European Groundshot—addressing Europe's cancer research challenges: a Lancet Oncology Commission

The Lancet Oncology European Groundshot Commission on Cancer Research

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Cancer Research in Europe: Setting the Scene

Cancer Research in Europe in the meta COVID era

We have reached a critical inflection point for cancer research in Europe. Our challenge is unequivocal - how best can research play a transformative role in promoting more efficient and effective prevention, facilitating earlier diagnosis, delivering better, safer and potentially more cost effective and affordable treatments and ensuring enhanced quality-of-life for citizens, patients and those living beyond cancer? Furthermore, how do we address this challenge through the prism of the significant impact of the COVID-19 pandemic and other externalities (e.g. Brexit, the war in Ukraine)? Crucial to informing a person-centred cancer research agenda for Europe is the need for accurate, timely granular data that capture the current landscape of research activity. Too often opinion, even if expert, has trumped intelligence in the genesis and implementation of cancer research agendas. In this *Lancet Oncology European Groundshot Commission on Cancer Research*, we have first focussed on generating the data that shine a penetrating light on the current European cancer research landscape, highlighting its strengths but most particularly capturing its weakness, contrasting areas that have perhaps received an over-emphasis of effort with those which have been underserved and lacked support. Analysing these data and deploying the resulting intelligence underpins a series of Essential Recommendations and a Call to Action, which if acted upon, will help create and nurture a cancer research culture that can deliver holistic pragmatic solutions that translate into better outcomes for European citizens.

One of the unintended consequences of the pandemic, with rapid repurposing of health services and introduction of national lockdowns in response to widespread SARS-Cov-2 infection, has been the adverse impact that these measures have had, and their continuing legacy, on cancer services, on cancer research across Europe and most importantly on cancer patients.[1-3] The indirect effects of COVID-19 on cancer will form a continuous thread through this *Lancet Oncology Commission*, as their impact on cancer research and cancer control have been all-encompassing and their consequences seem set to persist over the next decade. [4] Our data intelligence, delineating the impacts of COVID on cancer, will be presented in detail, but just to emphasise the scale of the problem, we estimate that ~1 million cancer diagnoses

may have been missed across Europe during the pandemic.[5] There is also emerging evidence of cancer stage-shift; of significant delays in cancer care delivery precipitating more complex treatments for patients whose cancer has not been caught at its earliest stage. [6]

These issues will ultimately compromise current survival trajectories and contribute to inferior quality-of-life for European cancer patients and those living beyond cancer. COVID has regrettably exposed a lack of resilience in cancer health systems. Its impacts across the cancer continuum, from screening/diagnosis to treatment, survivorship and supportive care, allied to its debilitating effect on cancer research, are set to contribute to increased cancer morbidity/mortality, and if not addressed as a matter of urgency, to prompt a cancer epidemic over the next decade. [7]

A combination of applying research modelling approaches to determine predicted survival, coupled with recent analyses of emerging cancer data, suggests that much of the success achieved in improving cancer outcomes over the last 2.5 decades in Europe may potentially be reversed by the impact that the pandemic has had over the last two and a half years. [8] Crucially, in the context of this *Lancet Oncology Commission,* there has been an unsettlingly negative impact on cancer research, with significant reductions in cancer clinical trial activity, disruption to discovery cancer research efforts and major reductions in cancer research funding. [9]

This *Lancet Oncology Commission* provides the crucial intelligence that defines the current landscape of cancer research in Europe, exposes the key gaps and informs a re-prioritisation of the European cancer research agenda over the next decade. Critically, we focus on those research gaps and inequalities in cancer research, that if addressed, would create a more effective cancer research ecosystem that significantly shifts the dial and reimagines cancer research and its implementation across Europe. Simply continuing to dedicate resource and effort on a narrow research agenda is no longer desirable or viable – we must follow the data and act on what they reveal.

Cancer research domains of particular strength in Europe

There are many research domains where Europe can be categorised as being internationally excellent or world-leading. The European continent (not just the EU27)

is a leader in cancer discovery science. Strengths are evident in cancer biology, cancer models, cancer diagnostics and early detection, new medical technologies and personalised treatments, precision oncology, vaccines, immunotherapies and drug-antibody conjugates, and paradigm shifts in neo-adjuvant therapy, especially for immunotherapy.

Cancer Biology Discovery and Cancer Model systems: In the deployment of cancer models, the discovery/development of organoids as a simplified multicellular system to elucidate critical drivers of cancer, has allowed precise definition of distinct mechanisms of tumour cell killing and helped determine emerging drug resistance.[10-12] Creation of "living biobanks" for multiple tumour types provides an excellent platform for driving cancer research and innovation.[11-14] Having appropriate well-characterised model systems has been a critical driver in the rapid development of drug-sensitivity screening models (now widely-used across the cancer research community), which have predictive value in multiple tumour types and can act as a guiding system for precision oncology research.[13-15] Organoid platforms are being finessed to broaden their applicability, not only in cancer, but across the research continuum.[15] Recently, they provided the key platform to identify super killer/serial killer cytotoxic T-cells and have been fundamental in developing innovative immunotherapy approaches.[16]

Congruent with the application of organoid models has been the creation/deployment of a variety of animal model systems that recapitulate the tumour biology of multiple cancer types, facilitating evaluation of the effectiveness and safety profiles of innovative treatment modalities at the pre-clinical stage, Europe has shown particular strengths and has pursued innovation in animal models, particularly Genetically Engineered Mouse Models (GEMMs) [17] and Patients-Derived Xenographs (PDXs). [18] The importance of animal model systems and their relevance to cancer is supported by the UK's Medical Research Council recent announcement of a multi-million investment in a National Mouse Genetics Network, with cancer as a key cluster.[19]

Early Detection research: From an early detection perspective, the NELSON randomized trial in lung cancer has changed the mind-set of many, because of the convincing early detection rates achieved in female and male populations, with an impact on survival.[20] New European-driven developments in ultra-thin rapid next-generation CT-scanning and AI-enhanced early detection (and prediction) [21] will

further empower robust early detection, enhanced by robotic read-out systems and machine learning approaches that provide increasing precision/speed in early cancer detection. That this will be accompanied by a lowering of costs will help drive the dual imperative of saving people's lives, while also delivering value-based care.[22]

Cancer Diagnostics and Precision Oncology: There has been a significant push in Europe to embrace new medical technologies, developing and deploying these innovative tools to enhance cancer diagnosis and treatment. Cancer biomarkers and genomic testing are critical enablers to help unlock the promise of precision oncology. A robust cancer biomarker infrastructure must be embedded across European health systems, to ensure their deployment as drivers of innovation in all European countries. Cancer biomarkers must also be considered in the context of the In Vitro Diagnostics Regulation, [23] which may still pose certain challenges including non-compliance of laboratory-developed tests, prompting cancer biomarker shortages and increased costs. Embedding cancer biomarkers within real-world oncology delivery and providing genomic testing across Europe, whilst ensuring that inequity gaps for patients are narrowed, not widened, must be the goal. [24] Critically, cancer patients must be firmly at the centre of a cancer biomarker-driven precision oncology research agenda, with research on value-based care informing appropriate biomarker use. Maximal collection and analysis of real-world data (RWD) on deployment of biomarkers in cancer care, learning from potentially every patient outcome, should be our goal.

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 and spare cancer treatment sequelae for those who will gain no therapeutic benefit. Our recent health economic analyses have underlined the potential for cancer biomarkers to deliver value for money. [25-27] However, we also found a paucity of studies that employ detailed health economic analysis to inform research on the feasibility of incorporating cancer biomarkers/genomic testing into mainstream cancer care, highlighting the need for wider deployment of health economic evaluation to inform value-based care.

Radiation Therapy and Theranostics: Europe has shown international leadership in nuclear medicine and the development/use of theranostics. In common cancers such

as prostate, development of a Prostate-specific membrane antigen (PSMA)-guided radioactive nuclide diagnostic/treatment approach is a major high-tech success story.[28-32] PSMA-PET detects the site of recurrent prostate cancer, enabling new radio-therapeutic/surgical strategies for oligometastatic disease.[30] In parallel, PSMA ligands labelled with various therapeutic isotopes have been effective in metastatic castration-resistant prostate cancer.[31, 32] One of these ligands, PSMA-617, recently received marketing authorization in the US, only 7 years after its chemical synthesis was published.[33] Notably, almost all radio-ligands for PSMA-targeted imaging and therapy were designed and developed by academic centres, underlining the enormous potential for translational cancer research in Europe. Encouraged by these successes, second-generation PSMA ligands have been rapidly translated from chemical design to phase III studies, investigating new theranostic targets, such as the chemokine receptor CXCR4, and fibroblast activation protein.[34] Similarly, in precision radiation therapy development, new-generation MRI-guided radiotherapy systems will lead to highly hypo-fractionated high-precision delivery, profoundly changing the radiation therapy landscape and providing viable options that are ultra-competitive with the more expensive proton therapy alternatives.[35]

Vaccine development: Overall, there are strengths in cancer vaccine expertise across Europe. Successful development of the preventative Human Papilloma Virus (HPV) vaccine and its implementation to protect girls from cervical cancer (and more recently both sexes from HPV-driven cancers such as oropharangeal cancer) had its origins in the pioneering research of 2008 Nobel Prize winner Harald Zurhausen and the Deutsche Krebsforschungs Zentrum DKFZ.[36] More recently, Europe has been at the forefront of the COVID vaccines development, deploying mRNA personalized vaccine approaches for vaccination strategies in solid tumors.[37-39] Long peptide vaccine developments [40] are also highly relevant in this field.

Tumour Immunology and Immunotherapy: Tumour immunology/immunotherapy are further examples of recognised research strengths in Europe. The early work on anti-PD1 (nivolumab, pembrolizumab), is both a seminal development and an exemplar of European research strength.[41] It also regrettably represents a prime example of how such a blockbuster asset can escape a successful valourization pathway in Europe. Recognition of the importance of immunogenic cell death has been pivotal, particularly

for classifying chemotherapeutic drugs and enhancing combination strategies.[42-44] Europe is also a global leader in determining the impact of the microbiome on cancer treatment efficacy, in particular treatments employing immune-checkpoint inhibitors.[45-49] This discovery science has informed clinical trials, opening up a microbiome-management approach to optimise anti-tumour responses.[50] Characterising the immune component of the tumour micro-environment has been critical in developing tumour "immunoscores";[51] detailing immune-enhancing and immunosuppressive components fundamental to our understanding of the immune environment. This work highights that manipulation of the immune system and the tumour microenvironment represent a pivotal target in successful cancer therapy development.[52-54]

Immunotherapy is currently undergoing its next revolution, Translating discovery science in advanced disease in melanoma and its roll-out in multiple tumour types represented the first paradigm shift; now rapidly followed by development of adjuvant therapy approaches,[55-60] initially in palpable node-positive melanoma stage III patients.[55] This neo-adjuvant immunotherapy paradigm is now achieving a highly significant reduction in clinical relapses, more cures, shorter treatment cycles, and less surgery, initially in melanoma.[55-57] Subsequently, it has also been deployed effectively to avoid rectal cancer surgery in almost all patients,[58] with similar results for head and neck,[59] bladder[60] and locally-advanced lung cancer. [61].[62]

Cancer research challenges in Europe

Highlighting Europe's cancer research gaps: While we have emphasised exemplars of research excellence and front-line innovation in cancer discovery science that can be enhanced through further support at European level, there are also a number of substantial overarching research challenges that must be addressed. The focus of this *Lancet Oncology European Groundshot Commission on Cancer Research* is to identify and codify these research challenges and deploy the intelligence revealed to propose a broader, more person-centred data-informed cancer research agenda for all of Europe, not just the EU27. Cancer prevention research, for example, has not had the attention (nor the funding) that it deserves. From an early diagnosis perspective, screening recommendations from as far back as 2003 have not been fully implemented, while screening currently only focusses on 3 of the 200+ cancers that

exist. More of our early detection research needs to be translated into pathways to early diagnosis, catching cancer at its earliest stage.

Similarly, our ability to convert research discovery into therapeutic innovation is compromised by regulatory, implementation and scale-up challenges. More support is required for academic-led clinical trials/real world evidence studies. Health services research and implementation science are critical to ensuring translation of research into clinical practice, but to date research focus and funding for these two critical areas has been woefully lacking. Overall, the lack of support for implementation science and health service/policy 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, there remains a distinct lack of focus on developing research programmes that address the physical, psycho-social and financial needs of cancer survivors.

Highlighting Europe's research infrastructure gaps: From an infrastructure perspective, gaps are evident We need to occupy the vanguard of the digital health revolution, ensuring well-structured data-warehouses, databanks and IT-systems to support rapid deployment of machine learning and accelerated analytic approaches. We need to facilitate precise analysis of the impact of new diagnostic and therapeutic approaches on healthcare, on the real-world impact of new treatments, and on new prevention and life-style adaptation strategies. These developments are currently hampered by the fragmented health informatic architecture of Europe, with different healthcare systems, different levels of economic development and differing health care priorities (given that health policy and healthcare cosing are national-level functions). However, a great advantage that we must build on is that research policies are defined and research funding is allocated both at national and at European level, providing an opportunity to break drown traditional silos and enhance the value of cancer research and its translation across the continent of Europe. This is particularly relevant, given the opportunities already highlighted (Europe's Beating Cancer Plan, EU Cancer Mission), as well as other opportunities through Horizon Europe's research funding programmes. Critical to this is the need for the bioinformatic, statistical and advanced data analytics skills and frameworks to drive a digital health agenda that places

significant emphasis on data intelligence and its deployment to underpin cancer research and its real-world translation for the benefit of human health and wellbeing.

Europe also lags behind other countries, particularly the USA, in the speed with which discoveries and innovations are valourised in clinical trials, or particularly in RWE studies. Many innovations unfortunately take a transatlantic journey to the USA where the final successful development is more often realised and brought to market. However, for Europe with its tradition of social health systems and health technology assessments, translation of innovation into clinical services and systems may provide better value. Speed of regulatory approval can be associated with greater uncertainty around clinically-meaningful benefit.[63]

For both Europe and the USA, though, one of the critical lacunae in innovation remains the poor quality of real-world data studies, reinforcing the need for better data strategies for post marketing studies. Through more data-empowered morpho-molecular analysis, coupled with linkage to clinical information, we are realising the unique nature of every cancer patient. Consequently, the classical research paradigm will probably shift in the near future, based on our digital capabilities, to one where collecting and analysing real-world data from all oncology patients is the norm. In this context, new financing models such as coverage linked with evidence development, may aid evidence generation (both clinical and economic), to support formal reimbursement schemes. in the real life setting.

Cancer Research in Europe – the opportunity beckons

For many European countries, cancer is the leading cause of premature mortality/morbidity, and a major economic burden for citizens and societies. The human and financial costs of cancer to Europe and its citizens will continue to grow over the next decade. 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, coupled with a need to ensure that cancer research and innovation address these disparities, so as to reduce the inequalities divide that exists between and within European countries. The cancer research strengths of Europe, though evident in a number of key domains as already

illustrated, are currently unevenly distributed, and do not necessarily align with the cancer priorities of individual European countries, an area we explore in more detail in defining the landscape of cancer research activity across Europe.

Despite these challenges, there have been some encouraging chinks of light within the overall European cancer control and research landscapes. Crucially, European Commission President Ursula von der Leyen has championed the need for a clearer strategic focus on health, as exemplified by her call for a stronger European Health Union as part of an ambitious "health in all policies" agenda. Previous incumbents of her office have rather shied away from this strategic focus, relying instead on the oft-used phrase that "heath is a national competency". If there is one irrefutable truth that the current pandemic has taught us, particularly in the context of the rightly-praised collaborative COVID vaccine development effort and the rapid delivery of effective vaccines to European citizens, it is that collaboration between countries, jurisdictions and sectors is absolutely essential – cancer, just like COVID-19, is a global health problem, which requires global collaborative solutions, at scale.

This re-orientation of the narrative, championing enhancement of our health and well-being as part of a pan-European effort, was recently reinforced by the conclusions of the Conference on the Future of Europe, which called for more pan-European cooperation in health care and research **(Box 1)** [64] 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-focussed research-driven agenda such as what we are proposing, are what are urgently required to address the challenges that cancer poses. Putting patient- and citizen- focussed (and approved) research at the heart of a pan-European cancer strategy will act as a critical driver of enhanced health outcomes.

Prioritising Cancer: Europe's Beating Cancer Plan and the EU Cancer Mission

Early in her tenure, the European Commission President tasked her Health and Food Safety Commissioner Stella Kyriakides with developing an ambitious overarching plan for cancer, emphasising the importance of tackling this common disease that was diagnosed in 2.7 million citizens and led to >1.3 million deaths in the EU in 2020. Following a period of development and a degree of consultation, an overarching

Europe Beating Cancer Plan was launched by Commissioner Kyriakides on the eve of World Cancer Day, February 3rd 2021. The 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 **(Box 2),** and a series of accompanying supporting actions. On 16th February 2022, the European Parliament ratified Europe's Beating Cancer Plan, the first time that Europe has developed a consolidated approach to address a disease that is overtaking cardiovascular disease as the most common cause of premature death in Europe.

From a research perspective and thus of critical importance to this *Lancet Oncology Commission,* cancer was selected as one of five research "missions" of the EU, emphasising the importance placed on cancer research as integral to national cancer control planning. Irrefutable evidence generated by this *Commission* and by others indicates that those patients treated in research-active hospitals have significantly better outcomes than those who are not. [65] The interim report of the Cancer Mission Board *"Conquering Cancer: Mission Possible"* was published towards the end of 2020. [66] A number of key research themes were identified, echoing the pillars of Europe's Beating Cancer Plan. The Cancer Mission Implementation Plan envisions *"Improving the lives of more than 3 million people by 2030 through prevention, cure and for those affected by cancer including their families, to live longer and better"* The four Mission objectives are: Understanding of cancer; Prevention and early detection, Diagnosis and treatment, and Quality-of-Life for patients and their families, supported by a series of activities **(Box 3).** [66] Additionally, the Cancer Mission espouses the following guiding principles **(Box 4);** noble ambitions, but they must be underpinned by an appropriate critical evidence base, as we have sought to do in this *Lancet Oncology Commission.*

Cancer Research in Europe; the Political Dimension

Politically, as Europe's Beating Cancer Plan and the Cancer Mission were being developed and socialised, a significant focus on cancer emerged within the European Parliament. The European Beating Cancer Committee (BECA) hearings received substantial evidence submissions from stakeholders from across the cancer community, The establishment of a new cross-party European Parliament Challenge Cancer Intergroup with secretariat provided by the European Cancer Patient Coalition (ECPC), (Europe's largest umbrella cancer patient advocacy organisation), provides a

complementary voice to the existing Members of the European Parliament Against Cancer (MAC); these two cross-party European Parliamentary groups emphasise the commitment of MEPs to cancer issues. Political support is critical in driving a cancer research agenda as Europe navigates turbulent economic, social and political waters in the wake of the COVID-19 pandemic, the Ukrainian war and economic contractions.

Cancer Research in Europe: Moonshot or Groundshot

The aims and specific objectives of the Europe Beating Cancer Plan and in particular the Cancer Mission echo the US Cancer Moonshot,[67] with its aspiration *"to accelerate efforts to prevent, diagnose and treat cancer"* and perhaps more controversially to *"achieve a decade of progress in just 5 years,"* as articulated in a previous Lancet Oncology Commission *"Future Cancer Research Priorities in the USA."* [68] On Wednesday 3rd February 2022, US President Joe Biden announced the re-ignition of the Moonshot (Cancer Moonshot 2.0 if you like), with an aim of reducing cancer deaths by 50% in the next 25 years.[69] But does Europe really need another Cancer Moonshot? In developing the *Lancet Oncology European Groundshot Commission on Cancer Research,* we argue that a more citizen- and patient- focussed, less techno-centric cancer research approach is a more appropriate response to the challenges that cancer poses in Europe. Cancer research prioritisation for Europe must reflect what is happening on the ground and be underpinned by a clear evidence base that collects, analyses and interprets data, turning information into crucial intelligence to define the current cancer research landscape, empower a more holistic person-focussed cancer research culture and inform cancer research priorities and their implementation across all of Europe going forward. The use of objective intelligence to inform cancer research prioritisation in Europe has been our North Star in the development of this *Commission*

The Lancet Oncology Commission: Generating the evidence base

The *Lancet Oncology Commission* is supported by a significant number of new analyses, uncovering novel insights, combined with intelligence recently generated by members of the *Commission*. Crucially, this cancer research intelligence has been enhanced with significant input from members of the Focussed Topic Networks[70] of the European Cancer Organisation (E.C.O). E.C.O. is the largest multi-professional cancer organisation in Europe, bringing together >40 European health and care professional societies and 20 patient advocacy groups, with a mission to reduce the

burden of cancer, improve outcomes and quality of care for cancer patients, through multidisciplinarity and multiprofessionalism. E.C.O convenes oncology professionals and patients to agree policy, advocate for positive change and be the united voice of the European cancer community. Initially, E.C.O. established 8 Focussed 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. The COVID pandemic prompted E.C.O to also establish a Special Focused Network on the Impact of COVID-19 on Cancer[71] and in response to the war in Ukraine, E.C.O. joined with the American Society of Clinical Oncology (ASCO) to form an E.C.O-ASCO Special Focussed Network on the Impact of the War in Ukraine on Cancer. [72] The 10 Focussed Topic Networks which have inputted to this *Commission* are highlighted in **Fig 1.**

Additionally, there have been major contributions through specific partnerships with pan-European organisations including ECPC, the European Academy of Cancer Sciences (a pan-European body which convenes clinicians and scientists to provide evidence-based advice to underpin policy for the prevention, management and palliation of cancer in Europe), the Organisation of European Cancer Institutes (OECI), (a cancer research network that promote greater cooperation among European Cancer Centres and Institutes), and the International Cancer Research Partnership (ICRP), (a unique alliance of >150 cancer research organizations that captures and maintains the only public repository of publically-funded cancer research globally).

A significant challenge for Europe, both for the Beating Cancer Plan and the Cancer Mission, are the inequalities in relation to many aspects of cancer health systems and services, including screening, diagnosis, treatment, and supportive care, particularly in CEE countries Illuminating such inequalities within national cancer research agendas is critical for developing new policies that deliver better patient outcomes.

Ensuring a person-centred data-enabled European cancer research agenda

The *Lancet Oncology European Groundshot Commission on Cancer Research* is also informed by a number of 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. [73] This led to development of the *European Cancer Patient's Bill of Rights*[74] **(Box 5),** launched with cross-political party support in the European Parliament in Strasbourg on World Cancer Day 2014. The Bill of Rights, co-created by patients and health professionals, was developed as a catalyst for change and an empowerment tool for cancer patients across Europe. One of its three components was a commitment to optimal cancer care, underpinned by research and innovation (see **Box 5,** 2nd Article of the Bill of Rights). The Bill of Rights and its implementation across Europe received the prestigious 2018 European Health Award at Gastein.

Congruent with development of the *Bill of Rights* was the launch of the *Europe of Disparities in Cancer* initiative **(Box 6),** [75] led by ECPC, with input from European health professionals. The *Europe of Disparities in Cancer* initiative forms the bedrock of ECPC's cancer inequalities agenda. A critical evidence-informed output from this initiative 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, [76] published as part of CanCon, the EU Joint Action on Cancer Control.

The 70:35 Vision for cancer control and research in Europe

The twin initiatives described above**,** with their citizen- 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. This Vision was co-created 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. [77] Research and innovation form a critical pillar to support delivery of this 70:35 vision **(Box 7).**

In this *Lancet Oncology Commission*, we have collected and analysed high resolution data on cancer research activity and its funding in Europe, with a particular emphasis on CEE countries. This high quality intelligence provides the narrative for current cancer research being performed in Europe and informs our 12 Recommendations. It is also a key driver of a citizen- and patient- centred research-informed Call to Action to ensure that the European cancer research agenda (and more importantly its

implementation) addresses the challenges that Europe citizens face in their daily lives, including a burgeoning East-West divide in cancer research and in cancer care that, if not addressed, will ultimately undermine robust cancer control in CEE countries.

Methodology

Definitions of Europe

The different definitions of Europe employed in this *Lancet Oncology Commission* are indicated in **Box 8**

Determining inequalities in cancer survival

The third cycle of the CONCORD programme[78] analysed individual records for 37·5 million patients diagnosed with one of 18 common cancers world-wide, during 2000–2014, including ~15 million cancer patients diagnosed in Europe. Data were provided by 157 population-based cancer registries in 31 European countries, 22 of which provided data with national coverage. Most registries submitted data for patients diagnosed between 2000 and 2014, with follow-up to 2014. We used the cohort approach to estimate survival for patients diagnosed during 2000–2004 and 2005–2009 and the period approach[79] for patients diagnosed during 2010–2014.

We estimated 5-year net survival, i.e. the cumulative probability of surviving up to 5 years since diagnosis after correcting for other causes of death (background mortality), using the Pohar Perme estimator, [80] which takes unbiased account of the higher competing risks of death in elderly people. Survival estimates were age-standardised using the International Cancer Survival Standard (ICSS) weights[81] for adults and by assigning equal weights to the three age-specific estimates (0–4, 5–9, and 10–14 years) for children.[82]

Determining inequalities in Cancer Mortality

Official death certification data for 22 cancer anatomical sites and estimates of resident populations, based on official censuses, for European countries, were extracted from the World Health Organization (WHO) database.[83] All cancer deaths were recoded according to the 10th Revision of the International Classification of Diseases.[84] Age-specific rates for quinquennia of age (from 0-4 to 85+ years) were computed. Age-standardized mortality rates per 100,000 person-years, based on the world standard

population were obtained for each calendar year and sex, and for western and CEE regions, separately. The number of avoidable deaths in 2016 in CEE countries was estimated by applying the age- and sex-specific western European rates to the corresponding CEE populations. Similarly, avoided deaths from all cancers combined over the period 1991-2016 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 to the observed ones.

Bibliometric analysis of European Cancer Research Outputs

Cancer research papers (articles and reviews) were identified in the Web of Science (WoS) through a complex filter with the names of 396 specialist oncology journals and 384 title words/phrases as previously described.[85] The filter was calibrated and had a precision, p, of 0.95 and a recall, r, of 0.98. Additionally, we identified biomedical research papers with a second filter, containing a long list of 172 address words/contractions in oncology. Numbers of papers in each subject area, year-by-year, from the world, the 44 European region countries as a group **(Table 1),** and from each of them individually, were extracted to underpin our landscape mapping analysis.

The sets of papers were further analysed with a series of sub-filters based on title words, and on names of specialist journals. Identified papers captured cancer research outputs across 14 research domains **(Table 2a),** such as genetics and surgery, but also including domains such as paediatrics (childhood cancers). They also identified papers relating to 17 anatomical cancer sites **(Table 2b)** e.g. breast, lung, colon etc. For each of these 31 subject areas, annotated with tetragraph and trigraph codes, we determined numbers of papers from each of the 44 European region countries in the 12-year period (2009 – 2020), and from the European region as a whole. These data allowed comparison of the amount of research on each anatomical site with the relevant disease burden (in DALYs) for the European region as a whole. It also provided potential for data intelligence to determine which European countries had tailored their cancer research portfolio to take proportional account of the distribution of the cancer burden between anatomical sites. Tinting of the cells **(Tables 3, 4a, 4b, 5)** is based on a five point Likert significant statistical scale, ranging from very weak (pink) through to very strong associations (dark green).

Patterns of International Cooperation

The activities of the EU have already stimulated much co-authorship in cancer research within the region - and not just between the 27 Member States (MS). 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 over the 12-year study period). For each country, we compared the numbers of papers published in cooperation with each of the other nine countries, and with nine non-European countries, as a percentage of the totals of its international papers with the percentage presence of each country in world cancer research *minus* the contribution of the original country. For example, of 42,812 German papers with international collaboration, with a total of 118,719 individual country contributions, Sweden co-authored 3899 (3.28%), but South Korea only 1125 (0.95%). Of 1,196,119 cancer papers *without* a German author, and with a total of 1,491,804 national contributions, Sweden contributed 17,653 (1.18%) and South Korea 54,180 (3.63%). So Sweden was a preferred partner of Germany by a factor of 3.28/1.183 = 2.8, but for South Korea the ratio was 1.183/3.63 = 0.26, so it was non-preferred.

Actual Citation Impact

Citation counts for each paper (2009-20), year by year, were downloaded from WoS. Five-year citation counts (Actual Citation Impact, ACI) beginning in the publication year were calculated. A five-year window was used as a compromise between the need for immediacy (i.e., citations for recent papers) and stability (i.e., inclusion of the peak year for citations, usually the second or third year after publication).

Bibliometric analysis of Research Outputs for the Organisation of European Cancer Institute (OECI) Centres

Our filter was applied to WoS, and the numbers of papers, year by year, determined for the world; the European Union (EU27), plus Iceland, Norway, Switzerland, Turkey and the UK, and for the group of 19 European countries (EU19) with one or more OECI-accredited centres. These were: Belgium, Czech Republic, Denmark, Estonia, Finland, France, Hungary, Ireland, Italy, Lithuania, Netherlands, Norway, Portugal, Romania, Spain, Slovenia, Sweden, Turkey, and the UK, The 51 OECI cancer centres are listed in **Table 6.** To determine the amount of collaboration, sums of the outputs of the three latter groups of individual countries/centres were compared with totals for

each group. We also applied sub-field filters to each of the four entities that identified papers in different research domains and different anatomical sites (**Table 7).** These mainly consisted of lists of title words, and (for some sub-fields), journal name-strings. They were combined into a series of search statements that could be applied directly to WOS, in combination with the cancer research and appropriate geographical filters.

Cancer research activity by gender

Gender of authors was captured through https://gender-api.com as previously described.[86] This assigns sex of names across Europe from a database of 4 million names, categorising them into regional- or country-level coding. Gender of project principal investigators was determined using https://gender-api.com, ORCID (https://orcid.org/) and internet searches when first names were not provided.

Cancer research funding

Projects supporting principal investigators in European countries (**Appendix I**) between 2010 and 2019 (inclusive) were extracted from the ICRP database[87] (n=20761, total value €10.8 billion (B)) or provided in excel by partner organizations whose historic data was not yet included in the database due to General Data Protection Regulation (GDPR) or other constraints. To complement ICRP data, Framework Programme 7 (FP7) and Horizon 2020 (H2020) projects active in calendar years 2010-2019 inclusive and relevant to cancer research (keyword search using terms cancer, oncol*, malign*, tumor*/tumour*, *oma, melanom*,leuk*) were extracted from the EU CORDIS database[88] (2010-2019, n=3212, total value €5.4bn - only project funding to partners in European countries was included) and projects funded by the Swedish Research Council (2016-2019, n=471, total value €0.5bn) were extracted from WorldReport. [89] Other cancer-relevant projects from WorldReport were already included in the ICRP database. For non-ICRP data, manual review of projects with low numbers of keywords was conducted to exclude projects without a specific focus on cancer research. Non-ICRP projects were coded by ICRP to one or more CSOresearch domains and cancer anatomical sites.

A list of funding organizations whose data were included in the analysis is indicated in **Appendix II**. Projects whose funding data were not in Euros ((Canadian Dollars (CAD), US Dollars (USD), Sterling (GBP), Swedish Kroner (SEK)) were converted to Euros using the 2019 average annual exchange rate, [90] to avoid trends solely due to

currency fluctuations. Analyses represent the full value of the projects active in the relevant time frame. To complement the detailed analyses based on aggregated project-level data, estimates of overall cancer research funding by other European cancer research funding organizations, 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 International Agency for Research on Cancer (IARC) list of global cancer research funders. [91] This approach was limited to data available in the public domain; for biomedical research funders, it was not always possible to identify spend that was specifically dedicated/relevant to cancer research. A further limitation in capturing overall cancer research spend was that details of funding from pharmaceutical companies were generally not available in the public domain.

Cancer prevention research funding

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. [91] The database was updated to include the years 2019-2021, bringing the total number of cancer research funders identified in the World and in Europe to 4998 and 1477 respectively. A methodology based on a keyword analysis of all cancer research papers in the WoS from 2008 to 2021 was developed with cancer researchers to extract prevention research publications. A “bottom-up” approach was applied; funding acknowledgements were used to identify funders active in prevention research and assess current trends. Cancer prevention has a broad scope. For the purpose of this Commission, the following three areas were included: Etiology, Prevention and Early Detection, Diagnosis, and Prognosis. Tertiary prevention was excluded.

Mapping European Outcomes and the Cancer Research Landscape

Inequalities in survival between European countries

Real-world data from population-based cancer registries across Europe provide comprehensive intelligence that facilitates estimation of survival for cancer patients in Europe after adjustment for risks of death from other causes, which differ between countries by age, sex, and over time. These data are an important metric for the overall effectiveness of a country’s/region’s health system in managing cancer, from early diagnosis through treatment delivery to final outcome.[92] For this *Lancet Oncology*

Commission, survival estimates were provided by CONCORD[93] for 157 population-based cancer registries in 31 European countries, 22 of which provided data with 100% population coverage. We deployed these data to determine the overall cancer survival landscape of and the key inequalities in survival between European countries.

Our overall findings indicated that survival varied substantially between European countries and regions. For several countries in Northern (Finland, Iceland, Norway, Sweden) and Western Europe (Belgium, Germany, Switzerland), age-standardised 5-year net survival for patients diagnosed during 2010-2014 was the highest in Europe for many of cancers evaluated. In contrast, survival was lowest in the majority of the CEE countries evaluated (Bulgaria, Poland, Romania, Slovakia and Russian Federation). However, in certain Southern (SE) and Eastern European countries, five-year survival for liver, lung and pancreatic cancer was comparable with or higher than in Northern European (NE) countries. Denmark, which alone of the Nordic countries had previously exhibited poorer survival, [94] is closing the survival gap with its Nordic neighbours; for patients diagnosed during 2010-2014, five-year survival in Denmark was among the highest in Europe for cancers of the rectum, breast (women), cervix and brain, as well as for lymphoid malignancies and melanoma of the skin. In the United Kingdom (UK), which like Denmark has also exhibited lower survival (EUROCARE; International Cancer Benchmarking Partnership (ICBP)), [95] five-year net survival from the CONCORD programme[93] for patients diagnosed during 2010-2014 with cancers of the stomach, pancreas, lung, ovary and brain was similar to that seen in certain CEE countries. Five-year survival in the UK was high in the European range only for melanoma. Europe-wide differences in survival were particularly marked for cancers of the oesophagus, stomach and rectum, melanoma and lymphoid malignancies, particularly for patients diagnosed during 2010-14 **(Fig 2a-c, Fig 3a-c).**

Regional variation in survival within European countries

For a substantial proportion of cancers, five-year net survival also varied widely within countries **(Fig 4a-c).** Regional variations in Southern and Eastern Europe (France, Italy, Poland, Spain and Russian Federation), were more pronounced than in Central Europe (Germany, Switzerland) and the UK. Five-year survival increased steadily for many cancers between 2000-2004 and 2010-2014, particularly for colon/rectal

cancers, and lymphoid malignancies, but for some cancers (e.g. oesophageal, liver, pancreatic, lung), age-standardised five-year net survival still remains below 20%.

Inequalities in cancer mortality across Europe

Cancer mortality has shown substantial variation across different EU countries. The highest mortality rates, particularly for men, have been recorded in Eastern Europe, with a greater than twofold difference in total cancer mortality between the highest (> 250 per 100,000 in men, in Hungary) and the lowest (~110 per 100,000, found in most Nordic countries, and in Switzerland,).[97] A significant proportion of the higher cancer mortality in Eastern Europe is due to lifestyle factors, (use of tobacco, consumption of alcohol, and particular dietary choices) [98] however, part of the inequalities in cancer mortality in certain European countries reflect inadequate cancer management. [99]

Previously, we used cancer registration data from EUROCARE-5 and a modelling approach employing different survival scenarios to estimate the number of avoidable cancer deaths in the EU, based on survival estimates across EU 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 EU countries, then ~50,000 additional cancer deaths would be avoided each year.[100] If cancer survival in all EU countries could be raised further to the level of the 75th percentile, then >100,000 cancer deaths would be avoided annually. These data were the critical evidence that informed our 70:35 Vision, 70% average survival for at least 10 years across the EU by 2035. [77] Here, we update these data analyses, with additional analyses specifically comparing Western and Eastern Europe to inform the *Lancet Oncology Commission* recommendations in relation to building research capacity and capability to help improve outcomes in all European countries.

Persisting East/West differences across Europe in cancer mortality

When CEE countries gained access to the EU in 2004, large differences were 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 recent years and estimate the potential number of avoidable cancer deaths, assuming that such a gap would be closed.

We present age-standardized mortality rates from cancer sites per 100,000 person-years in Western Europe (WE) and CEE, in 2010 and in 2016, together with number of deaths observed in 2016 and percent change between the two rates **(Table 8).** From 2010 to 2016, in men, mortality rates for all cancers combined declined from 131.5/100,000 to 122/100,000 (-7.1%) in WE, and from 177 to 168 (-5%) in CEE, i.e. there was a persisting 38% excess in CEE versus WE. Corresponding rates in women declined from 80.7 to 78 (-3.4%) in WE, and from 95.9 to 94.8 (-1.2%) in CEE (excess 22%).

In WE, male rates declined in most cancer sites (e.g. Hodgkin's Lymphoma (HL) (-22.9%), larynx (-17.3%), testis (-16.7%), and stomach cancer (-16%). Unfavorable patterns with documented rises in mortality were seen for pancreatic (+3.3%) and renal cancers (+4.2%). Overall declines were smaller in women (-3.4%), due to persisting rises in tobacco-related cancers. Major decreases were observed in mortality from HL (-39.1%), thyroid (-16.7%), and stomach cancer (-15.3%). Unfavorable trends were detected in lung (+6.2%), larynx (+5.3%), pancreas (+5%), oral cavity/pharynx (+3.7%/3%) and liver cancers (+0.6%). Highest mortality rates were for breast (14.4/100,000), lung (14/100,000), and colorectal (8.9/100,000) cancer.

In CEE countries, greater variability was observed in both rates and trends. In men, major declines in rates were observed for HL (-22.9%) and stomach cancer (-19.5%). Unfavorable patterns of mortality were registered for skin (+13.7%), multiple myeloma (MM) (+7.8%), Non-Hodgkin's lymphomas (NHL) (+6.5%), liver (+6.1%), testis (+5.5%), bladder (+3.5%), and prostate (+1.3%). Similarly, in women, major declines in rates were observed in HL (-20.7%) and stomach cancer (-18.5%). Increased mortality was registered for lung (+17.7%), bladder (+7.2%), oral cavity and pharynx (+14.4%), pancreas (+7.5%), oesophagus (+6.6%), MM (+6.2%), liver (+6.1%), skin (+4%), and breast cancer (+2.6%).

In **Table 9,** we indicate predicted avoidable deaths from major cancer sites in 2016 in CEE countries, assuming they had the same mortality rates as WE. A total of 55,239 cancer deaths (40,804 men/14,435 women) would have been avoided in CEE countries in 2016. In **Figure 5,** we present the estimated avoided deaths from total cancer mortality in men and women from Western and CEE countries, between 1991

and 2016, applying the peak age-specific mortality rates in 1990 (light grey) as constant. In WE, we estimate a total of ~5 million avoided cancer deaths (over 3 million men and almost 2 million women), while only 62,000 (about 52,500 men and 9,700 women) avoided deaths were predicted in CEE countries. A total of approximately 55,000 deaths would have been avoided in CEE countries in 2016, if they had exhibited the same mortality rates as in the WE region.

For 2016, our current data indicate that the major differences between the two regions were observed in men for lung cancer (30.8/100,000 men in West vs 47.1/100,000 in CEE countries), colorectal cancer (14.4 vs 21.7), oral cavity and pharynx (4.1 vs 8.5). Major differences between female rates were for stomach (2.5 vs 4.1), intestine (8.9 vs 11.2), and uterus (3.9 vs 8.5). In the early 2000's, total cancer mortality rates were 194/100,000 in CEE countries versus 155/100,000 in Western countries (25% difference) in men, and 104/100,000 in women in both the regions.

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 intelligence to help inform political discourse on the relevance, prioritisation and implementation or research. Scientometrics (the analysis of scientific outputs) provides a well-validated tool to underpin both evidenced-based requirements analysis and criterion-based benchmarking for European cancer research.[101] Here, we deploy scientometrics to define the landscape of cancer research activity across Europe between 2009 – 2020, and use this granular intelligence to frame an evidence-based consideration of how best to ensure that the optimal cancer research is enacted within the Cancer Mission and robustly informs Europe's Beating Cancer Plan.

<u>Cancer Research Activity by European Region</u>

In the twelve years (2009-2020) leading up to the start of COVID-19 pandemic, the European region published 39.4% of all biomedical research, but only 33.8% of cancer research **(Figure 6a).** Its output of cancer research papers also grew more slowly (5.1% *per annum*) than that of the world (8.1% *p.a.*) **(Figure 6a),** suggesting that despite significant investment, total cancer research productivity in Europe has been

contracting.[85] Why this is happening is illuminated by a sub-analysis of the outputs by high income 'old' European countries (EU15 pre 2004) and newer EU13 countries that joined post 2004 (EU13 post 2004). Our findings are stark. Whilst the wealthy EU15 countries have collectively enjoyed a doubling of cancer research activity during the study period, EU13 (CEE) countries have languished behind **(Figure 6b).** These data suggest that the actions started under EU Research Commissioner Philippe Busquin's European Research Area (ERA) and accelerated from the 6th European Framework research programme onwards, have not succeeded in delivering the trans-European cancer research equity and equality that was part of their intended impact.[102] 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 CEE countries.

Cancer Research Activity in Central and Eastern Europe

Other work that we have completed on mapping cancer research in newer EU13 CEE countries suggests that certain countries are escaping this 'low output' trap e.g. Poland.[103,104] As already indicated, the COVID pandemic has had a significant negative impact on cancer research activity and its funding in Europe (particularly from the charity/Non Governmental Organisation (NGO) sector), while both COVID and the Russian-Ukrainian war are likely to have a major negative impact on research funding for cancer in the foreseeable future.[105] Beyond just the capacity to retain an active research community due to these externalities, the low research activity of the EU13 that we highlight here **(Figure 6b)** is likely to have a direct impact on population cancer outcomes in these countries for many years to come.[106]

Cancer Research activity and Brexit

Additional to the pandemic and the Russia-Ukraine conflict, the impact of Brexit and the European Union's contraction to EU27 on cancer research activity, previously articulated by us[107] has already been detrimental and will continue to negatively impact European cancer research outputs. [108] In addition to these data, which starkly delineated the detrimental impact of Brexit on cancer research and the cancer research workforce, the work that we present here is also revelatory, highlighting the significant gap in outputs when we compare EU28 (UK included) versus EU27 (UK not included) research activity **(Figure 6b).** The gap is sizeable, reflecting the fact that the

UK is a significant powerhouse 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 other EU27 MSs.

Paediatric Cancer Research activity

Specific domains such as paediatric oncology research outputs **(Figure 6c)** 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.[109] lending support to the specific request for a paediatric cancer research uplift, as proposed by the International Society of Paediatric Oncology (SIOP), [110] and supported by this study. Our analysis provides a revealing picture of how different domains in adult versus paediatric cancers (for both solid and haemato-oncology tumours) are balanced across the EU's portfolio, building on our previous work with SIOP Europe, the *Lancet Commission for Sustainable Care for Children with Cancer* in 2020[111] and the *Lancet Oncology Series Improving Cancer Care for Children and Young Adults* in 2013.[112] Paediatric oncology is thus embedded as a recognised domain for research prioritisation within the Cancer Mission.

Cancer Research Activity by Collaboration

When it comes to choice of countries with whom to collaborate, European countries tend to be governed by traditional ties - language, cultural background, geographical proximity. Within Europe, strong cancer research linkages were detected between most pairs of countries, while European interactions with countries in for example East Asia were much weaker **(Table 3).** Tinting of the cells shows which countries were preferentially chosen as partners by the ten European region countries. Thus, Iran was non-preferred by all ten European region countries except for Turkey, while Turkey was non-preferred by all nine European countries. In contrast, Switzerland was a preferred partner by all the other nine countries, especially its neighbours with whom it shares common languages: Germany, Italy and France. The converse was also true. The UK was well represented in the research portfolio of its European partners, and it also favoured them, especially Sweden and the Netherlands, as well as Austria. Perhaps surprisingly, the USA is a non-preferred country for European countries, particularly compared with Canada, and even with Brazil. [There were, of

course, many more co-authored papers between Europe and the USA than with Brazil, but fewer relative to their respective presences in world cancer research.]

Europe has seen a range of strategic collaborative initiatives, some of which have yielded significant impact. One initiative that deserves mention is the Ireland-Northern Ireland-US National Cancer Institute Cancer Consortium[113] which led to a doubling of joint cancer research outputs on the island of Ireland, a significant increase in field-weighted citations and a series of joint research activities between cancer researchers on the island of Ireland and their US counterparts. These have delivered significant benefit to cancer systems and cancer patients on the island of Ireland over a 20+ year period, serving as a model for future collaborative strategic approaches.[113]

The recently established UK-USA axis on cancer research represents another important development, [114] but for both the UK and the US, the overall commitment to global cancer research i.e. in collaboration with LMICs, remains very limited (<4% of overall research activity). [114] In a similar way, Europe's commitment to collaborate with LMICs in cancer research is also disappointingly low.[114] Only 3.9% to less than 0.5% of Europe's research is co-authored with LMIC researchers. Thus, despite Europe's substantial expenditure on cancer research, its overall support of global cancer research has been extraordinarily poor.

Cancer Research Activity by Disease Burden

A further significant policy question that we have posed in this *Lancet Oncology Commission* is to what extent European cancer research reflects both the burden of sites-specific cancers and overall Disability Adjusted Life Years (DALYs) lost to cancer, both overall in Europe and within individual countries/regions? For certain site-specific cancers, our data indicate that the volumes of research activity are commensurate with their burden across Europe, with some e.g. haemato-oncology (HAE) even having higher than expectational levels of research activity. However, major cancer anatomical sites such as lung and colorectal, irrespective of European region, are significantly under-researched when compared with their relative disease burdens, as too are hepato-biliary and upper GI cancers **(Figure 7 a-d).** Remarkably, patterns for anatomical site-specific research are similar for all groupings. For some under-researched anatomical cancer sites, the amount of research may be as little as

one fifth of what would be proportionate e.g. 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. This "deep dive" 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 **(Table 4a and b).** Addressing such research deficits requires high-resolution strategic insight in order to understand potential causes and inform tangible solutions.[115] Such strategic mis-alignment is further reflected when we evaluate cancer research performance in individual European countries vis-à-vis overall cancer burden (as measured by DALYs). Whilst some countries have clearly developed national strategies that drive proportional levels of cancer research aligned to the countries' disease burden, many have not, particularly CEE countries. Although many of this latter group are lower-middle income CEE countries, UK and Ireland are notable high income additions to this deficit in research proportionality **(Figure 8).**

Cancer Research Activity by Gross Domestic Product

Broadly speaking, the level of cancer research outputs across Europe follows the country's wealth ($r^2 = 0.94$) **(Figure 9),** with four nations (UK, Italy, France, Germany) collectively dominating. A combination of huge national investment and collaborations between comprehensive cancer centres in these countries have acted as potent drivers of research activity.[116] In spite of the overall strength of this "top four", many other countries and groupings within Europe also deliver highly-cited cancer research **(Figure 9),** However, the impact of the low volumes of research being produced by EU13 i.e. mainly CEE countries, remains very low.

Cancer Research Activity by Research Domain

For the five largest cancer research domains (genetics (GENE), prognosis (PROG), surgery (SURG), systemic (CHEM), and pathology (PATH), there is a fairly even distribution of research between leading high-income European countries. However, in epidemiology (EPID), the four Scandinavian countries, followed by the Netherlands and the UK, are very strong. (Iceland is even stronger, RC = 5.21.) In clinical trials (CLIN), Belgium and Switzerland are the strongest countries. In palliative care (PALL),

Norway, Ireland, and Denmark are relatively the strongest, and could perhaps assist the southern Mediterranean countries of Spain, Italy and Greece. Ireland's strength may reflect the All-Ireland Institute of Hospice and Palliative Care, a product of the Ireland-Northern Ireland-US National Cancer Institute Cancer Consortium.[113]

The Impact of European Cancer Research

The impact of cancer research from certain European countries e.g. Netherlands, Germany and UK, as measured by ACI, has been consistently on par with that of the USA **(Figure 10a, 10b).** The most striking finding, however, is for the EU13 (which, in addition to low research volumes, also have a low research impact, 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

Finally, in this particular analysis section of the *Lancet Oncology Commission*, we address a very significant research policy topic that has arisen in the last decade, the question of gender equality (or more precisely its lack) within research, here focussing 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 (CEE), and research groups in Nordic and Benelux countries have done the most to promote women, with the highest levels of women in both first author and last (senior) author positions **(Figure 11a, b).** However, 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 11b).** In Germany, a recognised powerhouse of European cancer research, the number of females in senior author positions is disappointingly low, less than 25%.

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. The majority of principal investigators were men (65%) with only 35% women, reflecting the results of the analysis of senior authors on gender inequality.

Comprehensive Cancer Centres and Comprehensive Cancer Infrastructures

Driving the research agenda

Comprehensive Cancer Centres (CCCs) **(Box 9)** and Comprehensive Cancer Infrastructures have a key role to play in European cancer research and care agendas. The EU's 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"*. [117] It articulates that the purpose of this Network is "*to ensure that each EU citizen or cancer patient has access to and could benefit from high-quality cancer research and care".* 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 Flagship Initiative 5 of Europe's Beating Cancer Plan[118] **(Box 10).** Allied to these statements, the 'Porto Declaration' of May 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 healthcare system",* [119] echoing our 70:35 vision.

CCCs as research hubs and research drivers

A total of 51 CCCs and large clinical centres in 19 MSs in Europe have been accredited by OECI to date (**Table 6)**. There are 12 centres in Italy and eight in France, but in ten countries, there is only a single accredited centre. Mapping of existing structures for translational, clinical and outcomes research shows that CCCs and large clinical centres are key drivers of research (the first 40 centres accredited by OECI produce ~12,400 peer reviewed papers annually). [120] Additionally, within the German Cancer Aid/German Cancer Society accreditation programmes there are 14 designated "Oncologische Spitzenzentren" with a high degree of cancer research. [121] Furthermore, EACS has developed a Designation of Research Excellence for CCCs, which has to date designated two centres. [122] Disease-specific accreditation programmes are also available from professional organisations: breast cancer (European Society of Breast Cancer Specialists (EUSOMA)), [123] neuro-endocrine tumours (European Neuroendocrine Tumour Society (ENETS)), [124] and prostate

cancer (European Association of Urology (EAU)), [125] while the European Society of Medical Oncology (ESMO) leads an accreditation programme in palliative care. [126]

A number of European networks of CCCs 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; [127] Cancer Core Europe, linking seven CCCs to help drive a precision oncology agenda, with a particular focus on early-phase clinical trials[128] and the European Organisation for Research and Treatment of Cancer (EORTC), aligning multiple stakeholders for delivery of high-quality translational and clinical trial research. [129]

Capturing the research activity of OECI centres

The outputs of papers for each of the four groups (World, EUR32, EUR19, OECI), year by year, are presented in **Table 10**. European research output has grown more slowly than that of the world, reflecting the rapid increase in papers from China. However, the growth in outputs for the 51 OECI-accredited centres as a grouping has increased slightly faster than the world as a whole, 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, OECI-accredited centres accounted for slightly over one quarter of the total for the top 19 European countries by output (**Table 11)**, but this varied greatly, with Nordic countries at 50% and CEE countries at <15%. The sum of the outputs of the 51 OECI accredited centres exceeded the total by 68%, representing papers with authors affiliated to different OECI-accredited centres (thus, collaboration) but because there are many more centres than countries, this figure cannot be directly compared with the 30% for the 19 countries individually. The sum of the outputs is much larger than the corresponding figures for Europe countries as a whole (EUR32) (+ 40%) and the world (+34%), with 199 countries in the WoS data. This suggests 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 12)** clinical trials are the most highly represented, followed by targeted therapy, epidemiology, and radiotherapy.

However, the centres collectively do relatively little research on quality-of-life. This domain, together with screening and palliative care, is relatively neglected. For research on cancer anatomical sites (**Table 13)**, differences are less than those by research domain; they show a welcome focus of the OECI-accredited centres on oesophageal and lung cancers, which are often relatively neglected in Europe (**Table 7a-d**). OECI-accredited centres' concentration on breast and skin cancers relative to that of the world, reflects the greater burden associated with these cancers in Europe.

A key questions 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, which tend to be those who elected to go for OECI certification and have been accredited. OECI-accredited centres saw a 100% growth of relevant cancer research publications from 2012-2021, compared to a 59% growth in the EUR32 group **(Table 10).** As a result, the proportion of cancer research papers from OECI-accredited centres within the EUR19 group rose from 22.2% to 28.0%. This confirms what OECI has observed during its accreditation processes. Larger CCCs, often supported by a small but targeted enabling central budget, are able to galvanise the full resources of universities/ 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 CCCs with a central governance, bringing together high-quality clinical care, clinical research, and translational research, and in many cases, discovery science.[130] Academic output has increase longitudinally in a substantial fashion as a result of more significant collaborations between the clinic and the laboratory.

Geographical differences within the EUR19 were also observed (**Table 11)**. But the number of papers per annual GDP in both the two countries and five country groups show a remarkable congruence, ranging from 24 papers per billion euros GDP in France to 45 papers in Italy, albeit that purchasing power of the euro in those country groups has not been adjusted for. Scientific outputs of CEE countries comes out at above the average for European countries, which is a promising development. Networking between centres is vital to cancer research; it is universally acknowledged that key scientific challenges cannot be effectively tackled by cancer centres/institutes

acting alone. These collaborations involve investigators in multiple locations with a team science mentality, for example performing deep -omics studies at scale, and publishing results of clinical trials involving large numbers of patients in multiple sites.

Clinical Research in Comprehensive Cancer Centres

Critical mass and integration are also important for maintaining a throughput of high quality clinical trials, focussing on investigator-led studies. Not only are numbers of eligible patients within the network vital, but also protected time for academic clinicians, supported by a team of research nurses, study coordinators and other professionals. These resources are generally more available in larger CCCs. This is confirmed by our findings (**Table 12);** a higher preponderance of OECI-certified CCCs significantly exceeding EUR32/EUR19 outputs in Clinical Trials (Phases 1-3); targeted therapies including immuno-oncology; genetics and discovery science; radiotherapy and epidemiology. One surprise is the lower ratio of surgical studies, which may be from University Hospitals not yet formed into CCCs or part of the OECI network.

Regarding clinical trials overall (**Figure 12 (A, B))**, in 48 accredited OECI centres, the number of open clinical trials and patients recruited annually divides into two designated groups. OECI CCCs and OECI Cancer Centres (CC). The alignment across the two designations is remarkable. In the 31 CCCs, there is a large throughput of prospective interventional clinical trials, recruiting significant numbers of patients, with a median of 534 patients annually. This is 3.8 times greater than their CC counterpart, even without addition of observational or biomarker-driven studies. CCCs enrolled around 10% of patients to prospective interventional trials, compared to 3.4% within CCs (**Figure 12C)**. Phase I and I/IIA trials are especially concentrated in the large CCCs (**Figure 12D)**, with critical mass of expertise and patients to conduct such studies. Median CCCs conducted 23 studies, compared to the CC median of 2. The very largest CCCs have around 100 open studies at any one time.

Research budgets of CCCs and CCs, adjusted by purchasing power parity in the country in which the centre is located, are commensurate with the volume/spread of clinical research in the two groups, with median annual research budget of CCCs (€26.3M) 5 times greater than the median CC (**Figure 13C)**. However, some quite large cancer centres in Europe devote comparatively few financial resources to research, with concomitantly lower clinical research outputs (**Figures 13A,13B)**.

The Funding of European Cancer Research

Public sector/governmental funding for cancer research in Europe

The Cancer Mission, the European Beating Cancer Plan, the EU for Health Programme, Horizon Europe and others all provide significant opportunities for research funding at supra-regional level. But 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 intelligence on the European cancer research landscape. National Funding Agencies should also align their funding schemes to relevant "in country" research priorities.

Collaboration, including strategic partnerships between research funding organizations, 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)[87] is an alliance that in 2022 includes more than 150 cancer research organizations 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 $100bn US dollars (USD) in cancer research funding since 2000. ICRP member organizations submit project-level data for their research portfolios to the ICRP database,[88] including PI name, host institution, city, country, funding organization, project title, abstract, start and end date, and total funding amount. Each project is assigned to one or more cancer anatomical sites and research domain. The research domain classification (CSO) includes 34 codes, grouped into six categories (Biology, Aetiology, Prevention, Early Diagnosis and Prognosis, Treatment, and Survivorship and Cancer Control). All fields (with the exception of funding amount) are visible on the ICRP public website; funding amount is visible to partners who contribute data. The database includes current and historic projects, enabling researchers to identify potential collaborators and to avoid duplicating previous or existing research. It is estimated that ICRP captures over 60% of global cancer research funding.

Overview of European public sector/governmental funding for cancer research

From 2010-2019, a total of 24,394 individual projects (value €16.7 Billion (B)) were identified in the ICRP Database that could be coded to cancer anatomical site and

research domain **(Figure 14)**. From internet searches of annual reports, we estimate that an additional €4B of European cancer research was funded during this period, but could not be analysed in detail, as project-level data could not be sourced. Thus, the overall public sector funding for European cancer research (government or philanthropic) was estimated at €16B-€21B over the 10-year period **(Figure 14)**.

European Cancer Research Funding by research domain

Analysis of European cancer research funding by research domain **(Figure 15)** indicated that between 2010-2019, treatment (CSO5) received the highest level of investment, closely followed by biology (CSO1). Prevention (CSO3) received the least investment. Between 2010 and 2019, the pattern changed **(Figure 16)**, with increases in funding proportion to Diagnosis, Detection and Prognosis (CSO4) (from 19% to 23%), and Treatment (CSO5) (from 27% to 32%), suggesting that the research portfolio is becoming more translational/clinical. Funding for Biology (CSO1) and Aetiology (CSO2) decreased, (from 34% to 29% for CSO1 - Biology, and from 11% to 6% for CSO2 - Aetiology). Investment in Cancer Control and Survivorship research (CSO6) increased by 1.5 percent (5.6% to 7.1%), an encouraging trend. Research into primary prevention (CSO3) was very low, <4% of the overall European cancer research portfolio. However, there was a very small increase in the percent investment for Prevention research from 3.4% (2010) to 3.7% (2019). The research domain profile was similar to the international portfolio[131] (**Figure 15**), with a higher emphasis on discovery biology, diagnosis and treatment than on aetiology, prevention and cancer control/survivorship), reflecting our findings on cancer research outputs.

European Cancer Research Funding by cancer anatomical site

Investment in non-site-specific research was highest (>50%) (**Figure 17**); this included either basic/discovery research, or research relevant to multiple cancer sites (e.g. pain control/palliative care). 48% of codeable projects were related to specific cancer anatomical sites. **Figure 18** illustrates the percent investment by cancer anatomical site, compared to incidence and mortality trends for those cancer sites in Europe[132] Breast cancer research received the highest level of investment (18% of site-specific investment), followed by Colorectal cancer (12%) and Leukaemia (12%). The pattern of investment showed broad correlation with cancers of high incidence/mortality (**Figure 18**), but with some notable outliers (lung, bladder, stomach) where percent

investment was significantly lower than percent mortality, again reflecting our intelligence from mapping the cancer research landscape by publication output.

Our evaluation of European cancer research spend does have some limitations. At least €4bn (approximately 18%) of investment could not be included for in-depth analysis, as project-level data were not available in the public domain for coding. Investment by country is included (**Appendix III**) along with estimates of additional funding for cancer research that could not be coded in detail. While sharing data (project titles/abstracts) to enable detailed analysis of the funding landscape can be challenging, both due to data availability and obtaining permission to share data, inclusion of additional datasets would provide a fuller picture of the cancer research funding landscape, allowing research strengths and weaknesses to be calibrated and enabling collaboration and further investment to fill gaps in research. A full picture of the European research portfolio will also be invaluable in understanding more precisely the impact of COVID-19 on cancer research investment and capacity.

Strengthening cancer services and systems research for Europe

Ensuring precision oncology research is part of a broader research portfolio

The 'pharmaceuticalisation of cancer care' across Europe[133] 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 and systems research contribute significantly to better cancer outcomes for populations. Precision oncology has a critical place and is showing increasing promise, but needs to be proportionate and contextualised to its contribution to improved citizen/patient outcomes. The new generation of precision oncology medicines, including immuno-oncology are exciting and indicate clear potential; genuine advances were presented at the ASCO Conference in Chicago in June 2022, but these new agents are also expected to collectively contribute to 70% of total cost of active care in Europe by 2025,[134] reopening the cost versus value debate. Furthermore, there is now ample evidence that a substantial proportion of research in precision biopharmaceuticals is not delivering clinically meaningful benefit.[135]

An overemphasis on precision oncology also risks reinforcing the notion that achieving the best for patients can simply be addressed by ensuring cutting-edge technologies

are available,[135] ignoring the wider social and economic contexts within which people live and that will ultimately influence their outcomes.[136,137] Accumulating evidence shows that novel biopharmaceutical treatments tend to deliver value at the margins at best and may not contribute significantly to reducing cancer mortality at population level,[138] Investing more in biomedical research and technologies, without building the wider cancer research base, is therefore unlikely to deliver better, more affordable, more equitable progress in European cancer outcomes, without addressing the health system barriers to optimum cancer care delivery.[139]

The value of health systems/implementation science research

It is health systems which fund, organise and deliver cancer care. The wider political, economic and societal context within which they are embedded define the accessibility, affordability, equity and outcomes of cancer control interventions[140, 141] These aspects set the parameters for policies/strategies that help protect people's health (e.g. legislation on unhealthy commodities such as tobacco and alcohol), define options for early detection and prevention (e.g. HPV vaccination), 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 the science by defining research ecosystems and prioritising what will help realise the greatest improvements in outcomes.[142]

Health systems, and the cancer services and systems within them are complex. To address the myriad factors which ultimately influence patient outcomes at the individual and population level, requires a more balanced research portfolio which prioritises health policy and systems research (HPSR) as well as implementation science. This would enable a much deeper understanding of the multiple factors acting at different levels, their interconnections, and the priorities, agency and power of the various actors within and across systems that influence cancer outcomes. [138] This requires convening a wide range of scientific disciplines and professions, from political science to applied health services research, implementation science to epidemiology, geography to economics and anthropology to behavioural psychology. However, most cancer research funders do not consider these domains a priority for funding, potentially because the impact that investment in cancer systems and policy research is at national/international level and not immediately visible to clinical and

patient communities. 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 to ensuring equitable, efficient cancer care, research delivery and sustainable funding e.g. HTA, commissioning and reimbursement systems, and pharmaceutical regulation. [143] However, the benefits for outcomes, affordability and equality achieved by implementing multi-layered governance from mandated clinical practice guidelines through to sophisticated HTA mechanisms, coupled to pricing and reimbursement models is not being universally replicated across all European countries.[144,145]

Implementation science as a driver of innovation

No innovation improves patient care and outcomes without first navigating its way through the health system. Healthcare systems determine the breadth and extent of innovation by creating the environment for translational and clinical research. Implementation and scale-up, both intrinsic aspects of health systems strengthening, further determine whether an innovation is affordable and pro-equity. Yet in a system where you pay to play so to speak, global cancer research largely focuses on discovery science and systemic therapies.[146, 147] A recent analysis reviewing publication outputs in lung cancer found that 60% of research focused on systemic therapies and discovery science research, compared to 8% on radiation research, 4% on early diagnosis and 2% on screening research. [148]

What gains could potentially be made from a greater emphasis on implementation science for early diagnosis and more effective curative loco-regional treatments? Improving our understanding of how to minimise disparities in access to care through health services research, could make a huge difference to population-level survival, yet for example only 2% of radiation research is devoted to this area.[149] There is an urgent need for cancer research funders, particularly federal and philanthropic, to re-assess the balance of their research portfolio investments and their overall strategic direction. Areas like precision oncology will only prosper and deliver within in a fully-fledged health system, informed by health systems/ implementation science research.

Cancer Prevention Research Activity and Funding in Europe

Who funds cancer prevention research in Europe?

Our analysis reveals that 11% of cancer research papers published between 2008 and 2021 focussed on prevention research and were supported by 243 European funders, representing 16% of all European cancer research funders **(Figure 19b).** European not-for-profit prevention research funding organizations account for 45% of the total spend **(Figure 20a).** Governmental sources (including the European Commission) represent 31% of cited organizations**,** but received 48% of funding acknowledgements in our dataset **(Figure 20b).** While a direct link between funding acknowledgements and funding received cannot be established, it nevertheless provides indirect intelligence of which funder may 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 organizations. Maybe unsurprisingly, only 8% of prevention research funders are for-profit entities, while they account for 17% of funders of all cancer research **(Figure 20a).**

Cancer prevention research funders are present in 23 European countries (94% EU). Number of funding acknowledgements per country were compared as an indicator of overall spend on cancer prevention research. UK, Germany and Italy are the three most acknowledged countries in cancer prevention research publications. Restricting the scope of funding acknowledgments to not-for-profit organizations, UK, Spain and Sweden are the most active in cancer prevention research **(Table 14).**

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 prevention research centers/research networks. Out of the 32 European research networks identified, only two are involved in (but not dedicated to) prevention research, reflecting wider structural issues where major CCCS are 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 levels in prevention research funding indicates that Europe does slightly better, with more European cancer research

funders in prevention research (16%) than in the World (12%) **(Figure 21a, 21b)**. European not-for-profit organizations are also more involved in prevention research, accounting for 45% of European cancer prevention research funders **(Figure 20a)** and representing 13% of all European not-for-profit organizations funding cancer research **(Figure 21b)**. In comparison, 34% of cancer prevention research funders in the World are not-for-profit entities **(Figure 20a)**, representing only 7% of all not-for-profit organizations funding cancer research **(Figure 21a)**. European not-for-profit organizations are acknowledged in 31% of cancer prevention research papers; this percentage drops to 20% for the World **(Figure 20b)**.

Cancer prevention research funding is another relevant element of comparison. 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 is primarily due to the multiplication of not-for-profit organizations and governments involved in prevention research, as the number of other types of funding e.g. industry has stagnated. However, while interest in prevention research is growing globally, the last six years have seen a slowdown in the growth rate and spend by European cancer prevention research funders **(Figure 22).**

Primary prevention: a (consistently) neglected research area

A break-down by research domains within cancer prevention reveals that secondary prevention is the most funded area (52% of European cancer prevention research funders), closely followed by aetiology (47%) **(Figure 22a)).** Primary prevention is the least-funded area, though higher in Europe (25%), compared to the World (20%) **(Figure 23a).** This means that <4% of the 1477 European cancer research funders identified are interested in primary prevention research, concordant with the outputs (bibliometric) analysis and reflecting 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 papers **(Figure 23b, 23c).** In contrast, they 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 acknowledgements.

These results are in line with earlier studies that identified primary prevention as the cancer research domain attracting the least funding.[91] Investment in primary prevention has often been neglected partly because the impact may take several decades to emerge, and is difficult to measure. But primary prevention also offers the most advantageous approach to reducing cancer (and other Non Communicable Diseases (NCDs)), by reducing exposure to common risk factors and therefore producing important co-benefits for health.[150]

Our findings on cancer prevention, particularly primary prevention underfunding, led to additional analysis on cancer prevention and implementation science. Implementation science links research and practice to accelerate development and delivery of public health improvement approaches.[151] It is thus crucial to ensuring that cancer prevention is effective. A sample of 2000 European cancer prevention research papers from the last five years was checked and coded to identify implementation science projects. Only 7% of European cancer prevention research papers were classified as implementation (9% in the World), demonstrating that cancer prevention research, and especially implementation science, remain underfunded, in comparison to other research areas. This imbalance must be rectified, otherwise enhancing cancer prevention and adhering to World Cancer Research Fund/ American Institute for Cancer Research lifestyle recommendations will be compromised. [152]

Early Detection of Cancer – the need for better screening and earlier diagnosis

Research to promote early detection of cancer

While enhancing cancer prevention research is a critical (but under-resourced) component to 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 which 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 one third of cancer cases in Europe can be positively impacted by an early detection approach, including some of the commoner causes of cancer mortality, (breast, colorectal cancer).[153] The International Agency for Research on

Cancer (IARC) estimates that women who attend breast cancer screening appointments have a 40% reduction in their risk of dying from breast cancer, [154] with over 21,000 deaths per annum prevented, [155] Secondary prevention also makes sense from a health economic perspective; the total cost associated with managing late-stage colorectal cancer is at least 10 times higher than for early-stage disease.[156]

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 certain cancers in Europe.[157] These recommendations included a shared commitment by EU MSs to implement systematic population-based national (or regional) screening programmes for breast, colorectal (respectively the third and 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 for cervical cancer and 20 for colorectal cancer. [158] Despite improvements in cancer screening since 2003, It is an indictment of European cancer screening policies and their implementation that almost 20 years later, population-wide screening programmes are not universal in all European countries, leading for example to cervical cancer mortality over four times the EU average in Romania.[159]

Disparities in coverage for cancer screening

Coverage of respective target populations by screening also remains very low, at 14% on average across the EU for colorectal cancer. [160] Wide disparities exist, both across European countries, with breast cancer screening coverage for instance ranging from 6 to 90%,[161] and across social groups, as women of lower socio-economic have less access to screening, Over 12,000 deaths could be avoided annually from breast cancer, if maximal coverage was achieved throughout the EU. [162] Cancer screening programmes achieving the best coverage were also those with the most rapid recovery from the pandemic, showing how best practices in screening directly relate to 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 country. In countries where

population-based cancer screening programmes were actively implemented, examination coverage rates ranged between 17%-84% (breast cancer screening), 1%-53% (colorectal cancer screening), and 4%-71% (cervical cancer screening).[163] These figures are not acceptable and must be improved. Coverage of >70% of the target population by screening (recommended by WHO) was only achieved by five EU MSs and the UK for breast cancer, by no EU MS for colorectal cancer, and by one EU MS for cervical cancer. [164] Additionally, participation rates of >65%, (European Council of Health Ministers target), was only achieved by nine EU MSs and the UK in breast cancer, by only two EU MSs in colorectal cancer, and by three EU MSs in cervical cancer [165] While a more recent focus on seeking to improve what are exceedingly disappointing figures may yield a degree of improvement, these data and the associated health inequities that the lack of national comprehensive screening coverage has precipitated, are inextricably linked with inadequate adherence by both policy-makers and medical professionals to the quality metrics required. This, allied to a variety of organisational issues, are hampering both access to and participation of those at risk in efficient screening to ensure the earlier detection of cancer.

Broadening of cancer screening programmes to other cancers

There have been significant considerations on developing additional cancer screening programmes for other cancer anatomical sites, with a particular focus on lung cancer. While WHO and the EU co-funded Cancer Control Joint Action (CanCon) have indicated that further evidence is required,[166] recent research studies by European disease-based communities have provided evidence to support the case for low-dose computed tomography (CT) screening for lung cancer.[167] The development and roll-out of lung cancer screening would help in tackling the leading cause of cancer death in the EU, responsible for an estimated 296,140 deaths in 2018[168]

Early Diagnosis of Cancer

Despite many public health efforts, awareness of cancer warnings signs remains low among the public. [169] A more prominent role for primary care providers is essential for successful implementation of early detection strategies. [170,171] Although delivering optimal cancer screening can be highly effective, it only involves a very small minority of the 200+ cancer types that affect the European citizen. Currently, >75% of cancer cases are not detected through a screening approach; including 40 of the most

frequent and more lethal cancer types. Worryingly, a pan-European survey of >4,000 patients with cancer, revealed that for 30% of those patients whose cancer was detected outside of screening, their original diagnosis was not cancer, sometimes on multiple occasions, [172] emphasising 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 [173] can be effective, from clinical, female and health economic perspectives. For colorectal cancer, employing the Faecal Immunochemical Test (FIT) as a decision tool for triaging patients for colonoscopy was successfully employed to ensure early detection of colorectal cancer, despite the impact of COVID-19 and national lockdowns on the urgent diagnostic pathway. [174, 175] Not only did this approach help save lives, it also allowed colonoscopy capacity to be managed more efficiently. In lung cancer, low-dose computed tomography (LDCT), [167] can be targeted to at-risk populations. Self-collection approaches for screening (e.g HPVCheck)[176] are increasingly being adopted.

Inefficiencies and workforce pressures in diagnostic pathology

Critical to achieving a robust cancer diagnosis is timely patient referral for diagnostic confirmation and accurate cancer staging, both of which inform decisions on optimal treatment decisions for the patient. However, in an All.Can survey, >25% of surveyed cancer patients highlighted that diagnosis, and in particular the tardiness of the diagnostic process, was the most inefficient aspect of their cancer journey, impacting negatively on their entire experience of care. [172] From a workforce perspective, pathologists and clinical scientists play a pivotal role in helping to deliver accurate and timely cancer diagnosis. However, workforce shortages for these disciplines are significant, as we previously highlighted in the *Lancet Series on Pathology and Laboratory Medicine*. [177] Lack of a suitably-trained pathology workforce will also impact on the ongoing development of precision oncology approaches, particularly as laboratory test complexity increases, including molecular profiling of individual patients' tumours, to help select patients for the most optimal therapeutic intervention.

Human papillomavirus (HPV) and cancer

HPV-driven cancers

HPV causes ~5% of all cancers in women and men worldwide.[178] From a European perspective, ~2.5% of cancers are attributable to HPV. Widely recognised as the causative agent in cervical cancer; it is also involved in the aetiology of anal, oropharyngeal, penile, vaginal and vulval cancers. There are around two hundred different types of HPV, twelve of which are associated with a high cancer risk.[178] HPV is responsible for ~87,000 of cancers across the WHO European region.[179] Recently, there has been a marked increase in the incidence of oropharyngeal cancers, particularly in men.[180] In the US, HPV-positive oropharyngeal cancer has overtaken cervical cancer as the most common HPV-associated cancer type.[181]

Screening for HPV-driven cancers

Cervical cancer screening can reduce cervical cancer mortality by up to 90%,[182] Currently, there are no screening programmes available for other HPV cancers, including those affecting men. More research is needed into potential screening programmes for these demographics. Dentists and dental hygienists also have an important role to play in 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 may reflect the indirect impact of the 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,[183] and is being adopted by an increasing number of countries in place of cytology-based screening.[184]

HPV Vaccination

An impressive 100% vaccine effectiveness has been demonstrated over 12 years in four Nordic countries; no cases of high-grade cervical dysplasia were found in a large sample of vaccinated women.[185] Incidence of genital warts (also caused by HPV) has also been significantly reduced by HPV vaccination.[186] The US Food and Drug Administration (FDA) has approved vaccination as a means of preventing head and neck cancers caused by HPV.[187] Vaccinating both sexes provides an effective and

faster approach to preventing or reducing the incidence of cancers and other HPV-related diseases **(Box 11).** A universal approach could the elimination of HPV-driven diseases possible, even with moderate levels of vaccination uptake (50-75%).[188] The European Centre for Disease Prevention and Control (ECDC) has indicated that universal vaccination is a cost-effective option to prevent all diseases where HPV is implicated. [189] A total of 26 EU countries now provide national HPV vaccination programmes for girls, while 40 of 54 countries across the WHO European region have national HPV vaccination programmes. A total of 26 countries within the WHO region are including boys in their national HPV vaccination programmes.

Research 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 drops to 59% in Western Europe and a lowly 40% in Eastern Europe. [190] 'Vaccine hesitancy' is linked to a number of factors including: 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.[191] However, these views may change with the recent success of COVID vaccines.

Lack of knowledge on HPV and cancer

Many people currently lack basic knowledge about HPV and its associated risks. In the UK, despite HPV systematic cervical cancer screening since 1988 and vaccination for girls from 2008, a survey found that only 37% of participants had even heard of HPV. [192] Of these, 70% were aware that HPV could be transmitted during sex, and ~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 17,000 Europeans across 10 countries found that 70% of participants were not aware that HPV could cause cancer in males. [193]

Prioritisation of Radiation Therapy and Surgical Oncology research in Europe

Radiotherapy and surgery are essential treatment modalities to help improve cancer outcomes, exert improved cancer control, and deliver appropriate palliation. Over 50% of cancer patients have an evidence-based intervention with radiotherapy and/or

surgery at least once in the course of thweir disease [ref]. However, there is a paucity of research focus/funding for these two important domains.

Gaps in Radiation oncology research

While radiation therapy is a core component of modern cancer treatment, the data that we have presented highlights a lack of prioritization of radiation research relative to 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 ~50% of all publications in this domain relate to the preparation/delivery of radiation therapy, combined-modality regimens, and dose fractionation studies, with very little focus on health services research, palliative care, and quality-of-life studies.[194] Trial-related publications represented only 5.1% of total radiation research output. These data emphasise the need to invest in research related to loco-regional cancer treatments such as radiotherapy. Randomized clinical trials are often difficult to execute - due to the complexity of radiotherapy innovations, high up-front investments and strong operator dependency. These challenges are further intensified by the limited research budgets available for radiation oncology research,[ref] and in the challenge of implementing the evidence into clinical practice.[ref] For instance, an anonymous, electronic survey, distributed to radiation oncologists through the European Society for Radiotherapy and Oncology – Global Impact: Radiation in Oncology (ESTRO-GIRO) initiative, revealed significant variation in hypofractionation, especially across specific curative approaches and between geographical regions, in spite of the available literature evidence.[195]

Since 2012, the ESTRO Health Economics in Radiation Oncology project (ESTRO-HERO) has focussed on health systems research, developing an evidence-base for radiotherapy availability, access, cost and reimbursement across European countries.[ref] To foster the diffusion and clinical implementation of innovative radiotherapy interventions, ESTRO-HERO is now developing an evidence-based value framework for radiation oncology.[ref] Analysis of available frameworks in oncology such as the ESMO Magnitude of Clinical Benefit Scale (ESMO-MCBS), the ASCO Value Framework, and the National Comprehensive Cancer Network Blocks indicated that these frameworks are not immediately transferable to loco-regional

cancer treatments such as radiotherapy. They require a greater focus on the patient perspective, considering the broad spectrum of endpoints that are most relevant to the patients undergoing radiotherapy; as well as a more blended approach to evidence-generation, diversifying for new radiotherapy technologies, techniques and treatments [REF]. [ref] Alternatives to randomized controlled trials have been suggested and are under evaluation, such as the model-based approach in proton-beam radiotherapy [REF], [ref] the R-IDEAL framework for MR-guided radiotherapy [ref] or the collection of RWE, as part of an evidence development programme.[ref]

In the context of the Europe's Beating Cancer Plan and the Cancer Mission, the need to collect radiation-relevant information deploying data analytics and AI approaches is evident, Such data should inform research developing predictive models for radiation treatment outcomes, empowering a more tailored and personalised approach for each patient's treatment. There ia a need to evaluate which new radiotherapy technologies and treatment modalities are emerging 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, while quality-of-life and patient-reported outcomes should be captured and assimilated. Turning this data into intelligence will both facilitate the best therapy for each patient but also allow patients' quality-of-life readouts to inform future research priorities for patients living beyond cancer.

To assure access to the most optimal radiation treatment for each cancer patient in Europe, a dual focus on treatment optimization, with the aim to guarantee the best clinical outcome and quality-of-life for the individual patient, and health system optimization, guaranteeing equitable access to valuable innovations, considering the societal perspective, is required. Beyond the need for research that deepens our understanding of how new radiotherapy interventions impact patient benefit, there is the need to perform research defining the value of these radiotherapy innovations, in order to support their implementation in the clinic. Focusing on health services research and implementation science approaches to address inequalities across Europe is urgently required, as these research domains have been underrepresented in radiation and radiotherapy research.

Gaps in surgical oncology research

Cancer surgery remains a critical yet underdeveloped domain for research. Through a services/systems lens, the World Bank's Disease Control Priorities 3 (DCP3)[196] focused on the trade-offs between centralized and de-centralized approaches to cancer surgery and capacity- 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. [197] However, the Lancet Oncology Commission *Global Cancer Surgery: delivering safe, affordable, timely cancer surgery*[198] took a deep, broader strategic view, highlighting both care and research needs and deficits: >80% of people diagnosed with cancer worldwide requiring a surgical procedure at some point in their treatment; ¾ of cancer surgery are judged to be unsafe, not delivered, or unaffordable. [199] Furthermore, this Commission found dramatic deficiencies in the research ecosystem to support cancer surgery.

Across Europe, cancer research funding organisations have not stepped up to the challenge of delivering more surgical oncology research. Perusal of the EU Clinical Trials register reveals that surgical oncology only comprises 6.1% of cancer clinical trials.ref In part this is a systemic problem. High-income funders are increasingly inward-looking, focused on discovery cancer science and biopharmaceutical research[199] Additionally, <4.5% of cancer research activity over the last decade was in collaboration with LMICs (of this cancer surgery research was <0.1%). Furthermore, there is little evidence that cancer surgery is a priority commensurate with the surgical need.[200] Reflecting on previous analysis in 2012 where, based on bibliometrics, <5% of total global (including European) cancer R&D expenditure was on surgery, little has changed. Our updated 2022 analysis found almost no progress. Instead, research funding organisations and advocacy groups continue to focus on access to cancer medicines. [201] The realpolitik of cancer surgery is that it remains marginalised, politically, on the European stage. However, with the rise of new advocacy movements, for example global diagnostics, [202] the opportunity exists to re-integrate cancer surgery as part of a broader political discourse, reflected in the Europe's Beating Cancer Plan focus on enhancing surgical oncology and emphassing its position as a pillar of cancer treatment.

European cancer surgical research has, however, innovated in numerous areas, for example in the impact of technology, in particular robotics and to a lesser extent minimally-invasive surgery. Technology innovation is fundamental to cancer surgery; however, robotics has had a highly disruptive impact on services and systems. What data we have, mainly from Nordic countries and the UK, strongly suggests that these novel technologies, if not properly implemented in a managed cancer care system, can be anti-equity, distorting cancer surgical systems which then adapt to deliver these high-cost, high-end technologies.[203] 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. [204]

Cancer surgery has, however, been a rich area for health services/policy research in Europe, with a long history of research into performance metrics, models of care, and surgical workforce. These analyses have helped underpin policy intelligence for national planning, reflecting the importance of a broad surgical oncology research strategy, embracing technological innovation and health systems research. [205]

Ensuring a Person-Centric Approach to Cancer Research and its translation

A Patient Centred Approach: The European Code of Cancer Practice

A patient-centred approach, where patient involvement and engagement is facilitated and promoted, helps bridge the gap between health research, policy, and patient-centred practice, increases transparency, leading to more meaningful outcomes. [206] In the Introduction to this *Lancet Oncology Commission*, we highlighted how the *European Cancer Patient's Bill of Rights* and the *Europe of Disparities in Cancer* initiatives helped deliver patient-centred cancer care and research activities across Europe. Continuing this theme, the recent establishment of the *European Code of Cancer Practice* by E.C.O. places patients at the centre of both cancer control and cancer research agendas in Europe. The *European Code of Cancer Practice* **(Figure 24)**[207] is a citizen and patient-centred initiative, highlighting the core requirements that people should expect, in order to receive good quality clinical cancer care and be involved in cancer research activities within their health system.

The Code sets out a series of 10 key overarching rights **(Box 12),** [207] signposting what European patients (whether they be paediatric, adolescent or adult) should expect

from their health system, including incorporation of research as a critical component at all stages of their cancer journey, in order to achieve the best possible outcomes. The Code has been co-produced by a team of cancer patients, cancer professionals and patient advocates, to underpin a framework for the delivery of optimal cancer care and patient-centred cancer research. The 10 rights provide specific support for the cancer patient and their family/carer and are articulated in detail in **Box 13.** [207]

Legitimacy of each of these 10 overarching rights has been underpinned by a combination of the best available medical literature, evidence-based guidelines and research intelligence,[207] including the *Essential Requirements for Quality Cancer Care (ERQCC)* series,[208] which have been developed by E.C.O. The *European Code of Cancer Practice* is designed to be of value and support to people with cancer, people at risk of cancer, people living beyond cancer, carers, parents/guardians, patient advocates, educators, researchers, health professionals and their trainees.

Currently, the Code has been translated into 28 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 both a ringing endorsement of the Code's relevance and impact in Europe, as well as an invaluable support for its widespread dissemination and implementation. The 10 overarching rights of the Code align to the Focussed Topic Networks hosted by E.C.O **(Figure 1).**

Living beyond cancer

Research on Cancer Survivorship

As 5-year and 10-year cancer survival from many cancers have improved substantially, there is a need for greater focus on ensuring that those living beyond cancer attain a better quality-of-life, both physically and psychologically, and are actively re-integrated into society. In Europe, research must focus on the challenges that increased levels of cancer survival will bring. There are now 20 million European citizens living beyond a cancer diagnosis and this will continue to rise.[ref] 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 to control their cancer. These issues may reflect physical (e.g. side effects,

complications, chronic pain, co-morbidities) and/or psycho-social aspects (e.g. cancer distress, cancer stigma, professional and financial difficulties, relationships, including intimacy and fertility.[209]

Comorbidities are particularly common in cancer patients,[210, 211] with research indicating that the majority of cancer patients report at least one comorbid condition. [212] Such comorbidities and their complications are very diverse - cardiovascular diseases (arrhythmias, heart failure, hypertension, myocardial infarction), thrombosis, stroke, pulmonary disorders, diabetes, obesity, dietary disorders, liver diseases, neurological and mental health disorders.. [213, 214] From a psycho-social perspective, the evidence indicates that psycho-oncology services must be an integral component of the comprehensive multidisciplinary care provided to cancer patients and survivors throughout their cancer journey. [215]

Inequalities in managing the long-term impacts of cancer

Unfortunately, management of the long-term impacts of cancer and its treatment is not consistent across European countries, emphasising the need to ensure equal access to survivorship care and support for European citizens. Additionally, the lack of consistency in regulations that should protect those living beyond cancer against financial, professional and social discrimination across different European countries propagates further inequities, compromising the cancer survivor's ability to live a full life. We need a more truly patient-centred approach, that aims for an optimal quality-of-life throughout the entire cancer journey and promotes active re-integration back into society **(Box 14).** [216] We also need new research-informed approaches to survivorship care. This includes developing risk-stratified pathways that optimize coordination between cancer specialists and primary care physicians, based on the "whole person" needs of the individual.[217]

Delivering a cancer survivorship research agenda

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,

[218, 219] in order (as part of a wider focus on cancer research) to embed cancer survivorship research as an active component of the Cancer Mission.[219] We have prioritised three distinct Cancer Survivorship Research and Innovation Pillars **(Box 15)** that we propose should be the thematic areas of particular focus for a European Cancer Survivorship Research and Innovation Plan. Within these pillars, we highlight the challenges **(Box 16 - 18)** and propose a series of recommended solutions that will firmly empower cancer survivorship research and innovation.

The Medical Cancer Survivorship Research and Innovation Pillar

Ten challenges have been identified that sit within the Medical Cancer Survivorship Research and Innovation Pillar **(Box 16).** For each challenge, a focussed solution is identified and articulated. Addressing the lack of integration of cancer survivorship research requires a commitment it be recognised, but more importantly resourced, within the overall European cancer research agenda. This can best be achieved by creation of a European Cancer Survivorship Research and Innovation Plan, which should be embedded within the Cancer Mission and aligned to delivering our 70:35 Vision. Prioritisation of its themes should be informed by a comprehensive mapping exercise of existing cancer survivorship research activities, so as to identify, quantify and prioritise specific survivorship research gaps. This prioritisation must clearly align to survivors' specific challenges (including for example in areas such as mental health; reconstructive surgery; fertility preservation; active rehabilitation). This can be achieved by ensuring that such prioritisation is done in collaboration with cancer survivors, their patient advocates, health professionals and cancer researchers. Cancer survivors must be empowered as "active participants" rather than "passive recipients" in research and innovation to enhance their quality-of-life.

The Socio-Economic Cancer Survivorship Research and Innovation Pillar

Six challenges have been identified within the Socio-Economic Cancer Survivorship Research and Innovation Pillar **(Box 17).** For each challenge, a focussed solution is identified and articulated. Research on identifying determinants of cancer inequalities linked to social rehabilitation of cancer survivors, including disparities present across Europe (in particular in CEE countries) should be prioritised. From a quality-of-life perspective, a combination of maximising use of existing approaches and creating/ evaluating new research tools will permit granular assessment of the quality-of-life

of cancer survivors, help identify social determinants of health and how cancer survivors can return to normal living.

Financial challenges of cancer must also be addressed. Research is required on precise economic evaluations of direct and indirect costs to those living beyond cancer (including levels of financial toxicity experienced by survivors and their families); aligning this to the proposed European Cancer Inequalities Register can help promote distinct actions to address this area of increasing relevance. Additionally, data need to be accumulated to measure the impact and cost-effectiveness of supportive care, rehabilitation, psychosocial and palliative care interventions on cancer survivors. Social issues such as access to work, education, insurance, loan, mortgage and the impact of financial toxicity must be prioritised within an adequately resourced cancer survivorship research and innovation agenda.

<u>The Politico-Legal Cancer Survivorship Research and Innovation Pillar</u>

Five challenges have been identified within the Politico-Legal Cancer Survivorship Research and Innovation Pillar **(Box 18).** For each challenge, a focussed solution is identified and articulated. Increasingly, it is important to characterise any legal aspects of discrimination for cancer survivors, deploying this intelligence to inform research on discrimination and how it can be mitigated. In this regard, the *Right to be Forgotten* [220-222] with its key roles 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. The *Right to be Forgotten* is now embedded in 5 European countries – it needs to be universally accepted in all European countries, as all cancer survivors require access to financial services. There are 4 additional countries who are at different stages of introducing the *Right to be Forgotten* (Ireland, Cyprus, Italy and Romania). A legal framework already exists in France since 2016, providing a model for Europe in general. Establishing a code of conduct in all European countries would remove the potential for discrimination against those living beyond cancer.

Defining and mitigating the stigmas associated with cancer is increasingly relevant and must be pursued, promoting a cultural shift to a more active survivorship-focussed approach. The lack of specific research on survivorship support and patient empowerment must be addressed. Investigating the potential role of comprehensive

survivorship clinics, allied with consideration of how survivorship care should be organized to help facilitate comprehensive and tailored long-term follow-up of individuals, providing dedicated and specific support without disrupting the medical units dealing with patients who still require active treatment. Specialists multidisciplinary teams in survivorship should be created and their expertise and activities promoted. Empowerment is also critical 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, right across Europe.

Many Patient Advocacy Groups have experienced significant difficulties in maintaining their activities due to the impact of the pandemic; developing and applying an appropriate model for financially supporting patient advocacy research activities is critical, so that they can continue to support those living beyond cancer.

The Critical Importance of Data for European Cancer Research

Data intelligence and COVID

If there is one important lesson that we have learned from the enormous challenges that COVID has posed for our society, it is the critical role of information and its conversion into data intelligence to inform policy and practice. Data intelligence is no longer just the preserve of scientific/healthcare communities; it is now embedded in the public consciousness and has become part of our daily norm. As a society, we are now more familiar with data– be it the daily numbers of people infected with SARS-CoV-2, percentage of the population vaccinated, or sadly, COVID death numbers. In a way, we have all become armchair "data experts". But data are not just being deployed to help mitigate the direct impact of COVID-19. They have also highlighted the indirect impact of the pandemic on life-threatening diseases such as cancer.

Data Intelligence and cancer

Given the impact of data science on unravelling the indirect impacts of the COVID pandemic on cancer, a critical component of the European cancer research effort must focus on empowering the responsible and effective use of health-relevant data. [223] Building a citizen-centred cancer knowledge network must be our goal. We now inhabit a digital society; we must explore ways to better harness the power of data, while ensuring that they are used in a safe and trustworthy manner. [224] Data

intelligence is pivotal to this *Lancet Oncology Commission*, informing the research that underpins development of better approaches to ensure optimal cancer control for European citizens. Combining multi-modal data sources and employing this improved intelligence to drive research and innovation, must be at the heart of efforts to deliver better outcomes and fair value for citizens/patients, for clinicians, for researchers and for economic/societal development across Europe. In particular, the ability to access and use data in near real-time will facilitate early diagnosis of cancer and accelerate development of innovative treatment approaches tailored to the needs of patients.

COVID and Conflict: externalities impacting the Cancer Research agenda

Externalities will have a highly relevant influence on the future of European cancer research. We have yet to fully understand the triple impact of the pandemic, Brexit and the ongoing war in Ukraine on investment in, and commitment to cancer research. There may be implications for the European Commission's ability to continue to support the Cancer Mission at the intended and required level. Economic shocks from the pandemic and war are having profound impacts on cost of living, which directly alters our population's philanthropic behaviours. **(Box 19)** Thus, we may see a huge contraction in donations for cancer research, severely damaging our aspirations.

<u>The critical role of data in addressing the impact of COVID on cancer</u>

By many measures, the COVID-19 pandemic has had a grave impact on Europe, both directly – most European countries have experienced high per capita COVID-19-related mortality and morbidity and indirectly, through its impact on non-COVID healthcare. At the nadir of the first pandemic wave (March-April 2020), we established a research study that collected and evaluated near real-time data from hospital trusts across the UK, measuring the impact of the pandemic on cancer diagnostic and treatment pathways. [225] Specifically, we focussed 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 either unwilling to see their doctor for fear of catching COVID, or unable to access GP/ specialist cancer services. While not as dramatic, the impact on treatment was also significant; four out of ten cancer patients experienced delays in delivery of their

chemotherapy. These data were the first in the UK to show the indirect impact of the pandemic on cancer and contributed to the decision to restore cancer services.

The impact of COVID at the European level

At a European level, these data prompted E.C.O. to establish a Special Focussed Network on the Impact of COVID-19 on Cancer. Extending our data analysis revealed the disastrous impact across the European continent **(Figure 25)** - 100 million missed screening tests, up to a million citizens who may have an undiagnosed cancer, significant delays/reductions in treatment (particularly systemic therapy, surgery) and significant impacts on cancer clinical trial activity and cancer research programmes. The effect on the cancer workforce is also revealing, with four out of ten cancer healthcare workers feeling burned out due to their herculean efforts, not only to control cancer, but also to contribute to infection control efforts of a beleaguered health system. Additionally, the analysis shows that three out of ten cancer healthcare workers exhibited symptoms of clinical depression.

Data as an advocacy and policy driver

These compelling data prompted E.C.O. to launch a *Time To Act* Campaign with the strapline "Don't let COVID stop you from tackling cancer." Translated into over 30 languages, this campaign was launched at European level in Brussels in May 2021 and has now been launched nationally in 12 European countries. It is accompanied by a Time to Act Data Navigator **(Figure 26),** facilitating evaluation of the impact of COVID on cancer by tumour subtype, by country or region, by treatment modality etc., providing an extremely informative tool for the European cancer community. The *Time to Act* Campaign, with its robust evidence base, its messaging of "Don't Delay", "Seek Help", "Don't Let COVID stop you from tackling cancer" and its highlighting of potential cancer symptoms to be aware of (e.g. a lump on the breast, difficulty swallowing, blood in the urine or faeces, unexpected weight loss) resonated widely across Europe, with significant political support. Both President von der Leyen and Commissioner Kyriakides referred to *Time to Act* and referenced its sobering statistics.[226, 227] These data are also highlighted in the Special Committee on Beating Cancer (BECA) report.[5] At all national *Time to Act* launches, Ministers of Health participated and were very supportive of the campaign, while presentation of local research data confirmed the

substantial impact of the pandemic on cancer patients/cancer healthcare systems in different European nations, highlighting the need for pan-European solidarity.

COVID and Cancer Research

The pandemic has had a chilling effect on cancer research across Europe; laboratories were shut and clinical trials delayed or cancelled altogether in the first pandemic wave. This has persisted for many months due to further waves and full/partial lockdowns in certain European countries. Whilst the medium-term impact of COVID-19 remains unclear, research data that we and others have generated suggest significant negative impacts, particularly on CEE countries. [5] The pandemic has highlighted that cancer research and cancer care are complex adaptive systems, which are 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 intelligence 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. The former have been able to benchmark treatment quality after radiotherapy/surgery across high-burden tumours, thus enabling clear evidence-to-policy links. 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 ~2 million euros over 5 years, 0·002% of the median estimated cost for developing a new therapeutic agent (>€9100M). Research data infrastructures supporting health policy and health systems research have also been critical for broader issues in cancer research as we have highlighted, such as understanding cancer inequalities.

The Impact of the war in Ukraine on Cancer Research in Europe

The challenge for cancer systems

The invasion of Ukraine by Russia (February 24, 2022) has added to the impact of the pandemic on European health systems, creating a massive humanitarian crisis. The impact of this conflict comes on top of eight years of low level war by Russian-backed forces in the Eastern Donbas region since 2014, which had already created huge challenges for healthcare systems. The impact of Ukrainian refugees in Europe is

creating new difficulties for cancer systems capacity, especially for CEE countries. Recognising these challenges and the need to provide much-needed support, E.C.O and ASCO established a joint E.C.O-ASCO Network on the Impact of the War in Ukraine on Cancer, leading to a series of activities including cancer data intelligence gathering in Ukraine and surrounding countries to inform actions on issues including medicines shortages, diagnostic and treatment capacity.

The Impact on cancer research

Whilst there has been much discourse on the war in Ukraine, what has gone relatively unnoticed is the profound impact that the war has had and will continue to have on clinical cancer research. Both Russia (upper-middle income) and Ukraine (lower-middle income) are unusual in their significant global impact on cancer research. Both are two of the largest contributors to clinical cancer research in the world, especially to industry-sponsored clinical research. Our analysis **(Table 14)** indicates that between 2014 and 2017, a total of n=636 cancer Randomised Control Trials (RCTs) were published (all led by high-income countries). Ukraine contributed to n=39 of these RCTs, one of the highest lower-middle income contributors (out of a total of 136) – placing it only just behind another lower-middle income country, India, a country over thirty times its size, which contributed to n=42 cancer RCTs. Countries in the upper-middle income category contributed to n=182 cancer RCTs. Russia was by far the largest contributor, with n=115 cancer RCTs. At the start of the war, an analysis of ClinicalTrials.Gov indicated that Ukraine had n=245 active pharmaceutical cancer clinical trials, of which 127 were actively recruiting. Corresponding figures for Russia were n=667 and 352, respectively, emphasising the significant impact that the war in Ukraine will potentially 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. Additional pressure has been applied to these companies through the so-called Yale List,[228] which has illuminated which companies have, and which have not, withdrawn from Russia. Many of the major pharmaceutical companies listed by the Yale List such as AstraZeneca, Pfizer, Glaxo Smith Kline (GSK) *et al* have taken the position to stop new investment

and new clinical trials, but to continue both pre-existing trial recruitments as well as supplying standard cancer medicines as per contractual arrangements.

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 in cancer research. China and India have significantly increased their research imprint. [229-231] The former has become particularly dominant, globally, in lung cancer research as well as discovery science, driving a revolution in immuno-oncology drug development. [148,230] Such research activities are both disruptive and opportunities for Europe. More widely, the Middle East and Latin America are also ramping-up cancer research activities, providing wider opportunities for European trans-national engagement. [232,233] In Sub-Saharan Africa, the challenges are different; countries on this continent require a higher level of capacity and capability building, with broader collaborative networks to enhance cancer research methodological skills from biostatistics to clinical trial design, as well as discovery science techniques. [234] All evidence shows that regions and countries that are outward-looking and engaged produce better, higher impact research.

A stronger focus on global cancer is crucial for Europe, catalysing it's own research agenda but also in solidarity with countries faced with their own unique challenges as they look to deliver innovative, effective cancer research. However, European cancer research funding organisations are failing to realise this potential or honour their global commitments to cancer control that they so often espouse. [199] We need a new strategic pact that focuses funds and effort on the wider global cancer agenda, rather than wealthy-to-wealthy country co-operation. Multiple *Lancet*/*Lancet Oncology* Commissions, as well as recent significant multi-stakeholder strategic reviews, [235] have created the opportunity for Europe to engage more widely and this Commission sets out an unrivalled global opportunity that needs to be grasped.

4. Recommendations and Call to Action

This *Lancet Oncology European Groundshot Commission for Cancer Research* has employed 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 impact of external factors including the COVID pandemic, Brexit and the war in Ukraine. Gaining this more granular understanding of the European cancer research landscape, its strengths and in particular its weaknesses, has empowered us to deploy this intelligence to inform a series of 12 Essential Recommendations **(see Box 20),** underpinning a Call to Action to ensure that cancer research is a pivotal driver of enhanced cancer control and improved quality-of-life for cancer patients and those living beyond cancer across Europe. Our recommendations are grouped under three thematic areas, informed by our interpretation of the data intelligence that we have generated:

- *Closing the European Cancer Research Divide*
- *Plugging the gaps in European cancer research and its funding*
- *Responding to current and future challenges*

For each of the 12 Recommendations, we provide an indication of how they can be achieved and a time frame for their implementation

Closing the European Cancer Research Divide

Essential Recommendation 1: Develop an implementation science focused research and innovation plan to help deliver an average of 70% 10-year survival for all cancer patients in Europe by 2035

This will be achieved by:

- **Setting yearly stretch targets** informed by data intelligence to accomplish **a step-change in cancer research** to address the **research gaps and cancer inequalities** that exist across Europe.
- Creating by 2023 a **European "Cancer Tracker,"** a patient- and citizen- facing research tool **to capture baseline parameters** such as stage at diagnosis, treatment delivered, lifestyle behaviours, comorbidities, social- economic, quality-of-ife and mortality data
- Deploying the Cancer Tracker to **benchmark and monitor** the impact of cancer research and **identify exemplars of best practice** that may be applied across Europe to help deliver the 70:35 Vision.

Essential Recommendation 2: 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 from advances in cancer research

This will be achieved by:

- Ensuring that cancer research and innovation are **recognised and appropriately resourced components** of National Cancer Control Plans

- Providing mechansims to **enhance cancer research capability and capacity** where it is needed

Essential Recommendation 3: 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

This will be achieved by:

- Establishing funded action plans **by 2024** that **empower transnational collaboration** by European partners **and capacity building in-region** in Central and Eastern European countries to ensure enhanced cancer research and innovation capability

Delivering the 70:35 Vision and ensuring equity in cancer research

Population-based cancer registries represent key tools that can be deployed to delineate cancer inequalities, evaluate the impact of cancer prevention research strategies and determine effectiveness of national health systems in providing the best care for cancer patients, regardless of their socio-economic status. Overall, the data we have generated emphasise that population-based intelligence is crucial to help in the precise delineation of the cancer inequalities that persist across Europe and in the development of data-informed research solutions to address these inequalities. Information on crucial factors such as stage at diagnosis, treatment delivered, lifestyle behaviours and socio-economic status, should be routinely collected nationally and shared Europe-wide, in order to both quantify their impact on survival and illuminate a pathway to narrow the inequalities divide, particularly in CEE countries.

Diverging patterns in cancer mortality between Western and CEE countries have continued to persist and - if anything – have increased over the last decade. There has been little evidence of the gap in cancer mortality being closed, though overall mortality has declined across Europe's geographic regions and countries. Our data emphasise the absolute need to prioritise cancer research and cancer control activities as rapidly as possible in Central and Eastern Europe. [Refs] Persisting unfavorable patterns in exposure to major cancer risk factors, including mainly tobacco, alcohol, and aspects of diet, together with residual environmental disadvantages explain part of the persistent gap.[236-238] 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, [239] a deficit which must be addressed as a matter of urgency. Ensuring

equitable cancer research activity across Europe is also critical, particularly given that research-active hospitals and cancer centres achieve better cancer outcomes than those which do not prioritise research within their remit.

Another area that our research has uncovered as crucial to a robust European cancer research agenda is data – and more specifically turning that data into intelligence to inform European cancer research priorities. Use of near real time data is crucial – we must ensure that the data that drive our research and innovation and their translation into benefit for cancer patients are available and analysed in a timely fashion, such that up-to-date data intelligence informs our research and innovation efforts.

4.3. Plugging the gaps in European cancer research and its funding

Essential Recommendation 4: 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

This 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 and colorectal*
- ***Investing 50% more in radiation oncology and surgical oncology research*** *to redress the lack of research funding in tehse two critical areas of cancer care*
- **Embedding socio-economic, health policy and systems** research into European cancer research, particularly in clinical research activities
- ***Doubling implementation science and outcomes research capacity*** *dedicated to cancer to ensure that research breakthroughs are translated more rapidly into clinical, societal and/or economic benefit*

<u>Addressing the cancer research expenditure gap</u>

Our analysis indicates that the total amount of non-pharma investment in cancer research in Europe is approximately €20-22B (2010-2019). The minimum equivalent figure for the USA over the same time period, sourced from the ICRP database, was $80.5B (around €76B), an almost 4 fold difference. Looking at investment per head shows an even wider gap - for Europe, the figure over this period was ~ €26 per head, a logfold lower than the US investment (minimum €234 per head). There is an urgent need to make significant additional investment in cancer research in Europe, in order

to narrow the overwhelming gap in spend per head between two international powerhouses of cancer research. So what is possible in terms of an uplift in cancer research spend? The UK's National Cancer Research Institute (NCRI) has tracked cancer research investment by UK funders since 2002;[240] the initial reported investment of £298m in 2002 doubled to £601m by 2011. The average annual UK increase in investment was approximately 5% until 2019.

Efforts to increase investment may however be stymied by the impact of the pandemic on cancer research funders, particularly the charitable sector, whose available funds to support cancer research have, and will be badly affected by the pandemic. [241] Recent analysis by the NCRI (UK) showed that in 2020/21, funding for UK cancer research dropped by 9% and fewer new cancer research projects were funded. [242]

Ensuring cancer research activities prioritisation for all Europeans

Our data intelligence indicates that European cancer research is largely dominated by discovery science, including biomarker research, and research into systemic therapy **(Table 5).** The emergence of translational cancer research as a major domain in the 2000's[243] has tended to 'capture' European cancer research, including public sector-funded research, within a more private-sector driven discovery science and biopharmaceutical paradigm) [244] Whilst there is considerable country-to-country differences by research domain, Europe is particularly strong (committed) in clinical trials, driven by research into targeted (systemic) therapies and, although volumetrically low, Europe has also made significant strides in driving forwards quality-of-life research activity **(Table 5),** a direction of travel to be welcomed.

However, surgery and radiotherapy, currently the most effective treatments we have to control cancer, have a significant number of countries under-committing to these research domains (surgery: Denmark, Finland, Portugal; radiotherapy: Greece, Israel, Finland, Czech Republic, Portugal, **(Table 5)**)**.** This direction of travel appears to be global, [245] with discovery science and biopharmaceutical research becoming the dominant spheres of cancer research, irrespective of income group.

Health systems research and implementation science

Healthcare systems are faced with the continual challenge of ensuring high-quality discovery science and applied research ultimately influences practice. It can take 17-

20 years to get clinical innovations into practice; <50% ever make it to the clinic. The answer for improving this damning statistic is through greater investment in implementation science – the second translational gap - which seeks to test strategies to enhance clinical innovation adoption, by considering health system dynamics and actors (patients, clinicians, providers, policy environment, industry) which could impede or facilitate evidence adoption, deploying this intelligence to ensure clinical- and population-level implementation of research discoveries. Allied to this requirement for a bigger focus on implementation is the need to have access to intelligence to inform the implementation. We are entering an era where RWE will be crucial to drive the implementation of innovation, so we must ensure that Europe has sufficient digitally maturity to collect, analyse and link these data to inform the rapid adoption of research and innovation within cancer health systems.

Implementation research in cancer prevention: a crucial need

There are evidence-based and cost-effective preventive interventions available for cancer. The current privileged focus on cancer treatment is not a cost-effective cancer control policy, unless 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 critical research areas - cancer prevention and implementation science research would yield significant return on investment. A more systematic and structured approach to cancer prevention in Europe would have a major impact at the public health, societal and economic level.

Ensuring cancer research is concentrated in areas of specific need

The landscaping mapping that we have performed in this *Lancet Oncology Commission* has shone a data-enabled light on European cancer research activity over the last twelve years prior to the COVID-19 pandemic. The results we have revealed through this data-driven approach reflect a mixed picture. 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 CEE region. There has been huge increases in cancer discovery science and biopharmaceutical-centred research, placing individual countries and, collectively, 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 which 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 which are affordable and equitable. The cancer research archaeology that we have defined provides objective data for considering today's 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.

Essential Recommendation 5: European cancer research funders and the European cancer research community must mitigate the impact of Brexit on European cancer research

- 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

The data generated clearly indicate a significant gap between research outputs from EU28 (including the UK) and EU27 (excluding the UK), one that is extremely unlikely to be bridged by increased research activity from the remaining EU27. Disappointingly, at time of writing, 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.

Essential Recommendation 6: The European cancer research community must develop proactive mechanisms to enhance gender equality in cancer research

This will be achieved through:

- ***Increasing female first authorship*** *of cancer research publications* ***to 45%*** *by 2027*
- ***Increasing female lead authorship*** *of cancer research publications* ***to 40%*** *by 2028*
- ***Increasing female leadership*** *of cancer research programmes* ***to 40%*** *by 2027*

Our data on female first and last author cancer research publications from European researchers clearly illustrate the significant gender gap that exists in the European cancer research community. While both CEE and Nordic countries show better gender ratios in first and last author publications, the performance by cancer research

powerhouses such as Germany is disappointing. A similar gender disparity is seen in cancer research leadership as judged by successful competitive research funding. Delving deeper into the reasons for better performance in terms of gender balance in certain European countries/regions and developing mitigation strategies based on this intelligence will hopefully improve the gender balance in cancer research outputs and cancer research leadership in Europe. This could be assisted by embedding programmes that provide formal leadership training for women within both research and the oncology workforce.

Essential Recommendation 7: European cancer funders and policy makers must mandate a step change in cancer prevention, cancer screening and early cancer detection research in order to reduce the burden of cancer for European citizens

This will be achieved by:

- *Delivering by 2023 a **research-informed approach to eliminate HPV-driven cancers** and other diseases caused by HPV by 2030*
- ***Monitoring exisiting screening programmes** against agreed performance metrics and **embedding new technological developments** to enhance the detection of cancer at its earliest stage*
- ***Introducing new screening programmes e.g. lung by 2023***
- *Ascertaining by 2024 through **behavioural research the barriers/reasons for lack of participation in cancer screening programmes across Europe**, with particular focus on underserved populations*
- *Developing **new approaches to facilitate early detection** of cancer, including the use of liquid biopsies*

<u>The need for research to eliminate HPV-driven cancers</u>

In 2019, E.C.O.'s Focussed Network on HPV launched a resolution to achieve the elimination of cancers caused by HPV. Critically, this included supporting research priorities such as new vaccine and screening technologies as well as new care and treatment modalities. More research is needed to improve the early detection of non-cervical cancers caused by HPV. Research is also required relating to the vaccination of women found to be HPV-positive at cervical cancer screening, as this could provide a potential pathway way to interrupt viral transmission in the community.

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 demonstrate what can be achieved when countries

work together to achieve a major public health goal. Action across the European region to deliver a research-informed approach to eliminate HPV-driven cancers and other diseases caused by HPV has the potential to save hundreds of thousands of lives and improve the quality-of-life of many more.

Advances in cancer screening research

Since the 2003 Council recommendations on cancer screening, a number of scientific/ technological developments have emerged in breast, colorectal and cervical cancer screening. These include new screening tests, such as full field digital mammography, or supplemental magnetic resonance imaging (MRI) in women with extremely dense breast tissue, faecal immunological test and/or endoscopy for colorectal screening and HPV testing for cervical cancer screening.[246,247] Implementing these new research innovations within screening programmes is proceeding apace. We view the development of risk-adapted screening approaches, particularly ones incorporating distinct strategies according to risk profile of screened individuals, making use of the latest technological developments, as a critical component of 21st century screening programmes, in order to accelerate earlier cancer diagnosis for European citizens.

New approaches to cancer early detection

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. [248,249] Cervical cancer early diagnosis is also being enhanced by the provision of self/home-based screening tests. FIT for colorectal cancer screening helps reduce the invasiveness of the procedure, which translates into a significant improvement in screening adherence. A significant new development has been the use of liquid biopsies, where detection of circulating cancer cells or tumour DNA in blood can underpin the early diagnosis of multiple cancers. [250] Combining this with multi-cancer detection approaches represents a significant opportunity to underpin more accurate early diagnosis.[ref]

Research on behavioural considerations in cancer screening and cancer detection

Crucially for all approaches to enhance screening, early detection and accurate cancer diagnosis, we need to understand in more detail from a behavioural perspective why

a European citizen does or doesn't attend their scheduled screening appointment, does or doesn't come forward with suspicious symptoms, does or doesn't engage with cancer patient pathways. Research to understand behavioural choice, cultural constraints and previously unrecognised barriers, particularly for disadvantaged/ underserved communities is critical to move the dial and enhance the early diagnosis of cancer across Europe.

Recommendation 8: European cancer funders and policy makers must establish an evidence-informed, research and innovation driven EU Network of Comprehensive Cancer Centres that aims to:

(A) Reduce inequalities in cancer diagnosis, care and access to clinical trials

(B) Strengthen the quality of translational, clinical and outcomes research in cancer in Europe

(C) Integrate clinical care and research to achieve better outcomes

This will be achieved through:

- *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 an EU Network of Comprehensive Cancer Centres, to be **completed by 2023***
- *Placing a focus on **posing and 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*

The European Commission is currently addressing the question of inequalities in a number of ways. Some are to map research capabilities and capacities. Others are to foster collaborations in smaller groupings, for instance twinning cancer centres in widening participation countries with more established CCCs or fostering team science. A third arm is to create an EU network of certified CCCs, and to build research capacities and capabilities in MSs. But at the moment such initiatives lack hard evidence as to whether managed processes of spreading resource will deliver better science for the benefit of cancer patients Europe-wide. Our data capture the impact both individually and collectively that CCCs are having, emphasising the benefits of a network approach. Integration within and between CCCs needs to be achieved at multiple levels. For governance, a critical component is a CCC Board, bringing together cancer research leaders with clinical leads in cancer and patient advocates. OECI has recently published guidance to establish an effective governance framework, [251] At an organisational level, researchers need to be integrated with

clinical colleagues; formally through programme structures, or through multi-disciplinary teams; informally, through colloquia, regular meetings and 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

Comprehensive Cancer Infrastructures and inequalities

A critical component of this Comprehensive Cancer Infrastructures approach will be addressing the inequalities that are being experienced across Europe, in diagnosis, in treatment and care, and in access to clinical trials. A crucial infrastructural need to help achieve this goal is the strengthening of the quality of translational, clinical and outcomes research/implementation science and ensuring that they are integrated with clinical care delivery. Research indicates that patients who are diagnosed and treated in specialist cancer centres (including, but not limited to, CCCs) have better access to advanced diagnosis and therapy, and to clinical trials, reflected in better outcomes than those patients treated in general hospitals. [252] Europe's Beating Cancer Plan aims to ensure that 90% of eligible patients have access to CCCs by 2030. Currently, a number of MSs have no accredited CCCs and many do not yet have regional/local networks linking cancer research and care, organised around CCCs. A mapping exercise in 2017, performed as part of the EU Joint Action on Rare Cancers, [253] showed that only 13 MSs had Cancer Networks covering the whole country.

Development of an EU 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. Additionally, in order to have maximum reach within countries as part of the envisaged infrastructure, effective local cancer networks will be required, supplemented by extended multi-disciplinary teams and digital and video-consultation infrastructure A variety of funding sources could be deployed to help support the establishment of this EU Network of Comprehensive Cancer Centres.

Strengthening research excellence will also require collaborative infrastructures across Europe, drawing on different aspects of the Cancer Mission and the European Beating Cancer Plan

Essential Recommendation 9: As a matter of urgency, European cancer funders and policy makers must establish a European Cancer Survivorship Research and Innovation plan and ensure its implementation, in order to address the research gaps, that if solved, would help enhance the lives of the 20 million European citizens living with and beyond cancer

This will be achieved by:

- *Ensuring a **research-enabled focus** on the **medical, socio-economic 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/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*

Embedding cancer survivorship research

As already highlighted, 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 beyond cancer. However, as indicated in E.C.O's European Code of Cancer Practice, ~20 million Europe citizens have survived cancer[254] and it is incumbent upon the European cancer community to significantly enhance our engagement with cancer survivors and promote and instigate a cancer survivorship research agenda, in order to ensure that the specific challenges and needs of those living 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 cancer patient must have a survivorship care plan, underpinned by research. [255] A recently published study highlights the importance of capturing detailed European data on cancer care and quality-of-life for cancer survivors

Interdisciplinary survivor-centred research must be promoted and should include development of new tools to facilitate survivorship research. To ensure an international dimension, the European Cancer Survivorship Research and Innovation Plan should be designed and pursued in collaboration with international partners. The paucity of specific research programmes for childhood, 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 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.

The challenges, potential solutions and recommendations that we articulate build on previous work of the EACS, emphasising the key challenges and solutions to ensure that cancer survivorship research and innovation is firmly embedded within the European cancer research agenda. As part of our recommendations, we call for establishment of a European Cancer Survivorship Research and Innovation Plan to ensure a research-informed approach for those living with and beyond cancer. Additionally, in order to ensure that the 20 million voices are heard, we call for establishment of a European Cancer Survivorship Day.

Responding to current and future challenges

Essential Recommendation 10: The European cancer research community must accelerate the research response to the indirect impacts of the COVID-19 pandemic on cancer, with particular emphasis on the deployment of accurate, timely cancer intelligence for patient benefit

This will be achieved by:

- *Building on the work of the European Cancer Organisation on the **7-Point Plan** and the **Data Navigator** to mitigate the impact of COVID to establish by 2023 a **near real time dashboard** that captures and quantifies the impact of the COVID-19 pandemic on all aspects of the cancer pathway, on clinical trials participation and on the cancer workforce*
- *Deploying this intelligence to **inform research interventions to mitigate** current and future impacts of the pandemic*

The COVID-19 pandemic and the associated disruptions to cancer systems have dramatically affected cancer screening and early detection. In the context of its *Time To Act* campaign on the impact of COVID-19 on Cancer, we estimate that 100 million cancer screening tests were not performed in Europe, while urgent referrals of suspected cancer patients were cut by up to half. As a result of this cancer backlog, 1 million cancer patients could be undiagnosed in Europe. At national level, as shown by the 'Cancer and COVID-19 Data Navigator',[256] the impact of the pandemic on cancer screening programmes has exceeded 70% in several European countries,

such as Austria, Belgium, Czech Republic and Poland. Importantly, these disruptions are expected to lead to significant future excess mortality from cancer. All these data indicate that urgent action must be prioritised to advance cancer screening/early detection across Europe, clearing the COVID-19-associated backlog and tackling pre-existing deficiencies to ensure a lower cancer burden in Europe moving forward.

COVID and the political narrative

More broadly, the COVID-19 pandemic has focussed 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, 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 have tended to drive the political narrative of European cancer research, divorced from discussions of value and affordability. There has been a relentless narrative about innovation in cancer research, without wider consideration of research into the enabling environment, i.e. research translation into clinical practice, services, systems and policy. In the meta-pandemic era, 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; 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 impact of the COVID-19 pandemic has resulted in an unprecedented economic contraction in 2020, with EU real GDP falling by 6.1%, more than 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 a significant indirect contributing factor to poorer outcomes. Why? It is clear from a wide variety of research outputs over the last 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. Why is this important for patient outcomes? Because improving patient outcomes is critically empowered by a research-active health system that supports a

wide range of fundamental/discovery and applied cancer research and their transition into patient-centric translation.

COVID and health systems' resilience

Aside from strategic questions about where Europe should now focus, COVID-19 has exerted a further downward pressure on cancer services and systems across Europe. The OECD report Health at a Glance: Europe 2020[257] reflects the fact that many European countries were 'burning hot' (i.e. over-capacity) even prior to the pandemic. Critically, there was no capacity to expand or headroom to absorb systemic shocks. 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. **(Box 19)** Routine referrals during the pandemic collapsed in most European countries, meaning that fewer cancers were detected and that those that are eventually detected are at a later stage, meaning worse prognosis. In addition to directly worsening outcomes, this will lead to sicker, more advanced cancer patients needing treatment which has a higher care burden, which, when added to an already overheated system, is likely to indirectly worsen overall patient outcomes. Such systemic effects have two downstream impacts on research. The first is to reduce the headroom for clinical cancer research, as capacity and funding are potentially diverted into routine care; the second is a political-policy mismatch. This is why the over-focus on discovery science and biopharmaceutical research does not lead to better population outcomes. If the pandemic has had the damaging impact that the data intelligence suggest, then Europe will see a significant decline in its 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 critical 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 performed in Europe (and must continue to be delivered going forward), into improved outcomes for patients and make a significant contribution to healthier and more productive societies. Despite the negative impacts that have been all-pervading, it is critical that we redouble our efforts to ensure that cancer does not become the forgotten "C" in the fight against COVID.

Essential Recommendation 11: As a matter of extreme urgency, the European cancer research community must investigate how research can help mitigate the impact of the war in Ukraine on cancer

- *Building on the work of the European Cancer Organisation – American Society of Clinical Oncology (E.C.O – ASCO) Special Network on the Impact of the War in Ukraine on Cancer, immediately collecting **monthly data on the impact of the conflict** on patients, cancer services, medicines and other shortages, workforce gaps, in Ukraine and in neighbouring countries.*
- *Based on our data on the current significant impact on cancer clinical trials in both Ukraine and Russia, developing a plan by 2023 on how best to **mitigate the impacts of the conflict on cancer clinical trials activity across Europe***

The Clinical Cancer Research Dilemma

Clinical cancer research finds itself in unchartered territory. The conflict-induced loss of cancer centres which are such major recruiters to global RCTs will have a significant impact. Many major clinical trials will be delayed, as new centres of varying capacity are incorporated and some will undoubtedly fail to recruit. Many of the cancer trials in the Ukraine also had participation of major centres in CEE countries such as Romania (**see Table 14**). If such trials are stopped, this will further reduce infrastructural investment and debilitate cancer clinical trial activity in CEE countries. More long term, it is not clear whether industry will consider it too high risk to place cancer clinical research in CEE 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 CEE. Whilst this is understandably not the major focus for the European Commission at this moment of writing, it is clear that for the Cancer Mission to succeed, it will require that these externalities, which fall heaviest on CEE countries, are central to informing strategic planning and funding going forward.

Essential Recommendation 12: 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 and Middle Income Countries

This 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-and Middle-Income Countries*
- *Developing innovative funding mechanisms to encourage **a 50% uplift by 2024** in support for joint research between European and Low-and Middle-Income Countries*

- ***Doubling collaborative research activity** between Europe and Low-and Middle-Income countries **by 2027***

While 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 significantly increase cancer research collaborations between Europe and the Rest of the World, in particular co-creating a broad portfolio of research activities across the LMIC continuum, where without immediate action nearly 70% of global cancer deaths will occur by 2040.[14] Currently, we collectively devote <4.5% of our cancer research to activities with LMICs, 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 LMICS face.

Reimagining cancer research and its implementation in Europe: A Call To Action

It has been a difficult two and a half years for the European cancer community as it sought to deliver optimal cancer care and produce high-quality cancer research under unprecedented pressures as COVID-19 ravished our society. But the pandemic has also highlighted our lack of resilience, prompting much reflection on whether the ways in which we delivered cancer care and research pre-COVID best served our citizens, patients and society. While getting back to normal was frequently invoked, it quickly became clear that normal wasn't good enough. A new normal emerged as the direction of travel with the oft-quoted wish to "build back better" pervading many parts of society. In cancer research, there is an unrivalled opportunity to embrace this "build back better" option. In this *Lancet Oncology Commission*, we position the European Groundshot and its Essential Recommendations within a Call to Action to "Reimagine Cancer Research and its Implementation In Europe". The research response to COVID 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 us to a better place, as citizens, as patients and as societies. Follow the science, Follow the Data has become our modus operandum. We now have the opportunity to deploy a similar approach in cancer as we have done with COVID.

Reimagining cancer research and its robust implementation provides us with an opportunity to think differently, to embrace a more team science approach, to nurture true innovation, and to be unencumbered by barriers or pressure points that would previously have prompted paralysis. While the intelligence that we have generated has highlighted the particular challenges that we face in Central and Eastern Europe, a focus on research capacity building, directed funding and twinning approaches to enhance cancer research activity, its quality and its implementation in CEE countries has 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 *Lancet Oncology Commission*, we can start to reimagine a more equality-focussed, people-centred, data-enabled cancer research ecosystem that mandates that the best science and most promising innovation are delivered at pace and at scale so that our 70:35 Vision is delivered by 2035.

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The pandemic shows the importance of co-ordination among European countries to protect people's health, both during a crisis and in normal times when we can tackle underlying health conditions, invest in strong health systems and train the healthcare workforce. The European Health Union will improve EU-level protection, prevention, preparedness and response against human health hazards."

Box 1: Conclusions of the Conference on the Future of Europe[64]

Flagship Initiative 1: A new Knowledge Centre on Cancer
Flagship Initiative 2: The European Cancer Imaging Initiative
Flagship Initiative 3: Eliminate cervical cancer and other cancers caused by human papillomaviruses
Flagship Initiative 4: Europe's Beating Cancer Plan will put forward a new EU-supported Cancer Screening Scheme
Flagship Initiative 5: An EU Network linking recognised National Comprehensive Cancer Centres in every Member State
Flagship Initiative 6: The new 'Cancer Diagnostic and Treatment for All' initiative,
Flagship Initiative 7: Alongside the 'Genomic for Public Health' project, the European Initiative to Understand Cancer (UNCAN.eu)
Flagship Initiative 8: Funded by the EU4Health programme, the Commission will launch the 'Better Life for Cancer Patients Initiative'
Flagship Initiative 9: In 2021, the Commission will establish a Cancer Inequalities Registry.
Flagship Initiative 10: In 2021, the Commission will launch the 'Helping Children with Cancer Initiative'

Box 2: The ten Flagship Initiatives of the European Beating Cancer Plan

Specific Objective 1: Improve the understanding of cancer
1.1 Establish the 'UNCAN.eu' platform
1.2 Better understand healthy versus cancer cells at individual and population level
1.3 Better understand cancer-patient molecular, cell, organ, organismal interactions
1.4 Determine the role of genetics in cancer

Specific Objective 2: Prevention including screening and early detection (prevent what is preventable)
2.1 Develop a one-stop cancer information centre on prevention
2.2 Boost research and innovation into risk assessment
2.3 Conduct implementation research on cancer prevention
2.4 Establish synergies on prevention with other missions
2.5 Optimise and improve access to existing screening programmes
2.6 Develop new methods and technologies for screening and early detection
2.7 Develop early predictors/tests

Specific Objective 3: Optimise diagnostics and treatment
3.1 Support the creation of a Network of Comprehensive Cancer Infrastructures (CCIs)
3.2 Develop twinning programmes
3.3 Develop a clinical trial programme on diagnostics
3.4 Develop a clinical trial programme on treatments

Specific Objective 4: Support quality of life
4.1 Collect and analyse data on today's unmet needs of cancer patients and survivors
4.2 Set up of the European Cancer Patient Digital Centre
4.3 Develop early predictors for quality of life
4.4 Design monitoring programmes for survivors of childhood cancer

Box 3 Specific Objectives and Activities of the EU Cancer Mission[66]

- Ensure equity and access to knowledge, research and care
- Promote innovation.
- Allow for risk taking
- Work with “the coalition of the willing”
- Communication and citizen engagement

Box 4 Guiding principles of the Cancer Mission

i. ***Article 1***
The right of every European citizen to receive the most accurate information and to be proactively involved in his/her care.

ii. ***Article 2***
The right of every European citizen to optimal and timely access to appropriate specialised care, ***underpinned by research and innovation.***

iii. ***Article 3***
The right of every European citizen to receive care in health systems that ensure improved outcomes, patient rehabilitation, best quality of life and affordable healthcare.

Box 5 The European Cancer Patient's Bill of Rights[74]

Cancer Control
Establish a European Centre for Cancer Control
Implement the relevant policy recommendations produced by EPAAC and CanCon

Cancer Registries
Develop mechanisms to promote increased registration of cancer incidence, prevalence and mortality across Member States

Multidisciplinary Teams(MDT)
Promote patient-centred MDT cancer care delivery as the Standard of Care

Cancer Health Literacy
Make cancer health literacy a patient–enabled European public health priority
Develop European cancer patient navigation pilot projects

Screening and Early Diagnosis
Remove educational and socio-economic barriers for European citizens in accessing cancer screening programmes

Access to optimal care
Issue guidelines on optimal radiotherapy capacity(equipment/manpower) in Europe
Provide patients with accurate surgical oncology activity data to allow informed decision-making on choice of accredited hospital/cancer centre

Identify and catalogue cancer medicine shortages to inform future healthcare policies
Facilitate access to life-preserving and life-enhancing therapeutic interventions through a harmonised European Health Technology Assessment (HTA)

Cancer Survivorship and patient rehabilitation
Develop an integrative EU Cancer Survivorship Plan
Protect cancer survivors from employment discrimination

Box 6 Recommendations from the Europe of Disparities Initiative[75]

Our aim is to reach 70% survival on average beyond 10 years for all European citizens by 2035, improving both the length and quality of cancer patients' survival

This "70:35 Vision" will be addressed by:

Sharing and implementing good practice in cancer diagnosis and care. An actively managed, systematic approach to identifying and sharing good practice in cancer control and the best available cancer care across European countries and regions is needed. We envisage that this process by itself would raise long term patient survival from an average of about 50% to around **60%**, which is already being achieved in certain European countries.

More intense research and innovation in discovery, translational, clinical and health-related cancer sciences. If at the same time as sharing and establishing good clinical cancer practice, we also sustain and increase the intensity of research and innovation and the rapid translation of this research and innovation into clinical practice, there is the real potential for a further increment in long-term survival towards **70%** and improvement in both quality of life and the patient experience.

Box 7 The 70:35 Vision: Achieving an average of 70% long term survival by 2035[77]

Europe	All countries contained within the continent between Asia & the Atlantic Ocean: the Ural Mountains & the Ural River are generally considered the Eastern boundary (en.wikipedia.org/wiki/Europe)
Central & Eastern Europe	Bulgaria, Romania, Czech Republic, Hungary, Poland (our scope excludes Moldova, Ukraine, Belarus and Russia which also belongs in this UN category)
European Union (EU)	Political and Economic Union of 27 Member States. 447 milion population (5.8% global population) (en.wikipedia.org/wiki/European_Union)
WHO EURO region	Countries that are formally managed by EURO office of World Health Organisation (en.wikipedia.org/wiki/List_of_WHO_regions)
EU-15	EU countries pre-2004 Austria, Belgium, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, Netherlands, Portugal, Spain, Sweden, UK (left EU 2021)
EU-13	All EU countries that joined after 2004, including all Central and Eastern European EU countries

Box 8 Definitions of Europe deployed in this Lancet Oncology Commission

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/discovery science

3. A University partnership as part of the Centre, or strong University and Research Institute links

4. Extensive international networking in research and clinical trials • Educational programmes for clinicians, researchers and patients

Box 9 Definition of a Comprehensive Cancer Centre[117]

To *"establish, by 2025, an EU Network linking recognised National Comprehensive Cancer Centres in every Member State. The EU Network will enable the uptake of quality-assured diagnosis and treatment processes, including training, research and clinical trials. This cross-border collaboration of Centres will improve patients' access to high quality diagnostics and care including the latest innovative treatments. The Plan aims to ensure that 90% of eligible patients have access to such Centres by 2030".*

Box 10 Flagship Initiative 5 of Europe's Beating Cancer Plan[118]

Box 11 The European Parliament, in its resolution on vaccine hesitancy adopted in 2018, welcomed *"the encouraging progress made in the fight against HPV diseases and cancers thanks to vaccination programmes against the HPV virus' and called on Member States 'to further develop these programmes and explore ways to increase coverage rates and prevent other forms of cancer, for example by including boys in vaccination programmes.*

Box 11 European Resolution on Vaccine Hesitancy[187,188]

1. You have a right to equal access to affordable and optimal available cancer care, including the right to a second opinion.
2. 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.
3. 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.
4. You have a right to receive care from a specialised multidisciplinary team, ideally as part of a cancer care network.
5. You have a right to participate in Shared Decision-Making with your healthcare team about all aspects of your treatment and care.
6. You have a right to be informed about ongoing research relevant to you, and your ability and eligibility to participate in research.
7. You have a right to discuss with your healthcare team your priorities and preferences to achieve the best possible quality of life.
8. You have a right to receive optimal supportive and palliative care, as relevant, during any part of your cancer journey.
9. You have a right to receive and discuss with your care team a clear, managed and achievable plan for your survivorship and rehabilitation.
10. 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.

Box 12: The 10 Rights of the European Code of Cancer Practice[207]

1) You have a right to equal access to affordable and optimal available cancer care, including the right to a second opinion.
Patients are encouraged to enquire as to whether their hospital/cancer centre delivers good quality clinical cancer practice as defined by clinical guidelines and whether their outcomes are compatible with national or international standards.

2) 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.
Patients and their care givers must receive clear and compassionate communication, with recommendations for how they may prepare for a medical consultation

3) 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.
Patients need to have access to information about the quality of the cancer service providing their treatment

4) You have a right to receive care from a specialised multidisciplinary team, ideally as part of a cancer care network.
Cancer care must be delivered by a specialised multidisciplinary team, bringing together wide-ranging expertise, including cancer research, and linked through frameworks such as Cancer Care Networks to the wider health system

5) You have a right to participate in Shared Decision-Making with your healthcare team about all aspects of your treatment and care.
Shared Decision Making must be supported, where the professional explains the options and recommendations of their multidisciplinary team, but the decision is taken by the patient in consultation with the health professional.

6) You have a right to be informed about ongoing research relevant to you, and your ability and eligibility to participate in research.
This is a critical part of the European Code of Cancer Practice and aligns with the ethos and activities of the *Lancet Oncology European Cancer Groundshot Commission.* Cancer research must be an integral component of delivering better cancer outcomes for patients and contribute to improved patient experience and better quality of life.

7) You have a right to discuss with your healthcare team your priorities and preferences to achieve the best possible quality of life.
Improved quality of life should be paramount, both during and following treatment, including consideration of the patient's emotional and social well-being. Research in this area must be enhanced to deliver for those living with and beyond cancer.

8) You have a right to receive optimal supportive and palliative care, as relevant, during any part of your cancer journey.
Close integration should occur between oncology and palliative care services, supporting delivery of early palliative care to enhance patient symptoms and quality of life, reduce hospital admissions and potentially, improve patient survival.

9) You have a right to receive and discuss with your care team a clear, managed and achievable plan for your survivorship and rehabilitation.
The 20 million cancer survivors in Europe require support to ensure that they can return to as many of the activities of normal living as possible. Each patient should have a survivorship care plan that clearly articulates the requirements for their support, including the need for cancer research in this often overlooked domain.

10) 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.

Re-integration into normal life and the workplace is critically important to those living beyond cancer. Cancer survivors should be free of any discrimination that arises as a consequence of their disease.

Box 13: The 10 Rights of the European Code of Cancer Practice (expanded version) [207]

- Cancer survivors' follow-up, late effect management and tertiary prevention needs to be anticipated, personalized and implemented into care pathways, with active participation of survivors and relatives.
- Improvement of early detection of patients' needs and their access to rehabilitation, psychosocial and palliative care services is required.
- An integrated and multiprofessional care approach with a coordination of community care providers and services are needed to implement a survivorship care plan that enhances patient's self-management and quality-of-life

Box 14: Adopting a new approach for cancer survivors[216]

- The Medical Cancer Survivorship Research and Innovation Pillar
- The Socio-economic Cancer Survivorship Research and Innovation Pillar
- The Politico-Legal Cancer Survivorship Research and Innovation Pillar

Box 15 The three Cancer Survivorship Research and Innovation Pillars

Challenges within the Medical Cancer Survivorship Research and Innovation Pillar
Challenge 1.1: Insufficient integration of cancer survivorship research within overall cancer research activity in Europe
Challenge 1.2: Lack of a European Cancer Survivorship Research and Innovation Plan
Challenge 1.3: Lack of robust data intelligence to underpin cancer survivorship research prioritisation
Challenge 1.4: Research activities often do not underpin cancer survivors' needs
Challenge 1.5: Lack of integration of patients into the research and innovation agenda, with limited active involvement in survivorship research
Challenge 1.6: Limited interdisciplinary research activity in the survivorship domain and a paucity of survivorship research tools
Challenge 1.7: Lack of appreciation of the potential value of the international collaborative research dimension
Challenge 1.8: Paucity of specific research programmes for children, adolescents and young adult survivors
Challenge 1.9: Lack of focus on Palliative/End of Life research
Challenge 1.10: Improve cancer survival such that an average of 70% survival is achieved across Europe by 2035 (the 70:35 vision)

Box 16: Delineating the Challenges within the Medical Cancer Survivorship Research and Innovation Pillar

Challenges within the Socio-Economic Cancer Survivorship Research and Innovation Pillar

Challenge 2.1: Lack of detailed knowledge of the specific social determinants of cancer inequalities that impact on cancer survivorship

Challenge 2.2: Paucity of relevant tools to assess Quality of Life in cancer survivors

Challenge 2.3: Lack of accurate robust data on the economic burden of cancer for cancer survivors

Challenge 2.4: Paucity of data on the impact and cost effectiveness of interventions for cancer survivors

Challenge 2.5: Lack of financial support for cancer survivorship research at European level

Challenge 2.6: Limited integration of social issues into cancer survivorship research activities

Box 17: Delineating the Challenges within the Socio-Economic Cancer Survivorship Research and Innovation Pillar

3. Challenges within the Politico- Legal Cancer Survivorship and Innovation Pillar
Challenge 3.1: Limited detailed intelligence on the legal aspects of discrimination for cancer survivors
Challenge 3.2: Lack of research on the legal aspects of reintegration of cancer survivors back into society
Challenge 3.3: Paucity of research that specifically focusses on the activities and requirements of Cancer Patient Advocacy Groups
Challenge 3.4: Lack of knowledge of the stigma associated with cancer
Challenge 3.5: Lack of specific research on survivorship support for patients and for patient empowerment

Box 18: Delineating the Challenges within the Politico-Legal Cancer Survivorship Research and Innovation Pillar

Public finances have taken a considerable hit and fiscal divergence between Member States has increased. Deficit and debt ratios have soared in all Member States. High debt ratios are expected to persist, remaining above pre-pandemic levels over the next decade. This will have major contraction impacts on cancer research especially in Central and Eastern Europe.

The COVID-19 crisis has aggravated a number of pre-existing vulnerabilities. Internal imbalances related to high government and private debt have increased, driven by the recession and measures taken to address the COVID-19 crisis. Moving forward, new risks may emerge as a result of structural transformations accelerated by the COVID-19 crisis. This is likely to focus EU countries on only supporting cancer research with high return on investment e.g. biopharmaceuticals.

The challenge of boosting socioeconomic resilience has become more apparent. Less-resilient Member States, territories and sectors found it harder to withstand and respond to the crisis. Differences in resilience across the EU will have a bearing on social, economic and territorial cohesion, as well as convergence within the euro area and the effectiveness of the single monetary policy. Supporting cancer services and systems will be dissociated from research, with priority funding going into the former,

Box 19 External challenges to cancer research and its funding

Essential Recommendation 1: Develop an implementation-focused research and innovation plan to help deliver an average of 70% 10-year survival for all cancer patients in Europe by 2035.

Essential Recommendation 2: 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 from advances in cancer research

Essential Recommendation 3: 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

Essential Recommendation 4: 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

Essential Recommendation 5: European cancer research funders and the European cancer research community must mitigate the impact of Brexit on European cancer research

Essential Recommendation 6: The European cancer research community must develop proactive mechanisms to enhance gender equality in cancer research

Essential Recommendation 7: European cancer funders and policy makers must mandate a step change in cancer prevention, cancer screening and early cancer detection research in order to reduce the burden of cancer for European citizens

Essential Recommendation 8: European cancer funders and policy makers must establish an evidence-informed, research and innovation driven EU Network of Comprehensive Cancer Centres that aims to:

A: Reduce inequalities in cancer diagnosis, care and access to clinical trials
B: Strengthen the quality of translational, clinical and outcomes research in cancer in Europe
C: Integrate clinical care and research to achieve better outcomes

Essential Recommendation 9: As a matter of urgency, European cancer funders and policy makers must establish a European Cancer Survivorship Research and Innovation plan and ensure its implementation, in order to address the research gaps, that if solved, would help enhance the lives of the 20 million European citizens living with and beyond cancer

Essential Recommendation 10: The European cancer research community must accelerate the research response to the indirect impacts of the COVID-19 pandemic on cancer, with particular emphasis on the deployment of accurate, timely cancer intelligence for patient benefit

Essential Recommendation 11: As a matter of extreme urgency, the European cancer research community must investigate how research can help mitigate the impact of the war in Ukraine on cancer

Essential Recommendation 12: 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 and Middle Income Countries

Box 20 Essential Recommendations of the Lancet Oncology European Groundshot

- UNCAN.eu
- The EU Cancer Screening Scheme
- The European Health Data Space
- The European Cancer Information System
- The European Cancer Patient Digital Centre
- The European Cancer Inequalities Registry
- The European Cancer Imaging initiative
- The Partnership on Personalised Medicine
- The Cancer Survivor Smart Card
- The Inter-speciality Cancer Training Programme

Box 21 Aligning with the Cancer Mission

Prevention, Early Detection and Screening Network
HPV Action Network
Health Systems and Treatment Optimisation Network
Quality Cancer Care Network
Digital Health Network
Workforce Network
Survivorship and Quality of Life Network
Inequalities Network
Special Network: Impact of COVID-19 on Cancer
Add link to War in Ukraine network

Figure 1 The European Cancer Organisation's 10 Focussed Topic Networks

Figure 2a. Age-standardised 5-year net survival (%) for adults (15-99 years) diagnosed during 2010-2014 in Europe, by country: cancers of the oesophagus, stomach, colon, rectum, liver and pancreas

Footnote: survival estimates are ranked from highest to lowest. Where data were available for more than one registry in a given country, the survival estimates were derived by pooling the data for that country, but excluding data from registries for which the estimates were considered less reliable because 15% or more of patients were (a) lost to follow-up or censored alive within five years of diagnosis, or if diagnosed in 2010 or later, before 31 December 2014, or (b) registered only from a death certificate or at autopsy, or (c) with incomplete dates (i.e., unknown year of birth, unknown month or year of diagnosis, or unknown year of last vital status). Data with 100% coverage of the national population. § Estimate flagged as less reliable because the only available estimates were from a registry or registries in this category. † Estimate not age-standardised.

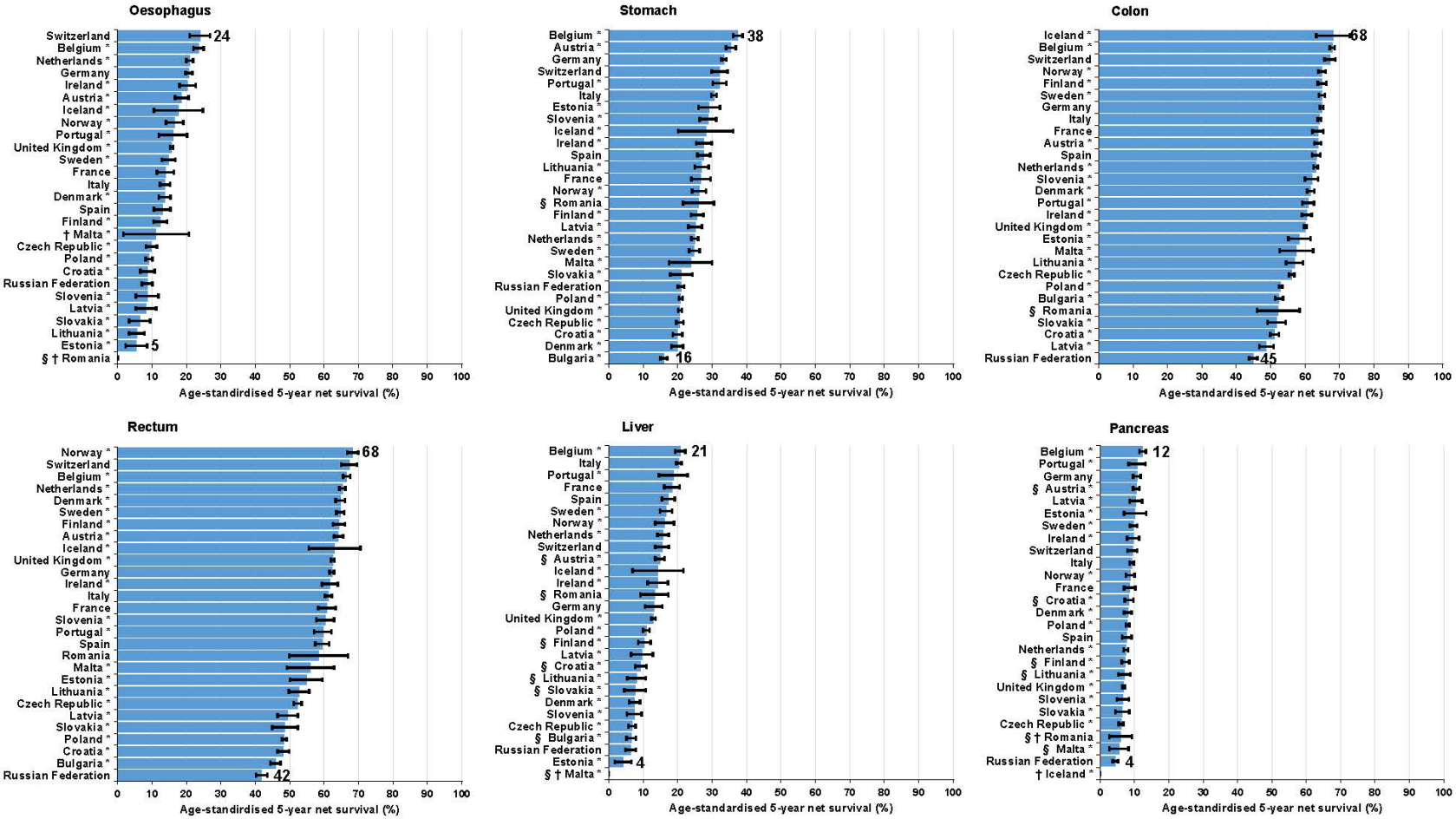
Figure 2b. Age-standardised 5-year net survival (%) for adults (15-99 years) diagnosed during 2010-2014 in Europe, by country: cancers of the breast (women), cervix, ovary and lung, melanoma of the skin, and cancer of the prostate

Footnote: survival estimates are ranked from highest to lowest. Where data were available for more than one registry in a given country, the survival estimates were derived by pooling the data for that country, but excluding data from registries for which the estimates were considered less reliable because 15% or more of patients were (a) lost to follow-up or censored alive within five years of diagnosis, or if diagnosed in 2010 or later, before 31 December 2014, or (b) registered only from a death certificate or at autopsy, or (c) with incomplete dates (i.e., unknown year of birth, unknown month or year of diagnosis, or unknown year of last vital status). Data with 100% coverage of the national population. § Estimate flagged as less reliable because the only available estimates were from a registry or registries in this category. † Estimate not age-standardised.

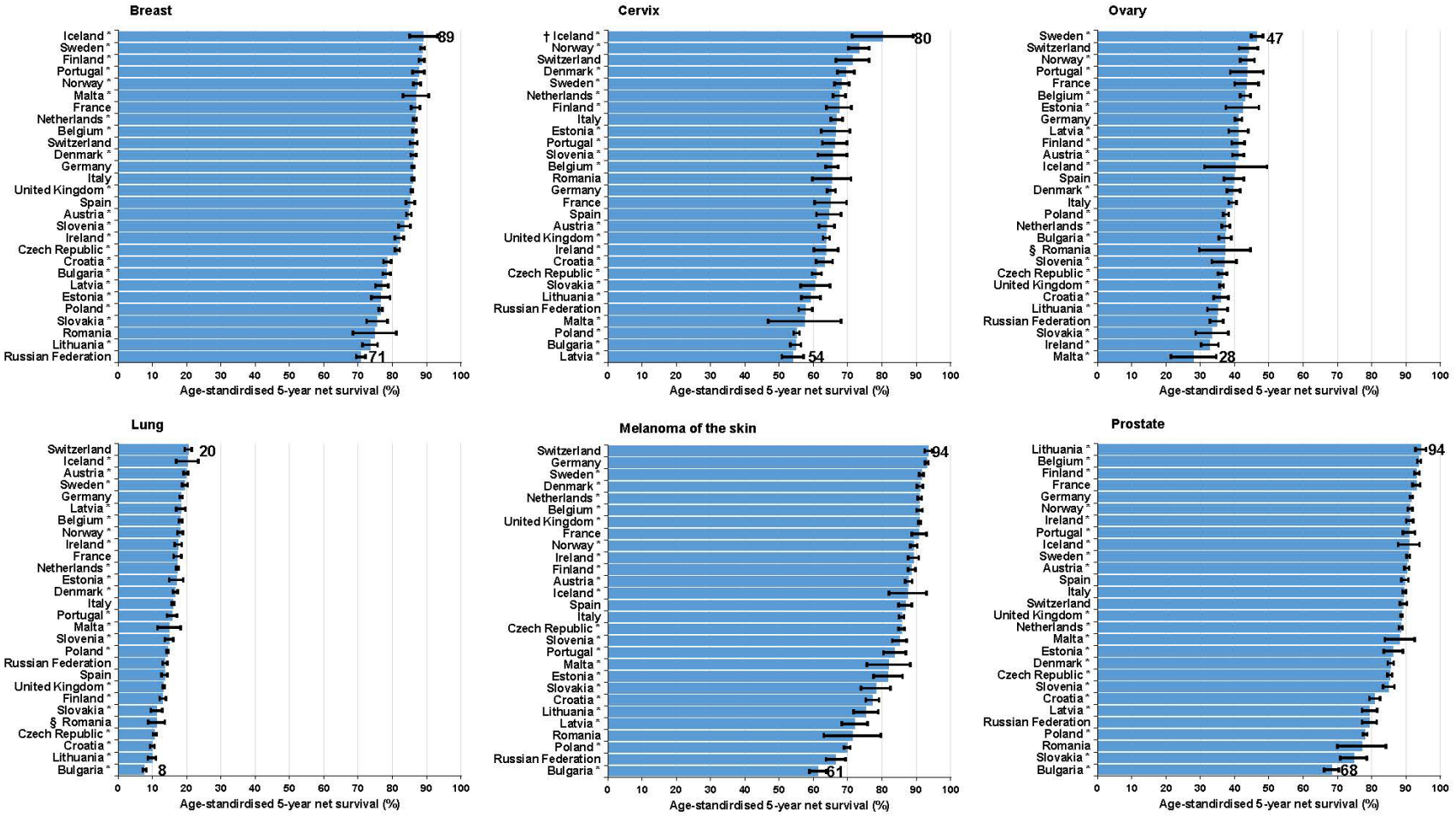
Figure 2c. Age-standardised 5-year net survival (%) for patients diagnosed during 2010-2014 in Europe, by country: adults (15-99 years) diagnosed with a tumour of the brain, or a myeloid or lymphoid malignancy, and children (0-14 years) diagnosed with a tumour of the brain, or a lymphoma or acute lymphoblastic leukaemia (ALL)

Footnote: survival estimates are ranked from highest to lowest. Where data were available for more than one registry in a given country, the survival estimates were derived by pooling the data for that country, but excluding data from registries for which the estimates were considered less reliable because 15% or more of patients were (a) lost to follow-up or censored alive within five years of diagnosis, or if diagnosed in 2010 or later, before 31 December 2014, or (b) registered only from a death certificate or at autopsy, or (c) with incomplete dates (i.e., unknown year of birth, unknown month or year of diagnosis, or unknown year of last vital status). Data with 100% coverage of the national population. § Estimate flagged as less reliable because the only available estimates were from a registry or registries in this category. † Estimate not age-standardised.

a)


Oesophagus
Switzerland
Belgium *
Netherlands *
Germany
Ireland *
Austria *
Iceland *
Norway *
Portugal *
United Kingdom *
Sweden *
France
Italy
Denmark *
Spain
Finland *
† Malta *
Czech Republic *
Poland *
Croatia *
Russian Federation
Slovenia *
Latvia *
Slovakia *
Lithuania *
Estonia *
§ † Romania
24
5
0 10 20 30 40 50 60 70 80 90 100
Age-standirdised 5-year net survival (%)
Stomach
Belgium *
Austria *
Germany
Switzerland
Portugal *
Italy
Estonia *
Slovenia *
Iceland *
Ireland *
Spain
Lithuania *
France
Norway *
§ Romania
Finland *
Latvia *
Netherlands *
Sweden *
Malta *
Slovakia *
Russian Federation
Poland *
United Kingdom *
Czech Republic *
Croatia *
Denmark *
Bulgaria *
38
16
0 10 20 30 40 50 60 70 80 90 100
Age-standardised 5-year net survival (%)
Colon
Iceland *
Belgium *
Switzerland
Norway *
Finland *
Sweden *
Germany
Italy
France
Austria *
Spain
Netherlands *
Slovenia *
Denmark *
Portugal *
Ireland *
United Kingdom *
Estonia *
Malta *
Lithuania *
Czech Republic *
Poland *
Bulgaria *
§ Romania
Slovakia *
Croatia *
Latvia *
Russian Federation
68
45
0 10 20 30 40 50 60 70 80 90 100
Age-standardised 5-year net survival (%)
Rectum
Norway *
Switzerland
Belgium *
Netherlands *
Denmark *
Sweden *
Finland *
Austria *
Iceland *
United Kingdom *
Germany
Ireland *
Italy
France
Slovenia *
Portugal *
Spain
Romania
Malta *
Estonia *
Lithuania *
Czech Republic *
Latvia *
Slovakia *
Poland *
Croatia *
Bulgaria *
Russian Federation
68
42
0 10 20 30 40 50 60 70 80 90 100
Age-standirdised 5-year net survival (%)
Liver
Belgium *
Italy
Portugal *
France
Spain
Sweden *
Norway *
Netherlands *
Switzerland
§ Austria *
Iceland *
Ireland *
§ Romania
Germany
United Kingdom *
Poland *
§ Finland *
Latvia *
§ Croatia *
§ Lithuania *
§ Slovakia *
Denmark *
Slovenia *
Czech Republic *
§ Bulgaria *
Russian Federation
Estonia *
§ † Malta *
21
4
0 10 20 30 40 50 60 70 80 90 100
Age-standardised 5-year net survival (%)
Pancreas
Belgium *
Portugal *
Germany
§ Austria *
Latvia *
Estonia *
Sweden *
Ireland *
Switzerland
Italy
Norway *
France
§ Croatia *
Denmark *
Poland *
Spain
Netherlands *
§ Finland *
§ Lithuania *
United Kingdom *
Slovenia *
Slovakia *
Czech Republic *
§ † Romania
§ Malta *
Russian Federation
† Iceland *
12
4
0 10 20 30 40 50 60 70 80 90 100
Age-standirdised 5-year net survival (%)

b)


Breast
Iceland ^
Sweden ^
Finland ^
Portugal ^
Norway ^
Malta ^
France
Netherlands ^
Belgium ^
Switzerland
Denmark ^
Germany
Italy
United Kingdom ^
Spain
Austria ^
Slovenia ^
Ireland ^
Czech Republic ^
Croatia ^
Bulgaria ^
Latvia ^
Estonia ^
Poland ^
Slovakia ^
Romania
Lithuania ^
Russian Federation
89
71
0 10 20 30 40 50 60 70 80 90 100
Age-standirdised 5-year net survival (%)
Cervix
† Iceland ^
Norway ^
Switzerland
Denmark ^
Sweden ^
Netherlands ^
Finland ^
Italy
Estonia ^
Portugal ^
Slovenia ^
Belgium ^
Romania
Germany
France
Spain
Austria ^
United Kingdom ^
Ireland ^
Croatia ^
Czech Republic ^
Slovakia ^
Lithuania ^
Russian Federation
Malta ^
Poland ^
Bulgaria ^
Latvia ^
80
54
0 10 20 30 40 50 60 70 80 90 100
Age-standirdised 5-year net survival (%)
Ovary
Sweden ^
Switzerland
Norway ^
Portugal ^
France
Belgium ^
Estonia ^
Germany
Latvia ^
Finland ^
Austria ^
Iceland ^
Spain
Denmark ^
Italy
Poland ^
Netherlands ^
Bulgaria ^
§ Romania
Slovenia ^
Czech Republic ^
United Kingdom ^
Croatia ^
Lithuania ^
Russian Federation
Slovakia ^
Ireland ^
Malta ^
47
28
0 10 20 30 40 50 60 70 80 90 100
Age-standirdised 5-year net survival (%)
Lung
Switzerland
Iceland ^
Austria ^
Sweden ^
Germany
Latvia ^
Belgium ^
Norway ^
Ireland ^
France
Netherlands ^
Estonia ^
Denmark ^
Italy
Portugal ^
Malta ^
Slovenia ^
Poland ^
Russian Federation
Spain
United Kingdom ^
Finland ^
Slovakia ^
§ Romania
Czech Republic ^
Croatia ^
Lithuania ^
Bulgaria ^
20
8
0 10 20 30 40 50 60 70 80 90 100
Age-standirdised 5-year net survival (%)
Melanoma of the skin
Switzerland
Germany
Sweden ^
Denmark ^
Netherlands ^
Belgium ^
United Kingdom ^
France
Norway ^
Ireland ^
Finland ^
Austria ^
Iceland ^
Spain
Italy
Czech Republic ^
Slovenia ^
Portugal ^
Malta ^
Estonia ^
Slovakia ^
Croatia ^
Lithuania ^
Latvia ^
Romania
Poland ^
Russian Federation
Bulgaria ^
94
61
0 10 20 30 40 50 60 70 80 90 100
Age-standirdised 5-year net survival (%)
Prostate
Lithuania ^
Belgium ^
Finland ^
France
Germany
Norway ^
Ireland ^
Portugal ^
Iceland ^
Sweden ^
Austria ^
Spain
Italy
Switzerland
United Kingdom ^
Netherlands ^
Malta ^
Estonia ^
Denmark ^
Czech Republic ^
Slovenia ^
Croatia ^
Latvia ^
Russian Federation
Poland ^
Romania
Slovakia ^
Bulgaria ^
94
68
0 10 20 30 40 50 60 70 80 90 100
Age-standirdised 5-year net survival (%)

c)

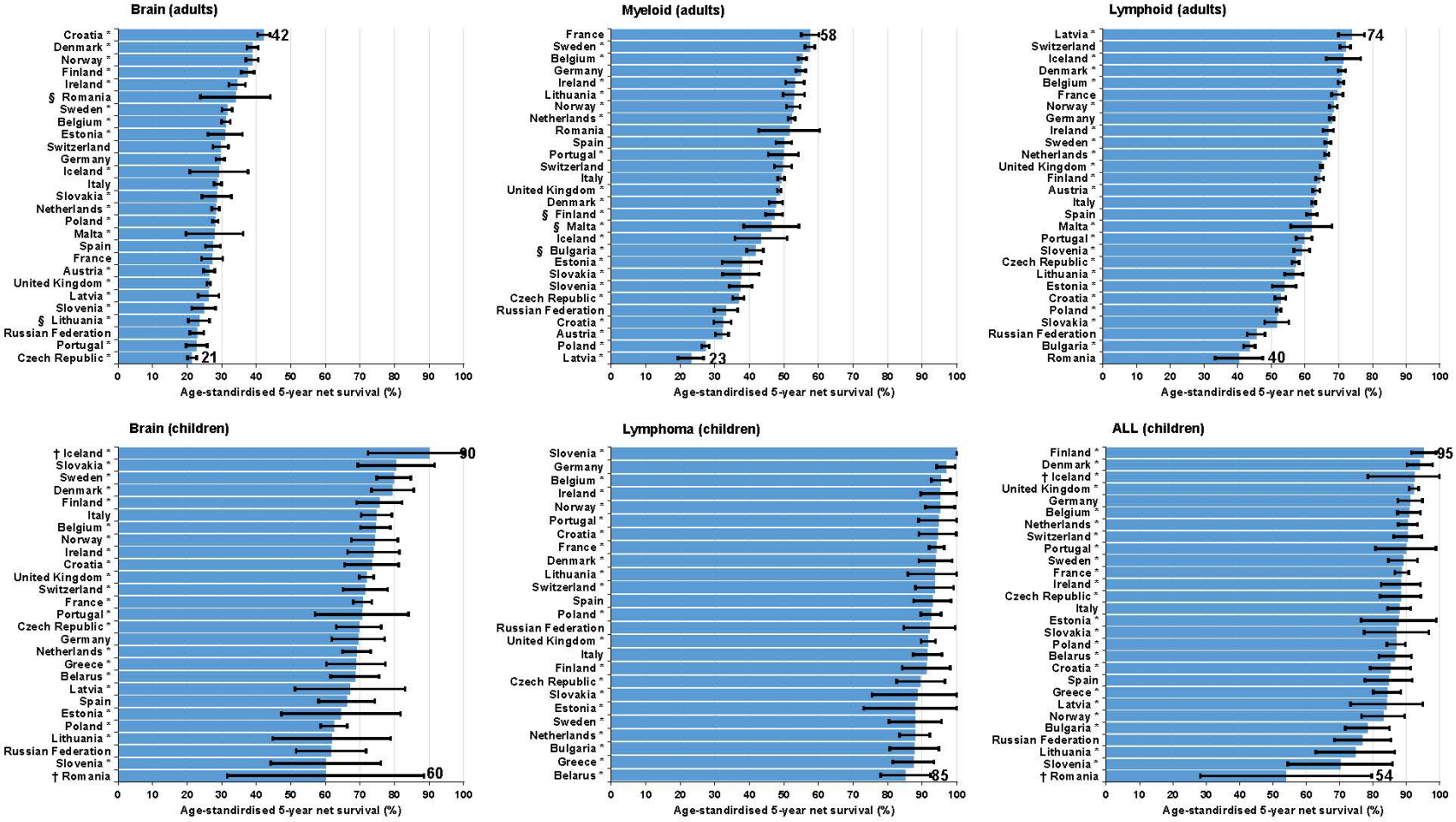

Brain (adults)
Croatia *
Denmark *
Norway *
Finland *
Ireland *
§ Romania
Sweden *
Belgium *
Estonia *
Switzerland
Germany
Iceland *
Italy
Slovakia *
Netherlands *
Poland *
Malta *
Spain
France
Austria *
United Kingdom *
Latvia *
Slovenia *
§ Lithuania *
Russian Federation
Portugal *
Czech Republic *
42
21
0 10 20 30 40 50 60 70 80 90 100
Age-standirdised 5-year net survival (%)
Myeloid (adults)
France
Sweden *
Belgium *
Germany
Ireland *
Lithuania *
Norway *
Netherlands *
Romania
Spain
Portugal *
Switzerland
Italy
United Kingdom *
Denmark *
§ Finland *
§ Malta *
Iceland *
§ Bulgaria *
Estonia *
Slovakia *
Slovenia *
Czech Republic *
Russian Federation
Croatia *
Austria *
Poland *
Latvia *
58
23
0 10 20 30 40 50 60 70 80 90 100
Age-standirdised 5-year net survival (%)
Lymphoid (adults)
Latvia *
Switzerland
Iceland *
Denmark *
Belgium *
France
Norway *
Germany
Ireland *
Sweden *
Netherlands *
United Kingdom *
Finland *
Austria *
Italy
Spain
Malta *
Portugal *
Slovenia *
Czech Republic *
Lithuania *
Estonia *
Croatia *
Poland *
Slovakia *
Russian Federation
Bulgaria *
Romania
74
40
0 10 20 30 40 50 60 70 80 90 100
Age-standirdised 5-year net survival (%)
Brain (children)
† Iceland *
Slovakia *
Sweden *
Denmark *
Finland *
Italy
Belgium *
Norway *
Ireland *
Croatia *
United Kingdom *
Switzerland *
France *
Portugal *
Czech Republic *
Germany
Netherlands *
Greece *
Belarus *
Latvia *
Spain
Estonia *
Poland *
Lithuania *
Russian Federation
Slovenia *
† Romania
90
60
0 10 20 30 40 50 60 70 80 90 100
Age-standirdised 5-year net survival (%)
Lymphoma (children)
Slovenia *
Germany
Belgium *
Ireland *
Norway *
Portugal *
Croatia *
France *
Denmark *
Lithuania *
Switzerland *
Spain
Poland *
Russian Federation
United Kingdom *
Italy
Finland *
Czech Republic *
Slovakia *
Estonia *
Sweden *
Netherlands *
Bulgaria *
Greece *
Belarus *
85
0 10 20 30 40 50 60 70 80 90 100
Age-standirdised 5-year net survival (%)
ALL (children)
Finland *
Denmark *
† Iceland *
United Kingdom *
Germany
Belgium *
Netherlands *
Switzerland *
Portugal *
Sweden *
France *
Ireland *
Czech Republic *
Italy
Estonia *
Slovakia *
Poland *
Belarus *
Croatia *
Spain
Greece *
Latvia *
Norway *
Bulgaria *
Russian Federation
Lithuania *
Slovenia *
† Romania
95
54
0 10 20 30 40 50 60 70 80 90 100
Age-standirdised 5-year net survival (%)

Figure 3a. International variation in age-standardised 5-year net survival (%) for adults (15-99 years) diagnosed during 2010–2014, by European region: cancers of the oesophagus, stomach, colon, rectum, liver and pancreas

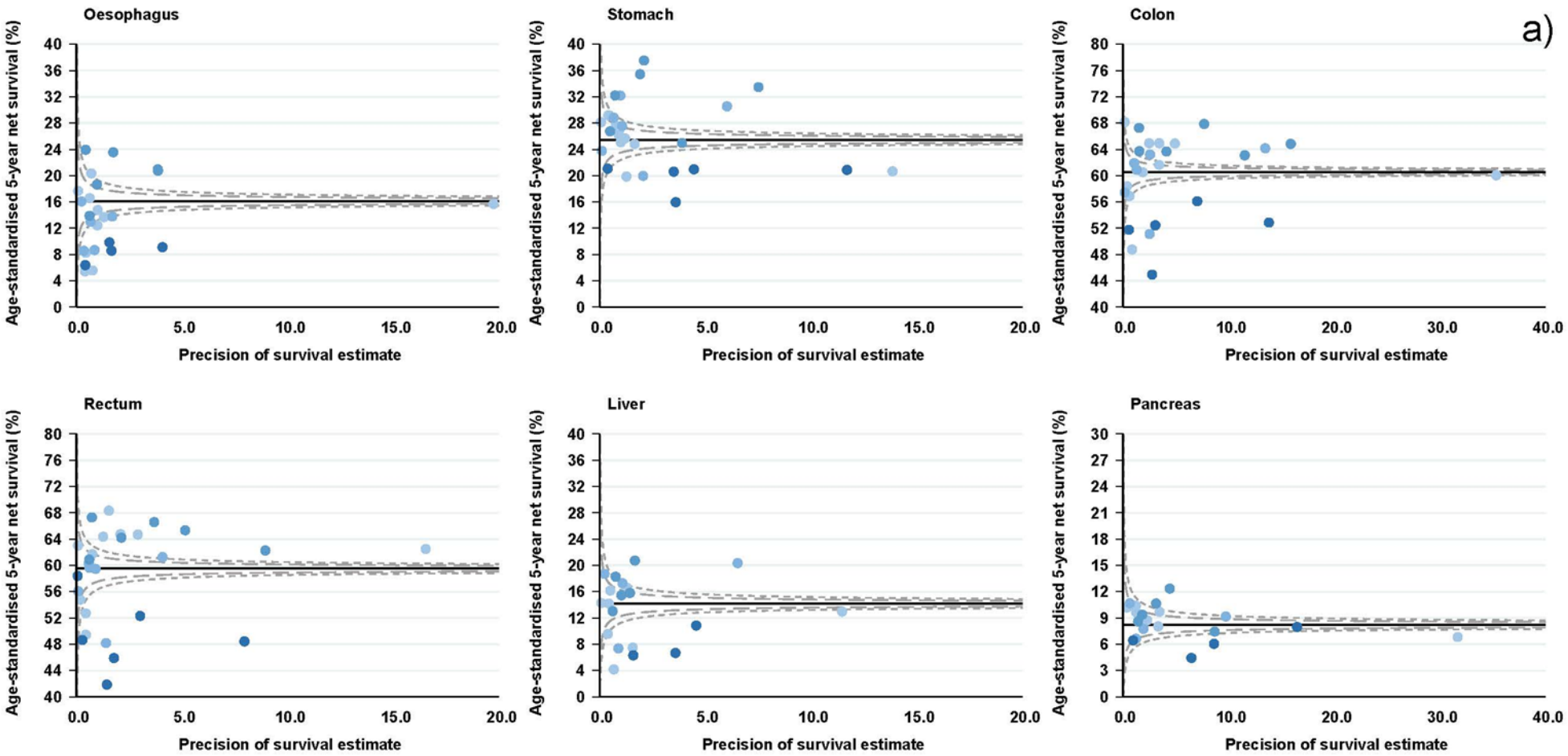
Footnote: funnel plot with each national survival estimate plotted against its statistical precision (the inverse of its variance). The target value is the pooled estimate for all participating countries in the same period. Only age-standardised estimates are included. Control limits for 95% and 99.8% are shown. The wider control limits to the left emphasise the increased variability expected between survival estimates that are less statistically precise, while the narrower limits to the right emphasise the reduced variability between more precise estimates (Quaresma et al. 2014).

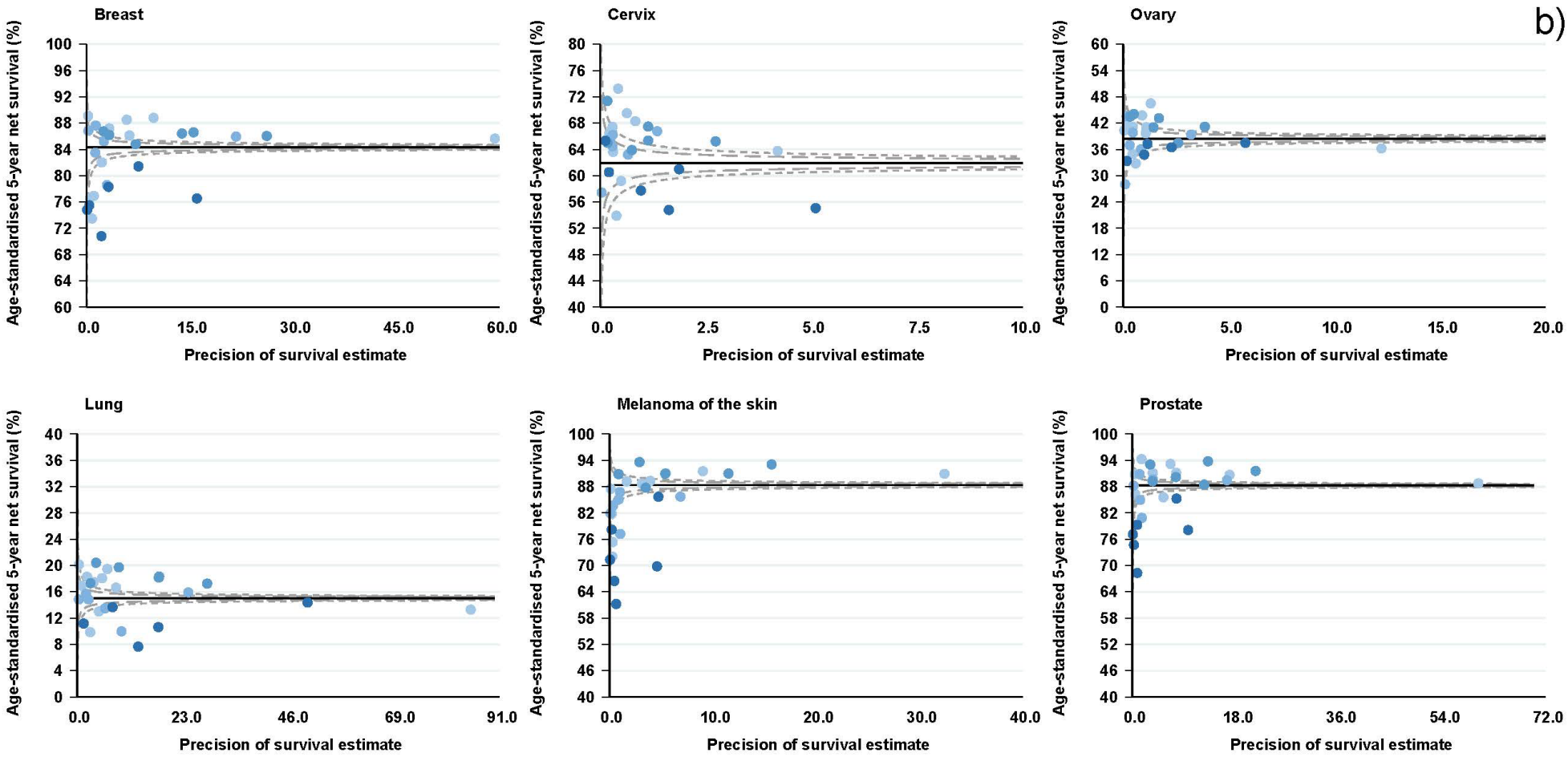
Figure 3b. International variation in age-standardised 5-year net survival (%) for adults (15-99 years) diagnosed during 2010–2014, by European region: cancers of the breast (women), cervix, ovary and lung, melanoma of the skin, and cancer of the prostate

Footnote: funnel plot with each national survival estimate plotted against its statistical precision (the inverse of its variance). The target value is the pooled estimate for all participating countries in the same period. Only age-standardised estimates are included. Control limits for 95% and 99.8% are shown. The wider control limits to the left emphasise the increased variability expected between survival estimates that are less statistically precise, while the narrower limits to the right emphasise the reduced variability between more precise estimates (Quaresma et al. 2014).

Figure 3c. International variation in age-standardised 5-year net survival (%) for patients diagnosed during 2010-2014, by European region: adults (15-99 years) diagnosed with a tumour of the brain, or a myeloid or lymphoid malignancy, and children (0-14 years) diagnosed with a tumour of the brain, or a lymphoma or acute lymphoblastic leukaemia (ALL)

Footnote: funnel plot with each national survival estimate plotted against its statistical precision (the inverse of its variance). The target value is the pooled estimate for all participating countries in the same period. Only age-standardised estimates are included. Control limits for 95% and 99.8% are shown. The wider control limits to the left emphasise the increased variability expected between survival estimates that are less statistically precise, while the narrower limits to the right emphasise the reduced variability between more precise estimates (Quaresma et al. 2014).


a)
Oesophagus
Stomach
Colon
Rectum
Liver
Pancreas
Age-standardised 5-year net survival (%)
Precision of survival estimate


b)
Breast
Cervix
Ovary
Lung
Melanoma of the skin
Prostate
Age-standardised 5-year net survival (%)
Precision of survival estimate

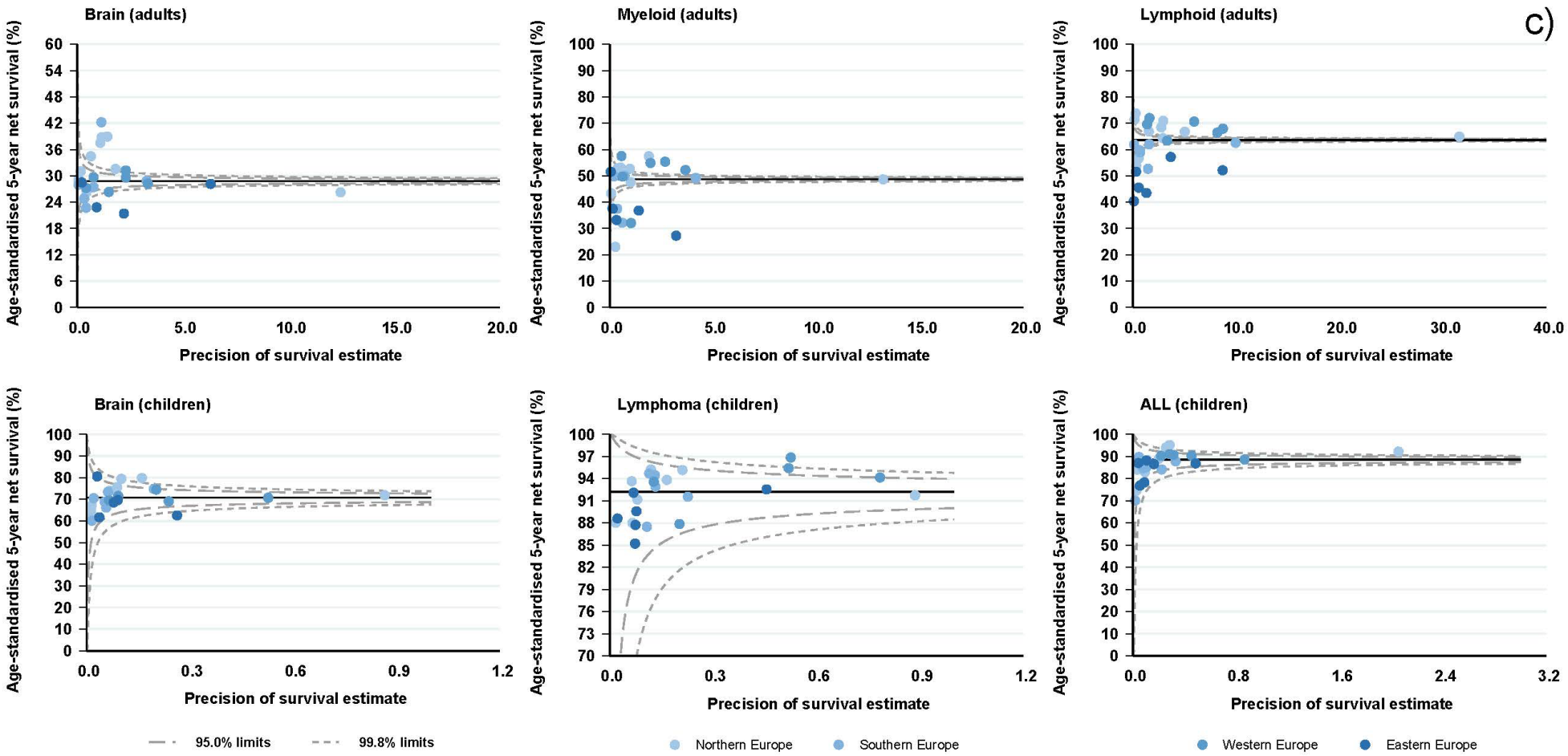

c)
Brain (adults)
Myeloid (adults)
Lymphoid (adults)
Brain (children)
Lymphoma (children)
ALL (children)
Age-standardised 5-year net survival (%)
Precision of survival estimate
95.0% limits
99.8% limits
Northern Europe
Southern Europe
Western Europe
Eastern Europe

Figure 4a. Regional variation in age-standardised five-year net survival (%) in European countries with more than one participating population-based cancer registry: adults (15-99 years) diagnosed during 2010–2014 with a cancer of the oesophagus, stomach, colon, rectum, liver or pancreas

Footnote: Each box-plot shows the range of survival estimates among all cancer registries for which suitable estimates were obtained in each country. Survival estimates considered less reliable are not included. The vertical line inside each box represents the median survival estimate among all contributing registries (the central value in the range, or 50th centile). The box covers the inter-quartile range (IQR) between the lower and upper quartiles (25th and 75th centiles). Where there are only a few widely scattered estimates, the median may be close to the lower or upper quartile. The extreme limits of the box-plot are 1.5*IQR below the lower quartile and 1.5*IQR above the upper quartile. Open circles indicate “outlier" values, outside this range.

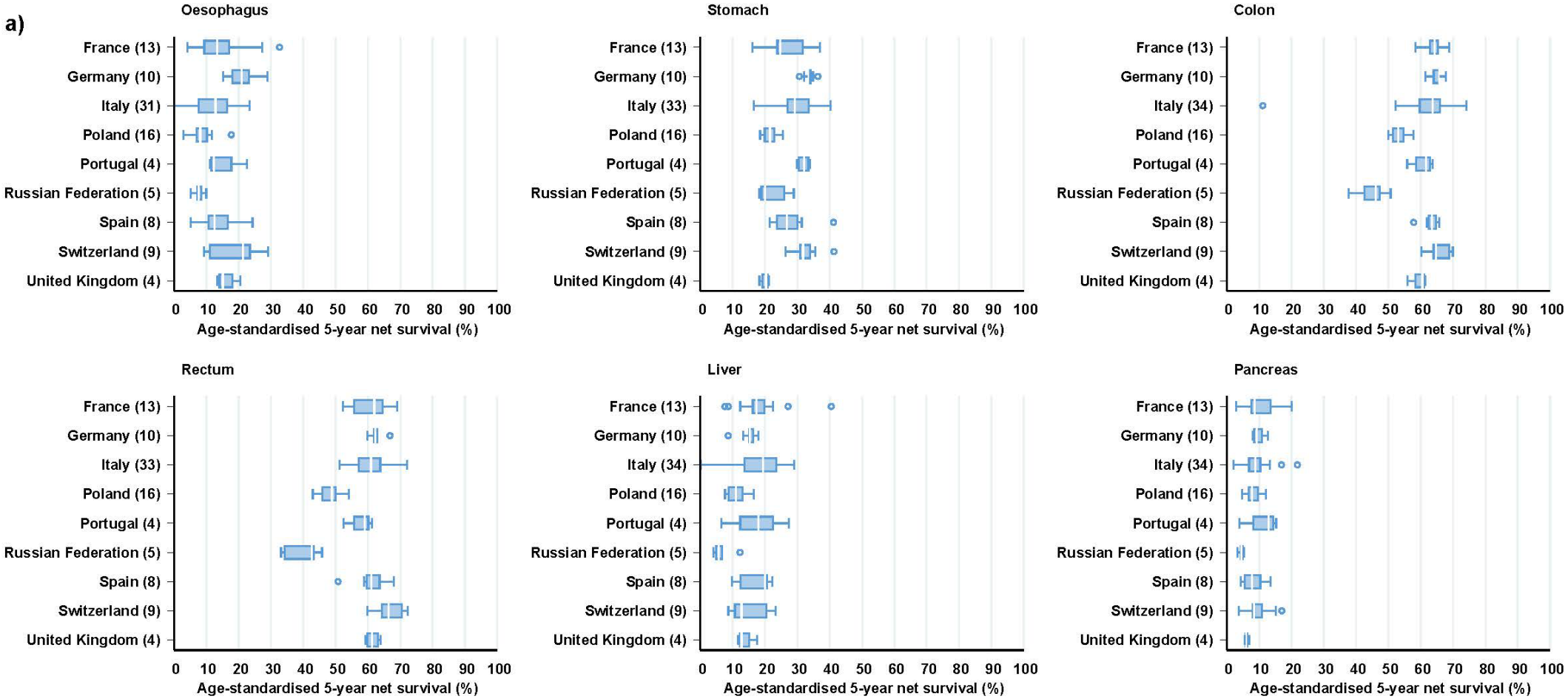
Figure 4b. Regional variation in age-standardised five-year net survival (%) in European countries with more than one participating population-based cancer registry: adults (15-99 years) diagnosed during 2010–2014 with a cancer of the breast (women), cervix, ovary or lung, melanoma of the skin, or cancer of the prostate

Footnote: Each box-plot shows the range of survival estimates among all cancer registries for which suitable estimates were obtained in each country. Survival estimates considered less reliable are not included. The vertical line inside each box represents the median survival estimate among all contributing registries (the central value in the range, or 50th centile). The box covers the inter-quartile range (IQR) between the lower and upper quartiles (25th and 75th centiles). Where there are only a few widely scattered estimates, the median may be close to the lower or upper quartile. The extreme limits of the box-plot are 1.5*IQR below the lower quartile and 1.5*IQR above the upper quartile. Open circles indicate “outlier" values, outside this range.

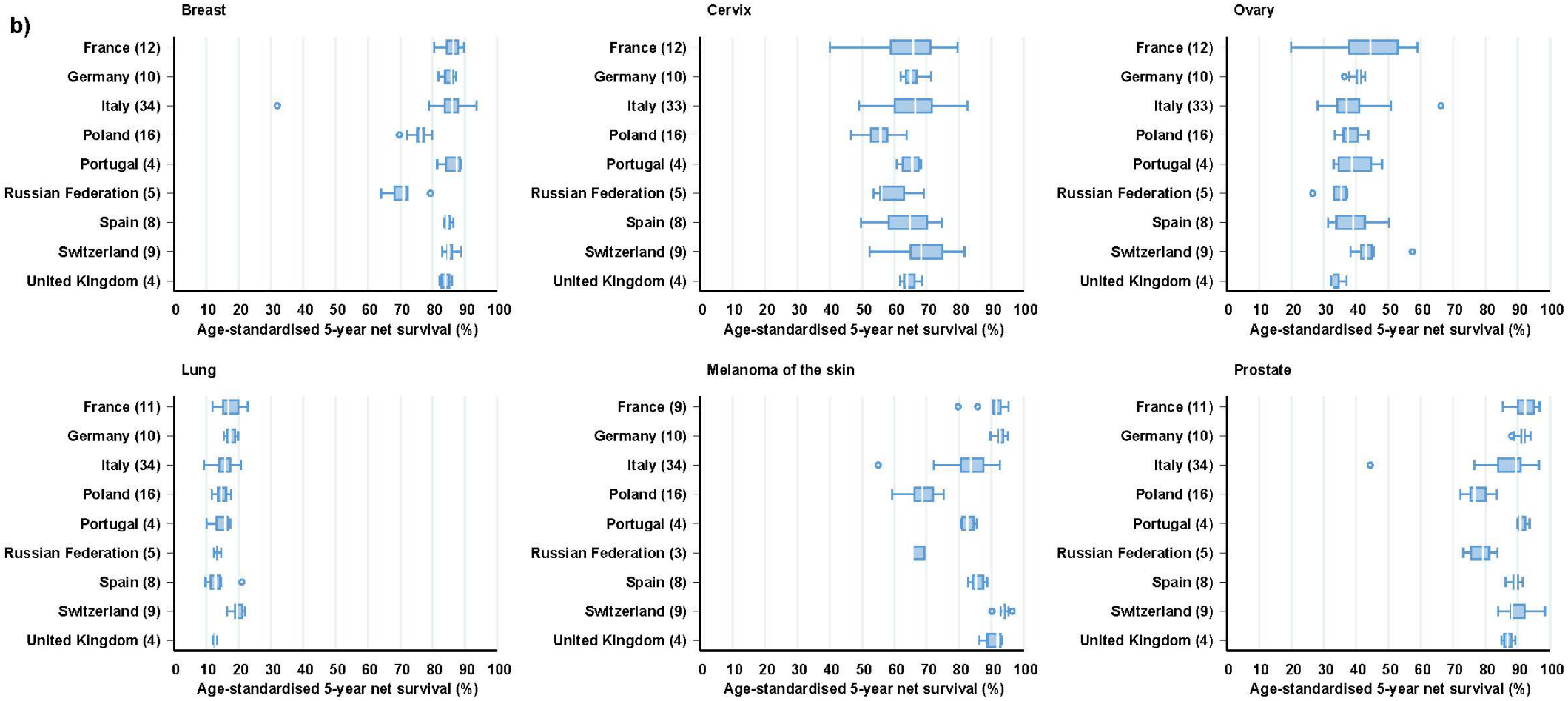
Figure 4c. Regional variation in age-standardised five-year net survival (%) in European countries with more than one participating population-based cancer registry: adults (15-99 years) diagnosed with a tumour of the brain, or myeloid or lymphoid malignancy, and children (0-14 years) diagnosed with a tumour of the brain, or lymphoma or acute lymphoblastic leukaemia (ALL)

Footnote: Each box-plot shows the range of survival estimates among all cancer registries for which suitable estimates were obtained in each country. Survival estimates considered less reliable are not included. The vertical line inside each box represents the median survival estimate among all contributing registries (the central value in the range, or 50th centile). The box covers the inter-quartile range (IQR) between the lower and upper quartiles (25th and 75th centiles). Where there are only a few widely scattered estimates, the median may be close to the lower or upper quartile. The extreme limits of the box-plot are 1.5*IQR below the lower quartile and 1.5*IQR above the upper quartile. Open circles indicate “outlier" values, outside this range.

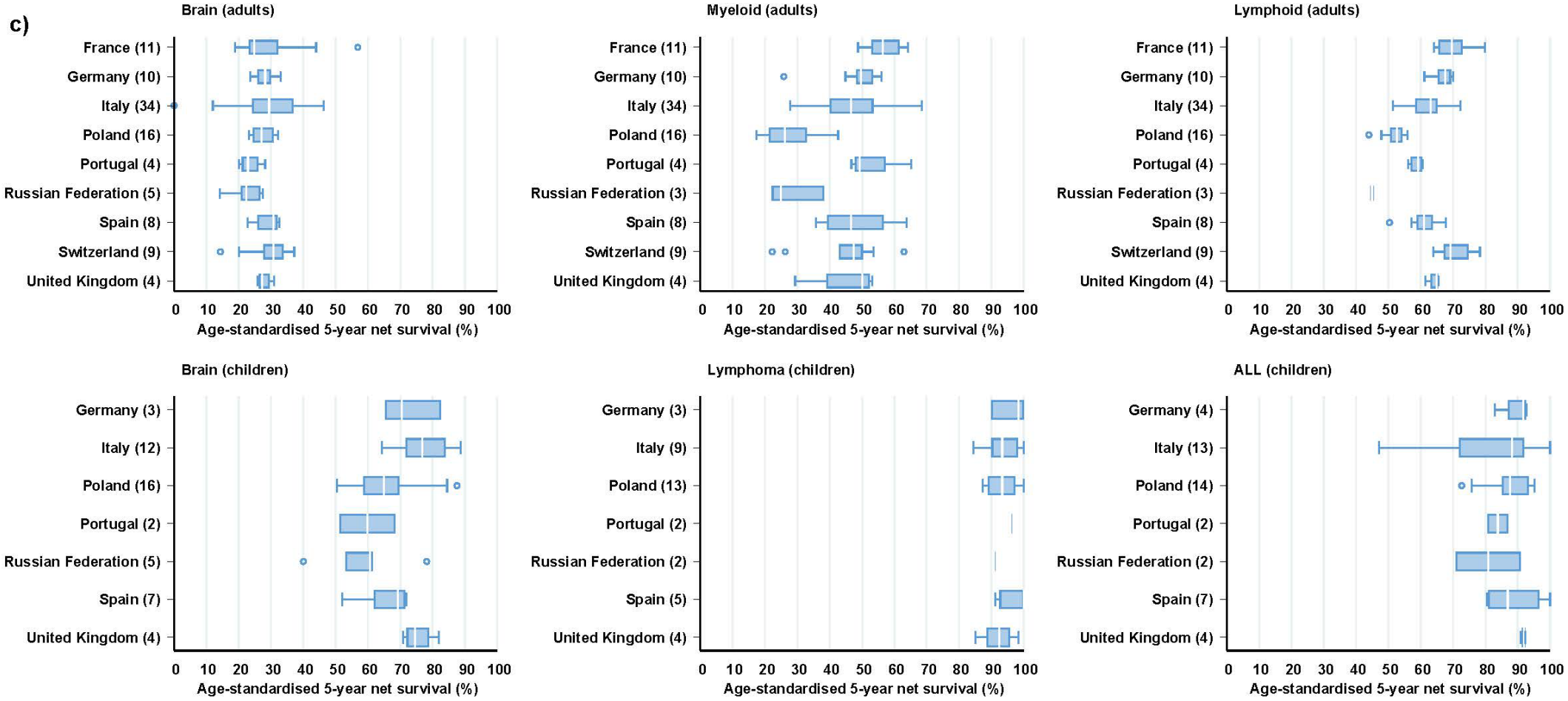
a)


Oesophagus
Stomach
Colon
Rectum
Liver
Pancreas
France (13)
Germany (10)
Italy (31)
Italy (33)
Italy (34)
Poland (16)
Portugal (4)
Russian Federation (5)
Spain (8)
Switzerland (9)
United Kingdom (4)
0 10 20 30 40 50 60 70 80 90 100
Age-standardised 5-year net survival (%)

b)


Breast
France (12)
Germany (10)
Italy (34)
Poland (16)
Portugal (4)
Russian Federation (5)
Spain (8)
Switzerland (9)
United Kingdom (4)
0 10 20 30 40 50 60 70 80 90 100
Age-standardised 5-year net survival (%)
Cervix
France (12)
Germany (10)
Italy (33)
Poland (16)
Portugal (4)
Russian Federation (5)
Spain (8)
Switzerland (9)
United Kingdom (4)
0 10 20 30 40 50 60 70 80 90 100
Age-standardised 5-year net survival (%)
Ovary
France (12)
Germany (10)
Italy (33)
Poland (16)
Portugal (4)
Russian Federation (5)
Spain (8)
Switzerland (9)
United Kingdom (4)
0 10 20 30 40 50 60 70 80 90 100
Age-standardised 5-year net survival (%)
Lung
France (11)
Germany (10)
Italy (34)
Poland (16)
Portugal (4)
Russian Federation (5)
Spain (8)
Switzerland (9)
United Kingdom (4)
0 10 20 30 40 50 60 70 80 90 100
Age-standardised 5-year net survival (%)
Melanoma of the skin
France (9)
Germany (10)
Italy (34)
Poland (16)
Portugal (4)
Russian Federation (3)
Spain (8)
Switzerland (9)
United Kingdom (4)
0 10 20 30 40 50 60 70 80 90 100
Age-standardised 5-year net survival (%)
Prostate
France (11)
Germany (10)
Italy (34)
Poland (16)
Portugal (4)
Russian Federation (5)
Spain (8)
Switzerland (9)
United Kingdom (4)
0 10 20 30 40 50 60 70 80 90 100
Age-standardised 5-year net survival (%)

c)


Brain (adults)
France (11)
Germany (10)
Italy (34)
Poland (16)
Portugal (4)
Russian Federation (5)
Spain (8)
Switzerland (9)
United Kingdom (4)
0 10 20 30 40 50 60 70 80 90 100
Age-standardised 5-year net survival (%)
Myeloid (adults)
France (11)
Germany (10)
Italy (34)
Poland (16)
Portugal (4)
Russian Federation (3)
Spain (8)
Switzerland (9)
United Kingdom (4)
0 10 20 30 40 50 60 70 80 90 100
Age-standardised 5-year net survival (%)
Lymphoid (adults)
France (11)
Germany (10)
Italy (34)
Poland (16)
Portugal (4)
Russian Federation (3)
Spain (8)
Switzerland (9)
United Kingdom (4)
0 10 20 30 40 50 60 70 80 90 100
Age-standardised 5-year net survival (%)
Brain (children)
Germany (3)
Italy (12)
Poland (16)
Portugal (2)
Russian Federation (5)
Spain (7)
United Kingdom (4)
0 10 20 30 40 50 60 70 80 90 100
Age-standardised 5-year net survival (%)
Lymphoma (children)
Germany (3)
Italy (9)
Poland (13)
Portugal (2)
Russian Federation (2)
Spain (5)
United Kingdom (4)
0 10 20 30 40 50 60 70 80 90 100
Age-standardised 5-year net survival (%)
ALL (children)
Germany (4)
Italy (13)
Poland (14)
Portugal (2)
Russian Federation (2)
Spain (7)
United Kingdom (4)
0 10 20 30 40 50 60 70 80 90 100
Age-standardised 5-year net survival (%)

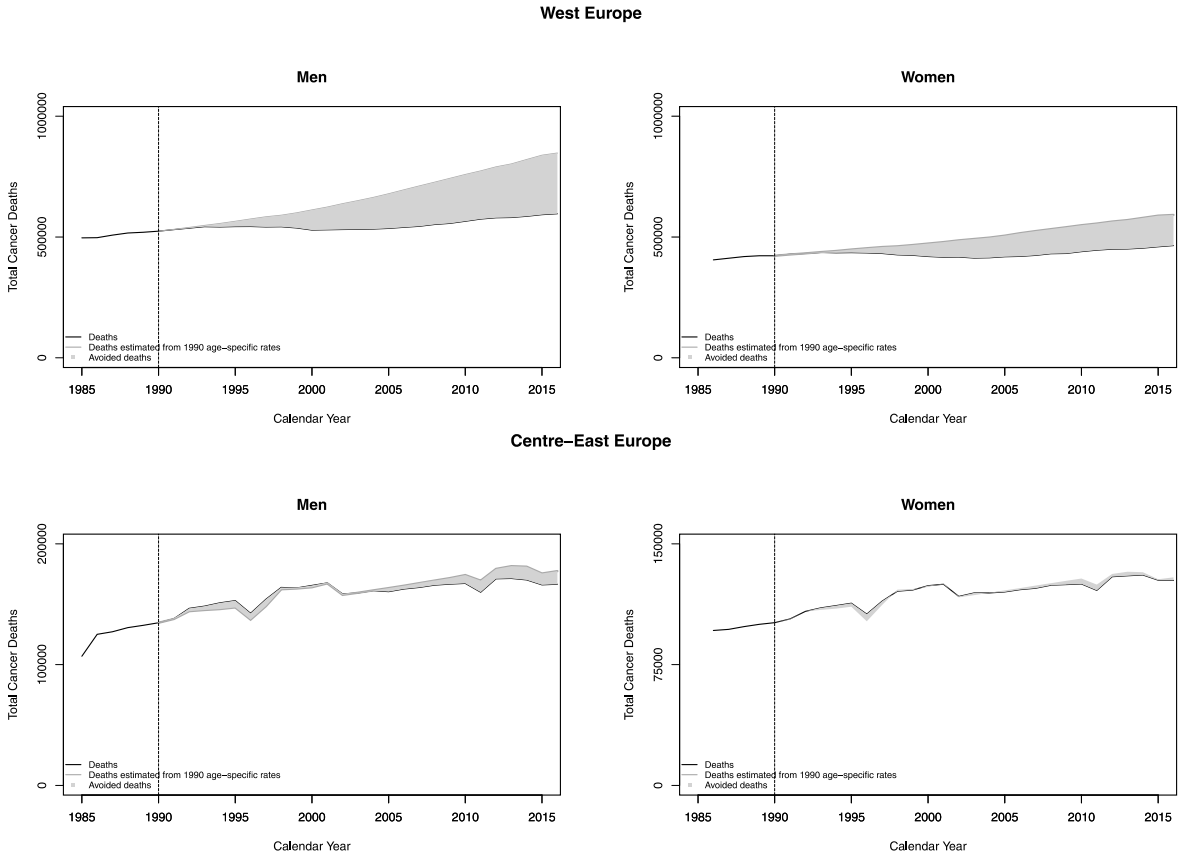


Figure 5 Estimated avoided total cancer deaths from 1991 to 2016, applying the peak age-specific mortality rates in 1990 (light grey area) as constant, in West and Centre-East Europe, men and women, separately.

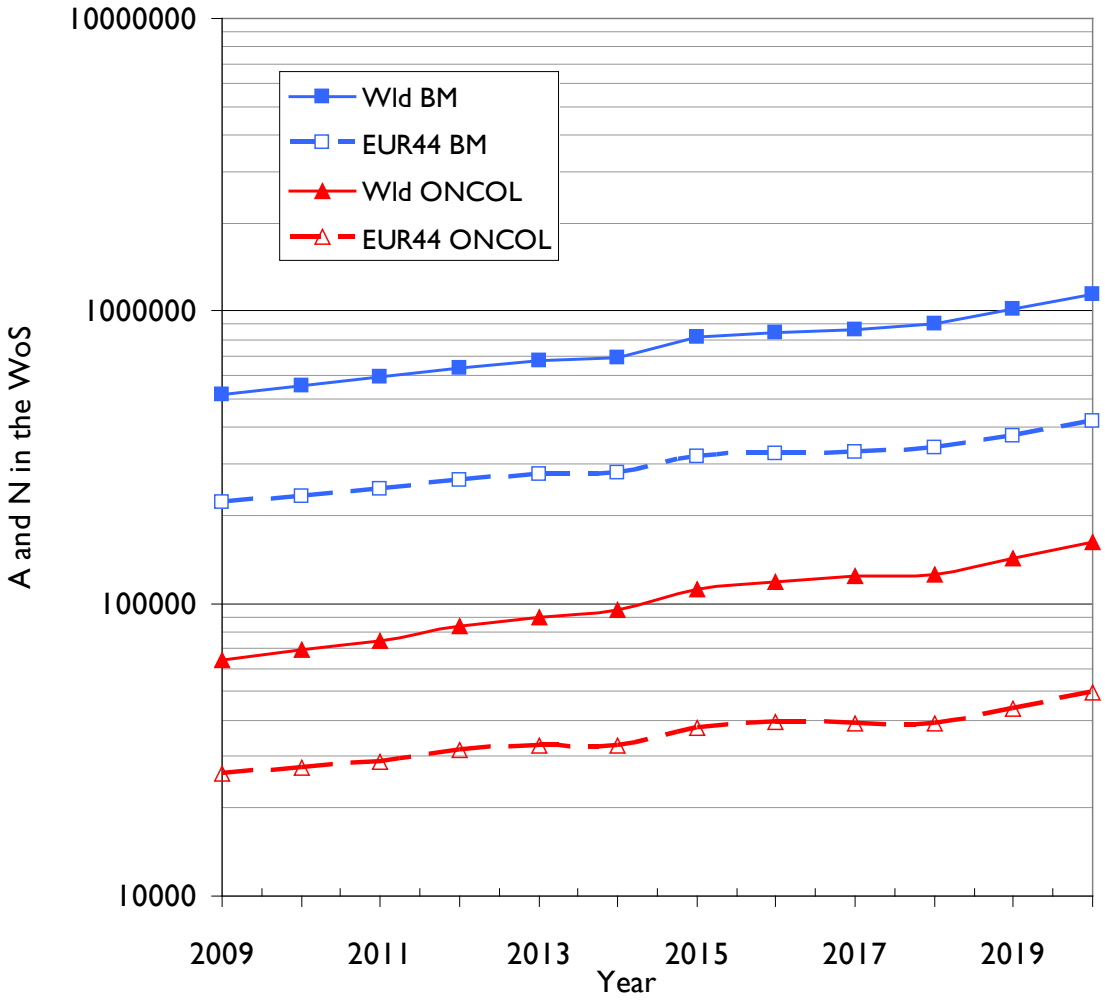


Figure 6a. Outputs of biomedical research papers (BM) and of cancer research papers (ONCOL) from the world and from the 44-country European region (EUR) in the Web of Science, 2009-20. *Logarithmic ordinate scale.*

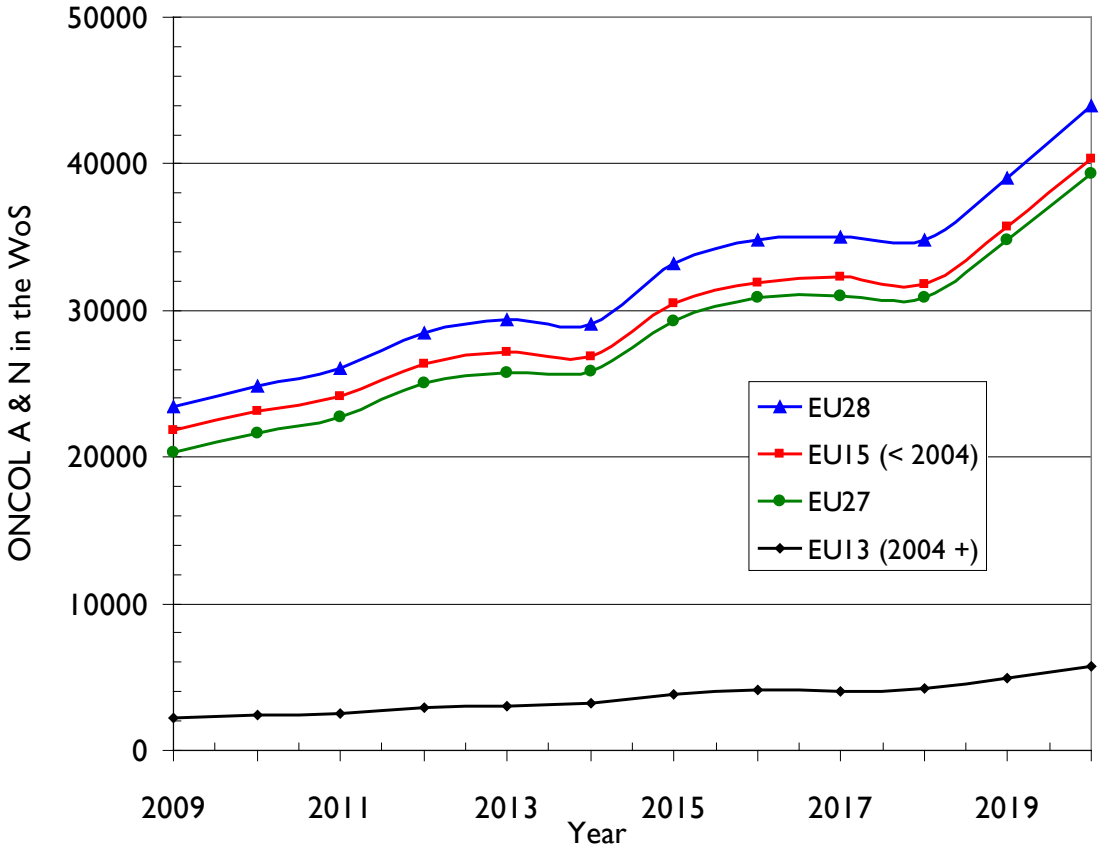


Figure 6b. Outputs of cancer research papers (ONCOL) from four groups of European countries in the Web of Science, 2009-20. *EU28 = European Union to 2020; EU27 = European Union after 2021; EU15 = European Union prior to 2004; EU13 = Member States joining the EU in 2004 and after.*

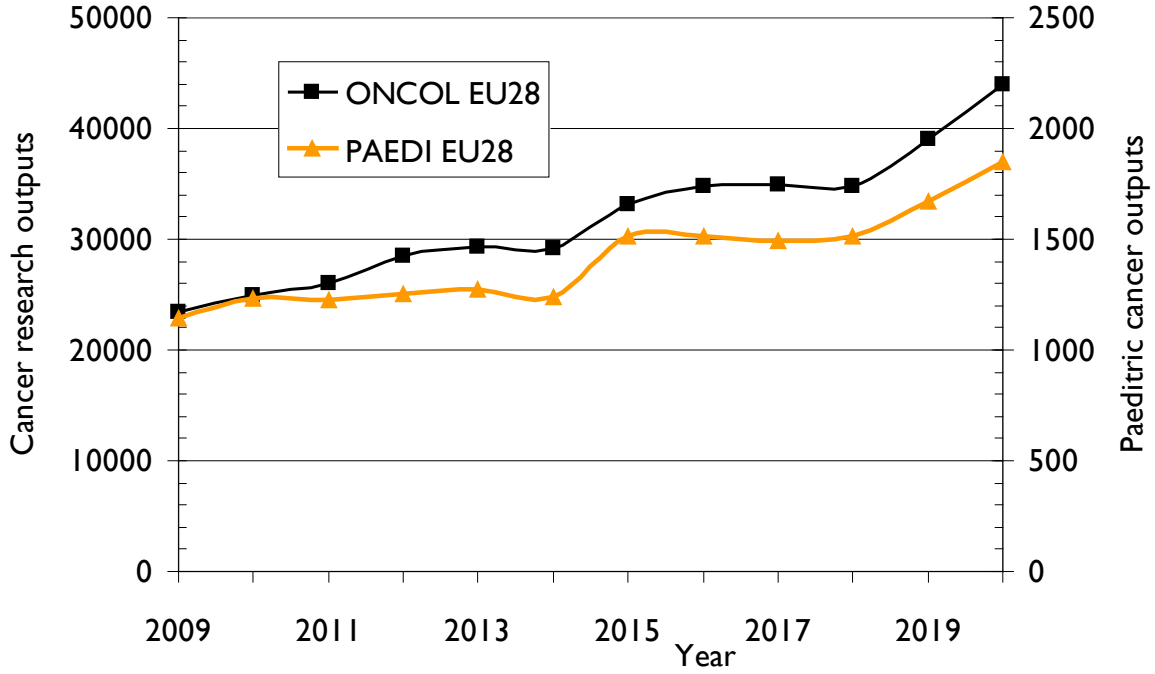


Figure 6c. Paediatric cancer outputs from the EU28 Member States, compared with outputs of all EU28 cancer research papers, 2009-20.

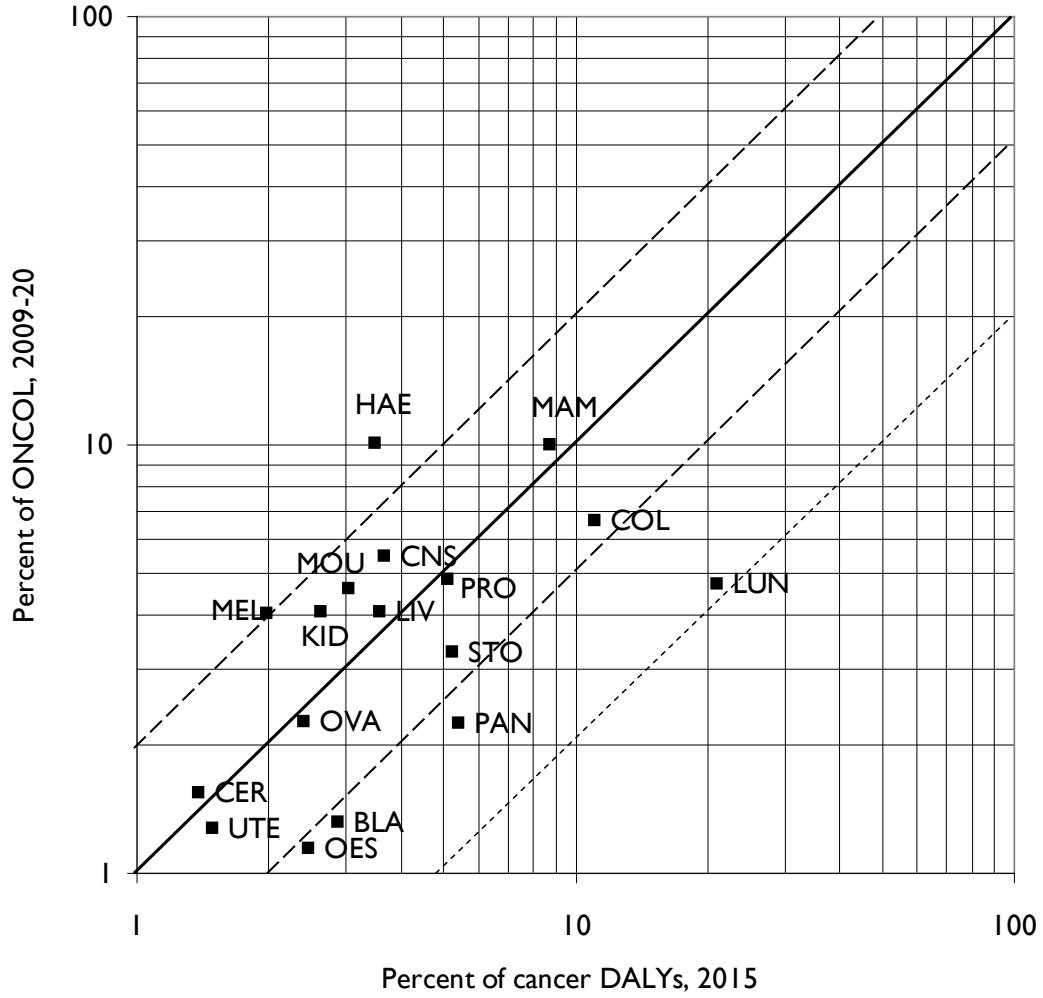


Figure 7a. Outputs of cancer research papers from the European region on individual cancer anatomical sites (for codes, see Table 2b) compared with the percentage of the burden from these cancers in 2015 (WHO data on DALYs). *Dashed lines represent outputs twice and half the equivalent percentage; dotted line represents an output of one fifth the equivalent percentage. Logarithmic scales.*

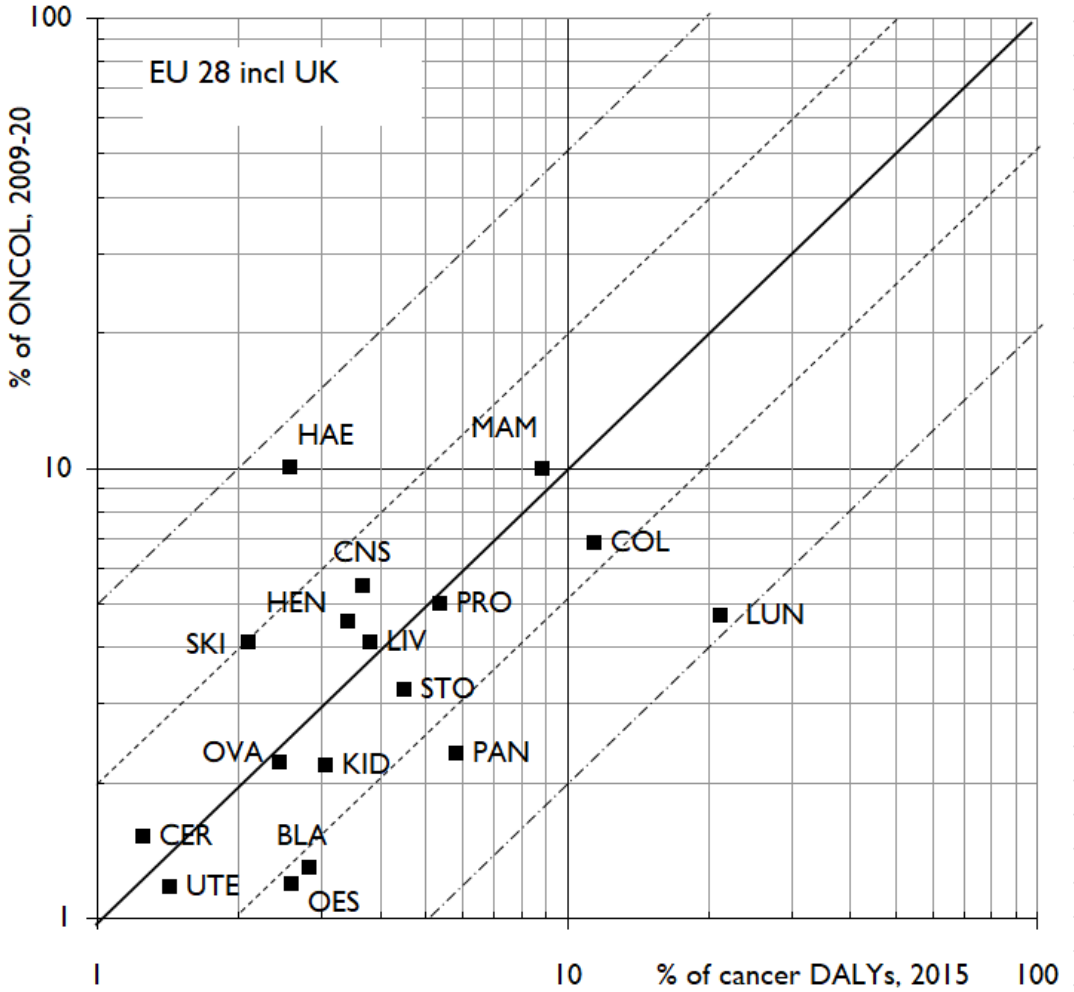


Figure 7b. Outputs of cancer research papers from the European Union (28 Member States, including the UK) on individual cancer anatomical sites (for codes, see Table 2b) compared with the percentage of the burden from these cancers in 2015 (WHO data on DALYs). *Dashed lines represent outputs twice and half the equivalent percentage; chain dotted line represents an output of one fifth the equivalent percentage. Logarithmic scales.*

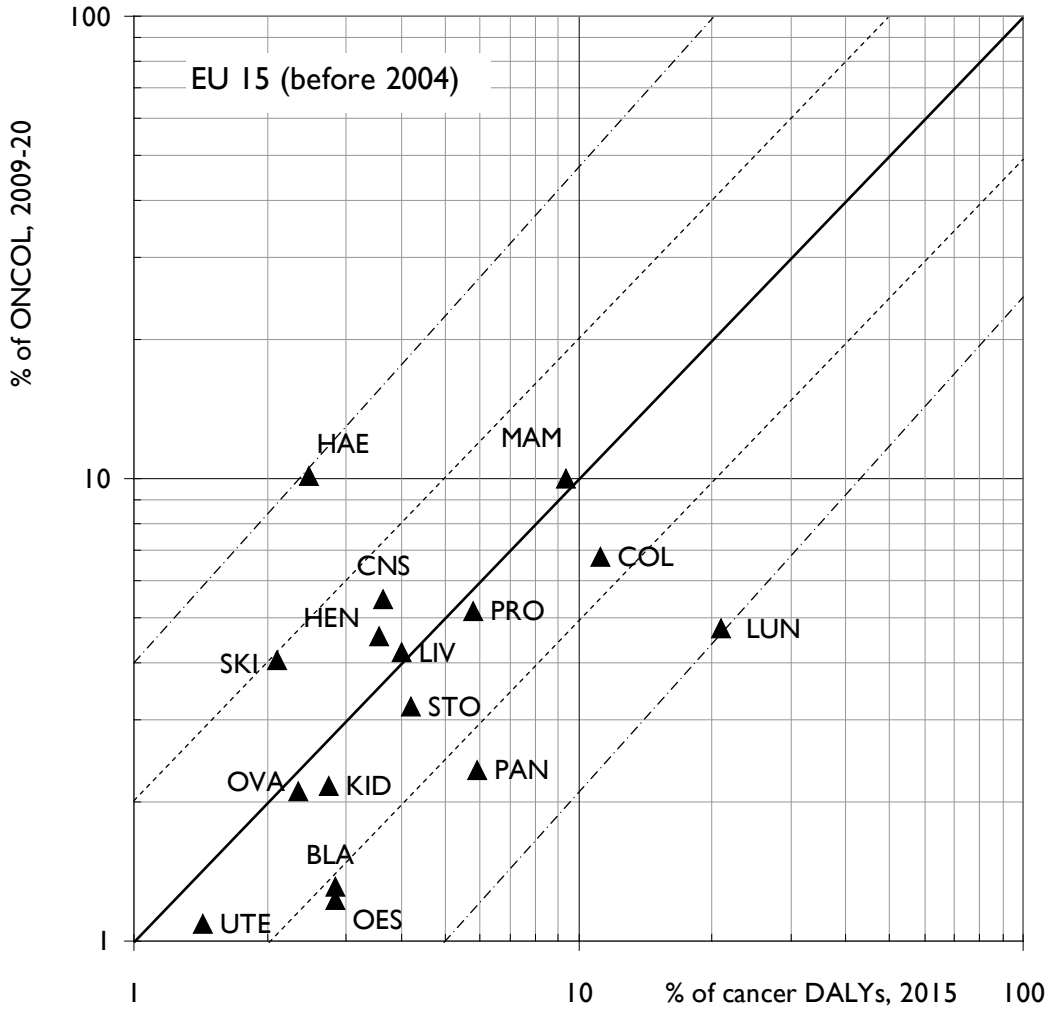


Figure 7c. Outputs of cancer research papers from the European Union in 2003 (before enlargement) on individual cancer anatomical sites (for codes, see Table 2b) compared with the percentage of the burden from these cancers in 2015 (WHO data on DALYs). *Dashed lines represent outputs twice and half the equivalent percentage; chain dotted line represents an output of one fifth the equivalent percentage. Logarithmic scales.*

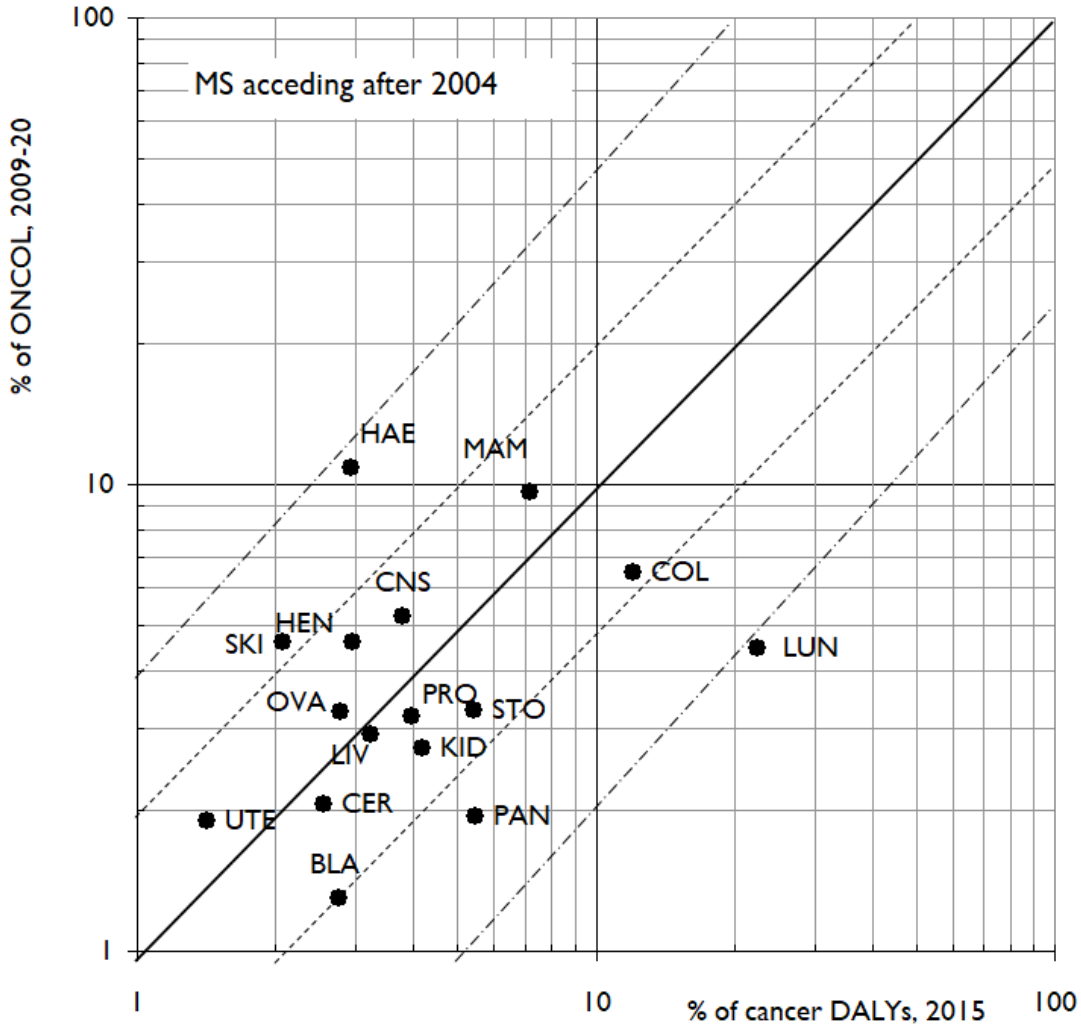


Figure 7d. Outputs of cancer research papers from the 13 Member States of the European Union that acceded in 2004 or after on individual cancer anatomical sites (for codes, see Table 2b) compared with the percentage of the burden from these cancers in 2015 (WHO data on DALYs). *Dashed lines represent outputs twice and half the equivalent percentage; chain dotted line represents an output of one fifth the equivalent percentage. Logarithmic scales.*

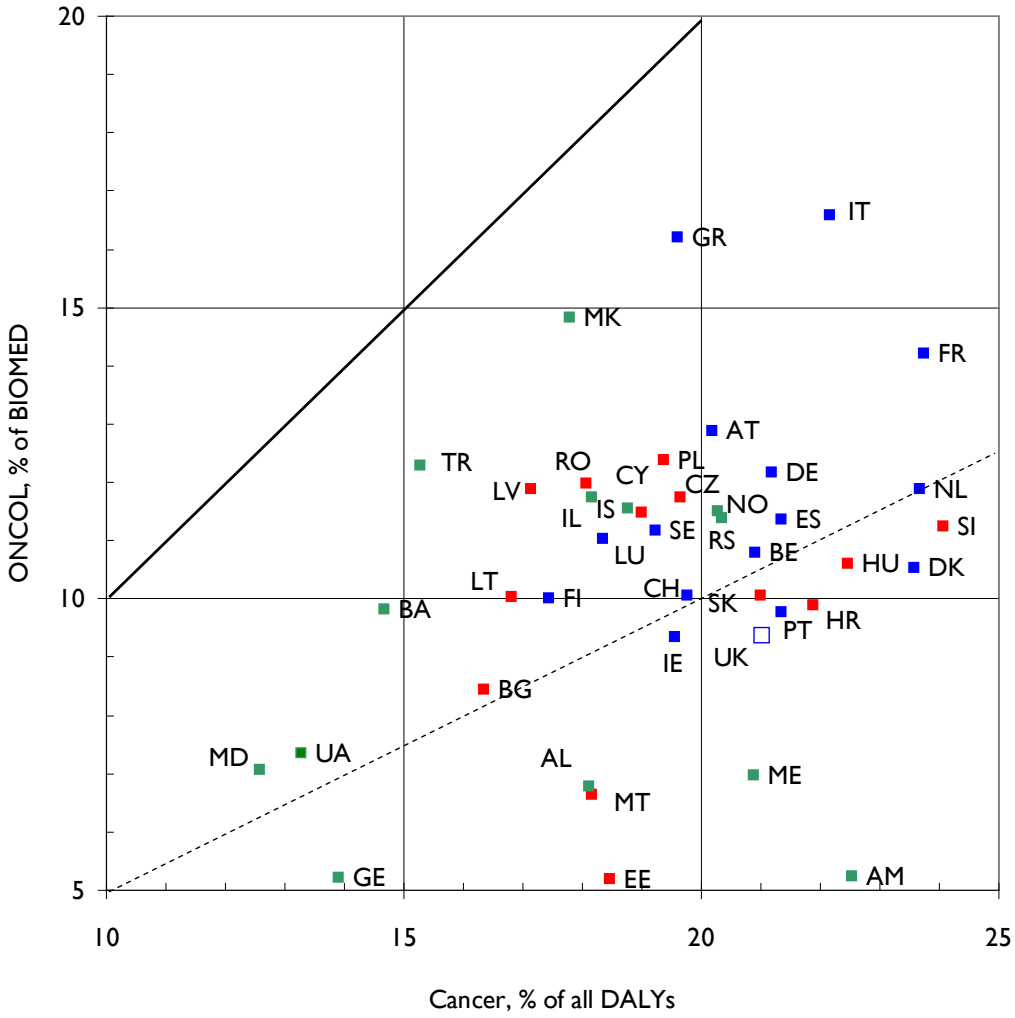


Figure 8. Output of cancer research, percent of all biomedical research, for countries in the European region (for codes, see Table 1), 2009-20 compared with the percentage of their overall disease burden attributable to cancer, 2015. (WHO data) *Dashed line represents outputs half the equivalent percentage. Blue squares: EU Member States prior to 2004; red squares: EU Member States acceding in 2004 and later; green squares: non-EU countries; blue hollow square: a former EU Member State (UK).*

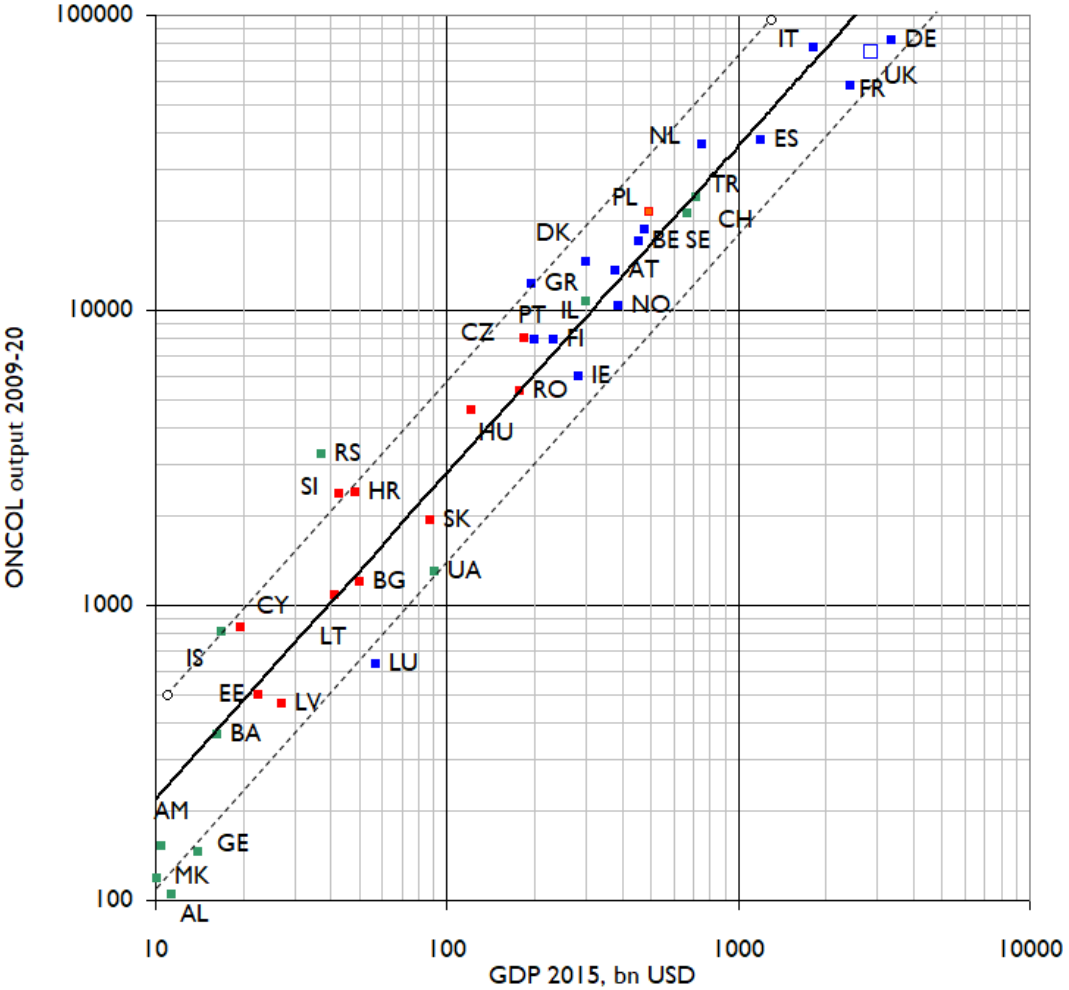


Figure 9. Comparison of the cancer research outputs from individual countries within the European region with their wealth (gross domestic product in 2015, billions of US dollars). *Logarithmic scales. Dashed lines show outputs twice and half the amounts expected from the least-squares trend-line. Blue squares: EU Member States prior to 2004; red squares: EU Member States acceding in 2004 and later; green squares: non-EU countries; blue hollow square: a former EU Member State (UK).*

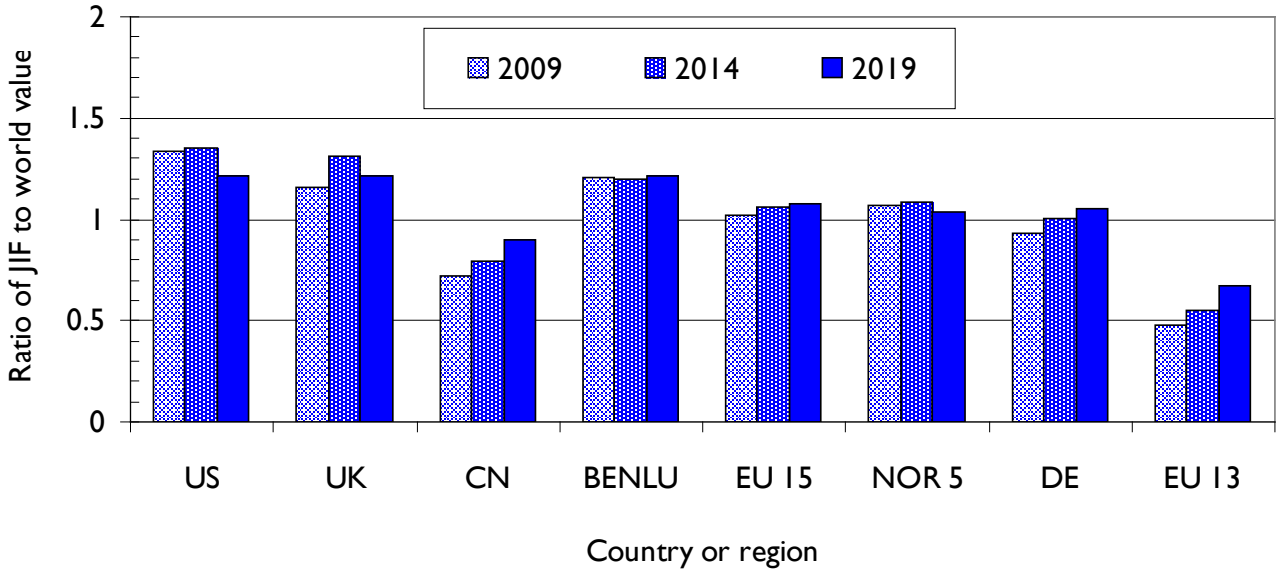


Figure 10a. Mean Journal Impact Factor for cancer research papers from nine countries or world regions, relative to world mean. *US = United States; UK = United Kingdom; CN = Canada; BENLU = Belgium, Netherlands, and Luxembourg; EU 15 = EU MS up to 2003; NOR 5 = five Nordic countries; DE = Germany; EU 13 = accession MS in 2004 and after;*

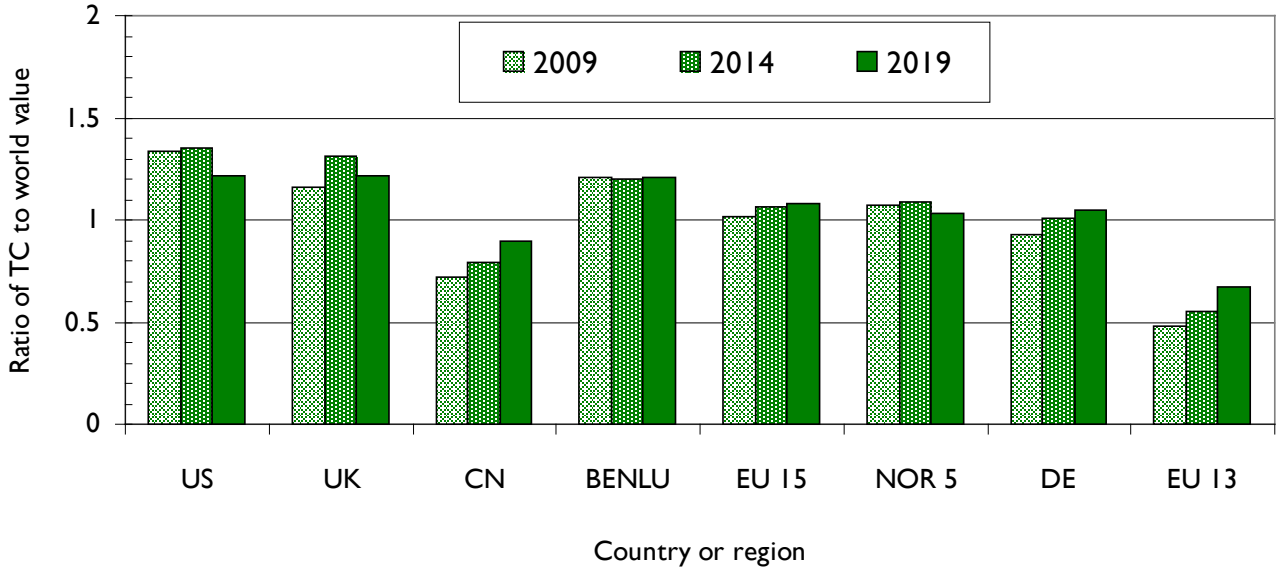


Figure 10b Mean citations for cancer research papers from nine countries or world regions, relative to world mean. *US = United States; UK = United Kingdom; CN = Canada; BENLU = Belgium, Netherlands, and Luxembourg; EU 15 = EU MS up to 2003; NOR 5 = five Nordic countries; DE = Germany; EU 13 = accession MS in 2004 and after;*

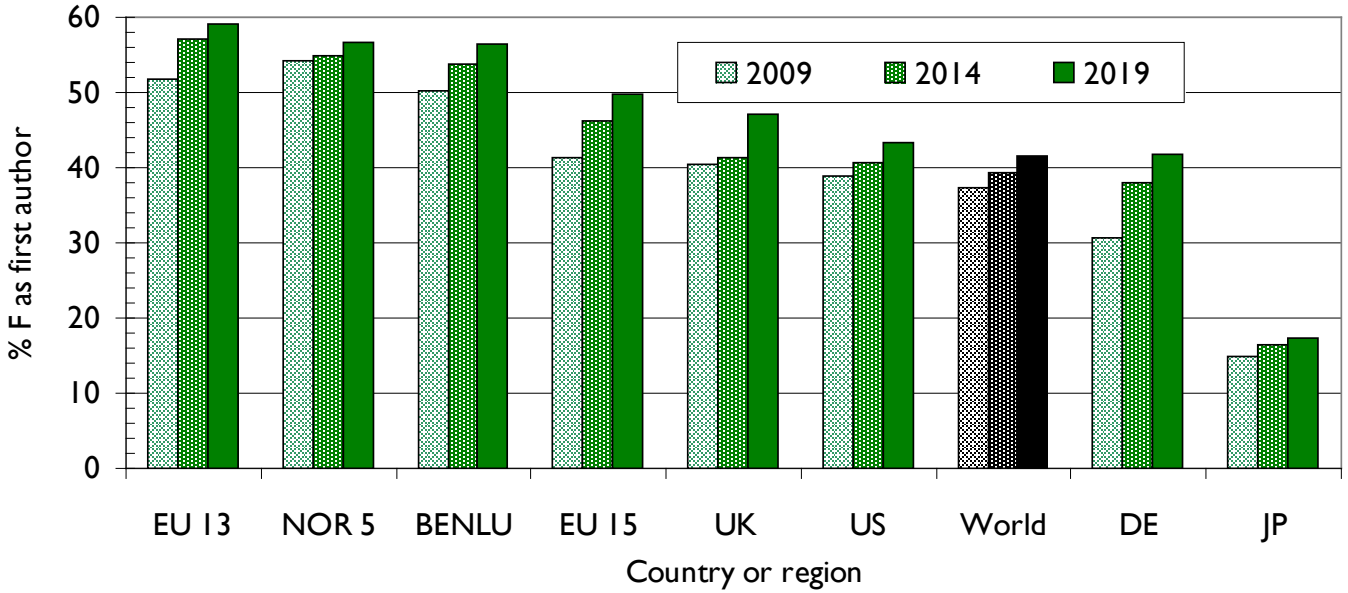


Figure 11a. Percentage of females in first author position for nine countries or regions in cancer research. *EU 13 = accession MS in 2004 and after; NOR 5 = five Nordic countries; BENLU = Belgium, Netherlands, and Luxembourg; EU 15 = EU MS up to 2003; DE = Germany; JP = Japan (given as comparison to reflect very low involvement)*

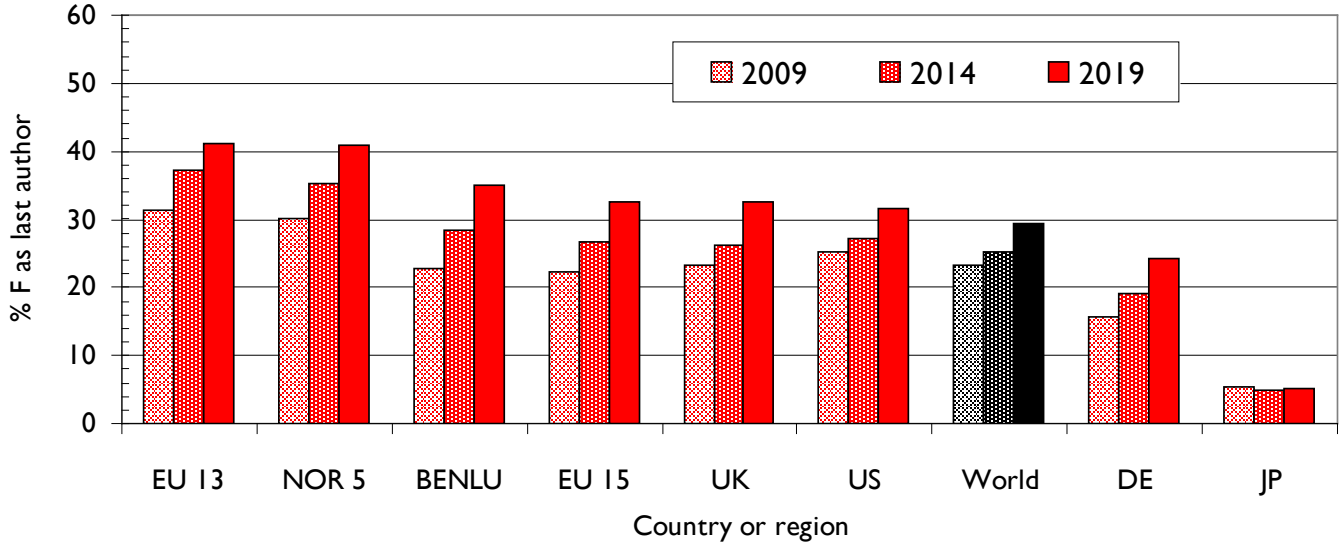
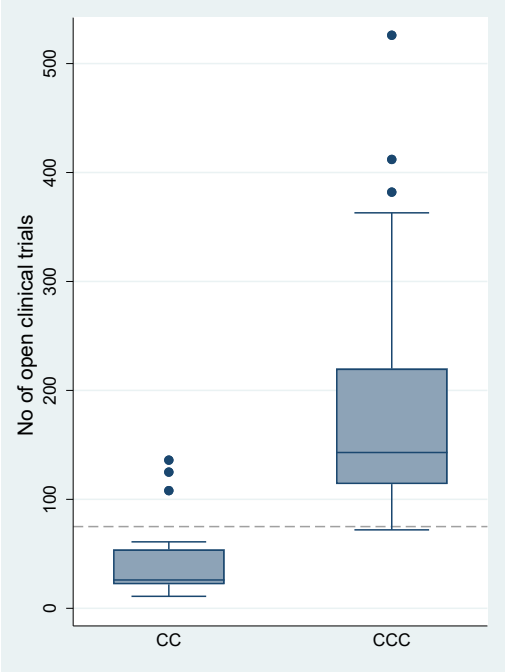
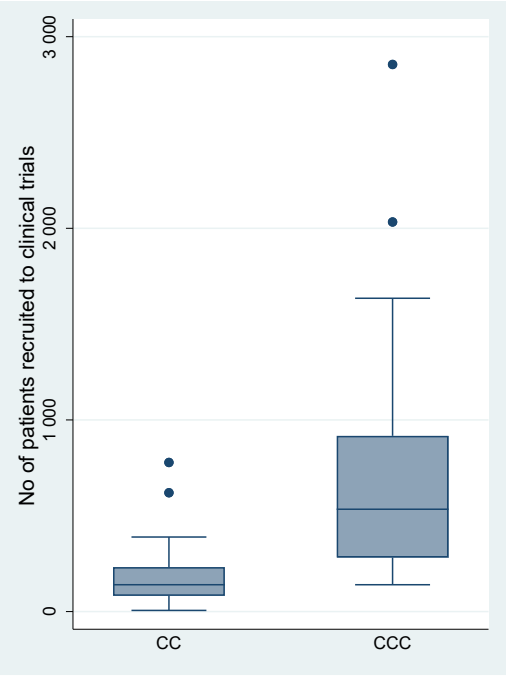


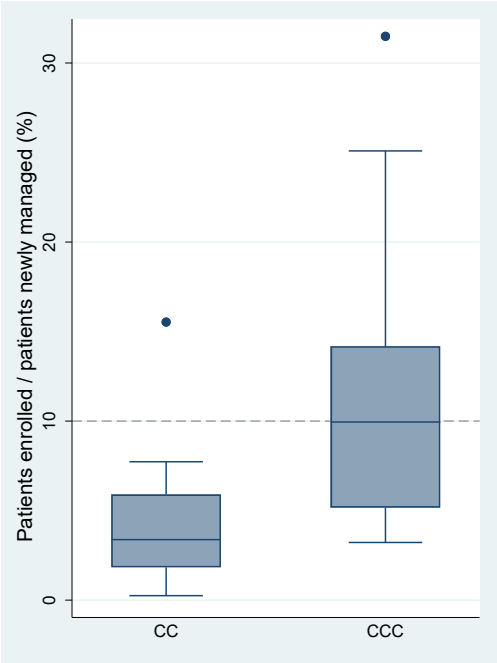
Figure 11b. Percentage of females in last (expected to be senior) author position for nine countries or regions in cancer research. *EU 13 = accession MS in 2004 and after; NOR 5 = five Nordic countries; BENLU = Belgium, Netherlands, and Luxembourg; EU 15 = EU MS up to 2003; DE = Germany; JP = Japan (given as comparison to reflect very low involvement)*


No of open clinical trials
0
100
200
300
400
500
CC
CCC

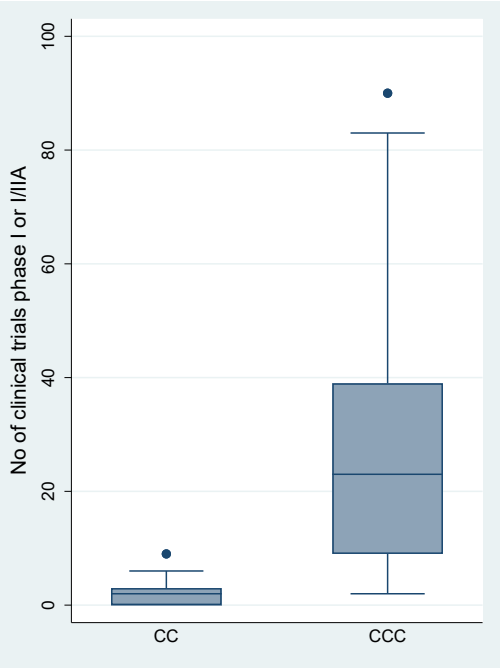
A


No of patients recruited to clinical trials
0
1 000
2 000
3 000
CC
CCC

B

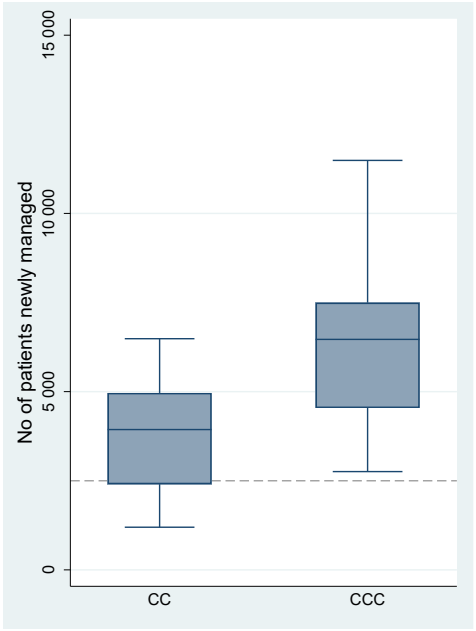


C

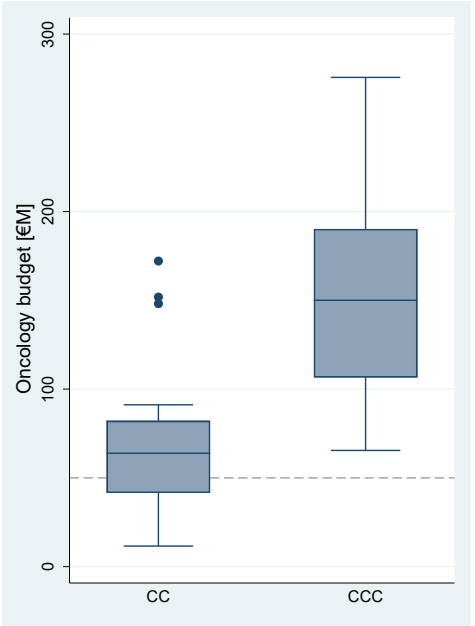


D

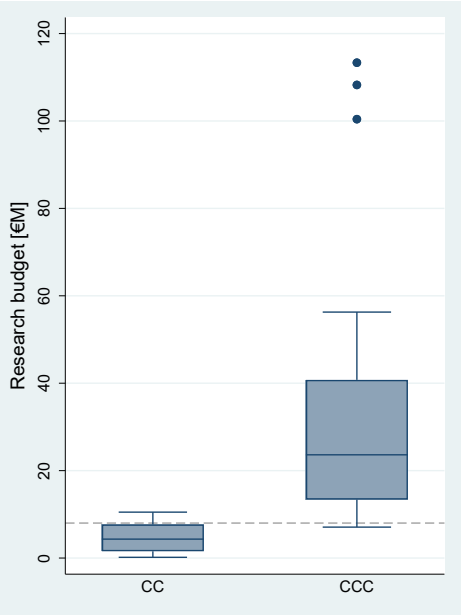
Figure 12 (A-D). Figure 12A shows the annual number of clinical trials open to recruitment at two clusters of OECI designated centres: Cancer Centres (CCs); and Comprehensive Cancer Centres (CCCs). CCs: 17: CCCs: 31; Median CC: 26; Median CCC: 143; Dotted line: 75 open trials (guide mininmum for OECI CCCs) . Figure 4B shows annual number of patients recruited: Median CC: 138; Median CCC: 534. Figure 4C shows the % of Patients enrolled in prospective interventional trials (Phases I-III)/patients newly managed in the centre: Median CC: 3.38%; Median CCC: 9.95%. Dotted line: 10% of newly managed patients enrolled in prospective interventional trials (guide minimum for OECI CCCs). Figure 4D shows number of open Phase I/IIA at the centres: Total Nº of centres: 45; CCs: 16; CCCs: 29; Median CC: 2; Median CCC: 23.


No of patients newly managed
0
5 000
10 000
15 000
CC
CCC

A


Oncology budget [€M]
0
100
200
300
CC
CCC

B



C

Figure 13. Figure 13A shows the annual number of patients newly managed in two clusters of OECI designated centres: Cancer Centres (CCs) and Comprehensive Cancer Centres CCCs). Total Nº of centres: 49; CCs: 18; CCCs: 31: Median CC: 3,936 pts; Median CCC: 6,466 pts. Dotted line: 2,500 patients newly managed in the centre (the OECI designation minimum for CCCs). Figure 13B shows the annual oncology care budget of the two sets of centres, adjusted by the purchasing power parity (PPP) of the Euro: Median CC: €63.9M; Median CCC: €150M; Dotted line: 50 €M oncology care budget, the nominal OECI designation minimum. Figure 13C shows the annual oncology research budget adjusted by PPP; Total Nº of centres: 48; CCs: 17; CCCs: 31; Median CC: €4.3M; Median CCC: €23.6M. Dotted line: €8M research budget (the OECI designated minimum for CCCs).

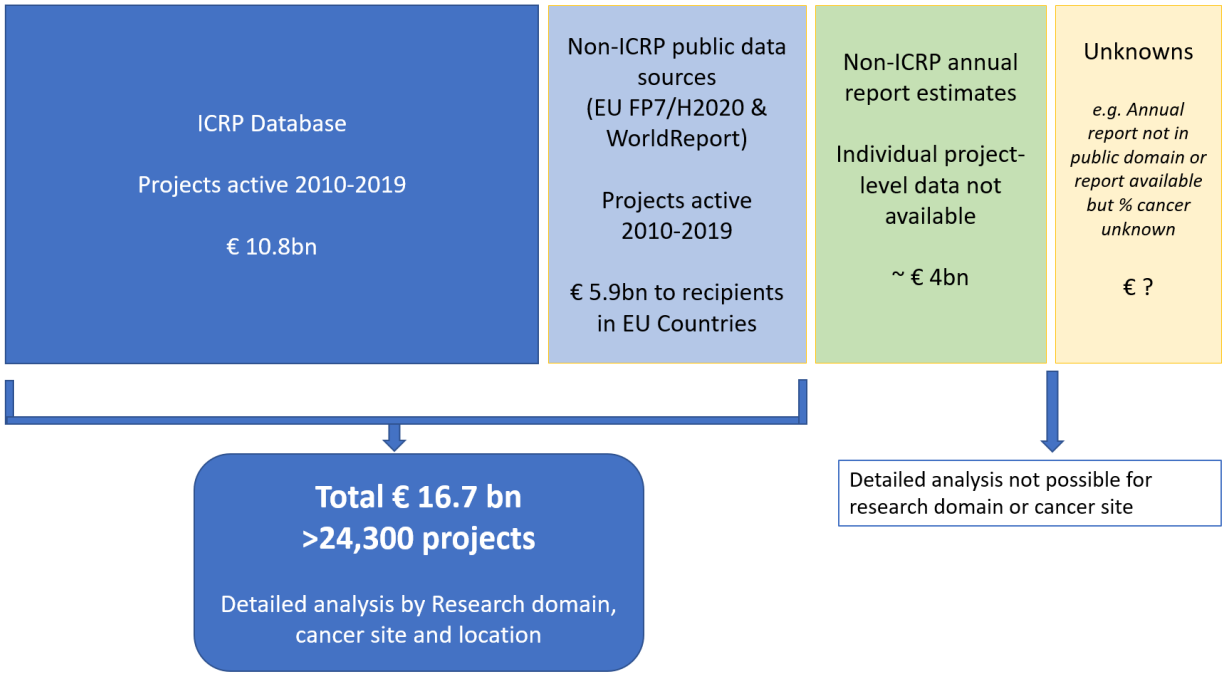


Figure 14 Overview of public sector/charitable and governmental funding for cancer research in Europe (in euro)

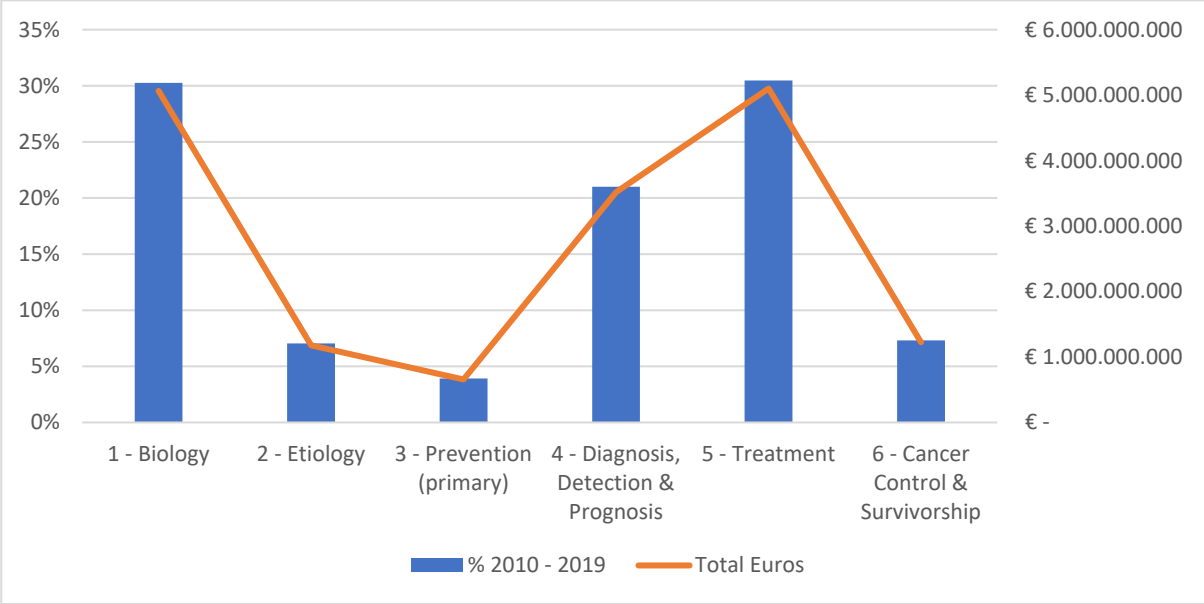


Figure 15 Investment in European cancer research by research domain (2010 – 2019)

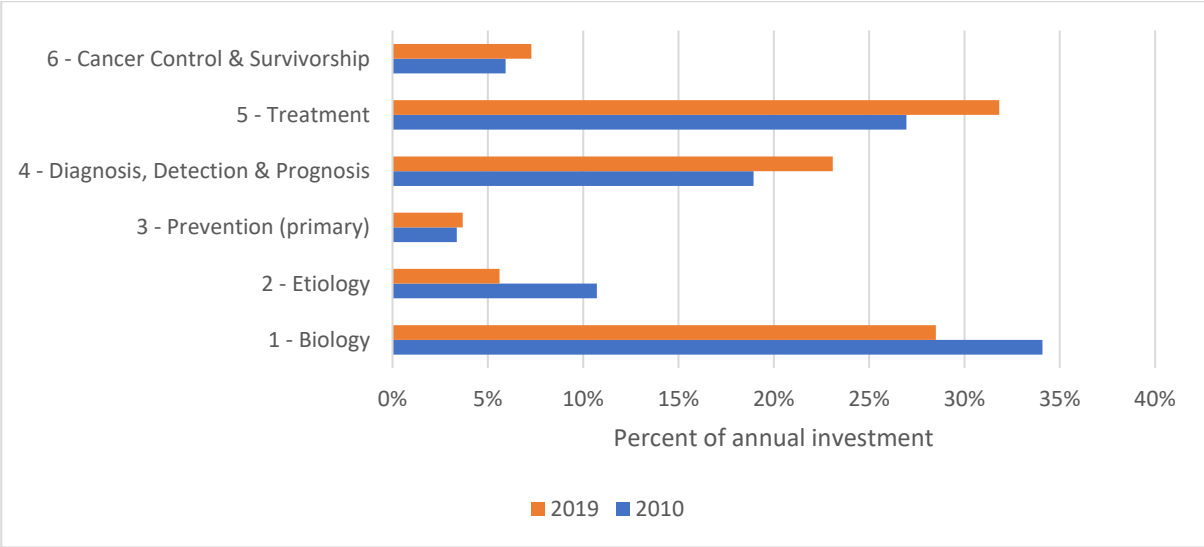


Figure 16 Changes in cancer research investment by research domain (2010 – 2019)

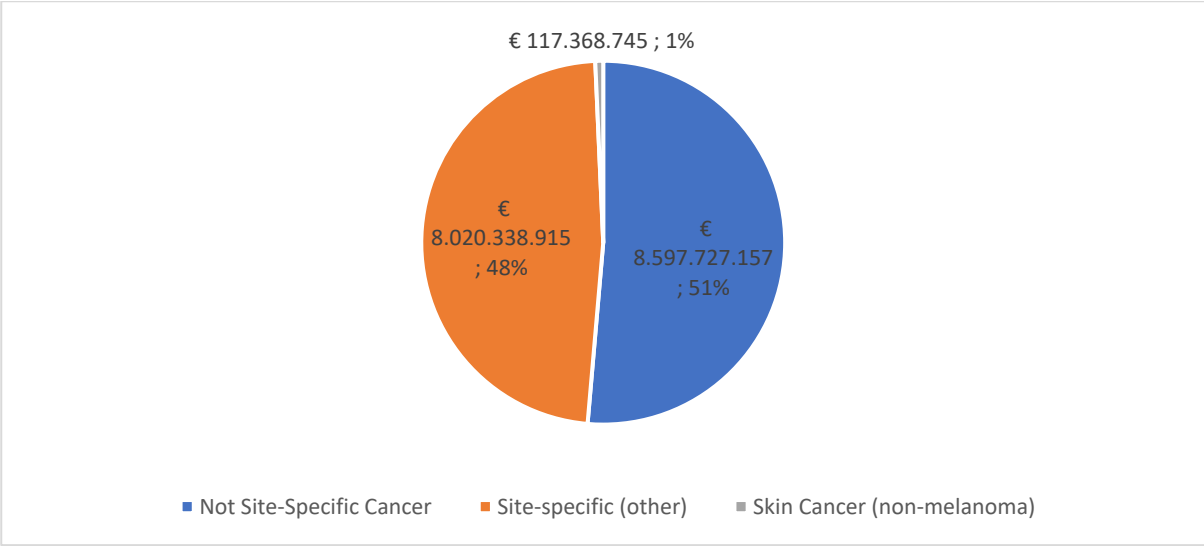


Figure 17 European cancer research spend, not site specific versus site specific cancer

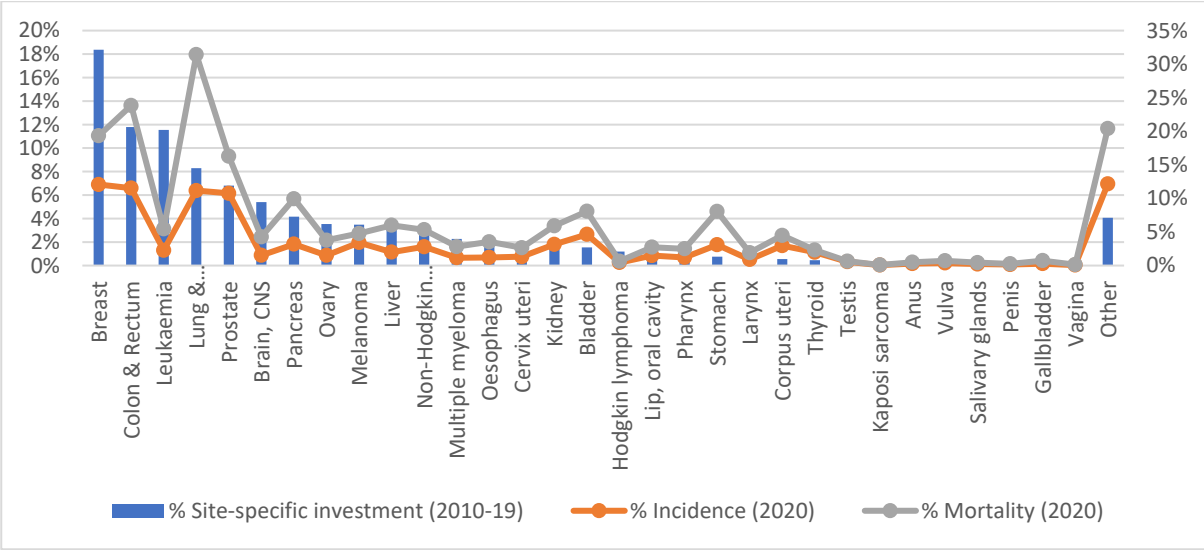


Figure 18 European investment in cancer research (2010 – 2019) – % investment in types of cancer compared to % incidence and mortality (2020)

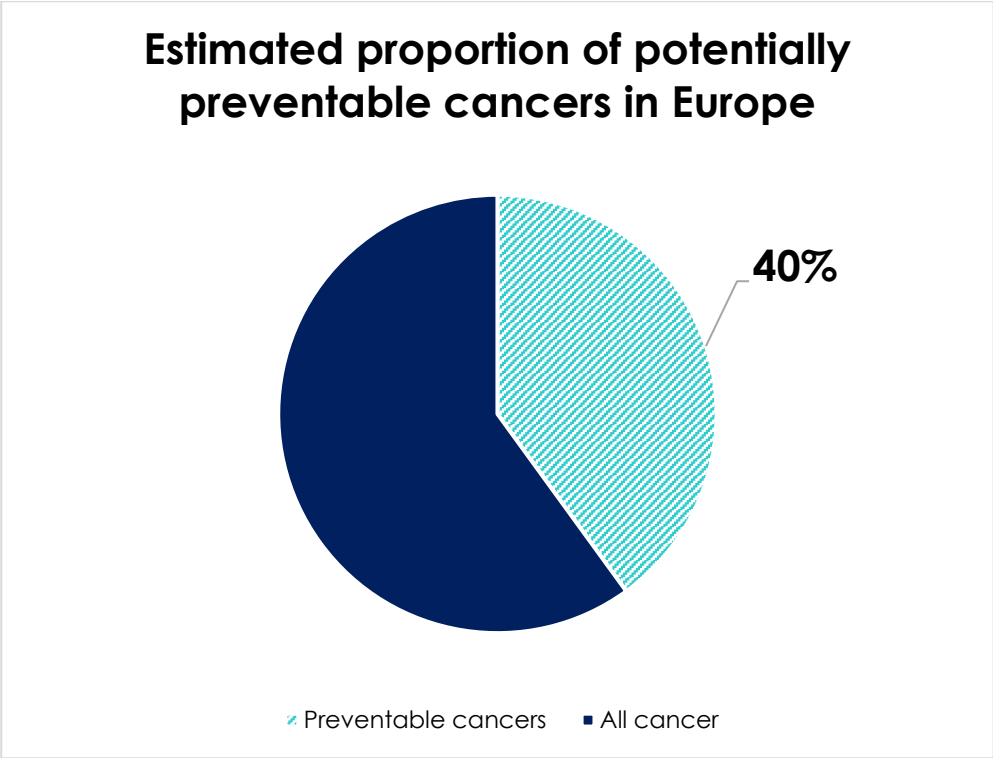


Figure 19a Estimated proprotion of potentially preventable cancers in Europe

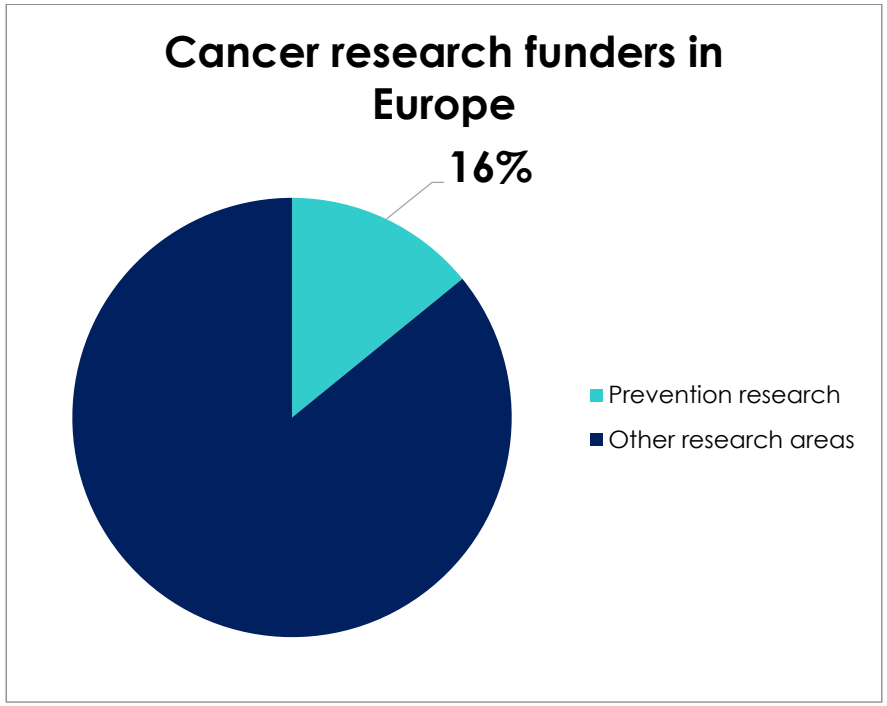


Figure 19b Cancer research funders in Europe Prevention v Others

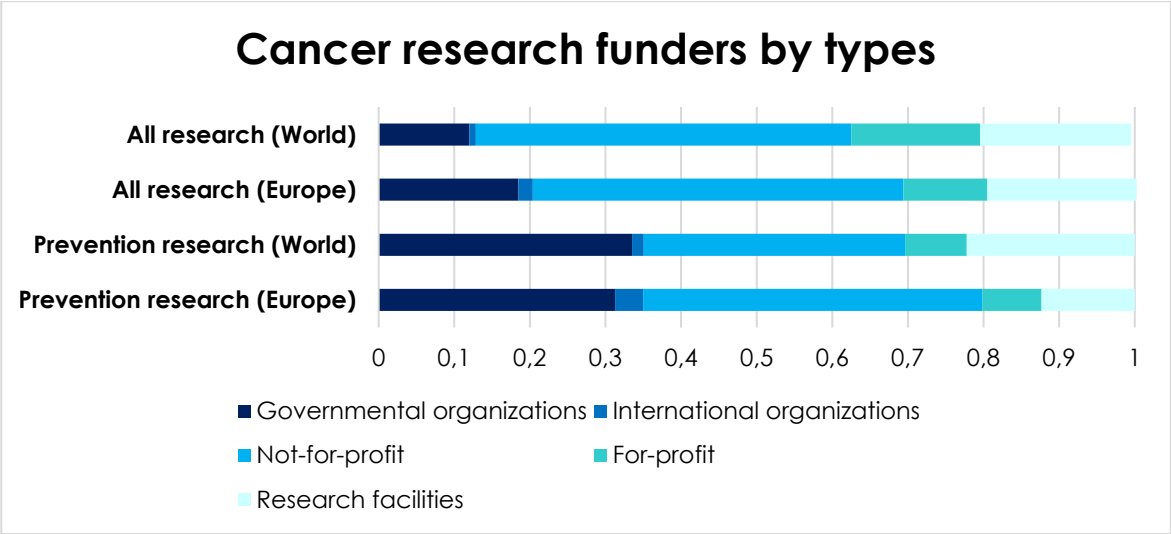


Figure 20a Cancer Research Funders by research type Prevention V All

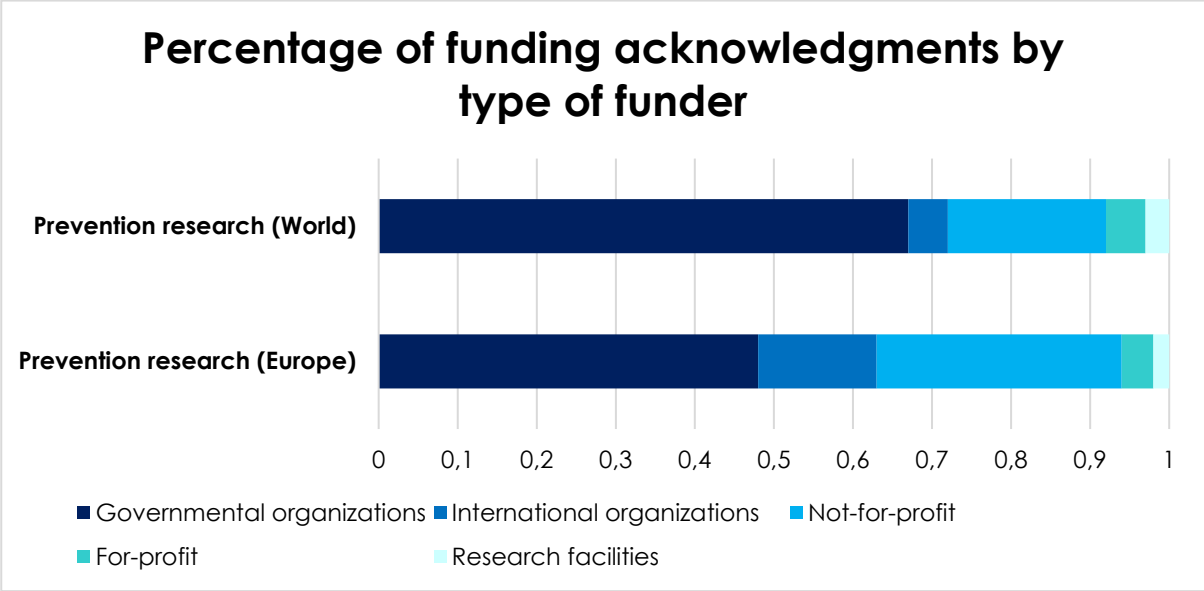


Figure 20b Percentage of funding acknowledgement by funder type

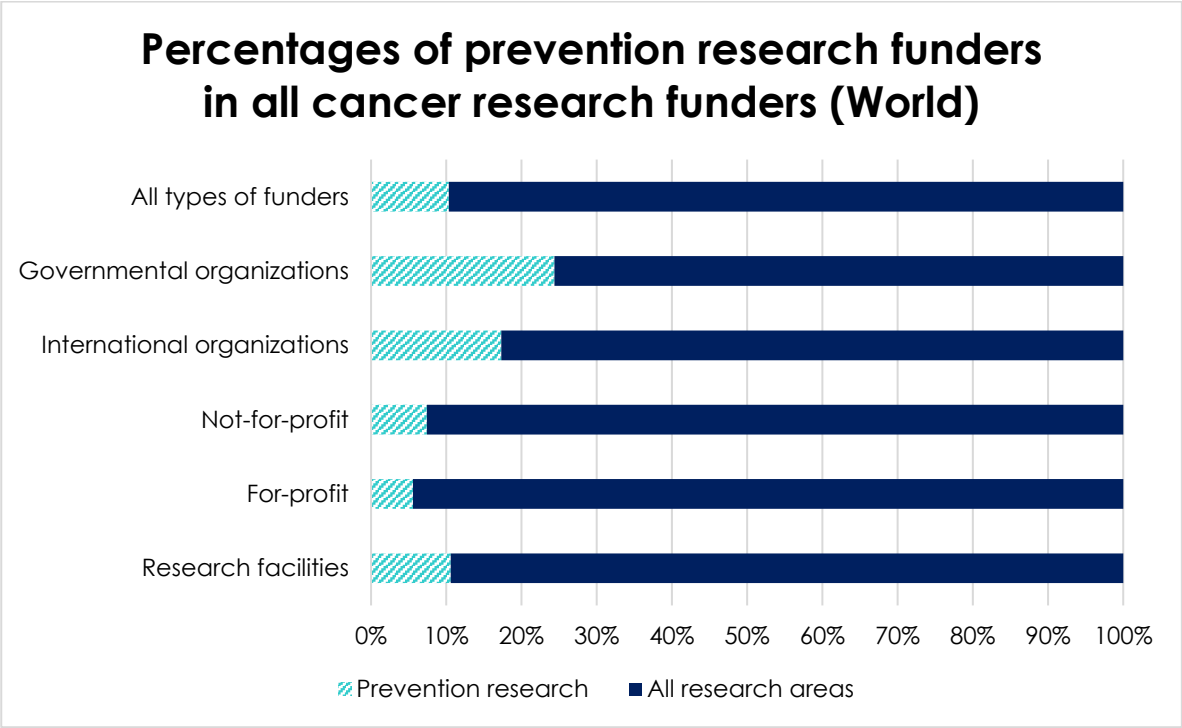


Figure **21a** Percentage of prevention research funders within all cancer research funders (World)

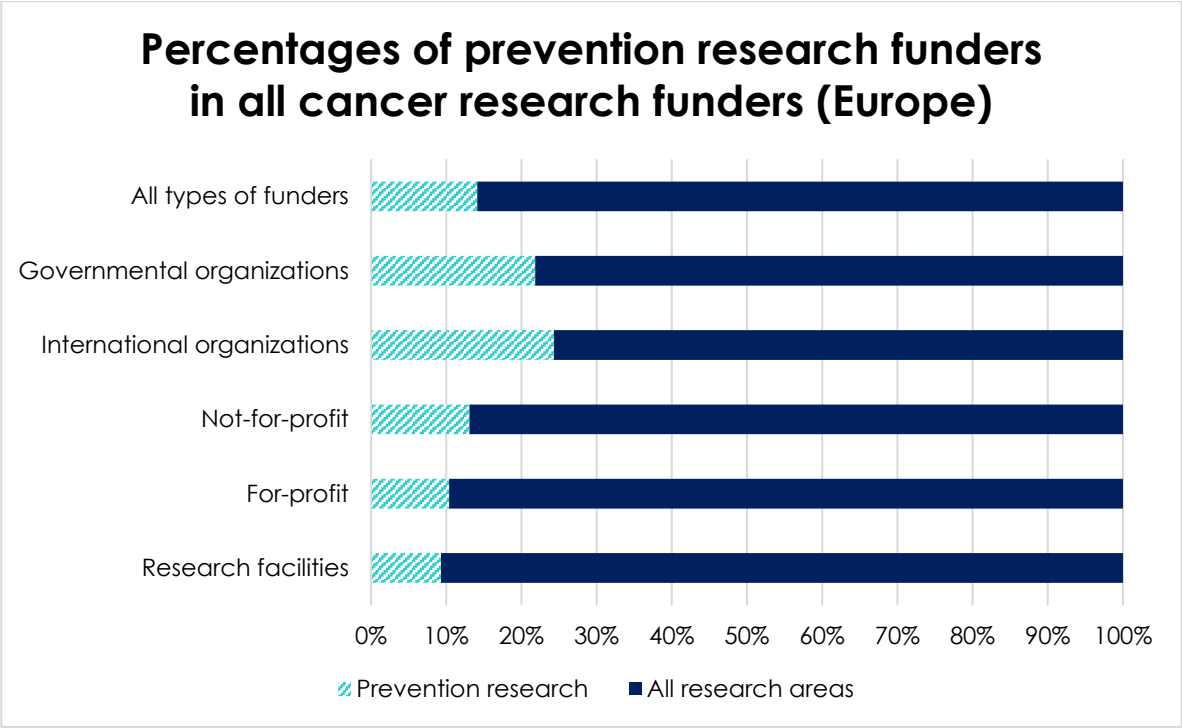


Figure 21b Percentage of prevention research funders within all cancer research funders (Europe)

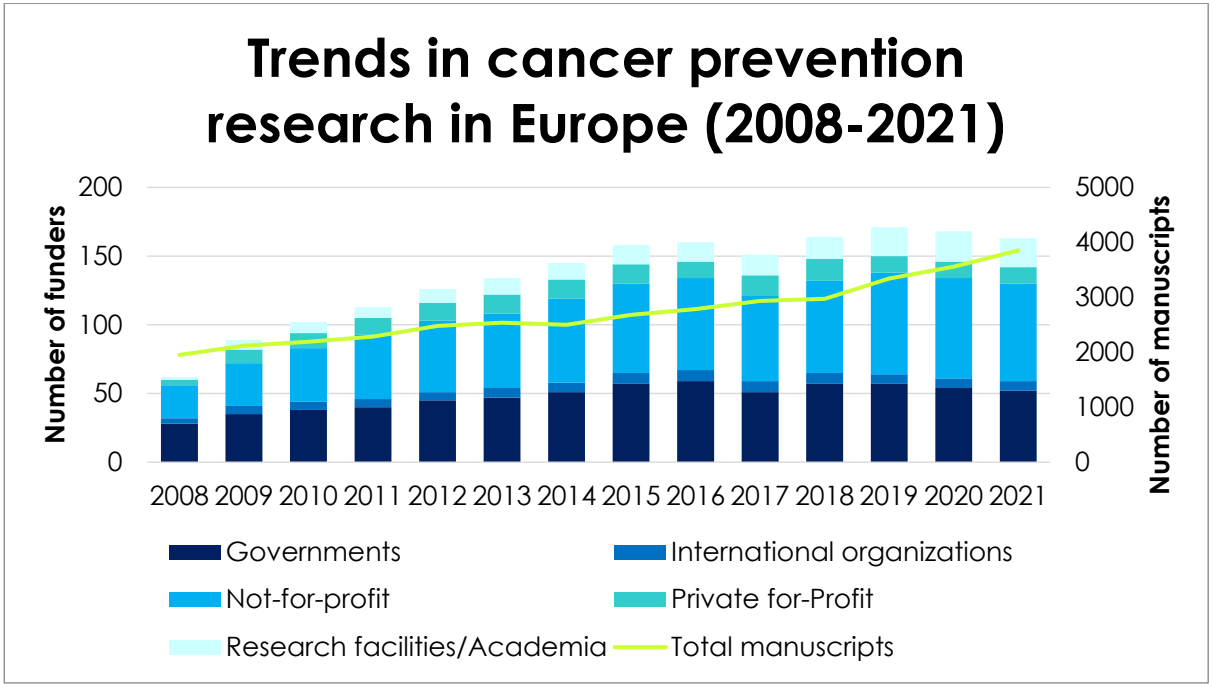


Figure 22 Trend in Cancer Prevention Research in Europe (2008 – 2021)

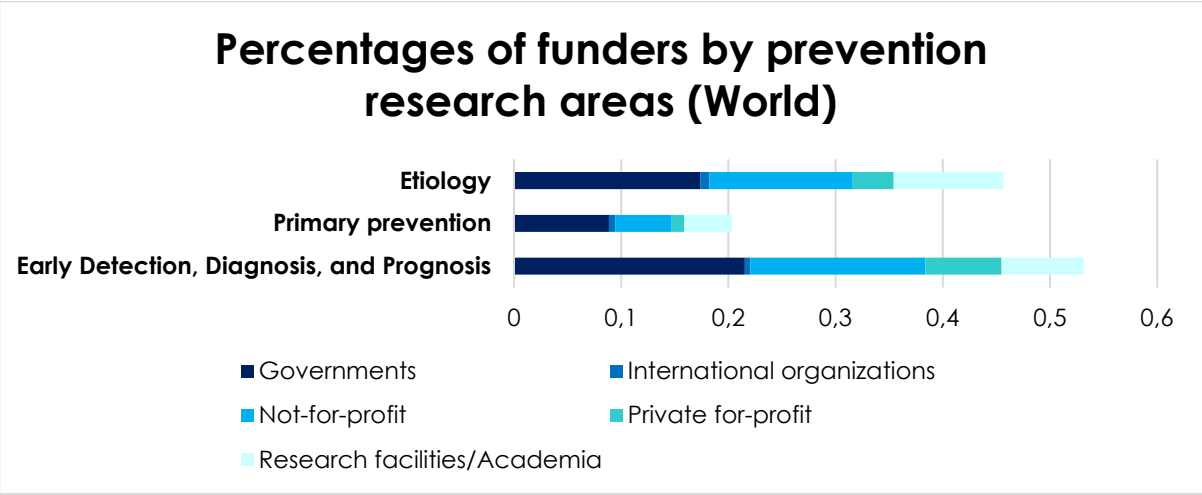


Figure 23a Percentage of funders by prevention research area (World)

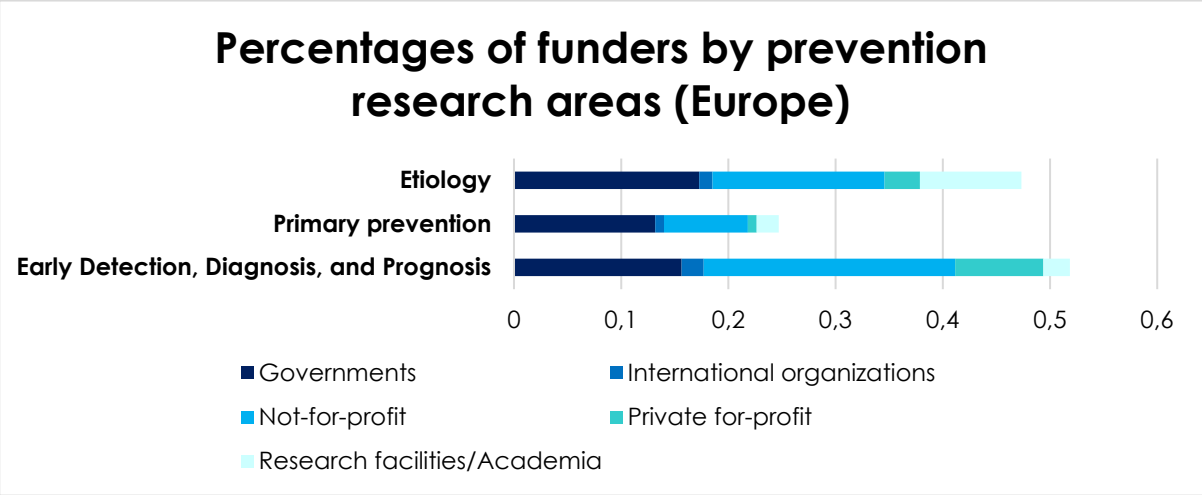


Figure 23b Percentage of funders by prevention research area (Europe)

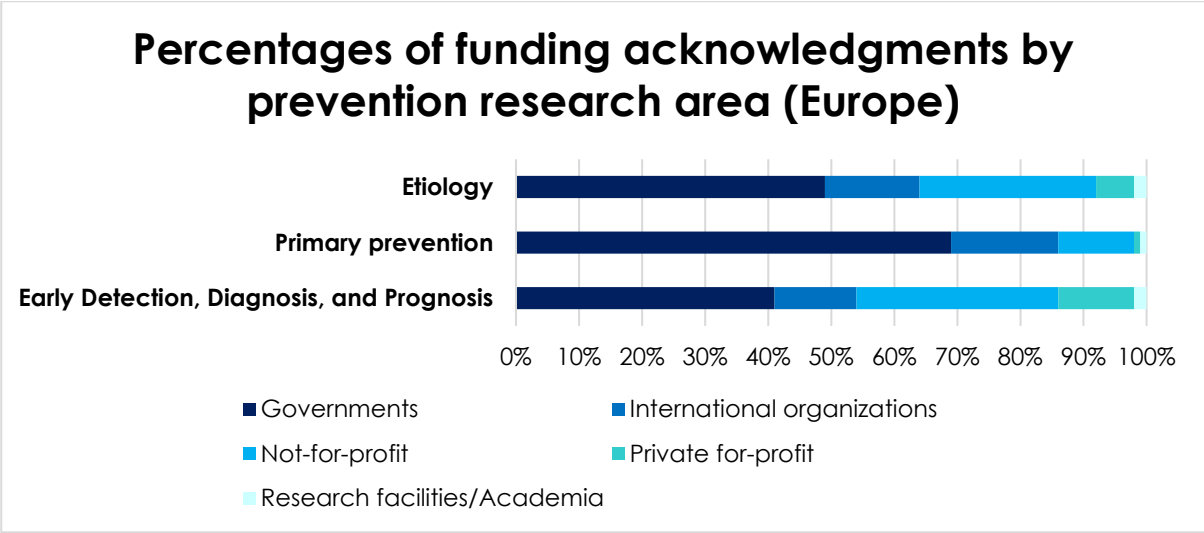


Figure 23c Percentage of funding acknowledgements by prevention research area (Europe)

Figure 24 European Code of Cancer Practice

Figure 25 Summary of European data on the impact of the COVID-19 pandemic on cancer

Figure 25 Impact of the COVID pandemic on cancer at European level. Time to Act Data Navigator is a visialisation tool that can be used to capture different impacts of the pandemic which can be searcehd by impact on cancer site, by treatment, by diagnosis by country etc

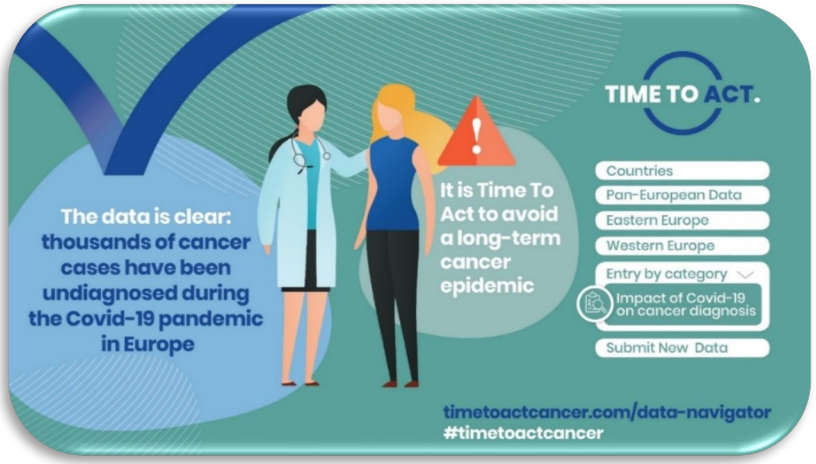

TIME TO ACT.
The data is clear: thousands of cancer cases have been undiagnosed during the Covid-19 pandemic in Europe
It is Time To Act to avoid a long-term cancer epidemic
Countries
Pan-European Data
Eastern Europe
Western Europe
Entry by category
Impact of Covid-19 on cancer diagnosis
Submit New Data
timetoactcancer.com/data-navigator
#timetoactcancer

Table 1. The 44 countries in the European region evaluated in this study, with ISO2 codes and populations (millions).

Country	*ISO2*	*Pop*	*Country*	*ISO2*	*Pop*	*Country*	*ISO2*	*Pop*
Albania	AL	2.9	Germany	DE	80.7	North Macedonia	MK	2.1
Armenia	AR	3.0	Greece	GR	11.0	Norway	NO	5.2
Austria	AT	8.5	Hungary	HU	9.9	Poland	PL	38.6
Belgium	BE	11.3	Iceland	IS	0.3	Portugal	PT	10.4
Bosnia Herceg	BA	3.8	Ireland	IE	4.7	Romania	RO	19.5
Bulgaria	BG	7.2	Israel	IL	8.1	Serbia	RS	8.9
Croatia	HR	4.2	Italy	IT	59.8	Slovakia	SK	5.4
Cyprus	CY	1.2	Latvia	LV	2.0	Slovenia	SI	2.1
Czech Republic	CZ	10.5	Liechtenstein	LI	0.04	Spain	ES	46.1
Denmark	DK	5.7	Lithuania	LT	2.9	Sweden	SE	9.8
Estonia	EE	1.3	Luxembourg	LU	0.6	Switzerland	CH	8.3
Faroe Islands	FO	0.05	Malta	MT	0.4	Turkey	TR	78.7
Finland	FI	5.5	Moldova	MD	4.1	Ukraine	UA	44.8
France	FR	64.4	Montenegro	ME	0.6	United Kingdom	UK	64.7
Georgia	GE	4.0	Netherlands	NL	16.9			

Table 2a. List of 14 research domains for the analysis of cancer research outputs in the European region and (for comparison) in the world, 2011-20. *Note: some papers described more than one type or domain of research, and some did not indicate any domain.*

Research	*Code*
Systemic	CHEM
Clinical trials	CLIN
Diagnosis	DIAG
Epidemiology	EPID
Basic/Genetics	GENE

Research domain	*Code*
Paediatrics	PAED
Palliative care	PALL
Pathology	PATH
Prognosis	PROG
Quality of life	QUAL

Research domain	*Code*
Radiotherapy	RADI
Screening	SCRE
Surgery	SURG
Targeted therapy	TARG

Table 2b. List of 17 anatomical sites for the analysis of cancer research outputs in the European region and (for comparison) in the world, 2011-20. *Note: some papers described research on more than one anatomical site, and some did not indicate any site.*

Site	*Code*
Bladder	BLA
Brain	CNS
Breast	MAM
Cervix	CER
Colorectal	COL
Head and neck (oral)	MOU

Site	*Code*
Haematological	HAE
Kidney	KID
Liver	LIV
Lung	LUN
Melanoma	SKI
Oesophagus	OES

Site	*Code*
Ovary	OVA
Pancreas	PAN
Prostate	PRO
Stomach	STO
Uterus	UTE

Table 3. The preference of ten countries in the European region (columns) for other countries (rows) as partners in cancer research, 2009-20, and with ten other leading countries. *Cells with preference > 2 tinted green, if > 1.414 tinted pale green, if < 0.707 tinted pale yellow, if < 0.5 tinted pink.*

Partner country↓	*DE*	*IT*	*UK*	*FR*	*ES*	*NL*	*TR*	*SE*	*CH*	*PL*
Switzerland	5.43	3.71	2.41	3.38	2.41	2.60	1.86	1.66		1.74
Sweden	2.78	2.28	3.43	2.44	2.48	3.12	1.61		1.79	2.35
Netherlands	2.86	2.45	2.89	2.52	2.45		1.58	2.51	2.30	2.03
Spain	2.20	3.05	2.40	2.80		2.37	1.82	1.96	2.06	2.20
France	1.99	2.44	1.99		2.33	2.04	1.41	1.63	2.36	1.67
United Kingdom	1.84	1.97		1.93	1.94	2.22	1.20	2.10	1.68	1.46
Germany		1.69	1.59	1.66	1.56	1.91	1.28	1.53	2.86	1.63
Italy	1.58		1.60	1.91	1.99	1.58	1.31	1.23	2.03	1.42
Poland	1.80	1.64	1.38	1.56	1.76	1.57	1.60	1.51	1.21	
Australia	1.18	1.17	2.17	1.29	1.18	1.36	0.77	1.27	1.14	1.27
Canada	1.17	1.11	1.41	1.36	1.03	1.26	0.75	0.93	1.13	1.13
Brazil	0.62	0.88	0.75	0.87	1.00	0.55	0.96	0.49	0.64	0.87
USA	0.60	0.63	0.60	0.51	0.53	0.51	0.67	0.47	0.55	0.44
Turkey	0.40	0.44	0.33	0.39	0.44	0.37		0.32	0.40	0.50
Iran	0.27	0.32	0.31	0.20	0.16	0.24	1.34	0.52	0.23	0.33
Japan	0.29	0.28	0.30	0.30	0.27	0.24	0.40	0.26	0.26	0.24
South Korea	0.26	0.28	0.26	0.28	0.32	0.22	0.45	0.20	0.22	0.32
India	0.18	0.19	0.29	0.22	0.17	0.15	0.43	0.17	0.18	0.25
China	0.13	0.09	0.16	0.11	0.08	0.10	0.12	0.15	0.09	0.10

Table 4a. Relative commitment (RC) to cancer research overall, and on first nine anatomical sites (for codes, see Table 2b) by 20 leading European region countries. *Cells with RC > 2 tinted green, if RC > 1.414 tinted pale green, if RC < 0.707 tinted pale yellow, if RC < 0.5 tinted pink.*

ISO2	*HAE*	*MAM*	*COL*	*CNS*	*PRO*	*LUN*	*HEN*	*LIV*	*KID*
DE	1.37	0.81	0.92	1.30	1.27	0.71	0.86	0.80	1.13
IT	1.43	0.93	1.01	0.96	1.16	0.87	1.08	0.93	1.09
UK	1.17	1.12	1.12	0.80	1.29	0.74	0.86	0.55	0.87
FR	1.47	0.98	0.88	1.03	1.05	0.91	0.80	0.83	1.30
ES	1.37	1.07	1.29	0.83	1.05	1.02	0.87	0.65	1.07
NL	1.18	1.11	1.41	0.85	1.27	0.91	1.01	0.53	0.87
TR	1.33	1.12	0.81	1.06	1.13	0.92	1.10	0.72	1.65
SE	1.28	1.27	1.23	0.84	1.79	0.55	0.68	0.42	0.78
CH	1.43	0.89	0.75	1.29	1.18	0.87	0.95	0.73	0.83
PL	1.25	1.07	0.98	0.93	0.68	0.92	1.00	0.35	1.14
BE	1.24	1.16	0.95	0.72	1.28	0.93	0.84	0.65	0.90
DK	1.38	1.19	1.49	0.83	1.22	0.83	0.77	0.42	0.81
AT	1.59	0.89	0.85	1.03	1.23	0.84	0.66	0.71	1.53
GR	1.42	1.14	1.10	0.69	0.92	1.11	1.11	0.66	0.99
IL	1.98	0.97	0.91	1.06	0.62	0.64	0.96	0.42	0.68
NO	1.12	1.39	1.41	1.15	1.28	0.78	0.62	0.45	0.52
FI	1.18	1.39	1.07	0.59	2.31	0.44	1.23	0.36	0.97
CZ	2.26	0.68	0.99	0.89	0.76	0.59	0.70	0.42	2.11
PT	0.84	1.34	1.00	0.83	1.04	0.58	0.90	0.62	0.81
IE	0.94	1.61	1.54	0.60	1.54	0.77	0.81	0.40	0.85

Total	43308	42848	28498	23586	20952	20229	19789	17334	9609
% of wld	*40.2*	*35.0*	*37.0*	*34.2*	*38.5*	*27.0*	*32.9*	*23.4*	*34.5*

Table 4b. Relative commitment (RC) to cancer research on second eight anatomical sites (for codes, see Table 2b) and all cancer research (ONCOL) by 20 leading European region countries. *Cells with RC > 2 tinted green, if RC > 1.414 tinted pale green, if RC < 0.707 tinted pale yellow.*

ISO2	*SKI*	*STO*	*OVA*	*PAN*	*CER*	*BLA*	*UTE*	*OES*	*ONCOL*	% wld
DE	1.43	0.72	0.84	1.25	0.50	1.25	0.62	0.77	81325	6.46
IT	1.37	0.77	0.99	1.08	0.58	1.10	1.07	0.34	76218	6.05
UK	1.09	0.64	1.11	0.85	0.78	0.99	0.76	1.19	73948	5.87
FR	1.30	0.50	0.86	0.88	0.84	0.94	0.74	0.44	56596	4.49
ES	1.36	0.64	0.85	0.89	0.70	1.42	0.96	0.32	37213	2.95
NL	1.12	0.78	0.87	0.90	1.08	1.30	0.89	1.57	36127	2.87
TR	0.86	1.05	1.23	0.68	1.05	1.69	2.36	0.38	23818	1.89
SE	1.02	0.73	0.97	0.99	0.88	1.15	1.03	1.22	21250	1.69
CH	1.51	0.46	0.69	0.68	0.57	1.27	0.60	0.57	21085	1.67
PL	1.50	0.76	1.99	0.75	0.92	1.02	2.16	0.45	18386	1.46
BE	1.19	0.56	1.35	0.66	1.13	0.80	1.07	0.52	16895	1.34
DK	1.20	0.57	1.65	0.67	1.14	1.13	0.84	0.46	14301	1.14
AT	1.78	0.50	1.09	0.69	0.80	2.28	0.79	0.50	13437	1.07
GR	1.34	0.85	1.35	1.16	1.00	1.45	1.58	0.49	12058	0.96
IL	1.41	0.48	1.32	0.81	0.44	0.79	0.89	0.25	10592	0.84
NO	0.91	0.80	1.58	0.90	1.34	0.64	2.12	0.60	10181	0.81
FI	0.87	0.72	1.53	0.86	1.18	1.17	1.44	0.90	7906	0.63
CZ	0.99	0.45	0.93	0.80	0.93	1.35	1.07	0.53	7898	0.63
PT	1.20	1.21	0.61	0.46	1.05	1.67	0.80	0.49	7883	0.63
IE	0.96	0.71	0.89	0.65	0.71	0.56	0.50	2.00	5877	0.47

Total	17269	14016	9712	9631	6638	5649	5496	4838	426869	33.9

Table 5. Relative commitment (RC) to cancer research in different research domains (for codes, see Table 2a) by 20 leading European region countries. *Cells with RC > 2 tinted green, if RC > 1.414 tinted pale green, if RC < 0.707 tinted pale yellow, if RC < 0.5 tinted pink*

.

ISO2	*GENE*	*PROG*	*EPID*	*SURG*	*CHEM*	*PATH*	*DIAG*	*RADI*	*TARG*	*PAED*	*CLIN*	*SCRE*	*QUAL*	*PALL*
DE	0.99	1.04	0.91	0.93	0.89	1.05	1.12	1.23	1.26	1.03	1.51	0.80	1.22	1.09
IT	0.86	1.00	0.90	1.14	1.06	0.98	1.06	0.89	1.57	0.97	1.49	0.75	0.75	0.76
UK	0.96	1.02	1.22	0.92	0.91	0.94	1.08	1.03	1.19	1.09	1.89	1.36	1.48	1.40
FR	0.87	1.00	1.10	0.89	1.08	0.83	0.94	1.29	1.62	1.09	2.02	0.93	0.94	0.69
ES	1.04	1.02	1.08	0.72	1.05	1.04	1.11	0.77	1.60	0.83	1.94	1.01	0.99	0.79
NL	0.91	1.18	1.30	1.03	0.95	1.10	1.23	1.72	1.23	1.27	1.97	1.76	2.34	1.63
TR	0.71	0.98	0.87	1.35	1.11	1.10	1.28	0.90	0.78	1.84	0.51	0.87	1.19	0.99
SE	1.18	1.24	1.98	0.73	0.76	0.98	1.05	0.96	0.83	1.44	1.43	1.48	1.64	1.36
CH	0.90	1.07	0.82	0.80	1.09	1.13	1.15	1.34	1.76	1.13	2.31	0.87	0.96	0.94
PL	1.14	0.80	0.92	0.72	1.06	0.89	1.06	0.87	1.18	1.08	1.41	0.58	1.10	0.92
BE	0.85	1.05	0.78	0.79	1.21	0.92	1.00	1.40	2.05	1.07	3.35	1.04	1.33	0.96
DK	1.04	1.19	2.10	0.68	0.85	1.01	1.19	1.34	0.98	1.23	1.97	1.57	1.71	1.46
AT	0.90	1.26	0.96	0.91	0.95	1.14	1.09	1.12	1.52	1.18	1.69	0.80	1.22	0.87
GR	0.99	1.01	1.29	1.03	0.99	0.95	1.12	0.67	1.20	0.85	1.42	0.74	0.89	0.76
IL	0.97	0.93	1.05	0.71	1.05	0.68	0.98	0.67	1.32	1.66	1.46	1.02	1.02	1.17
NO	1.14	1.32	2.05	0.73	0.70	1.14	0.90	0.99	0.71	1.13	1.55	1.96	2.32	2.16
FI	1.28	1.34	2.21	0.62	0.74	1.09	0.91	0.71	0.95	1.29	1.53	2.14	1.30	0.77
CZ	1.26	1.04	1.02	0.74	1.21	1.25	1.29	0.69	1.54	1.20	1.68	0.50	0.44	0.29
PT	1.00	0.83	0.92	0.54	0.94	1.02	1.09	0.51	0.81	0.81	0.67	1.08	1.42	1.28
IE	0.93	1.04	1.13	1.07	0.91	0.97	1.19	0.98	1.02	0.97	1.31	1.43	1.72	1.75

Total	76357	57622	49785	48965	44751	36493	28048	24767	20258	19948	14479	9423	8406	8085
% wld	31.2	33.3	33.9	32.0	33.6	33.4	37.5	37.8	38.4	40.7	39.9	37.1	42.4	35.5

Table 6. List of the 51 OECI accredited cancer centres, with their country (for ISO codes, see table footnote), and numbers of papers in the WoS in 2012-21 (N).

Centre name	*ISO*	*Centre name*	*ISO*
Karolinska Institutet	SE		
CRUK Cambridge Centre	UK	Azienda Unità Reggio Emilia	IT
Christie NHS Foundation	UK	Candiolo Cancer Institute	IT
King's Health Partners	UK	Centre Francois Baclesse	FR
Netherlands Cancer Institute	NL	TAYS Cancer Centre	FI
APHP Sorbonne, Paris	FR	Oncology Institute Ljubljana	SI
Ist. Nazionale dei Tumori di Milano	IT	Kuopio University Hospital	FI
Univ. Medisch Centrum Groningen	NL	Istituto Tumori Giovanni Paolo II	IT
Oslo University Hospital	NO	Anadolu Medical Center	TR
European Institute of Oncology, Milan	IT	TYKS Cancer Centre	FI
Institut Curie, Paris	FR	Inst. Valenciano de Oncologia	ES
Ist. Nazionale Tumori Regina Elena	IT	Institute "Prof. Dr. Ion Chiricuta"	RO
Centre Léon Bérard, Lyon	FR	Masaryk Memorial Cancer Inst.	CZ
Skane University Hospital	SE	National Institute of Oncology	HU
Policlinico San Martino	IT	Beaumont RCSI Cancer Centre	IE
IRCCS "Fondazione G. Pascale"	IT	Centro Oncologico Basilicata	IT
Sahlgrenska University Hospital	SE	Inst Português Oncol de Lisboa	PT
Maastricht University	NL	Inst Português Oncol do Porto	PT
Istituto Oncologico Veneto	IT	National Cancer Institute Vilnius	LT
Helsinki University Hospital	FI	Institut Cancérologie de l'Ouest	FR

IRCCS Instituto Clinico Humanitas	IT	AZ Groeninge	BE
Trinity St James's Cancer Institute	IE	Institut du Cancer Paris CARPEM	FR
Centro di Riferimento Oncologico	IT	Vejle Cancer Centre, Lillebaelt	DK
Institut Jules Bordet	BE	Tartu University Hospital	EE
Institut Paoli Calmettes	FR	Inst Port. Oncol de Coimbra	PT
Toulouse Oncopole	FR		

ISO country codes: BE = Belgium, CZ = Czech Republic, DK = Denmark, EE = Estonia, ES = Spain, FI = Finland, FR = France, HU = Hungary, IE = Ireland, IT = Italy, LT = Lithuania, NL = Netherlands, NO = Norway, PT = Portugal, RO = Romania, SE = Sweden, SI = Slovenia, TR = Turkey, UK = United Kingdom

Table 7 List of 14 research domains and top 14 anatomical sites into which cancer research was sub-divided

Research domain		*Anatomical site*	
Chemotherapy/SACT	Pathology	blood	liver
Clinical trials	Biomarkers	breast	lung
Diagnosis	Quality of life	central nervous system	oesophagus
Epidemiology	Radiotherapy	cervix	pancreas
Discovery Science/Genetics	Screening/Early Detection	colorectum	prostate
Paediatrics	Surgery	head & neck	skin
Palliative care	Targeted therapy inc I/O	kidney	stomach

Table 8. Overall age-standardized (world population) mortality rates from 22 selected cancers and all cancers combined per 100,000 men and women, in West and Centre-East Europe, separately, in 2010 and 2016, the number of deaths registered in 2016 and the percent change between the rates.

	West Europe								Centre-East Europe							
	Men				Women				Men				Women			
	2010	2016	Deaths	% change	2010	2016	Deaths	% change	2010	2016	Deaths	% change	2010	2016	Deaths	% change
Oral cavity, pharynx	4.31	4.11	16443	-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	20194	-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	25119	-16.0	2.94	2.49	16351	-15.3	12.60	10.14	10168	-19.5	5.02	4.09	5951	-18.5
Intestine (colon and rectum)	15.99	14.43	73870	-9.8	9.57	8.87	62676	-7.3	22.15	21.72	22561	-1.9	11.72	11.24	17228	-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	22064	-2.0	1.66	1.71	10728	3.0	2.96	3.14	3028	6.1	1.15	1.22	1742	6.1
Pancreas	7.54	7.79	36533	3.3	5.35	5.62	36602	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	143295	-12.5	13.16	13.97	73579	6.2	51.88	47.12	45771	-9.2	12.94	15.23	19206	17.7
Skin including melanoma	2.41	2.35	11297	-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	78050	-8.2					15.25	15.65	19907	2.6
Uterus (cervix and corpus)					3.93	3.88	20849	-1.3					9.03	8.49	10082	-6.0
Ovary					4.94	4.44	24066	-10.1					6.08	5.94	7173	-2.3
Prostate	11.50	10.15	63927	-11.7					12.56	12.72	14805	1.3				
Testis	0.24	0.20	537	-16.7					0.55	0.58	385	5.5				
Bladder	4.94	4.47	25957	-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	22307	4.2	1.71	1.72	11744	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's disease	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's lymphomas	3.52	3.30	16524	-6.3	2.08	1.94	13690	-6.7	2.92	3.11	2973	6.5	1.82	1.81	2543	-0.5
Multiple myeloma	2.07	1.94	10313	-6.3	1.37	1.23	8988	-10.2	1.53	1.65	1685	7.8	1.12	1.19	1787	6.2
Leukemias	4.37	4.12	20422	-5.7	2.69	2.48	15944	-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	596181	-7.1	80.74	77.97	464672	-3.4	176.98	168.17	166544	-5.0	95.93	94.79	127317	-1.2

Table 9. Avoidable deaths in Centre-East Europe in 2016: numbers of deaths from the major cancers, by sex, that would not have occurred if mortality rates had been the same as those seen in West Europe..

	Men	Women
Oral cavity, 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's disease	50	58
Leukaemias	236	68
All cancers (malignant and benign)	40,804	14,435

Table 10. Outputs of cancer research papers (articles + reviews in the WoS) for four groups, 2012-21. Ratios are outputs in 2020-21 divided by outputs in 2012-13.
EUR19 represents the European countries having at least one OECI accredited centre.

Year	*World*	*EUR32*	*EUR32/World %*	*EUR19*	*OECI*	*OECI/EUR19 %*
2012	83264	30841	*37.0*	23460	5215	*22.2*
2013	89417	31706	*35.5*	24264	5760	*23.7*
2014	95181	31705	*33.3*	24478	6079	*24.8*
2015	111829	36442	*32.6*	28368	7056	*24.9*
2016	118016	38129	*32.3*	29597	7894	*26.7*
2017	124396	38082	*30.6*	29668	7940	*26.8*
2018	125204	37890	*30.3*	29531	8101	*27.4*
2019	142966	42794	*29.9*	33468	9408	*28.1*
2020	162800	48705	*29.9*	38285	10783	*28.2*
2021	169976	50831	*29.9*	40120	11235	*28.0*
Ratio	*1.93*	*1.59*		*1.64*	*2.01*	

Table 11. The cancer research outputs in 2012-21, of two countries and five country groups within the EUR19 group, of the OECI accredited centres within the group, and of total OECI outputs within each group. Countries and groups ranked by the percentage of world cancer research papers. GDP = Gross domestic product of country or group in 2015, billion Euros

Country or group	*Component countries*	*GDP*	*Papers*	*% of world*	*Own OECI*	*% of total*	*All OECI*	*% of total*
Italy	IT	1627	73,550	*6.01*	19,757	*26.9*	24,375	*33.1*
British Isles	IE, UK	2808	73,224	*5.98*	19,107	*26.1*	25,233	*34.5*
France	FR	2160	52,148	*4.26*	12,449	*23.9*	17,894	*34.3*
BeNeLux	BE, NL	1076	46,474	*3.80*	12,619	*27.2*	18,067	*38.9*
Central and Eastern Europe	CZ, EE, HU, LT, RO, SI, TR	1169	43,359	*3.54*	3810	*8.8*	6428	*14.8*
Iberia	ES, PT	1243	43,060	*3.52*	1445	*3.4*	7983	*18.5*
Nordic	DK, FI, NO, SE	1264	42,551	*3.48*	18,685	*43.9*	21,521	*50.6*
19 countries		11,348	301,854	*24.6*	79,544	*26.4*	79,544	*26.4*
Overlap between groups			72,512		8,328			
% overlap			*24.0*		*10.5*			

Table 12. Outputs of cancer research papers in 14 research domains from the world, the EUR32 countries, the EUR19 ones, and the 51 accredited OECI centresThe right-hand column, "Ratio" indicates in which domains the OECI accredited centres are making the largest contribution, relative to that of the countries in which they are located. . Ratio is that of the percentages of the OECI accredited centres divided by those of the countries in which they are located, i.e., the EUR19 countries.

	Papers, 2012-21				*Percent of ONCOL*				*Ratio*
Domain	*World*	*EUR32*	*EUR19*	*OECI*	*World*	*EUR32*	*EUR19*	*OECI*	
discovery science/genetics	231878	65807	50684	15225	19.0	17.0	16.8	19.2	1.14
biomarkers	178687	54756	43333	13390	14.6	14.1	14.4	16.8	1.17
epidemiology	145846	45863	37831	11964	11.9	11.8	12.6	15.1	1.20
surgery	139851	44644	35098	8202	11.4	11.5	11.7	10.3	0.89
chemotherapy	134263	39530	31391	8769	11.0	10.2	10.4	11.0	1.06
pathology	110035	38054	29532	7423	9.0	9.8	9.8	9.3	0.95
diagnosis	74670	26402	20486	5157	6.1	6.8	6.8	6.5	0.95
radiotherapy	69546	25505	17632	5496	5.7	6.6	5.9	6.9	1.18
targeted therapy	53565	19262	15509	5303	4.4	5.0	5.1	6.7	1.30
paediatrics	52860	17506	13980	3681	4.3	4.5	4.6	4.6	1.00
clinical trials	34102	13462	11365	4769	2.8	3.5	3.8	6.0	1.59
quality of life	30006	12388	9743	1866	2.5	3.2	3.2	2.3	0.73
screening	24463	8610	7142	2030	2.0	2.2	2.4	2.6	1.08
palliative care	20535	7645	5844	1540	1.7	2.0	1.9	1.9	1.00
ONCOL	1223049	387125	301239	79471					

Table 13. Outputs of cancer research papers on 14 anatomical sites from the world, the EUR32 countries, the EUR19 ones, and the 51 accredited OECI centres. Ratio is that of the percentages of the OECI accredited centres divided by those of the countries in which they are located, i.e., the EUR19 countries.

	Papers, 2012-21				*Percent of ONCOL*				*Ratio*
Site	*World*	*EUR32*	*EUR19*	*OECI*	*World*	*EUR32*	*EUR19*	*OECI*	
breast	118276	38362	31009	9974	9.7	9.9	10.3	12.5	1.22
blood	99597	37410	29387	7849	8.1	9.7	9.8	9.9	1.01
lung	76771	19154	15122	4538	6.3	4.9	5.0	5.7	1.14
colorectal	75529	25852	20834	5234	6.2	6.7	6.9	6.6	0.95
liver	74127	16192	12389	2855	6.1	4.2	4.1	3.6	0.87
CNS	66832	21647	15643	3540	5.5	5.6	5.2	4.5	0.86
head & neck	58578	17868	13811	3706	4.8	4.6	4.6	4.7	1.02
stomach	56856	12597	9857	2402	4.6	3.3	3.3	3.0	0.92
prostate	50940	19496	15366	4283	4.2	5.0	5.1	5.4	1.06
skin	37716	16659	11635	3439	3.1	4.3	3.9	4.3	1.12
pancreas	31504	9244	6835	1730	2.6	2.4	2.3	2.2	0.96
kidney	26936	8397	6495	1630	2.2	2.2	2.2	2.1	0.95
cervix	22715	5829	4772	1202	1.9	1.5	1.6	1.5	0.95
oesophagus	19770	4425	3496	1168	1.6	1.1	1.2	1.5	1.27
ONCOL	1223220	387188	301275	79479					

Table 14. Top 12 most acknowledged countries in cancer research papers

Countries	**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** (governmental organisations)	**Percentages of funding acknowledgments for prevention research** (not-for-profit organisations)
United Kingdom	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%

(2008-2021).

Table 15

	Global RCTs		Total Cancer Research Output (publications)	
	Number	**%**	**Number**	**%**
Lower Middle n=84 RCTs				
India	42	50	27,601	67
Ukraine	39	46	801	2
Philippines	23	27	384	1
Egypt	12	14	6262	15
Georgia	6	7	78	0.2
Upper Middle n=182 RCTs				
Russian Fed.	115	63	4835	2
Brazil	94	52	15272	7
Romania	62	34	3457	2
China	56	31	154373	69
Mexico	56	31	4126	2

Table 15. Top 5 country-level participation in global RCTs published 2014-2017 by World Bank income category compared to their total cancer research outputs over same period

Appendix I

The 44 European region countries considered in this study, with ISO2 codes and populations (millions).

Country	*ISO2*	*Pop*	*Country*	*ISO2*	*Pop*	*Country*	*ISO2*	*Pop*
Albania	AL	2.9	Germany	DE	80.7	North Macedonia	MK	2.1
Armenia	AR	3.0	Greece	GR	11.0	Norway	NO	5.2
Austria	AT	8.5	Hungary	HU	9.9	Poland	PL	38.6
Belgium	BE	11.3	Iceland	IS	0.3	Portugal	PT	10.4
Bosnia Herceg	BA	3.8	Ireland	IE	4.7	Romania	RO	19.5
Bulgaria	BG	7.2	Israel	IL	8.1	Serbia	RS	8.9
Croatia	HR	4.2	Italy	IT	59.8	Slovakia	SK	5.4
Cyprus	CY	1.2	Latvia	LV	2.0	Slovenia	SI	2.1
Czech Republic	CZ	10.5	Liechtenstein	LI	0.04	Spain	ES	46.1
Denmark	DK	5.7	Lithuania	LT	2.9	Sweden	SE	9.8
Estonia	EE	1.3	Luxembourg	LU	0.6	Switzerland	CH	8.3
Faroe Islands	FO	0.05	Malta	MT	0.4	Turkey	TR	78.7
Finland	FI	5.5	Moldova	MD	4.1	Ukraine	UA	44.8
France	FR	64.4	Montenegro	ME	0.6	United Kingdom	UK	64.7
Georgia	GE	4.0	Netherlands	NL	16.9			

Appendix II

Funding organizations whose data contributed to the detailed analysis (€16.7 bn)

Funder	Source	Funder Country
EU	CORDIS	International
Alberta Innovates	ICRP	CA
Alex's Lemonade Stand Foundation	ICRP	US
American Cancer Society	ICRP	US
American Institute for Cancer Research	ICRP	US
American Society for Radiation Oncology	ICRP	US
AVON Breast Cancer Crusade	ICRP	US
Biotechnology & Biological Sciences Research Council	ICRP	UK
Blood Cancer UK	ICRP	UK
Breast Cancer Now	ICRP	UK
California Breast Cancer Research Program	ICRP	US
Canadian Association of Radiation Oncology	ICRP	CA
Canadian Institutes of Health Research	ICRP	CA
Cancer Research Society	ICRP	CA
Cancer Research UK	ICRP	UK
Cancer Research Wales - Ymchwil Canser Cymru	ICRP	UK
Children with CANCER UK	ICRP	UK
Congressionally Directed Medical Research Programs	ICRP	US
Department of Health	ICRP	UK
Economic and Social Research Council	ICRP	UK
Eunice Kennedy Shriver National Institute of Child Health and Human Development	ICRP	US
Fogarty International Center	ICRP	US
Fondation ARC pour la recherche sur le cancer	ICRP	FR
Fondazione AIRC	ICRP	IT
Fonds de la recherche du Québec – Santé	ICRP	CA
Francis Crick Institute	ICRP	UK
Health and Care Research Wales	ICRP	UK
KWF Kankerbestrijding / Dutch Cancer Society	ICRP	NL
Macmillan Cancer Support	ICRP	UK
Marie Curie Cancer Care	ICRP	UK
Medical Research Council	ICRP	UK
Melanoma Research Alliance	ICRP	US
National Cancer Institute	ICRP	US
National Human Genome Research Institute	ICRP	US
National Institute of Allergy and Infectious Diseases	ICRP	US

National Institute of Arthritis and Musculoskeletal and Skin Diseases	ICRP	US
National Institute of Biomedical Imaging and Bioengineering	ICRP	US
National Institute of Dental and Craniofacial Research	ICRP	US
National Institute of Diabetes and Digestive and Kidney Diseases	ICRP	US
National Institute of Environmental Health Sciences	ICRP	US
National Institute of Mental Health	ICRP	US
National Institute on Aging	ICRP	US
National Institute on Alcohol Abuse and Alcoholism	ICRP	US
National Institute on Drug Abuse	ICRP	US
Natural Sciences and Engineering Research Council	ICRP	CA
Northern Ireland Health & Social Care - R & D Office	ICRP	UK
Office of the Director	ICRP	US
Ontario Institute for Cancer Research	ICRP	CA
Pancreatic Cancer Research Fund	ICRP	UK
Pancreatic Cancer UK	ICRP	UK
Prostate Cancer Research	ICRP	UK
Prostate Cancer UK	ICRP	UK
Roy Castle Lung Cancer Foundation	ICRP	UK
Scottish Government Health Directorates - Chief Scientist Office	ICRP	UK
Susan G. Komen for the Cure	ICRP	US
Swedish Research Council	WorldReport	SE
Tenovus	ICRP	UK
The Anticancer Fund	ICRP	BE
The Pediatric Brain Tumor Foundation	ICRP	US
The Terry Fox Research Institute	ICRP	CA
Wellcome Trust	ICRP	UK
World Cancer Research Fund France	ICRP	FR
World Cancer Research Fund International	ICRP	International
World Cancer Research Fund Netherlands	ICRP	NL
World Cancer Research Fund UK	ICRP	UK
Worldwide Cancer Research	ICRP	UK
Yorkshire Cancer Research	ICRP	UK
INCa/DGOS	ICRP	FR

Appendix III

Research investment in Europe by country

Country	Project investment (2010-2019) EUR M Source: Projects coded to Research & Cancer Type (ICRP and other public data sources)	Estimated additional investment in cancer research EUR M Source: Annual reports in public domain
Albania	0.2	
Armenia	0.6	
Austria	177.9	69.3
Belgium	205	66
Bosnia and Herzegovina	0.5	
Bulgaria	2.1	
Croatia	11.9	
Cyprus	8.9	
Czech Republic	30.2	
Denmark	162.2	268
Estonia	11.9	10.8
Faroe Islands		
Finland	115.4	45.5
France	1482.8	253.5
Georgia		
Germany	890.8	2338
Greece	77.8	14.7
Hungary	30.6	
Iceland	10.5	3.6
Ireland	92.6	24.9
Israel	29.7	15.7
Italy	832.7	26.8
Latvia	7.8	
Liechtenstein	0	
Lithuania	2.6	
Luxembourg	11.8	
Malta		
Moldova, Republic Of	0.2	
Montenegro		
Netherlands	1343	0.2
North Macedonia		
Norway	65.8	414.6
Poland	37.1	
Portugal	57.8	119.5

Romania	3.3	
Serbia	5.6	
Slovakia	7.6	1.1
Slovenia	9.2	7.5
Spain	473.2	380
Sweden	771.5	197.1
Switzerland	312	
Turkey	10.4	
Ukraine	2.7	
United Kingdom	9251.6	
Total	**16700**	**4256.8**