology care budgets for comprehensive cancer centres (ie, €50 million). (C) The annual oncology research budget, adjusted by purchasing power parity, of cancer centres and comprehensive cancer centres. Data are from 17 cancer centres and 31 comprehensive cancer centres. The median annual oncology research budget of cancer centres was €4 million, and the median budget of comprehensive cancer centres was €24 million. The dashed line shows the guide minimum of research budgets for OECI-designated comprehensive cancer centres (ie, €8 million). OECI=Organisation of European Cancer Institutes.

**The funding of European cancer research**

*Overview of European public sector and governmental funding for cancer research*

From 2010 to 2019, 24 394 individual projects (with a total value of €16·7 billion) were identified in the ICRP database that could be coded to cancer anatomical site and research domain (figure 10). From internet searches of annual reports, we estimate that an additional €4 billion of European cancer research was also funded during this period, but could not be analysed in detail, because project-level data could not be sourced. Thus, the overall public sector funding for European cancer research (government or philanthropic) was estimated to be between €16 and €21 billion over the 10-year period (figure 10).



**Figure 10:** Overview of public sector, charitable, and governmental funding for cancer research in Europe FP7=Seventh Framework Programme. H2020=Horizon 2020. ICRP=International Cancer Research Partnership.

*European cancer research funding by research domain*

Analysis of European cancer research funding by research domain (figure 11) indicated that between 2010 and 2019, treatment (CSO5) received the highest amount of investment of the six research domains, closely followed by biology (CSO1). Prevention (CSO3) received the least investment. Funding for early diagnosis and prognosis (CSO4; from 18·9% to 23·1%), and treatment (CSO5; from 27·0% to 31·8%) increased from 2010 to 2019, suggesting that the research portfolio is becoming more translational and clinical (appendix p 36). Between 2010 and 2019, funding for biology decreased (CSO1; from 34·1% to 28·5%) and funding for aetiology decreased (CSO2; from 10·7% to 5·6%). Investment in cancer control (CSO6) increased by 1·4% (5·9% to 7·3%), an encouraging trend. Research into primary prevention (CSO3) was very

low, less than 4·0% of the overall European cancer research portfolio. However, there was a very small increase in the proportion of investment for prevention research between 2010 and 2019 (from 3·4% to 3·7%). The research domain profile was similar for the international portfolio,<sup>121</sup> with a higher emphasis on discovery biology, diagnosis, and treatment than on aetiology, prevention, and cancer control, or cancer survivorship, reflecting our findings on cancer research outputs.

*European cancer research funding by cancer anatomical site*

Investment was higher (51%) in non-site-specific research than for site-specific research (48%; appendix p 39).

Non-site-specific research included basic or discovery research, or research relevant to multiple cancer sites (eg, pain control and palliative care). The proportion of investment by cancer anatomical site compared with incidence and mortality trends<sup>55</sup> for those cancer sites in Europe is shown in figure 12. Breast cancer research received the highest amount of investment (18% of site-specific investment), followed by colorectal cancer (12% of site-specific investment), and leukaemia (12% of site-specific investment). The pattern of investment showed broad correlation with cancers of high incidence or mortality (figure 12), but with some notable outliers (eg, lung, bladder, stomach, and pancreas), for which proportion of investment was substantially lower than percent mortality, again reflecting our analysis from mapping the cancer research landscape by publication output.

Our evaluation of European cancer research investment does have some limitations. At least €4 billion (approximately 18%) of investment could not be analysed

in-depth, because project-level data were not available in the public domain. Investment by country is included (appendix pp 40–41), along with estimates of additional funding for cancer research that could not be coded in detail. A full picture of the European research portfolio will be invaluable in understanding more precisely the effects of the COVID-19 pandemic on cancer research investment and capacity.

### Who funds cancer prevention research in Europe?

Our analysis showed that 11% of cancer research papers published between 2008 and 2021 focused on prevention research, supported by 243 European funders, representing 16% of all European cancer research funders (appendix pp 42–44). European not-for-profit prevention research funding organisations accounted for 45% of total expenditure (figure 13A). Governmental sources (including the European Commission) represent 31% of cited organisations, but received 48% of funding acknowledgments in our dataset (figure 13B). Although a direct link between funding acknowledgments and funding received cannot be established, funding acknowledgments provide indirect evidence of which funder might be supporting relatively more or less research in cancer prevention, compared with other research domains. Thus, government funders support more cancer prevention research than typical not-for-profit organisations. Maybe unsurprisingly, only 8% of prevention research funders are for-profit entities, whereas these entities account for 17% of funders of all cancer research (figure 13A).

Cancer prevention research funders are present in 23 European countries (94% EU). The number of funding acknowledgments per country were compared as an indicator of overall expenditure on cancer prevention research. The UK, Germany, and Italy are the three most acknowledged countries in cancer prevention research

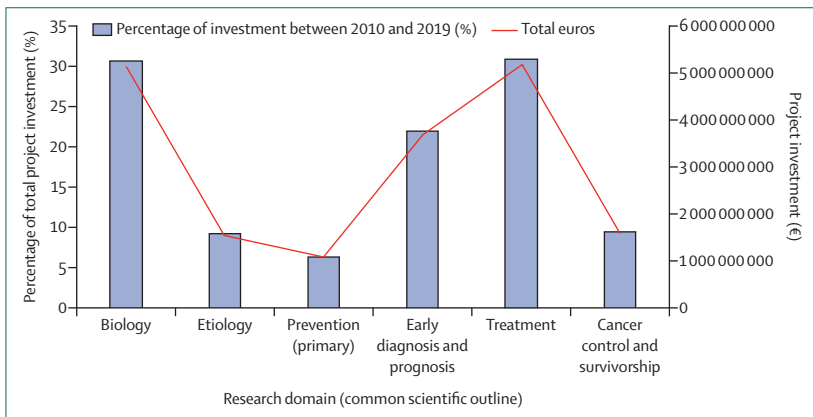


Figure 11: Investment in European cancer research projects by research domain between 2010 and 2019

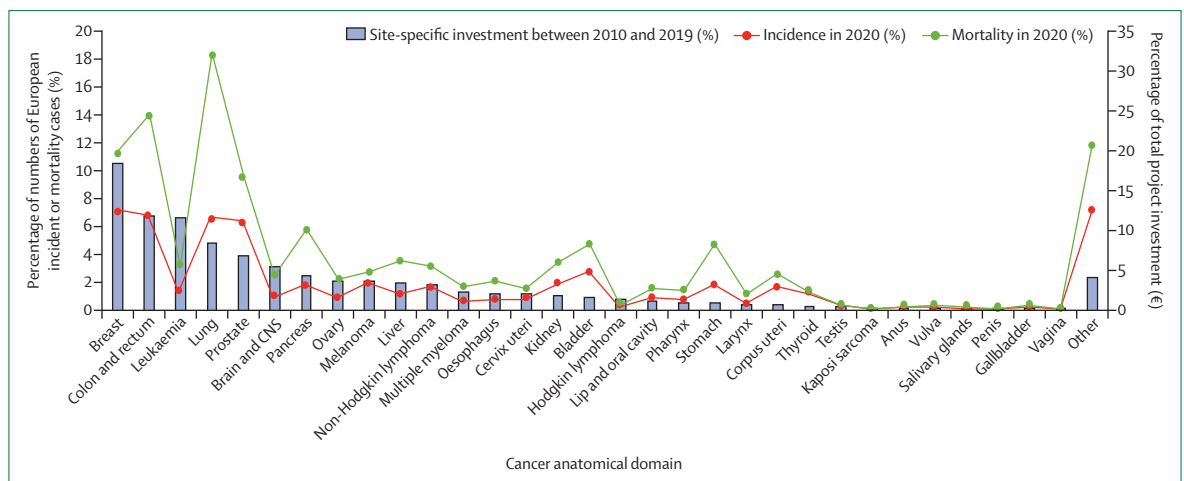


Figure 12: European investment in site-specific cancer research projects (as a percentage) between 2010 and 2019, compared with the incidence and mortality for site-specific cancers in 2020 (as percentages)

publications. Restricting the scope of funding acknowledgments to not-for-profit organizations, the UK, Spain, and Sweden are the most active in cancer prevention research (table 6).

Another element of the European cancer prevention research landscape is the absence of prevention research infrastructures. At European and national levels, infrastructure for cancer prevention tends to be fragmented. There are few examples of cancer prevention research centers. Of the 32 European research networks identified, only two are involved in (but not dedicated to) prevention research, reflecting wider structural issues of major comprehensive cancer centres being heavily focused on discovery science and biopharmaceutical research, including clinical trials.

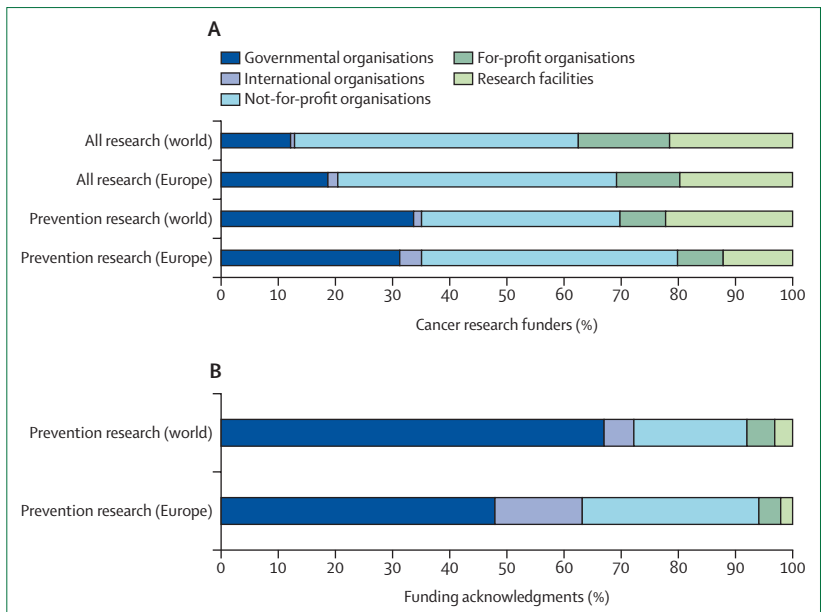
**Is Europe leading the way in cancer prevention research?**

A comparison between global and European prevention research funding indicates that Europe does slightly better than the whole world (appendix p 43) with more European cancer research funders in prevention research (16%) than in the world (12%). European not-for-profit organisations are also more involved in prevention research, accounting for 45% of European cancer prevention research funders (figure 13A) and representing 13% of all European not-for-profit organisations that fund cancer research (appendix p 43). In comparison, 34% of cancer prevention research funders in the world are not-for-profit entities (figure 13A), representing only 7% of all not-for-profit organisations funding cancer research (appendix p 43). European not-for-profit organisations are acknowledged in 31% of cancer prevention research papers, but this percentage drops to 20% for not-for-profit organisations in the whole world, excluding Europe (figure 13B).

The total number of European funding sources for cancer prevention research has more than doubled since 2008, resulting in a proportional increase in prevention research publications. This proportional increase is primarily due to the multiplication of not-for-profit organisations and governments involved in prevention research, because the number of other types of funding (eg, industry) has stagnated. However, although interest in prevention research is growing globally, the last 6 years have seen a slowdown in the growth rate and expenditure by European cancer prevention research funders (figure 14).

**Primary prevention: a consistently neglected research area**

A breakdown by research domains within cancer prevention reveals that secondary prevention is the most funded research area (51% of European cancer prevention research funders), closely followed by aetiology (46%; appendix p 44). Primary prevention is the research area with the least funding overall, though is more funded in Europe (25%) than in the world (20%; appendix p 43). Thus, less than 59 (<4%) of the 1477 European cancer



**Figure 13: Data on cancer research funding**  
 (A) Types of cancer research funders for prevention research and all research in Europe and in the world. (B) Percentage of funding acknowledgments for prevention research in Europe and in the world by type of funder.

	Percentages of funding acknowledgments for all research areas (all types of funders)	Percentages of funding acknowledgments for prevention research (all types of funders)	Percentages of funding acknowledgments for prevention research (funding from governmental organisations)	Percentages of funding acknowledgments for prevention research (funding from not-for-profit organisations)
UK	15%	13%	13%	12%
Germany	11%	11%	12%	7%
Italy	7%	10%	12%	8%
Spain	6%	10%	10%	12%
Sweden	9%	10%	9%	11%
France	12%	9%	11%	8%
Denmark	6%	6%	4%	7%
Netherlands	5%	5%	4%	5%
Belgium	4%	5%	6%	5%
Switzerland	5%	5%	4%	5%
Norway	3%	4%	5%	4%
Finland	4%	4%	6%	4%

The number of funding acknowledgments per country were compared as an indicator of overall spend on cancer prevention research. We measured acknowledgments of each country in all research areas with all types of funders, in prevention research with all types of funders, in prevention research with funding from governmental organisations, and in prevention research with funding from not-for-profit organisations.

**Table 6: Top 12 most acknowledged countries in cancer research papers between 2008 and 2021**

research funders identified are interested in research into primary prevention, which is concordant with our bibliometric analysis and reflects the long-term failure of research funding organisations to properly balance their research portfolios and funding. Not-for-profit funders represent 45% of secondary prevention funders, acknowledged in 32% of secondary prevention research

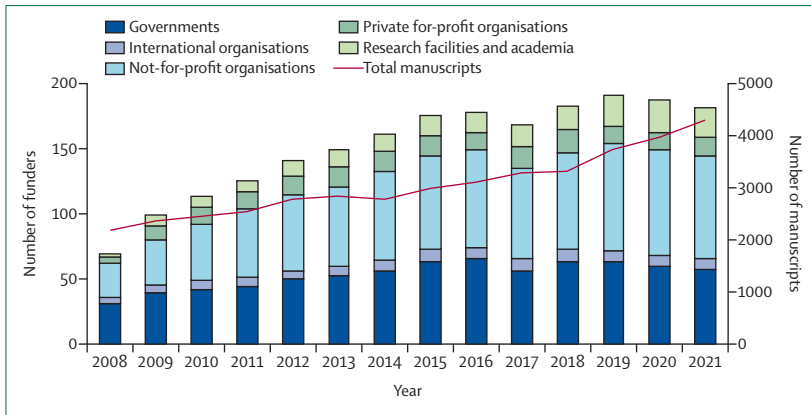


Figure 14: Number of funders, types of funders, and number of manuscripts in cancer prevention research in Europe between 2008 and 2021

papers (appendix p 44). By contrast, not-for-profit funders are acknowledged in only 12% of primary prevention research papers. Governments (including the European Commission) are active in primary prevention, with 56% of primary prevention funders identified as governmental entities and 86% of primary prevention research papers containing government funding acknowledgments.

Our findings on cancer prevention research, particularly that primary prevention research is underfunded, led to additional analysis on cancer prevention and implementation science. A sample of 2000 European cancer prevention research papers from the past five years were checked and coded to identify implementation science projects. Only 7% of European cancer prevention research papers were classified as implementation research and only 9% of global cancer prevention research papers were classified as implementation research. This finding shows that cancer prevention research, and especially implementation research, remain underfunded compared with other research areas. This imbalance must be rectified. Research funding organisations need to commit substantial strategic funding in this area and be willing to support health services and systems research.

## Section 8: strengthening cancer services and systems research for Europe

### Ensuring precision oncology research is part of a broader research portfolio

The so-called pharmaceuticalisation of cancer care across Europe<sup>122</sup> risks being somewhat reductionist in pursuing improving outcomes, pivoting research and public sentiment away from the evidence-based reality that early diagnosis, high-quality surgery and radiotherapy (de facto focusing on the precise delivery of cancer treatment), and health systems research contribute substantially to better, more equitable, and affordable cancer outcomes for populations. Precision oncology has an important place in this new research framework,<sup>123,124</sup> as evidenced by, for example, the impact of immuno-oncology, but precision oncology needs to be proportionate and contextualised to

its contribution to improving population outcomes. The new generation of precision oncology medicines, including immuno-oncology, are exciting and indicate clear potential to benefit patients, but these new drugs are also expected to collectively contribute to 70% of the total cost of active cancer care in Europe by 2025,<sup>125</sup> reopening the price and cost versus value debate. Furthermore, there is now ample evidence that a substantial proportion of research in precision biopharmaceuticals is not delivering new pharmaceutical technologies with clinically meaningful benefit.<sup>126</sup>

An overemphasis on precision oncology also risks reinforcing the notion that achieving the best outcomes for patients can simply be addressed by ensuring cutting-edge technologies are available,<sup>125</sup> ignoring the wider social and economic contexts in which people live, which will ultimately affect their outcomes.<sup>126,127</sup> Accumulating evidence shows that many novel biopharmaceutical treatments do not deliver clinically meaningful benefits, yet are reimbursed by national authorities, which means these treatments might not contribute substantially to reducing cancer mortality at a population level.<sup>128</sup> Therefore, investing more in biomedical research and technologies, without building the wider cancer research base, is unlikely to deliver better, more affordable, and more equitable progress in European cancer outcomes.<sup>129</sup>

### The value of health systems and implementation science research

Health systems fund, organise, and deliver cancer care. The wider political, economic, and societal context in which these health systems are embedded define the accessibility, affordability, equity, and outcomes of cancer control interventions.<sup>130,131</sup> These aspects set the parameters for policies and strategies that help protect people's health (eg, legislation on unhealthy commodities such as tobacco and alcohol); define options and ensure access to early detection and prevention (eg, HPV vaccination); and determine when and how people seek care, what treatments are available and where, who gets these treatments, their cost and cost-effectiveness, and the quality of care delivered. Health systems research frames science by defining research ecosystems and prioritising what will help realise the greatest improvements in patient outcomes.<sup>132</sup>

Health systems, and the cancer services and systems within them, are complex. Addressing the many factors that affect patient outcomes at the individual and population levels requires a more balanced research portfolio that prioritises health policy and systems research and implementation science. This research portfolio would enable a deeper understanding of the multiple factors acting at different levels; the interconnections of these factors; and the priorities, agency, and power of the various actors within and across systems that influence cancer outcomes.<sup>128</sup> Understanding these factors requires convening a wide range of scientific disciplines and

professions, from political science to applied health services research, from implementation science to epidemiology, from geography to economics, and from anthropology to behavioural psychology. However, most cancer research funders do not consider these domains a priority for funding. Strategic imbalances in funding and policy exist, leading to a devaluation of global cancer care due to a focus on marginal gains. Prioritisation and targeted investment could serve to address this imbalance.

There is an emerging understanding of political economy and its importance for ensuring equitable, efficient cancer care, research delivery, and sustainable funding (eg, health technology assessment [HTA], commissioning and reimbursement systems, and pharmaceutical regulation).<sup>133</sup> However, the benefits for outcomes, affordability, and equality achieved by implementing multilayered governance from mandated clinical practice guidelines through to sophisticated HTA mechanisms, coupled to pricing and reimbursement models, are not being universally replicated across all European countries.<sup>134</sup>

#### *Implementation science as a driver of innovation*

No innovation improves patient care and outcomes without first navigating its way through the health system. Implementation and scale-up, which are both intrinsic aspects of strengthening health systems, help to determine whether an innovation is affordable and equitable. Yet, in the current system, global cancer research largely focuses on discovery science and systemic therapies.<sup>3,135</sup> A 2016 analysis reviewing publication outputs in lung cancer found that 60% of research focused on systemic therapies and discovery science research, whereas 8% of research focused on radiotherapy research, 4% focused on early diagnosis, and 2% focused on screening research.<sup>136</sup>

What gains could potentially be made from a greater emphasis on implementation science for early diagnosis and more effective curative locoregional treatments? Improving our understanding of how to minimise disparities in access to care through health services research could make a great difference to population-level survival, yet for example only 2% of radiation research is devoted to this area.<sup>28</sup> There is an urgent need for cancer research funders, particularly federal and philanthropic, to reassess the balance of their research portfolio investments and their overall strategic direction. Promising areas like precision oncology will only prosper and deliver within a fully fledged health system, informed by health systems and implementation science research.

## **Section 9: screening and early detection research**

### **Research to promote early detection of cancer**

Although enhancing cancer prevention research is an important (but under-resourced) part of primary prevention policy development across Europe, it must be

accompanied by a clear strategic focus on research that improves secondary prevention, through earlier detection of cancer. When identified at an earlier stage, cancer is more curable and less expensive to treat. Additionally, health systems that deliver early detection through cancer screening and early diagnosis will ensure more cost-effective cancer control for citizens, patients, and society. Importantly, it is estimated that up to a third of patients with cancer in Europe could be positively affected by an early detection approach, including patients with more common cancers (eg, breast cancer or colorectal cancer).<sup>137</sup> IARC estimates that women who attend breast cancer screening appointments have a 40% reduction in their risk of dying from breast cancer,<sup>138</sup> with more than 21 000 global deaths prevented annually.<sup>139</sup> Secondary prevention is also important from a health economic perspective, for example the total cost associated with managing late-stage colorectal cancer is ten-times higher than the total cost associated with managing early-stage disease.<sup>140</sup>

### **Disparities in cancer screening**

In 2003, the European Council of Health Ministers issued recommendations for the implementation of cancer screening programmes to reduce the burden of some cancers in Europe.<sup>141</sup> These recommendations included a shared commitment by EU member states to implement systematic population-based screening programmes for breast cancer (the third leading cause of death due to cancer in the EU), colorectal cancer (the second leading cause of death due to cancer in the EU), and cervical cancer. These three cancers are collectively responsible for nearly 300 000 deaths in the EU annually. As of 2020, 25 EU countries had introduced population-based screening for breast cancer, 22 countries introduced population-based screening for cervical cancer, and 20 countries introduced this type of screening for colorectal cancer.<sup>142</sup> It is an indictment of European cancer screening policies and the absence of implementation research that population-wide screening programmes are not universal in all European countries, which has led for example to cervical cancer mortality being more than four-times the EU average in Romania.<sup>143</sup>

Coverage of respective target populations by screening also remains very low, at 14% on average across the EU for colorectal cancer.<sup>144</sup> Wide disparities exist, both across European countries (eg, breast cancer screening coverage ranging from 6% to 90%<sup>145</sup>) and across social groups. For instance, women with lower socioeconomic status have less access to breast screening than women with a higher socioeconomic status. More than 12 000 deaths could be avoided annually from breast cancer if maximal coverage were achieved throughout the EU.<sup>139</sup> Cancer screening programmes achieving the best coverage were also those with the most rapid recovery from the pandemic, showing how best practices in screening precipitate more equitable citizen access and increased resilience to health crises.



Disappointingly, all screening rates show wide variability between European countries and, in some cases, between specific regions within a country. In countries where population-based cancer screening programmes were actively implemented, examination coverage rates ranged between 17–84% (breast cancer), 1–53% (colorectal cancer), and 4–71% (cervical cancer).<sup>146</sup> However, research on these differences is essential for leveraging political and social change.

There have been important considerations of developing additional cancer research screening programmes for other cancer anatomical sites, with a particular focus on lung cancer. Although CanCon have indicated that further evidence is required,<sup>147</sup> research studies by European disease-based communities have provided evidence to support the case for low-dose CT screening for lung cancer.<sup>148</sup> The development and roll-out of lung cancer screening would help tackle the leading cause of cancer death in the EU, which was responsible for an estimated 296 140 deaths in 2018. However, lung cancer screening requires investment in national systems and implementation science research to succeed.

#### Early diagnosis of cancer

Despite many public health efforts, public awareness of warning signs of cancer remains low.<sup>149</sup> A more prominent role for primary health-care providers in the research agenda is essential for successful implementation of early detection strategies.<sup>150</sup> Currently, more than 75% of patients with cancer are not diagnosed through a screening approach, including patients with 40 of the most frequent and more lethal cancer types. Worryingly, a pan-European survey of more than 4000 patients with cancer reported that for 30% of those patients whose cancer was detected outside of screening, their original diagnosis was not cancer, sometimes on multiple occasions,<sup>151</sup> which emphasises the challenges for effective early cancer detection.

From a research perspective, risk-based early detection to help diagnose cancer is attractive, helping deliver earlier, better, and more equitable cancer diagnostic capacity for European citizens. For breast cancer, incorporation of genetic risk prediction based on family history and polygenic risk scores<sup>152</sup> can be effective from clinical and health economic perspectives. For colorectal cancer, the faecal immunochemical test was successfully used as a decision tool for triaging patients for colonoscopy to ensure early detection of colorectal cancer, despite the effects of COVID-19 and national lockdowns on the urgent diagnostic pathway.<sup>153–155</sup> Not only did this approach help to save lives, it also allowed colonoscopy capacity to be managed more efficiently.<sup>155</sup> In lung cancer, low-dose CT can be targeted to at-risk populations (eg, individuals who used to smoke).<sup>148</sup> Self-collection approaches for screening (eg, HPVCheck)<sup>156</sup> are increasingly being adopted. However, all these diagnostic innovations need rigorous preclinical and clinical

evaluation, much of which is becoming increasingly complex, requiring larger (ie, pan-European) populations to rapidly validate them.

Beyond this type of research, there is also a need for better studies addressing patient pathways to diagnosis. In an All.Can survey, more than 25% of patients with cancer and their caregivers highlighted that diagnostic pathways were a major issue for patients, negatively affecting their experience of cancer care.<sup>152</sup> There is a wider research need to examine the cancer workforce perspective in this area; general practitioners, nurses, allied health-care professionals, pathologists, and clinical scientists all play a pivotal role in helping to deliver accurate and timely cancer diagnosis. However, workforce shortages for these disciplines are substantial. For example, there are shortages in pathology capacity, which we previously highlighted in the *Lancet* Series on pathology and laboratory medicine.<sup>157</sup> Cancer nursing shortages have also been highlighted and need to be addressed.<sup>158</sup>

#### Section 10: secondary prevention—HPV and research

HPV causes approximately 5·0% of all cancers in women and men worldwide. From a European perspective, approximately 2·5% of cancers are attributable to HPV. Widely recognised as the causative agent in cervical cancer, HPV is also involved in the development of anal, oropharyngeal, penile, vaginal, and vulval cancers, and potentially, other cancers. There are around 200 different types of HPV associated with a high cancer risk.<sup>159</sup> HPV is responsible for approximately 87000 of cancer cases across the WHO European region.<sup>160</sup> In the past 5 years, there has been a marked increase in the incidence of oropharyngeal cancers, particularly in men.<sup>161</sup> In the USA, HPV-positive oropharyngeal cancer has overtaken cervical cancer as the most common HPV-associated cancer type.<sup>160</sup> Dentists and dental hygienists also have an important role to play in the opportunistic detection of oral lesions associated with oropharyngeal cancer, but more research is required to precisely delineate the benefits. The worrying recent increase in oropharyngeal cancer detection could reflect the indirect effect of the COVID-19 pandemic when dental surgeries were shut, often for many months.

From a screening perspective, HPV testing is recognised through the European Guidelines for Quality Assurance in Cervical Cancer Screening as the most accurate and effective method of cervical cancer screening.<sup>161</sup> Research has shown that cervical cancer screening can reduce cervical cancer mortality by up to 90%,<sup>162</sup> which has spurred a range of new implementation research programmes across Europe.

An impressive 100% vaccine effectiveness has been shown over 12 years in four Nordic countries; no cases of high-grade cervical dysplasia were found in a large sample of 2385 vaccinated women.<sup>163</sup> Global incidence of genital warts (also caused by HPV) has also been substantially

For All.Can see <https://www.all-can.org>

For the WHO Global Cancer Observatory see <https://gco.iarc.fr/>

For the HPV Information Centre see <https://www.hpvcentre.net>

reduced by HPV vaccination.<sup>164</sup> The US Food and Drug Administration has approved vaccination as a means of preventing head and neck cancers caused by HPV.<sup>165</sup> Vaccinating both sexes provides an effective and faster approach to preventing or reducing the incidence of cancers and other HPV-related diseases (appendix p 45). A universal approach for boys and girls could make the elimination of HPV-driven diseases possible, even with moderate levels of vaccination uptake (eg, 50–75% uptake) across Europe.<sup>160,166</sup> The European Centre for Disease Prevention and Control has indicated that universal vaccination is a cost-effective option to prevent all HPV-associated diseases,<sup>167</sup> which emphasises the importance of research that spans across domains, including health economics in this example.

Research also indicates that there is wide variation in European citizens' perceptions on the safety of HPV vaccination. In northern Europe, 73% of people believe that vaccines are safe, but this proportion decreased to 59% in western Europe and is only 40% in eastern Europe.<sup>168</sup> Vaccine hesitancy (appendix p 45) is linked to a number of factors: insufficient and inadequate information about vaccination; misinformation about potential side-effects; issues around trust in health authorities, doctors, and new vaccines; and a perception of low vaccine effectiveness.<sup>169</sup> However, these views could change in response to UK data from 2021 showing clear HPV vaccine efficacy,<sup>170</sup> along with the success of COVID-19 vaccines.

Many people currently do not have basic knowledge about HPV and its associated risks. In the UK, despite HPV systematic cervical cancer screening since 1988 and HPV vaccination for girls since 2008, a 2019 survey found that only 37% of participants had even heard of HPV.<sup>171</sup> Of these, 70% were aware that HPV could be transmitted during sex, approximately 40% recognised that HPV could cause oropharyngeal cancer, but only 64% were aware of the existence of a vaccine that could prevent HPV-associated disease. A study of 17000 Europeans across ten countries found that 70% of participants were not aware that HPV could cause cancer in men.<sup>172</sup> These findings clearly support the need for education and policy research to determine ways to reduce inequity, coupled with the need for research to challenge disinformation around HPV vaccination. Other viral risk factors, such as exposure to hepatitis B virus (HBV), can be addressed by vaccination campaigns and early oral treatment, to reduce the burden of hepatocellular cancer in the future. The European Cancer Network is advocating for greater awareness and action on HPV and hepatitis C virus programmes to achieve improvements in cancer reduction.

## Section 11: prioritisation of radiotherapy and surgical oncology research in Europe

Radiotherapy and surgery are essential treatment options to help improve cancer outcomes, exert improved cancer control, and deliver appropriate palliative care. More than

50% of patients with cancer have an evidence-based indication for radiotherapy or surgery, or both, at least once in the course of their disease.<sup>173</sup> However, there is a paucity of research focus and funding for these two important domains.

### Gaps in radiation oncology research

Although radiotherapy is a core component of cancer treatment, the data that we have presented highlight that radiation research is less prioritised than research on other cancer treatment modalities, particularly systemic therapy and precision oncology. Additionally, radiation research tends to be somewhat unbalanced. Previous analysis from a global perspective has shown that approximately 50% of all publications in the radiation research domain are focused on radiotherapy planning, radiotherapy delivery, combined-modality regimens, and dose fractionation. By contrast, studies on radiotherapy have very little focus on health services research, palliative care, and quality of life.<sup>48</sup> Trial-related publications represented only 5.1% of total radiation research output. Randomised clinical trials are often difficult to execute due to the complexity of radiotherapy innovations, high up-front investments for new technologies, and strong operator dependency. These challenges are further intensified by the limited research budgets available for radiation oncology research,<sup>48</sup> and by the challenge of implementing the evidence into clinical practice.<sup>174</sup> An anonymous, electronic survey distributed to radiation oncologists through the European Society for Radiotherapy and Oncology–Global Impact of Radiation in Oncology initiative (ESTRO–GIRO) revealed a substantial variation in hypofractionation regimens used, especially across specific curative approaches and between geographical regions, despite the available literature evidence to support this approach.<sup>175</sup>

To ensure access to the most optimal radiotherapy for each patient with cancer in Europe, a dual focus is required: one on treatment optimisation, with the aim to guarantee best clinical outcomes and quality of life for the individual patient; and the other on health system optimisation, guaranteeing equitable access to valuable innovations, considering the societal perspective. Beyond the need for research that deepens our understanding of how new radiotherapy interventions might benefit patients, there is also the need to perform research defining the value of these radiotherapy innovations, to support their implementation in the clinic. Focusing on health services research and implementation science approaches to address inequalities across Europe is urgently required, because these research domains have been under-represented in radiation and radiotherapy research.

Since 2012, the ESTRO Health Economics in Radiation Oncology project (ESTRO–HERO) has focused on health systems research, developing an evidence-base for radiotherapy availability, access, cost, and reimbursement

across European countries.<sup>173,176</sup> To foster the diffusion and clinical implementation of innovative radiotherapy interventions, ESTRO–HERO is currently developing an evidence-based value framework for radiation oncology.<sup>173,177</sup> This framework requires a greater focus on the patient perspective, which considers the broad spectrum of endpoints most relevant to patients undergoing radiotherapy. In addition to typical endpoints such as survival, quality of life, and toxicity, local control or organ-sparing are important clinical measures in the context of radiotherapy. Moreover, endpoints that appraise patient burden, quality of life, and economic consequences should be considered, including patient-reported outcome measures. A more homogeneous, yet blended, approach to evidence-generation, which can be diversified for new radiotherapy technologies, techniques, and treatments, should be used.<sup>178</sup> Alternatives to randomised controlled trials have been suggested and are under evaluation, such as the model-based approach in proton-beam radiotherapy,<sup>177</sup> the R-IDEAL framework developed for MRI-guided radiotherapy,<sup>178</sup> the embedding of randomisation into prospective cohort studies,<sup>179</sup> or the collection of real-world evidence.<sup>53</sup>

In the context of Europe's Beating Cancer Plan and the Cancer Mission, the need to collect radiation-relevant information deploying data analytics and artificial intelligence approaches is evident. These radiation-relevant data should inform research developing predictive models for radiotherapy outcomes, empowering a more tailored and personalised approach for each patient's treatment than what is currently available. There is a need to evaluate new radiotherapy technologies and treatment modalities that are emerging, also from the patient perspective, to ensure that radiotherapy innovations are accessible across Europe. Analysis of data from both clinical trials and in the real world will allow information on therapeutic efficacy and effectiveness, whereas quality of life and patient-reported outcomes should also be captured and assimilated. Turning these data into intelligence will facilitate the best therapy for each patient and allow patients' quality-of-life readouts to inform future research priorities for patients living beyond cancer.

#### Gaps in surgical oncology research

Cancer surgery remains an important yet underdeveloped domain for research. Through a services and systems lens, the World Bank's *Disease Control Priorities*, third edition<sup>180</sup> focused on the trade-offs between centralised and decentralised approaches to cancer surgery, and capacity-building and capability-building for the breadth of the surgical workforce needed to deal with cancer, including the challenges, both economic and practical, of scaling up different models.<sup>181</sup> However, the *Lancet Oncology Commission on global cancer surgery: delivering safe, affordable, timely cancer surgery*<sup>182</sup> took a deep, broader strategic view, highlighting both care and research needs and deficits, and finding that

more than 80% of people diagnosed with cancer worldwide required a surgical procedure at some point in their treatment, but that three-quarters of cancer surgeries are judged to be unsafe, not delivered, or unaffordable.<sup>118</sup> Our Commission has found dramatic deficiencies in the research ecosystem to support cancer surgery.

Across Europe, cancer research funding organisations have failed the challenge of delivering more surgical oncology research. A search in the EU Clinical Trials register shows that surgical oncology comprises only 6.1% of cancer clinical trials. Funders are increasingly inward-looking, focusing on discovery cancer science and biopharmaceutical research.<sup>118</sup> Additionally, less than 4.5% of cancer research activity over the past decade, of which research on cancer surgery was less than 0.1%, was in collaboration with low-income and middle-income countries. Furthermore, there is little evidence that cancer surgery and surgical research are priorities commensurate with the surgical need.<sup>181</sup> Previous analysis from 2012 showed that, based on bibliometrics, less than 5.0% of total global—including European—cancer research and development expenditure was on surgery.<sup>183</sup> Little has changed since then: our updated 2022 analysis presented here found almost no progress. Instead, research funding organisations and advocacy groups continue to focus on access to cancer medicines. The realpolitik of cancer surgery in Europe is that it remains politically marginalised. However, with the rise of new advocacy movements, such as global diagnostics,<sup>157,184</sup> the opportunity exists to reintegrate cancer surgery as part of a broader political discourse, reflected by the focus of Europe's Beating Cancer Plan on enhancing surgical oncology and emphasising its position as a pillar of cancer treatment.

European cancer surgical research has, however, innovated in numerous areas. For example, innovation exists on the impact of technology, particularly robotics and, to a lesser extent, minimally invasive surgery. Although technological innovation is fundamental to cancer surgery, robotics has had a highly disruptive effect on services and systems. What data we have, mainly from Nordic countries and the UK, strongly suggest that these novel technologies, if not properly implemented in a managed cancer care system, can be anti-equity, distorting cancer surgical systems that then adapt to deliver these high-cost, high-end technologies. As higher socioeconomic groups seek out novel technologies in the belief that they provide better outcomes, the reduction in patient flows to local hospitals can often cause services to shut, thus reducing access for more vulnerable patients who do not have the capacity to seek out novel technologies.<sup>185</sup> Technological innovation has often come at the expense of surgical systems' strengthening, primarily due to the failure to bring cancer surgery into the orbit of HTA and more managed systems planning.<sup>48</sup>

Cancer surgery has, however, been a rich area for research on health services and policy in Europe, with a long history of research into performance metrics, models of care, and surgical workforce. These analyses have helped underpin policy decisions for national planning, reflecting the importance of a broad surgical oncology research strategy, which embraces technological innovation and health systems research.<sup>186</sup> Surgical innovation, such as the development of total mesorectal excision for rectal cancers, has delivered very substantial improvements in patient outcomes, reflecting a crucial modality for future European research strategies that can deliver substantial improvements in population outcomes.<sup>187</sup>

### Section 12: ensuring a person-centred approach to cancer research and its translation

A patient-centred approach to cancer research is crucial to bridging health research, policy, and clinical practice. In the Introduction, we highlighted how the European Cancer Patient's Bill of Rights and the Europe of Disparities in Cancer initiatives articulated and supported the need for patient-centred cancer care and research across Europe. The European Code of Cancer Practice<sup>188</sup> was established in 2021, and places patients at the centre of both cancer control and cancer research agendas in Europe. This code (appendix p 46) is a citizen-centred and patient-centred initiative, highlighting the core requirements that people should expect in order to receive good quality clinical cancer care that also involves access to cancer research (eg, clinical trials).

The code sets out a series of ten key overarching rights (panel 2),<sup>188,189</sup> signposting what European patients should expect from their health system, including cancer research as an important component of their care. The code has been coproduced by a team of patients with cancer, cancer professionals, and patient advocates to underpin a framework for the delivery of optimal cancer care and patient-centred cancer research. The ten rights provide specific support for the cancer patient and their family or carer and are articulated in detail in the appendix (pp 47–48).<sup>189</sup> Legitimacy of each of these ten rights is underpinned by a combination of the best available medical literature, evidence-based guidelines, and research analysis,<sup>188,189</sup> including the Essential Requirements for Quality Cancer Care.<sup>190</sup>

The code has been translated into 31 languages, facilitating its dissemination and deployment across Europe. EU Health and Food Safety Commissioner Kyriakides has committed to use her office to support dissemination of the European Code of Cancer Practice, providing endorsement of the Code's relevance and importance in Europe, and providing invaluable support for its widespread dissemination and implementation. The ten rights of the Code align to ECO's Focused Topic Networks (figure 1).

#### Panel 2: The ten rights of the European Code of Cancer Practice<sup>188,189</sup>

- You have a right to equal access to affordable and optimal available cancer care, including the right to a second opinion
- You have a right to information about your own disease and treatment from your medical team and other reliable sources, including patient and professional organisations.
- You have a right to information about the quality and safety of care, the level of expertise, and the outcomes achieved for your type of cancer in the cancer care service where you are being treated.
- You have a right to receive care from a specialised multidisciplinary team, ideally as part of a cancer care network
- You have a right to participate in shared decision-making with your health-care team about all aspects of your treatment and care
- You have a right to be informed about ongoing research relevant to you, and your ability and eligibility to participate in research
- You have a right to discuss with your health-care team your priorities and preferences to achieve the best possible quality of life
- You have a right to receive optimal supportive and palliative care, as relevant, during any part of your cancer journey
- You have a right to receive and discuss with your care team a clear, managed, and achievable plan for your survivorship and rehabilitation
- You have a right to be fully reintegrated into society and protected from cancer-related stigma and discrimination, so that, in so far as is possible, you can return to work and a normal life

### Section 13: living beyond cancer

#### Research on cancer survivorship

Because 5-year and 10-year cancer survival from many cancers has improved substantially, there is a need for greater focus on ensuring that people living beyond cancer attain a better quality of life than what is currently the case, both physically and psychologically, which includes addressing the challenges of social and economic exclusion (eg, inability to access bank loans and travel insurance). In Europe, research must focus on these survivorship challenges. There are 20 million European citizens living beyond a cancer diagnosis and this number will continue to rise.<sup>49</sup> Improvements in survival are juxtaposed with a range of issues, either as a consequence of the cancer itself (or its comorbidities), or of the treatment the patient received for their cancer. The European research agenda needs to encompass a wide range of biomedical and socioeconomic survivorship challenges: physical (eg, side-effects, complications, chronic pain, and comorbidities); psychosocial (eg, cancer distress and cancer stigma); professional and financial (eg, loss of employment); and personal (eg, impact on relationships, including intimacy and fertility).<sup>191</sup>

Comorbidities are particularly common in patients with cancer, with research indicating that the majority of cancer patients report at least one comorbid condition.<sup>192,193</sup> From a psychosocial perspective, evidence indicates that psycho-oncology research must be an integral component of the comprehensive multidisciplinary approach to survivorship.<sup>194,195</sup> Unfortunately, management of the



For the European Cancer Inequalities Registry see <https://cancer-inequalities.jrc.ec.europa.eu>

long-term effects of cancer and its treatment is not consistent across European countries, which emphasises the need to widen the cancer survivorship research agenda. There is a need for a research-to-policy strategy that is patient-centred (appendix p 49).<sup>196</sup> We also need new research-informed approaches to survivorship care. Research-informed approaches include developing risk-stratified pathways that optimise coordination between cancer specialists and primary-care physicians, based on the complete needs of the individual.<sup>197</sup>

In association with EACS and ECPC, we focus on delineating specific survivorship research and innovation challenges that Europe is currently facing and propose tangible solutions that can be embedded within an overarching cancer survivorship framework. Previously, we performed in-depth analysis of the state-of-the-science in cancer survivorship and identified specific research domains that should be developed,<sup>49,198,199</sup> to (as part of a wider focus on cancer research) embed cancer survivorship research as an active component of the Cancer Mission.<sup>199</sup> We have prioritised three distinct cancer survivorship research and innovation pillars (appendix p 50) that we propose should be the thematic areas of particular focus. Within these pillars, we highlight challenges (appendix pp 51–53) and propose a series of recommended solutions to firmly empower cancer survivorship research and innovation.

#### *Pillar one: medical cancer survivorship research and innovation*

Ten challenges have been identified for this pillar (appendix p 51). Addressing the absence of cancer survivorship research integration requires a commitment that is resourced within the overall European cancer research agenda, which is best achieved by creating a European Cancer Survivorship Research and Innovation Plan, embedded within the Cancer Mission and aligned to our 70:35 Vision. Prioritisation of its themes should be informed by a comprehensive mapping exercise of existing cancer survivorship research activities, identifying, quantifying, and prioritising specific survivorship research gaps. Prioritisation must clearly align to survivors' specific challenges (in areas such as mental health, reconstructive surgery, fertility preservation, and active rehabilitation). Cancer survivors must be empowered as active participants instead of passive recipients in research and innovation to enhance their quality of life.

#### *Pillar two: socioeconomic cancer survivorship research and innovation*

Six challenges have been identified for this pillar (appendix p 52). Research on identifying determinants of cancer inequalities linked to social rehabilitation of cancer survivors, including disparities present across Europe (in particular in central and eastern European countries), should be prioritised. From a quality-of-life perspective, a combination of maximising the use of existing approaches and creating and evaluating new

research tools will allow for granular assessment of the quality of life of cancer survivors, and help to identify social determinants of health and how cancer survivors can return to normal living.

Financial challenges associated with cancer must also be addressed. Research is required on precise economic evaluations of direct and indirect costs to those living with and beyond cancer (including amounts of financial toxicity experienced by survivors and their families). Aligning this research to the proposed European Cancer Inequalities Registry can help promote distinct actions to address this area of increasing relevance. Social issues, such as access to work, education, insurance, loans, mortgages, and the effects of financial toxicity, must be prioritised within the research and innovation agenda.

#### *Pillar three: politico-legal cancer survivorship research and innovation*

Five challenges have been identified for this pillar (appendix p 53). Increasingly, it is important to characterise any legal aspects of discrimination for cancer survivors, deploying this evidence to inform research on discrimination and how it can be mitigated. The Right to be Forgotten<sup>200–202</sup> has a key role in sparing cancer survivors the challenges of potential financial toxicity, while promoting reintegration, equality, and social inclusion must be adopted across all European countries and jurisdictions. Although the Right to be Forgotten is currently embedded in six European countries (France, Belgium, the Netherlands, Luxembourg, Portugal, and Romania), it needs to be universally accepted in all European countries, because all cancer survivors require access to financial services without discrimination once they are considered cured. Equal access to financial services should not depend upon where a person chooses to live.

Defining and mitigating the stigmas associated with cancer is an increasingly relevant research area and must be pursued, promoting a cultural shift to a more active survivorship-focused approach. Investigating the potential role of comprehensive survivorship clinics should be prioritised. Additionally, consideration of how survivorship care should be organised, without disrupting the medical units dealing with patients who still require active treatment should be considered. Specialised multi-disciplinary teams in survivorship should be created and their expertise and activities promoted. Empowerment is also crucial and should be supported through patients' self-management. One size does not fit all, so flexibility is required. We need to deliver for all cancer survivors, across the whole of Europe.

## **Section 14: the importance of data for European cancer research**

One important lesson learned for European cancer research from the COVID-19 pandemic is the crucial role of data and its conversion into evidence to inform policy



and practice. Data and health analyses are embedded in the public consciousness and have become part of our daily norm. As a society, we are now more familiar with data, be it daily numbers of people infected with SARS-CoV-2, the percentage of the population who are vaccinated, or numbers of COVID-19-related deaths. But, data are not just being deployed to help mitigate the direct effects of the COVID-19 pandemic. Data have also highlighted the indirect effects of the pandemic on other life-threatening diseases such as cancer.

The role of data science for unravelling the indirect effect of the COVID-19 pandemic on cancer highlights the need to focus the European cancer research effort on empowering the responsible and effective use of health-relevant data, including building capacity and capability of cancer registries. Building a citizen-centred cancer knowledge network must be the goal.<sup>203</sup> We live in a digital society: we must explore ways to better harness the power of data while ensuring that these data are used in a safe and trustworthy manner.<sup>204</sup> Data analyses and their comparability are pivotal to this Commission, informing the research that underpins development of better approaches to ensure optimal cancer control for European citizens. Combining multimodal data sources and using this improved evidence to drive research and innovation must be central to efforts to deliver better outcomes and fair value for citizens, patients, clinicians, and researchers, and for economic and societal development across Europe. In particular, the ability to collate, access, and use data to inform tumour site-specific national audits, and transnational care audits (eg, for rare cancers) will need to be a major fulcrum of European cancer research, if health systems are to improve care access, quality, and outcomes.

### Section 15: externalities affecting the cancer research agenda

Externalities will have a major impact on the future of European cancer research. We have yet to fully understand the triple effect of the COVID-19 pandemic, Brexit, and the Russian invasion of Ukraine on investment in, and commitment to, cancer research across Europe. There might be implications for the European Commission's ability to continue to support the Cancer Mission and similarly for European countries, to support cancer research at the intended and required level. Economic shocks from the pandemic and the war are having profound effects on the cost of living, which directly alters our population's philanthropic behaviours (appendix p 54). Thus, we could see a huge contraction in donations for investment in cancer research, severely damaging our aspirations for equitably expanding cancer research activities across Europe.

#### The effect of the COVID-19 pandemic on cancer

By many measures, the COVID-19 pandemic has had a grave effect on Europe. The pandemic has had direct effects (most European countries have had high per

capita COVID-19-related mortality and morbidity) and indirect effects (impact on non-COVID-19 health care). At the nadir of the first pandemic wave (between March and April, 2020), we collected and evaluated near real-time data from hospital trusts across the UK, measuring the effect of the pandemic on cancer diagnostic and treatment pathways.<sup>205</sup> Specifically, we focused on 2-week wait times (a surrogate for urgent referrals) and chemotherapy delivery (measuring cancer treatment pathway robustness). Delays uncovered were extremely worrying: seven out of ten citizens were either unwilling to see their doctor for fear of being infected with SARS-CoV-2 or were unable to access general practitioner or specialist cancer services. The negative effect of COVID-19 on treatment was also substantial: delivery of chemotherapy was delayed for four of ten patients with cancer. These data were the first in the UK to show the indirect effect of the pandemic on cancer and contributed to the decision to restore cancer services. Several other studies have also highlighted the important role of data in influencing policy;<sup>5,206–208</sup> for example, the decision to delay colorectal cancer screening in the UK was rescinded in response to data from a population-based study,<sup>208</sup> and projections from several studies<sup>205,206</sup> on the impact of the pandemic are proving accurate and have affected policies. Worryingly, the cancer backlog (in both diagnosis and treatment) continues to be substantial because staff are still under strain after the COVID-19 pandemic, and many staff are choosing to leave or retire. Such studies reflect the power of data, cancer health policy, and systems research in informing national planning.

At a European level, these salutary data prompted ECO to establish a Special Focused Topic Network on the Impact of COVID-19 on Cancer. Extending our data analysis revealed the disastrous effects of the pandemic across the European continent (appendix p 55).<sup>5</sup> Across Europe, 100 million individuals missed screening tests and up to 1 million citizens might have an undiagnosed cancer. The COVID-19 pandemic also led to substantial delays and reductions in treatment (particularly systemic therapy and surgery) and notable effects on cancer clinical trial activity and cancer research programmes (appendix p 55). The effects of the pandemic on the cancer workforce are also worrying, with four of ten cancer health-care workers feeling burned out due to their great efforts to control cancer and contribute to infection control in a beleaguered health system (appendix p 55). Additionally, the analysis shows that three of ten cancer health-care workers exhibited symptoms of clinical depression (appendix p 55).

These compelling data prompted ECO to launch a Time To Act campaign with the strapline "Don't let COVID stop you from tackling cancer".<sup>5</sup> Translated into more than 30 languages, this campaign was launched in Brussels, Belgium, in May, 2021, and has now been operationalised nationally in 12 European countries. It is accompanied by a Time To Act data navigator (appendix p 56), facilitating

evaluation of the effect of COVID-19 on cancer by tumour subtype, by country or region, and by treatment modality. The data navigator provides an extremely informative tool for the European cancer community.<sup>5</sup> Both European Commission President, Ursula von der Leyen, and European Commissioner for Health and Food Safety, Stella Kyriakides, highlighted Time To Act and referenced its sobering statistics.<sup>209, 210</sup> These data are also emphasised in the Special Committee on Beating Cancer report.<sup>5</sup> At all national Time To Act launches, Ministers of Health participated and were very supportive of the campaign. At these launches, presentation of local research data confirmed the substantial effect of the COVID-19 pandemic on patients with cancer and cancer health-care systems in different European nations, highlighting the need for pan-European solidarity. Recognising the impact of the campaign, Time To Act received the prestigious Excellence in Communicating and Using Data Award at the 2022 Communiqué Awards (Brussels, Belgium), which highlights best practices in health-care messaging across Europe.

Patient advocacy organisations have also been active in research, using data to help define the effect of the pandemic on cancer patients and surveying their own patient communities to gain insights into the effect of the pandemic on patients, caregivers,<sup>211</sup> and cancer charities.<sup>212</sup>

The COVID-19 pandemic has had a substantially negative effect on cancer research across Europe; laboratories were shut and clinical trials delayed or cancelled in the first pandemic wave. This cessation of

cancer research persisted for many months due to further pandemic waves and full or partial lockdowns in most European countries. Although the medium-term impact of COVID-19 remains unclear, research data that we and others have generated suggest substantial negative impacts, particularly on central and eastern European countries.<sup>5</sup> The pandemic has highlighted that cancer research and cancer care are complex adaptive systems, easily disrupted by systemic shocks. Patient outcomes can rapidly change for better or worse, requiring national systems to constantly check and adapt their planning. Our work has exposed a more general weakness in European research ecosystems that, in many cases, are not capable of extracting actionable data from health information systems to inform research activities. The pandemic has also shone a light on the gulf between countries that have built clinical research ecosystems and deliver outputs, such as national audits, and those that have not. Yet, investment in these data research infrastructures remains challenging in many European countries. To put their value into context, the cost for developing a cancer audit research ecosystem is approximately €2 million over 5 years, or 0.002% of the median estimated cost for developing a new therapeutic agent (>€9100 million).

#### The effect of the Russian invasion of Ukraine on cancer research

The invasion of Ukraine by Russia (on Feb 24, 2022) has added to the effect of the COVID-19 pandemic on European health systems, creating a massive humanitarian crisis. The repercussions of the latest conflict builds on 8 years of low-level war by Russian-backed forces in the eastern Donbas region, which had already created huge challenges for health-care systems in Ukraine. The consequences of Ukrainian individuals taking refuge across Europe is creating new difficulties for the capacity of cancer systems, especially for central and eastern European countries. Recognising these challenges and the need to provide much-needed support, ECO and ASCO established a joint ECO–ASCO network on the impact of the war in Ukraine on cancer, leading to a series of activities, including cancer data gathering in Ukraine and surrounding countries, to inform actions on issues including medicines shortages, diagnostic capacity, and treatment capacity.

Although there has been much discourse on the war in Ukraine, what has gone relatively unnoticed is its profound effect on clinical cancer research. Both Ukraine (a lower-middle-income country) and Russia (an upper-middle-income country) are unusual in their substantial global contribution to cancer research. Both countries are two of the largest contributors to clinical cancer research in the world, especially industry-sponsored clinical research. Our analysis (table 7) indicates that between 2014 and 2017, 636 cancer randomised controlled trials were published. Ukraine contributed to 39 of these trials, one of the highest lower-middle-income contributors (out of 136 randomised controlled trials to which lower-middle-income countries

	Number of RCTs published*	Total cancer research output†	Percentage of total research output‡
<b>Lower-middle-income countries</b>			
India	42	27 601	67%
Ukraine	39	801	2%
Philippines	23	384	1%
Egypt	12	6262	15%
Georgia	6	78	<1%
Total	84	35	..
<b>Upper-middle-income countries</b>			
Russia	115	4835	2%
Brazil	94	15 272	7%
Romania	62	3457	2%
China	56	154 373	69%
Mexico	56	4126	2%
Total	182	182 063	..

RCT=randomised controlled trial. \*One RCT could involve one or more countries.  
 †Total number of cancer research papers published. ‡Percentage of total research output that are RCTs; percentages do not add up to 100% because data are exclusive to countries

**Table 7: Top five country-level participation in global RCTs published between 2014 and 2017 by World Bank income category compared with their total cancer research outputs between 2014 and 2017**

contributed). Countries in the upper-middle-income category contributed to 182 cancer randomised controlled trials. Russia contributed to 115 randomised controlled trials, by far the largest contributor out of all the upper-middle-income countries that contributed to cancer randomised controlled trials. At the start of the war, analysis of the ClinicalTrials.gov website indicated that Ukraine had 245 active pharmaceutical cancer clinical trials, with 127 trials that were actively recruiting. By comparison, Russia had 667 active pharmaceutical clinical trials at the start of the war, with 352 trials that were actively recruiting. These figures emphasise the substantial effect that the Russian invasion of Ukraine will have on cancer clinical trials activity in Europe.

For Europe, the conflict also emphasises the complex and political nature of pharmaceutical-driven research, as multinational corporations have come under increasing pressure to withdraw all engagement with Russia. Major pharmaceutical companies, such as AstraZeneca, Pfizer, and GlaxoSmithKline, have stopped new investment and new clinical trials in Russia, but continue both pre-existing trial recruitments and supplying standard cancer medicines as per contractual arrangements. This European conflict highlights the need for much better cancer intelligence data beyond disease burden (eg, infrastructure, cancer care workforce, and mapping of patient pathways) across European national boundaries; and a greater focus on building clinical research capacity and capability that can support other European countries.

### Section 16: safeguarding Europe as a global leader in cancer research

Europe is part of a global research community and the next decade will witness major expansions in countries across the world working on cancer research. China and India have substantially increased their research footprint.<sup>213,214</sup> China is particularly dominant, globally, in lung cancer research and discovery science, driving a revolution in immuno-oncology drug development.<sup>136,215</sup> Such research activities are both disruptive and opportunistic for Europe. More widely, the Middle East and Latin America are also increasing their cancer research activities, providing wider opportunities for European transnational engagement.<sup>215,216</sup> In sub-Saharan Africa, the challenges are different. Countries in sub-Saharan Africa require a higher level of capacity and capability building, with broad collaborative networks to enhance cancer research methodological skills from biostatistics to clinical trial design, and to enhance discovery science techniques.<sup>217</sup> All evidence shows that regions and countries that are engaged and outward-looking produce better, higher-impact research.

One area where Europe's research expertise would be beneficial is in geriatric oncology, ensuring that ageism is not a factor in research and care delivery in older adults.<sup>218</sup> The International Society of Geriatric Oncology Priorities Initiative highlights research as one of its four

key priorities,<sup>219</sup> emphasising its importance for older adults with cancer, who represent a major and rapidly growing demographic in global epidemiology.

A stronger focus on global cancer is crucial for Europe to catalyse its own research agenda and to work in solidarity with countries faced with their own unique challenges as they look to deliver innovative and effective cancer research. However, European cancer research funding organisations are failing to realise this potential, and are not honouring their global commitments to cancer control, which they so often espouse.<sup>116,118</sup> We need a new strategic pact that focuses funds and effort on the wider global cancer agenda, rather than wealthy-to-wealthy country cooperation. Multiple *Lancet* Commissions, *Lancet Oncology* Commissions, and important multistakeholder strategic reviews<sup>220</sup> have created the opportunity for Europe to engage more widely and this Commission emphasises an unrivalled global opportunity that needs to be grasped. However, the opportunities for Europe to engage in global cancer can only be realised through better funder-to-funder collaboration and transnational joint ventures to strategically address research capacity and capability in specific countries and regions. Across the world, many research projects run in parallel, supported by different European countries, with little strategic coordination.

### Section 17: recommendations and a call to action

This *Lancet Oncology* European Groundshot Commission on cancer research has used an evidence-based approach to capture and analyse information on key areas of relevance across the cancer continuum, including survival; mortality; research activity; research funding; cancer prevention and control; cancer treatment; survivorship; quality of life; and the effects of external factors including the COVID-19 pandemic, Brexit, and the Russian invasion of Ukraine. Gaining this more granular understanding of the European cancer research landscape, including its strengths and its weaknesses, has empowered us to deploy this evidence to inform a series of 12 recommendations (panel 3), underpinning a call to action to ensure that cancer research is a pivotal driver of enhanced cancer control and improved quality of life for patients with cancer and for those living beyond cancer across Europe. Our recommendations are grouped under three thematic areas, informed by our interpretation of the data we have generated through this Commission: (1) closing the European cancer research divide; (2) addressing the gaps in European cancer research and its funding; and (3) responding to current and future external challenges. For each of the 12 recommendations, we provide an indication of how they can be achieved and a timeframe for their implementation (panel 3).

#### Closing the European cancer research divide

Recommendation one is to develop a research and innovation plan focused on implementation science, to

**Panel 3: A call to action**

**Recommendation one: develop a research and innovation plan focused on implementation science, to help deliver a 70% average 10-year survival for all patients with cancer in Europe by 2035**

Recommendation one will be achieved by: setting yearly stretch targets and accomplishing a doubling in support for implementation science and health systems cancer research, particularly to address the cancer inequalities that exist across Europe; creating, by 2024, a European cancer tracker, a research programme that supports and develops cancer registries, and national audits to capture a range of baseline parameters (eg, data on stage at diagnosis, treatment delivered, lifestyle behaviours, comorbidities, socioeconomic status, quality of life, and mortality); and developing, by 2024, pan-European implementation science and health policy and systems research programmes using national data capture systems (eg, audits to benchmark and monitor the impact of cancer research and identify exemplars of best practice) that might be applied to help deliver the 70:35 vision.

**Recommendation two: embed the principles of equity and equality within the European cancer research agenda, so that all citizens and patients, no matter where they live, will benefit equally from advances in cancer research**

Recommendation two will be achieved by: ensuring that cancer research and innovation are recognised and appropriately resourced components of all national cancer control plans; and providing mechanisms to enhance cancer research capability and capacity in underserved jurisdictions through trans-European national collaboratives by 2025.

**Recommendation three: as a matter of urgency, to develop resourced time-bound European and national action plans to increase cancer research capacity and capability in central and eastern European countries by 25% by 2025**

Recommendation three will be achieved by: establishing funded action plans by 2024 that empower transnational collaboration by European partners and research capacity-building in-region in central and eastern European countries.

**Recommendation four: cancer research funding organisations and Europe's Cancer Mission must double the European cancer research budget to €50 per capita by 2030 and commit to supporting underserved research domains**

Recommendation four will be achieved by: doubling prevention research funding by 2025 and aiming for a 20% share of overall cancer research budgets by 2030; delivering a 50% increase by 2027 in research activity on cancers of high mortality that are currently under-researched, including lung, pancreatic, bladder, oesophageal, stomach, colorectal, and rare cancers; and investing 50% more in radiation and surgical oncology research to redress the absence of research funding in these two crucial areas of cancer care.

**Recommendation five: European cancer research funders and the European cancer research community must mitigate the effects of Brexit and other political challenges on European cancer research**

Recommendation five will be achieved by: recognising the UK's position as a leading cancer research driver in Europe, ensuring that the UK can continue to collaborate with European partners and contribute high-quality outputs to European cancer research and innovation activities.

**Recommendation six: the European cancer research community must develop proactive mechanisms to enhance gender equality in cancer research**

Recommendation six will be achieved by: increasing female senior authorship of cancer research publications from an average of 33% to an average of 45% by 2028, with a particular emphasis on the countries that are performing poorly; and increasing female leadership of cancer research programmes from an average of 35% to 45% by 2027 (figure 7).

**Recommendation seven: European cancer funders and policy makers must mandate a step change in cancer prevention, cancer screening, and early cancer detection research to reduce the burden of cancer for European citizens**

Recommendation seven will be achieved through a stronger, more citizen-enabled research focus on alcohol, smoking, diet, and environment and by: delivering, by 2023, a research-informed strategic approach to eliminate all human papillomavirus (HPV)-driven cancers and other diseases caused by HPV by 2030, which includes informing citizens of the benefits of screening and vaccination; supporting research programmes to monitor existing screening programmes against agreed performance metrics and embedding new technological developments to enhance the detection of cancer at its earliest stage; ascertaining, by 2024, through behavioural research, the barriers or reasons for minimal participation in cancer screening programmes across Europe, with particular focus on underserved populations; and developing new approaches by 2024 to facilitate early detection of cancer, including the use of liquid biopsies.

**Recommendation eight: European cancer funders and policy makers must continue to establish research-driven European networks of comprehensive cancer centres and other relevant networks**

Recommendation eight will be achieved by: completing a comprehensive mapping exercise of current comprehensive cancer centre capacity and activity in Europe by 2023; performing a needs analysis for the creation of a European network of comprehensive cancer centres, to be completed by 2023; and placing a focus on addressing relevant scientific challenges through a series of strategic funding calls, delivering impactful cancer research outputs primed for translation into better outcomes for European cancer patients.

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(Panel 3 continued from previous page)

**Recommendation nine: as a matter of urgency, European cancer funders and policy makers must establish a European cancer survivorship research and innovation plan to guide policy that will help enhance the lives of the 20 million European citizens living with and beyond cancer**

Recommendation nine will be achieved by: ensuring a research-enabled focus on the medical, socioeconomic, and politico-legal needs of cancer survivors, mediated through a series of focused funding calls by the European Cancer Mission, commencing in 2023; developing research activities that address both the physical and psychological or psychosocial aspects of those living with and beyond cancer; supporting through research and advocacy the implementation of the Right to be Forgotten to avoid financial toxicity for cancer survivors and ensuring that it is activated in all European countries by 2024; and establishing a European Cancer Survivors Day by 2024.

**Recommendation ten: the European cancer research community must accelerate the research response to the indirect effects of the COVID-19 pandemic on cancer, with particular emphasis on the deployment of accurate and timely cancer intelligence to build future resilience**

Recommendation ten will be achieved by: building on the work of the European Cancer Organisation (ie, the 7-point plan and the Time To Act Data Navigator) to mitigate the effects of COVID-19 by establishing, by 2023, a near real-time dashboard that captures and quantifies the effects of the COVID-19 pandemic on all aspects of the cancer pathway, on clinical trials participation, and on the cancer workforce; and deploying this intelligence to inform research interventions to mitigate current effects of the pandemic and build future pandemic resilience.

**Recommendation eleven: as a matter of extreme urgency, the European cancer community must address how research can help mitigate the effect of the Russian invasion of Ukraine**

Recommendation eleven will be achieved by: building on the work of the European Cancer Organisation and American Society of Clinical Oncology Special Network on the Impact of the War in Ukraine on Cancer, immediately collecting monthly data intelligence on the effects of the conflict on patients, cancer services, medicines, supply shortages, and workforce gaps, in Ukraine and in neighbouring countries; and developing a plan, by 2023, on how best to mitigate the effects of the conflict on cancer clinical trials activity across Europe, on the basis of our data on the detrimental effects of the war on cancer clinical trials in both Ukraine and Russia.

**Recommendation twelve: European cancer research funders and policy makers must commit to empowering European cancer researchers in driving an equitable global cancer research agenda, with particular emphasis on low-income and middle-income countries**

Recommendation twelve will be achieved by: committing to increasing cancer research activity between Europe and global partners by 50% by 2025, with a particular emphasis on low-income and middle-income countries; developing innovative funding mechanisms to encourage a 50% uplift by 2024 in support for joint research between European and low-income and middle-income countries; and doubling collaborative research activity between Europe and low-income and middle-income countries by 2027.

help deliver a 70% average 10-year survival for all cancer patients in Europe by 2035. Recommendation two is to embed the principles of equity and equality within the European cancer research agenda, so that all citizens and patients, no matter where they live, will benefit equally from advances in cancer research. Recommendation three is to, as a matter of urgency, develop resourced time-bound European and national action plans to increase cancer research capacity and capability in central and eastern European countries by 25% by 2025.

Overall, our data emphasise that population-based evidence is crucial to help in the precise delineation of the cancer inequalities that persist across Europe and in the development of evidence-driven research solutions to address these inequalities. Information on crucial factors, such as stage at diagnosis, treatment delivered, lifestyle behaviours, and socioeconomic status, should be routinely collected nationally and shared across Europe to quantify the effect of these factors on survival and illuminate a pathway to narrow inequalities between countries, particularly in central and eastern European countries.

Diverging patterns in cancer mortality between western European countries and central and eastern European countries have continued to persist and, if anything, have increased over the past decade. There has been little evidence of this gap in cancer mortality being closed, although overall mortality has declined across Europe's geographical regions and countries. Our data emphasise the need to prioritise cancer research and cancer control activities as rapidly as possible in central and eastern European countries.<sup>106,107,221</sup>

Persisting unfavorable patterns in exposure to major cancer risk factors, including tobacco, alcohol, and aspects of diet, together with residual environmental disadvantages explain part of the persistent gap.<sup>222-224</sup> However, delays in implementing research discoveries into screening and early diagnosis activities are also evident, together with delayed and inadequate adoption of modern therapeutic approaches for cancers amenable to treatment,<sup>224</sup> a deficit that must be addressed as a matter of urgency. Ensuring equitable cancer research activity across Europe is also important, particularly because research-active hospitals and cancer centres



achieve better cancer outcomes than those that do not prioritise research within their remit.

Another area that our research has uncovered as key to a robust European cancer research agenda is data and, more specifically, turning that data into evidence to inform European cancer research priorities. Use of near realtime data is crucial. The data that drive our research and innovation and their translation into benefit for patients with cancer should be made available and analysed in a timely fashion, so that up-to-date data inform research and innovation efforts. Europe needs a more systematic approach to patient experience data (patient preferences, patient reported outcomes) to understand patients' unmet needs, patient preferences and to better support quality of life and survivorship. Although the FDA has provided guidance on patient experience data after extensive public consultation, Europe is lagging behind providing a framework that facilitates the generation and regulatory assessment of patient experience data. Systematic generation of patient experience data should be part of our proposed European cancer survivorship research and innovation plan.

For the FDA guidance see <https://www.fda.gov/drugs/development-approval-process-drugs/cder-patient-focused-drug-development>

### Addressing the gaps in European cancer research and its funding

Recommendation four is that European cancer research funding organisations and Europe's Cancer Mission must double the European cancer research budget to €50 per capita by 2030 and commit to supporting underserved research domains. Our analysis indicates that the total amount of investment in cancer research in Europe between 2010 and 2019, excluding the private sector (eg, the pharmaceutical industry), was approximately €20 billion to €22 billion. The minimum equivalent figure for the USA over the same time period was \$81 billion (around €82 billion), which is almost four-times as much as the investment in Europe. Looking at investment per person shows an even wider gap. For Europe, investment per head between 2010 and 2019 was approximately €26 per person, which is about ten-times lower than the US investment per head (minimum €253 per person). There is an urgent need to make considerable additional investment in cancer research in Europe, to narrow the overwhelming gap in expenditure per person between two international powerhouses of cancer research. So what is possible in terms of an uplift in cancer research expenditure? The UK National Cancer Research Institute has tracked cancer research investment by UK funders since 2002;<sup>225</sup> the initial reported investment of £298 million in 2002 increased to £601 million by 2011. The average annual UK increase in investment was approximately 5% until 2019.

Efforts to increase investment could be hampered by the effect of the COVID-19 pandemic on cancer research funders, particularly the charitable sector, whose available funds to support cancer research have been, and will be, badly affected by the pandemic.<sup>226</sup> Analysis by the UK's

National Cancer Research Institute showed that, in 2020 and 2021, funding for UK cancer research dropped by 9% (ie, fewer new cancer research projects were funded than in previous years).<sup>227</sup>

Our data indicate that European cancer research is largely dominated by discovery science, including biomarker research and research into systemic therapy (appendix p 49). The emergence of translational cancer research as a major domain in the 2000s<sup>228</sup> has tended to keep European cancer research, including public sector-funded research, within a more private-sector-driven discovery science and biopharmaceutical framework.<sup>229</sup> Regarding research domains, although there are considerable differences between countries, Europe is particularly strong (committed) in clinical trials, driven by research into targeted (systemic) therapies and, although low in terms of total number of projects and publications, Europe has made substantial strides in increasing research on quality of life (appendix p 49), which is a positive development.

However, several European countries are under-committed to research on surgery and radiotherapy, which are currently the most effective treatments for controlling cancer. Denmark, Finland, and Portugal are under-committed to research on surgery, and Greece, Israel, Finland, Czech Republic, and Portugal are under-committed to research on radiotherapy (appendix p 37). This trend of research appears to be global,<sup>183</sup> with discovery science and biopharmaceutical research becoming the dominant spheres of cancer research, irrespective of income group.

Health-care systems are faced with the continual challenge of ensuring that high-quality discovery science and applied research ultimately affect clinical practice. It can take 17–20 years to get clinical innovations into practice, and less than 50% of innovations make it to the clinic. Improving this statistic requires greater investment in implementation science (ie, the second translational gap), which seeks to test strategies to enhance clinical innovation adoption by considering health system dynamics and actors (ie, patients, clinicians, providers, policy environment, and industry) that could impede or facilitate evidence adoption. This evidence is then used to ensure the clinical-level and population-level implementation of research discoveries. Allied to this requirement for a bigger focus on implementation is the need to have access to data from social science, political science, and cancer science. We are entering an era when real-world evidence will be crucial to drive implementation of innovation, so we must ensure that Europe has sufficient digital maturity to collect, analyse, and link these data to inform the rapid adoption of research and innovation within cancer health systems.

There are evidence-based and cost-effective preventive interventions available for cancer. The current privileged focus on biopharmaceuticals is not a long-term, cost-effective approach to cancer control policy, unless it is

complemented with public health strategies for cancer prevention. Reducing the number of people developing cancer should result in greater resources being available to provide those patients who require treatment with the most effective therapies available. Increased funding in crucial research areas (ie, cancer prevention and implementation science research) would yield substantial return on investment. A more systematic and structured approach to cancer prevention in Europe would have major effects at public health, societal, and economic scales.

Recommendation five is that European cancer research funders and the European cancer research community must mitigate the effects of Brexit and other political challenges on European cancer research. Successful cancer research activity that we have documented for the most powerful high-income countries is counterbalanced by clear stagnation for many other countries in the central and eastern European region. There have been huge increases in cancer discovery science and biopharmaceutical-centred research, placing individual countries and Europe on an equal strategic footing with the USA. However, this success has been achieved at the cost of leaving many other important domains of cancer research far behind. Taken together, the strategic analysis that we have undertaken and the results that we have generated reflect a potential mismatch with public rhetoric and the wider needs for improving patient and population outcomes that are affordable and equitable. The cancer research archaeology that we have defined provides objective data for considering the current European cancer research landscape, and how this can inform the most effective implementation of the Cancer Mission and Europe's Beating Cancer Plan going forward.

The data generated clearly indicate a notable gap between research outputs from EU28 (including the UK) and EU27 (excluding the UK), a gap that is extremely unlikely to be bridged by increased research activity from the remaining EU27. Disappointingly, at the time of writing this Commission, it appears the UK will not participate in EU funding programmes going forward. If the UK is not involved in EU collaborative cancer research and not part of Horizon Europe's research community, this will have an extremely detrimental effect on European cancer research activity and quality moving forward. Ultimately, patients with cancer will pay the price for this decision in terms of health-care outcomes. Lobbying to reverse this must be a matter of priority among the European cancer research community. It will also be important to consider maximising the involvement of other non-EU European countries in European cancer initiatives (eg, Switzerland and Norway).

Recommendation six is that the European cancer research community must develop proactive mechanisms to enhance gender equality in cancer research. Our data on female first and last (senior) authors of European cancer research publications clearly illustrate the

substantial gender gap that exists in the European cancer research community. Although both central and eastern European countries and Nordic countries show better gender ratios in first and last author publications than the rest of Europe and the rest of the world, the performance by cancer research powerhouses such as Germany is disappointing. A similar gender disparity is seen in cancer research leadership, which we assessed using our data on successful competitive research funding. Delving deeper into the reasons for better performance in terms of gender balance in some European countries or regions and developing mitigation strategies based on this evidence will hopefully improve the gender balance in cancer research outputs and cancer research leadership in Europe. Improving gender attitudes and balance could best be achieved by developing approaches that address gender biases related to senior author publications, leadership, and funding within research institutions and funding organisations, with a particular focus on certain poorly performing countries, thus empowering balanced female leadership in cancer research in Europe.

Recommendation seven is that European cancer funders and policy makers must mandate a step change in cancer prevention, cancer screening, and early cancer detection research to reduce the burden of cancer for European citizens. In 2019, ECO's Focused Topic Network on HPV launched a resolution to achieve the elimination of cancers caused by HPV.<sup>230</sup> Crucially, this initiative included supporting research priorities such as new vaccine and screening technologies, and ensuring best care and treatment modalities. More research is needed to improve the early detection of non-cervical cancers caused by HPV. Research is also required on vaccinations and treatment for women found to be HPV-positive at cervical cancer screening, because these vaccines could provide a potential pathway to interrupt viral transmission in the community. Replicating Australia's success rates should be our goal but this will depend on Europe-wide coordination and targeted action in those countries currently underperforming, and investment in resource and culturally appropriate public health campaigns.

In combatting HPV-driven cancers and championing a research-underpinned, prevention-led approach for their elimination, Europe has an unrivalled opportunity to be a global research leader and to show what can be achieved when countries work together to achieve a major public health goal. ECO's HPV Action Network is an exemplar model to build on.

Since the 2003 Council Recommendation (which is currently being revisited in Europe's Beating Cancer Plan) on cancer screening, several scientific and technological developments have emerged in breast, colorectal, and cervical cancer screening. These developments include new screening tests, such as full-field digital mammography, supplemental MRI in women with extremely

dense breast tissue,<sup>231</sup> faecal immunological test or endoscopy for colorectal screening, and HPV testing for cervical cancer screening.<sup>161</sup> We view the development of risk-adapted screening approaches that make use of the latest technological developments, particularly those that incorporate distinct strategies according to the risk profile of screened individuals, as a key component of contemporary screening research programmes.

Development of new tests and new approaches are helping to drive cancer screening and early diagnosis agendas. A good example is HPV DNA testing, which is now showing better results than pap-smear screening for cervical cancer screening.<sup>161</sup> Early diagnosis of cervical cancer is also being made possible by the provision of home-based screening tests. Faecal immunochemical tests for colorectal cancer screening helps reduce the invasiveness of the procedure, which translates into a marked improvement in screening adherence. An important new development has been the use of liquid biopsies, a technology that detects circulating cancer cells or tumour DNA in blood, which underpins the early diagnosis of multiple cancers.<sup>232</sup> Combining this technology with approaches that can detect multiple types of cancer provides an important European research opportunity to underpin more accurate early diagnosis.<sup>233</sup>

Crucially, for all approaches to enhance cancer screening, early detection of cancer, and accurate diagnosis of cancer, a better behavioural understanding of why a European citizen does or does not attend their scheduled screening appointment, does or does not come forward with suspicious symptoms, and does or does not engage with cancer pathways is needed. Social science research to understand behavioural choice, cultural constraints, and previously unrecognised barriers, particularly for disadvantaged and underserved communities, is key to enhance the early diagnosis of cancer across Europe.

Recommendation eight is that European cancer funders and policy makers must continue to establish research-driven European networks of comprehensive cancer centres and other relevant networks. The European Commission is currently addressing the question of inequalities in several ways. These strategies include mapping research capabilities and capacities; fostering collaborations in smaller groupings (eg, pairing cancer centres in widening participation countries with more established comprehensive cancer centres); or fostering team science. A third aim of the European Commission is to create a Europe-wide network of certified comprehensive cancer centres, and to build research capacities and capabilities in member states. However, such initiatives are currently not supported by hard evidence on whether managed processes of spreading resources will deliver better science for the benefit of cancer patients across Europe. Our data from the Commission capture the effect that comprehensive cancer centres are having both individually and

collectively, emphasising the benefits of a network approach. Integration within and between these centres needs to be achieved at multiple levels. For governance, a key component is a comprehensive cancer centre board, which would bring together cancer research leaders with clinical leads in cancer and patient advocates. At an organisational level, researchers need to be integrated with clinical colleagues, through programme structures or multidisciplinary teams; through informal colloquia and regular meetings; through seminars highlighting science and clinical challenges; or through incentivised collaborations such as pump-priming grants offered only to clinical groups working with laboratory colleagues. Patients and patient advocates need to be embedded into this structure.

A key component of using a comprehensive cancer centre infrastructure will be addressing the inequalities being experienced across Europe in prevention, diagnosis, in treatment and care, and in access to clinical trials. Strengthening the quality of translational, clinical, outcomes research, and implementation science and ensuring that these fields are integrated with the delivery of clinical care will help to tackle these inequalities using an infrastructural approach. Patients who are diagnosed and treated in research active cancer centres (including, but not limited to, comprehensive cancer centres) have better access to advanced diagnosis, therapy, and clinical trials, and better outcomes than patients treated in general hospitals.<sup>56,234</sup> Europe's Beating Cancer Plan aims to ensure that 90% of eligible patients have access to comprehensive cancer centres by 2030. Currently, several member states have no accredited comprehensive cancer centres and many do not yet have regional or local networks linking cancer research and care, which are usually organised around these centres. A mapping exercise in 2017, performed as part of the EU Joint Action on Rare Cancers,<sup>235</sup> showed that only 13 member states had cancer networks covering the whole country.

The development of a Europe-wide network of comprehensive cancer centres also provides an opportunity to ensure underpinning laboratory infrastructure is in place to help drive discovery research and its translation, at scale. Additionally, to have maximum reach within countries as part of the envisaged infrastructure, effective local cancer networks will be required, supplemented by extended multidisciplinary teams, and digital-consultation and video-consultation infrastructure. A variety of funding sources could be deployed to help support the establishment of this Europe-wide network of comprehensive cancer centres. Strengthening research excellence will also require collaborative infrastructures across Europe, drawing on different aspects of the Cancer Mission (appendix p 57) and Europe's Beating Cancer Plan.

Recommendation nine is that, as a matter of urgency, European cancer funders and policy makers must establish a European cancer survivorship research and

innovation plan to guide policy that will help enhance the lives of the 20 million European citizens living with and beyond cancer. As we have highlighted in this Commission, to date European scientific and clinical communities have tended to focus more on research into the diagnosis and treatment of cancer, rather than the more holistic challenge of living with and beyond cancer. However, as indicated in the European Code of Cancer Practice, approximately 20 million European citizens have survived a diagnosis of cancer.<sup>49,188</sup> Therefore, it is incumbent upon the European cancer community to substantially enhance engagement with cancer survivors and promote and instigate a cancer survivorship research agenda to ensure that the specific challenges and needs of individuals living with and beyond cancer are adequately addressed. Survivorship, rehabilitation, and reintegration into society are key pillars of the European Code of Cancer Practice; it is imperative that each patient with cancer has a survivorship care plan that is underpinned by research. Our study published in 2021 highlights the importance of capturing detailed European data on cancer care and quality of life for cancer survivors.<sup>49</sup> A cancer survivorship, rehabilitation, and reintegration plan for patients should also consider the crucial role of caregivers in helping secure the wellbeing of individuals living with and beyond a cancer diagnosis.

Interdisciplinary survivor-centred research must be promoted and should include the development of new tools to facilitate survivorship research. The paucity of specific research programmes for child, adolescent, and young-adult survivors should be addressed through age-adapted research programmes that best meet the needs of this demographic. The needs of the palliative-care community should also be addressed, through promotion of research early across the full spectrum of palliative care. All approaches should underpin best-practice sharing and promotion of survivorship research and innovation across Europe, aligning and empowering all stakeholders in a unity of purpose to help achieve the 70:35 Vision.

As part of our recommendations, we call for the establishment and implementation of a European cancer survivorship research and innovation plan to ensure a research-informed approach for individuals living with and beyond cancer. Additionally, to ensure that the 20 million voices of these individuals are heard, we call for establishment of a European Cancer Survivors' Day.

### Responding to current and future challenges

Recommendation ten is that the European cancer research community must accelerate the research response to the indirect effects of the COVID-19 pandemic on cancer, with particular emphasis on the deployment of accurate and timely cancer evidence to build future resilience. The COVID-19 pandemic and the associated disruptions to cancer systems have dramatically affected cancer care. In the context of the

Time To Act campaign on the effect of COVID-19 on cancer, we estimate that 100 million cancer screening tests were not performed in Europe, and urgent referrals of suspected cancer patients were cut by up to half. As a result of this cancer backlog, 1 million patients with cancer could be undiagnosed in Europe. At the national scale, as shown by the Time To Act data navigator, the effect of the pandemic on cancer screening programmes has seen a 70% reduction in European countries, such as Austria, Belgium, Czech Republic, and Poland. The disruptions to screening, early diagnosis, and timely treatment are all expected to lead to considerable future excess mortality from cancer.

More broadly, the COVID-19 pandemic has focused a spotlight on the substantial opportunity cost from current investments in cancer research, without a transparent and robust approach to linking this research to better, affordable, and more equitable outcomes. The UK's NHS Cancer Drugs Fund and the diffusion of robotic surgery across European cancer care systems are examples of how high-cost, techno-centric research has tended to drive the political narrative of European cancer research, divorced from the perspective of value and affordability.<sup>236,237</sup> There has been a relentless narrative about innovation in cancer research, without wider consideration of research into the enabling environment (ie, the translation of research into clinical practice, services, systems, and policy). In the era after the COVID-19 pandemic, given fiscal contractions across all countries, the need to inform European cancer services with research-empowered evidenced-based policy, and a robust consideration of the ever-rising burden and costs of care, is essential.<sup>24</sup> New research initiatives must focus on increasing the value of care (outcomes relative to cost) across the cancer pathway, minimising waste, and supporting responsible integration of innovation.

More fundamentally, the economic effect of the COVID-19 pandemic has resulted in an unprecedented economic contraction in 2020, with European real GDP falling by 6.1%, which is greater than the decrease during the global financial crisis of 2008. This current crisis calls for an urgent recalibration of public sector cancer research support to widen strategies beyond discovery science and biopharmaceutical research. Such a narrow focus is likely to be an important indirect contributing factor to poorer outcomes. Indeed, it is clear from a wide variety of research outputs over the past two decades that good outcomes are directly linked to research activity, but that this research activity needs to be broad, covering domains from public health and cancer through to surgery, radiotherapy, and palliative care. Therefore, improving patient outcomes is crucially empowered by a research-active health system that supports a wide range of fundamental research, discovery research, and applied cancer research and the transition of this research into patient-centric translation.

Aside from strategic questions about where Europe should now focus with regards to cancer research,

For the Time To Act data navigator see <https://www.europecancer.org/data-navigator/countries>

COVID-19 has exerted further downward pressure on cancer services and systems across Europe. The OECD report<sup>238</sup> *Health at a Glance: Europe 2020* reflects the fact that health-care systems in many European countries were already under pressure, even before the pandemic. Importantly, there was no capacity to expand systems to absorb systemic shocks such as the pandemic. The pandemic has not just illuminated these deficits, but has also acted as an additional weight on the entire cancer ecosystem, from social determinants to survivorship and end-of-life care (appendix p 41). Routine referrals during the pandemic collapsed in most European countries, which meant that fewer cancers were detected than before the pandemic and that the cancers that were eventually detected were at a later stage, meaning worse prognosis. In addition to directly worsening outcomes, this delay will lead to patients with more advanced disease needing treatment, leading to an increased care burden that, when added to already stretched health systems, could indirectly worsen overall patient outcomes. These outcomes highlight gaps in the cancer workforce and the need to support innovative clinical roles.<sup>158,239</sup>

Such systemic effects have two downstream consequences on research. The first is to reduce the headroom for clinical cancer research, as capacity and funding are potentially diverted into routine care; and the second is a political–policy mismatch. These downstream consequences are why the overfocus on discovery science and biopharmaceutical research does not lead to better population outcomes. If the pandemic has had the damaging effect that our data suggest, then Europe will see a substantial decline in its cancer outcomes over the next 5–10 years, which needs to be addressed as a matter of the greatest urgency. Thus, now more than ever, there is a crucial need to ensure that cancer is appropriately protected and prioritised within current and future European research agendas. Cogent solutions must be realised and acted upon that will translate the high-quality cancer research that is currently being done in Europe (and must continue to be delivered going forward), into improved outcomes for patients, which would make a substantial contribution to healthier and more productive societies. It is important that we redouble our efforts to ensure that cancer does not become forgotten in our efforts to tackle COVID-19.

Recommendation eleven is that, as a matter of extreme urgency, the European cancer community must address how research can help mitigate the effect of the Russian invasion of Ukraine. Clinical cancer research finds itself in uncharted territory. The conflict-induced loss of cancer centres in Ukraine, which are such major recruiters to global randomised controlled trials, will have a substantial effect. Many major clinical trials will be delayed as new centres of varying capacity are incorporated, and some will undoubtedly not be able to recruit. Many of the cancer trials in Ukraine also had participation of major centres in central and eastern European countries (eg, in Romania).

If such trials are stopped, this will further reduce infrastructural investment and debilitate cancer clinical trial activity in central and eastern European countries. In the future, it is not clear whether industry will consider it too high risk to place cancer clinical research in central and eastern European countries bordering Ukraine, particularly if, as the US National Intelligence Estimates suggest, we face a long, drawn-out war of attrition. Such a cessation of private sector investment could be hugely damaging to cancer research ecosystems in central and eastern European countries. Although this possibility is not currently the major focus for the European Commission, these externalities, which fall heaviest on central and eastern European countries, must be central to informing strategic planning and funding going forward if the Cancer Mission is to succeed.

Recommendation twelve is that European cancer research funders and policy makers must commit to empowering European cancer researchers in driving an equitable global cancer research agenda, with particular emphasis on low-income and middle-income countries. Although much of the focus of the cancer community in Europe has been directed towards refining and enhancing the European cancer research effort, Europe also has a substantial opportunity to provide international leadership and deliver tangible actions to address the challenge of cancer globally. We need to considerably increase cancer research collaborations between Europe and the rest of the world, particularly by co-creating a broad portfolio of research activities across the continuum of low-income and middle-income countries, where, without immediate action, nearly 70% of global cancer deaths will occur by 2040.<sup>116</sup> Currently, we collectively devote less than 5% of our cancer research to activities with low-income and middle-income countries, a paltry figure for areas of the world where the research need is greatest. We have a global responsibility to develop meaningful cancer research partnerships, enhancing research outputs to help address the increasing cancer burden that low-income and middle-income countries face.

### Reimagining cancer research and its implementation in Europe: a call to action

It has been a brutally challenging few years since the start of the COVID-19 pandemic for the European cancer community as it sought to deliver optimal cancer care and produce high-quality cancer research under unprecedented pressures. The effects of these circumstances at the time of writing of this Commission are far from over. The pandemic has highlighted a deficiency in systems' resilience, prompting reflection on whether the ways in which cancer care and research were delivered before the COVID-19 pandemic best served our citizens, patients, and society. It has become rapidly clear that returning to the so-called old normal will simply not be good enough. Improving cancer care, research, and education that focuses on the wellbeing of patients and society will



require renewed focus, drive, and creativity after the pandemic.

In cancer research, there is an unrivalled opportunity to make improvements in the field after the COVID-19 pandemic (ie, to build back better and smarter). In this *Lancet Oncology* Commission, we position future European cancer research endeavours as a groundshot, reflecting our aspirations to solve challenges on the ground,<sup>61,240</sup> and we present our recommendations within a call to action to reimagine cancer research and its implementation in Europe (panel 3). The research response to COVID-19 and its rapid transition to clinical care has been revelatory, particularly in the development and approval of the myriad of vaccine options and rapid-testing platforms that have brought citizens, as patients and societies, to a better place. We can now deploy a similar approach to cancer as we have done with COVID-19. We must achieve this by continuously following the science and the data. Reimagining cancer research and its implementation provides an opportunity to think differently, to embrace a more holistic end-to-end approach, by working closely with patient groups and the cancer workforce to nurture true pan-cancer innovation, and to be unencumbered by barriers or pressure points that would previously have prompted paralysis. Although the data that we have generated in this Commission have highlighted the challenges that we face in central and eastern Europe, a focus on research capacity-building and directed funding, and twinning approaches to enhance cancer research activity, its quality, and its implementation in these central and eastern European countries have the potential to be transformational. Coupled with a more nuanced and much broader portfolio of research and empowered by the ethos of implementation that we have articulated within this Commission, we can start to reimagine a more equality-focused, people-centred, and data-enabled cancer research ecosystem that mandates that the best science and most promising innovations are delivered at pace and at scale, so that the European 70:35 vision is delivered.

#### Contributors

ML and RS designed the concept. ML, RS, LD, SO, KO, AE, AS, CLV, CA, YL, PN, TC, AA, AC, and MA drafted the initial framework. AS, CLV, CA, and MPC performed primary analysis. All authors contributed to the writing of the manuscript. RS and ML are the lead commissioners. ML is the chair of the Commission and corresponding author.

#### Declaration of interests

ML declares honoraria from Bayer, Carnall Farrar, EMD Serono, Novartis, Pfizer, and Roche unrelated to this work and membership of the board of the European Cancer Organisation (ECO). AA declares Advanced NIH Fellowship unrelated to this work. AMB declares honorarium from Roche unrelated to this work and Presidency of Lung Cancer Europe. MC declares membership of the board of ECO and the European Society of Oncology Pharmacy. FC declares consultancy and advisory board membership of Amgen, Astellas/Medivation, AstraZeneca, Celgene, Daiichi-Sankyo, Eisai, GE Oncology, Genentech, Gilead, GlaxoSmithKline, Iqvia, MacroGenics, Medscape, Merck-Sharp, Merus, Mylan, Mundipharma, Novartis, Pfizer, PierreFabre, prIME Oncology, Roche, Sanofi, Samsung Bioepis, Seagen, Teva, and Touchime unrelated to this work. TC declares honoraria from AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, Roche, Merck Sharpe & Dohme, Pfizer, and Takeda

unrelated to this work. LD declares consultancy from the International Cancer Research Partnership unrelated to this work. FDN declares grants from the AIRC Foundation for Cancer Research, Associazione Italiana per la Ricerca sul Cancro, and Fondazione Piemontese per la Ricerca sul Cancro-ONLUS, and consultancy from Pierre Fabre unrelated to this work. JJ declares consultancy from AstraZeneca, Exact Sciences, and Merck Sharpe & Dohme unrelated to this work. DK declares honoraria from Merck Sharpe & Dohme unrelated to this work. TKo declares grants from Ipsen, AAA Pharma, Novartis, Isotope Technologies Munich, Victory Net Foundation, and Camulus, and honoraria or support from Cor2Ed, Ipsen, ECO, International Cancer Genome Consortium unrelated to this work. CLV received support from AIRC Foundation. YL is chair of the HERO VBHC and member of the European Society for Radiotherapy and Oncology (ESTRO) Scientific Committee, the Belgian College of Oncology, and a personal investigator on the European Organization for Research and Treatment of Cancer/ESTRO E2-RADIATE project. PS declares support from ECO and the European School of Oncology. SO, KO, AS, CA, PN, KA, MA, AC, MPC, ACo, CLD, AE, SE, MG, BJo, OK, TKu, GL, FM, JP, TP, RP, BR, ITR, MJS, GSB, JVH, EV, WW, UW, and RS declare no competing interests.

#### Acknowledgments

Change to ML is supported by grants from Health Data Research UK and the Medical Research Council and CLV is supported by the AIRC Foundation for Cancer Research.

Editorial note: The Lancet Group takes a neutral position with respect to territorial claims in published maps and institutional affiliations.

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