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Limitations of cancer care in Central and South-Eastern Europe: results of the international conference organized by the Central European Cooperative Oncology Group (CECOG)

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ABSTRACT

Profound disparities in cancer incidence and treatment outcomes, as well as accessibility of innovative EMA approved medications and technologies exist between Central, Eastern and South-Eastern (CEE) European countries and neighbouring Western European (WE) countries.

An international expert conference was held to discuss the current situation regarding the availability and affordability of innovative anti-cancer drugs in CEE, to define shortcomings in cancer care and to specify possible solutions to overcome the lack of access to anti-cancer medications in the region.

Consequently, all experts agreed that national prevention programs targeting smoking, obesity and alcohol consumption, and cancer screening programmes should be widely implemented in CEE countries. Considering limited healthcare resources in most CEE countries, an efficient allocation in a more structured way with clear cancer patient pathways to contain costs is needed. Also, more rapid reimbursement decisions and introduction of novel drugs in routine clinical practice, along with better access to clinical trials, are needed. There was consensus that higher investments into cancer care and more organized, value-oriented application of novel diagnostic and treatment approaches are necessary.

Furthermore, it was suggested that patient organisations should be more involved in cancer research, clinical research and reimbursement processes. Postulated were also higher investments into cancer care and more organized, value-oriented application of novel diagnostic and treatment approaches.

KEY WORDS: cancer care, inequality, access, cancer control plans.

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INTRODUCTION

Several pan-European studies on cancer outcomes report profound disparities in cancer care, survival and cancer-driven mortality across Europe, which have their roots in inequities in general wealth and health between European countries [1-3]. They are a consequence of highly different health care systems, with disparate populations and wide variations in technological, human and financial resources that are available for the care of cancer patients in different countries.

The increasing cancer burden that we experience in Europe will have a profound impact not only on patients and their families, but will also be a significant challenge for our healthcare systems and for the future economic competitiveness of Europe. While the simplest solution would be to increase spending on health in general, and cancer care in particular, it has been acknowledged that the problem is not simply about spending, but about spending wisely [4]. The problems lie not only in limitations in access to treatment, but also in deficits of prevention, screening and early diagnosis. Hence, cancer control policies have to be aligned with public health strategies related to disease prevention [5]. In addition, there has been an unprecedented wave of innovations in cancer treatment in the past few years, which may have a considerable budget impact and require new approaches to ensure timely patient access [6].

Against this background, the Central European Cooperative Oncology Group (CECOG) initiated a high-profile meeting with experts from Central and South-Eastern Europe to discuss the current situation of cancer care with the aim of developing joint approaches to tackle inequities in cancer care and to improve cancer patients' access to early diagnosis, followed by high-quality treatment with value-based medicines and technologies in the region.

THE STATUS QUO IN CANCER CARE IN CENTRAL AND SOUTH-EASTERN EUROPE

DIFFERENCES IN INCIDENCE AND MORTALITY RATES BETWEEN EU COUNTRIES

Europe accounts for 9% of the world's population but its share of global cancer cases and cancer deaths is about 25% [1]. Within the past three decades, cancer incidence has increased by approximately 30% across Europe and will continue to rise: In 2018, there were close to 4.23 million new cases of cancer in Europe, and this number is predicted to rise by almost a quarter to 5.2 million by 2040 [7, 8].

Studies show a North West to South East gradient of increasing incidence and mortality rates of tobacco-related and screening-detectable cancers, with a lack of decline in overall cancer mortality in Southeast European countries (SEE) [3, 9]. Data from EUROCARE-5 suggest less effective care as reason for the higher risk of cancer death in CEE, and worse stage-specific survival compared to the rest of Europe due to a restricted allocation of resources to healthcare (Table 1) [10-14].

Several causes of this discrepancy between Central, Eastern and South-Eastern Europe (CEE) and Western Europe (WE) have been proposed, including differences in distribution of risk factors, lack of primary prevention, lower access to cancer screening, later stage at diagnosis, more deadly cancer types, lower access to quality care, fewer available treatment options, lower availability of novel drugs, lack of access to specific equipment such as radiotherapy and to trained oncology specialists, lack of national cancer plans, and absence of comprehensive cancer registries [3, 15].

MAJOR GAPS IN HEALTHCARE EXPENDITURES AND COST OF CANCER ACROSS EUROPE

The distinct mortality trends in CEE and WE have been associated with large differences in health care budgets and the absolute investment in cancer care (Table 1) [16-20]. Health expenditure per capita strongly correlates with the gross domestic product (GDP) per capita and with the percentage of GDP allocated to healthcare [19]. While the population of WE are approximately four times larger than that of CEE, its GDP exceeds that of CEE more than 10-fold [19] (Fig. 1).

Similarly, a correlation between lower expenditure on oncology drugs and mortality-to-incidence ratio in CEE compared to WE have been shown in a cross-sectional analysis [3] (Fig. 2). While the percentage of GDP spent on oncology drugs was similar in both regions, the absolute expenditures on drugs per capita and per cancer case in CEE countries were 2.5 times less than in WE countries.

For radiotherapy, investments have been uneven across Europe and many countries face serious limitations. Whereas the Nordic countries, Belgium, the Netherlands, and Switzerland are well equipped with external beam machines, most countries in Central and South-Eastern Europe face substantial shortages and the urgent need to expand and modernise their equipment [21]. In many cases, the significant limitations in radiotherapy resources result in waiting lists, delays in initiation of radiotherapy and reduced effectiveness of radiation treatment [21]. It is estimated that at least a quarter of patients in Europe eligible for radiotherapy currently do not receive it [21]. At the same time, the demand for radiotherapy in the region is expected to grow by 16% by 2025 [22], requiring substantial additional investments.

However, spending is not the only factor explaining cancer survival differences. An analysis of results from published EUROCARE high-resolution studies on breast, colorectal, and prostate cancer found that countries with similar high or low total national health expenditures have different survival rates [23]. Ades *et al.* showed a strong correlation between the efficiency of a country's health policy and health expenditure and the breast cancer mortality/incidence ratio and that both variables are also directly associated with the speed of drug reimbursement [24].

TABLE 1. Expenditures on health, cancer care, 5-year survival rates and death rates across Central-Eastern and South-Eastern countries as compared to Austria

Country	Total health expenditure as % of GDP*	Cancer share of health expenditure**	5-year relative survival*** (all cancers)	Standardised death rates per 100,000 inhabitants#
Austria	10.8	6.8	59.43	243.4
Bulgaria	4.7	6.8	47.79	241.9
Croatia	6.9	6.9	53.42	335.7
Czech Republic	7.5	5.4	46.40	278.8
Estonia	6.5	5.8	39.92	299.1
Hungary	7.2†	–	–	345.9
Latvia	5.5	6.2	47.75	293.7
Lithuania	6.5	6.2	48.96	285.5
Poland	6.9	6.5	46.47	304.5
Romania	4.1	6.8	–	275.3
Slovakia	7.9	6.2	51.94	320.1
Slovenia	8.5	6.7	41.96	310.5
Northern Europe	–	58.24		
Central Europe	–	61.30		
Eastern Europe	–	50.91		
Southern Europe	–	58.91		
European average	9.4	50.34		

** latest available data; source [13], ** data from 2014; source [2], ** data from 2000-2007; source [14], † source [11], # data from 2015; source [12]*

OUT-OF-POCKET PAYMENTS FOR HEALTH SERVICES

A major financial burden for patients in CEE countries are out-of-pocket payments for health services [25-27]. Out-of-pocket payments are higher in countries where important health services are not included in the public benefit basket and/or cost-sharing of public payers is limited for some services. 18% of all health spending in the EU is borne directly by private households, ranging from 10% in France, Luxembourg or the Neth-

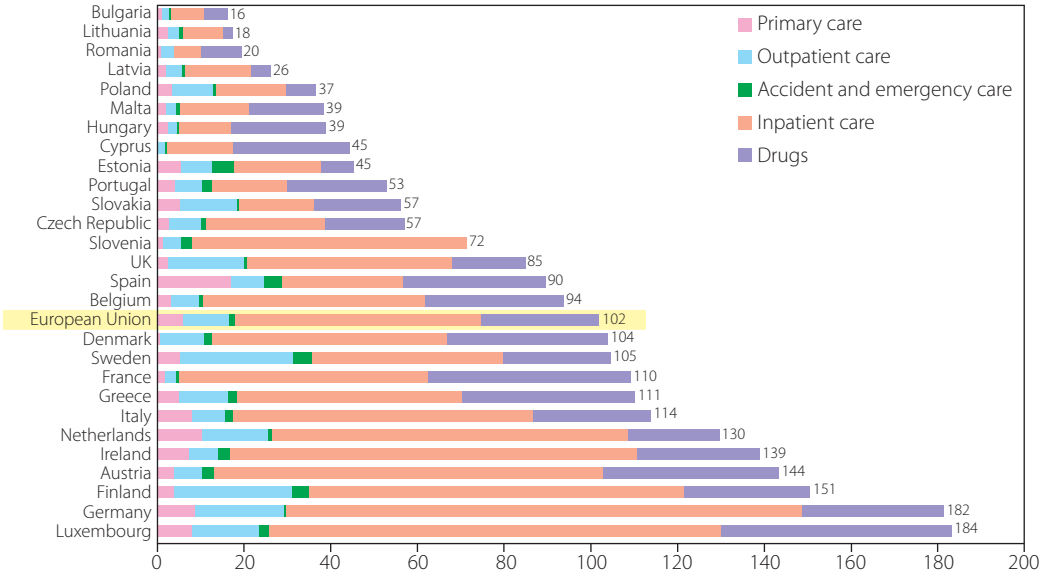

FIG. 1. Health-care costs of cancer per person in EU countries in 2009 by health-care service category. Data not adjusted for price differentials [84]

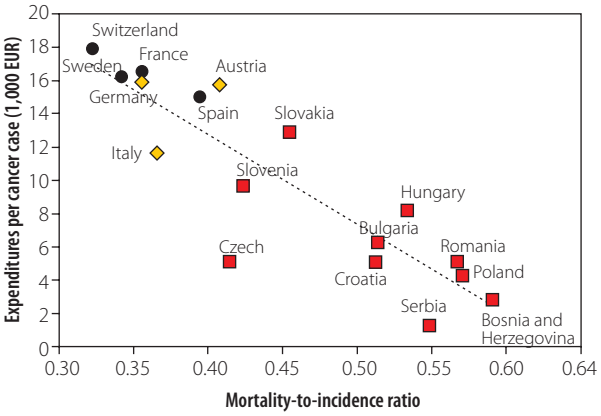

FIG. 2. Correlation of annual expenditures per new cancer case for antineoplastic drugs (ATC L01 class) and mortality-to-incidence ratio (2015, all cancers). Red squares represent Central and Eastern Europe countries, yellow rhombuses represent neighbouring Western Europe (WE) countries, and blue circles represent other WE countries [3]

erlands to over 40% in Bulgaria, Latvia and Cyprus (see supplement, Fig. S1).

SHORTAGES, RESTRICTIONS AND DELAYS OF ACCESS TO DIAGNOSTICS AND TREATMENTS IN EUROPE

Non-small-cell lung cancer (NSCLC) molecular testing – a paradigmatic example for targeted treatment

Lung cancer is the leading cause of cancer mortality worldwide [7] and also the most common cancer in CEE countries [8]. Since lung cancer consists of more than 50 histomorphological subtypes, diagnosis requires a comprehensive approach analysing anatomical, morphological and molecular features of the tumour to determine the most appropriate treatment option [28, 29].

Non-small-cell lung cancer (NSCLC) accounts for 80–85% of all lung cancers [29]. In 2016, a questionnaire-survey about molecular testing and NSCLC management in nine CEE countries (Bulgaria, Croatia, Czech Republic, Hungary, Israel, Poland, Slovakia, Slovenia, Turkey) showed that molecular testing of NSCLC samples is well established in these countries and most follow national or international guidelines but limited reimbursement significantly hampers molecular testing in general and reflex testing in particular [30].

These results were confirmed in a similar survey, initiated by CECOG in 2016 as a two-step-survey on the availability of different diagnostic procedures of NSCLC and the reimbursement landscape of drugs for NSCLC in CEE countries (Austria, Bulgaria, Croatia, Czech Republic, Hungary, Poland, Romania, Serbia, Slovakia and Slovenia) [29, 30]. In the first step, wide variations in both availability and reimbursement of diagnostic tests between CEE countries were observed. Not only is "reflex" testing often substituted by analyses performed only "on demand," but reimbursement of assessments varies widely between unavailability and payments by the health care system or even pharmaceutical companies. Analyses of reimbursement of modern drugs for the treatment of lung cancer in CEE showed also a highly divergent picture between various countries [31].

Anticancer drugs

The past two decades have seen major advances in diagnostic procedures and treatment technologies with the potential to save, improve and extend the lives of millions of people with cancer. But these improvements are associated with high expenditures that threaten the sustainability of health care systems globally. An economic study found that the average launch price of anticancer drugs, adjusted for inflation and health benefits (survival), increased by 10% annually or an average of $8,500 per year from 1995 to 2013 [32].

Several studies reported high discrepancies in the availability of innovative drugs to patients that most needed them [19, 24, 26, 33]. For example, huge delays in reimbursement across Europe have been shown in the case of the humanized anti-HER2 monoclonal antibody trastuzumab in the adjuvant and metastatic setting with marked differences in time to approval/reimbursement between WE and CEE countries of up to 12 years [33, 34].

This is in line with the second step of the above mentioned CECOG survey, which found that time from registration to reimbursement of targeted treatments like tyrosine kinase inhibitors or immune checkpoint inhibitors in NSCLC is usually long and could last one year or more [31].

Particularly in Eastern European countries with lower levels of economic development, the lack of availability is largely related to novel targeted agents, which gained market approval only in the past 10 years and are associated with high out-of-pocket costs [26]. In contrast, most of the cancer medications included in the updated version of the WHO model essential medicines list (EML) are usually available with no out-of-pocket cost to patients but shortages also affect EML medicines, e.g. tamoxifen and cisplatin, largely due to manufacturing and distribution issues [26]. In 2018, the European Association of Hospital Pharmacists (EAHP) found that shortages are getting worse compared to the results of the 2014 and 2017 surveys [35, 36]. Medicines' shortages in hospitals often last for weeks or even months, cause delay and cancellations in care, result in medication errors and, finally, in suboptimal patient care.

Besides the budget impact of innovative medicines, certain pricing and reimbursement policies interfere with timely patient access, in particular price benchmarking (external reference pricing) and parallel trade [37]. Delays imposed by health technology assessment (HTA) procedures and price negotiations, as well as characteristics

of health systems with low administrative capacities or with inefficiencies also undermine timely patient access to innovative treatments [38]. In addition to the discrepancies within European countries, there are also considerable regional differences across member states when it comes to spending on oncology drugs [39].

RADIOTHERAPY

Radiotherapy (RT) plays an important role in the curative and palliative setting next to surgery and chemotherapy with a general utilization proportion of ~50% [40]. To optimize the quality and availability of RT, guidelines have been proposed in 2005 by the European Society for Radiotherapy & Oncology (ESTRO) and in 2010 by the International Atomic Energy Agency (IAEA) [41, 42]. Nonetheless, at least one in four people needing radiotherapy does not receive it [21].

A report on actual and optimal RT capacity in 33 European countries described huge availability deficiencies of equipment, primarily teletherapy units [43]. Lack of qualified manpower for optimal delivery of radiotherapy services exacerbates the problem [44].

In 2012, projected needs of total RT capacity for 2020 estimate a general deficit of 25.6% with regard to RT units (n = 1698) and of 18.3% for radiation oncologists (n = 2429) compared with current guidelines [45]. Based on the expected proportion of new cancer patients that will require at least one course of radiotherapy by 2025, an increase in the number of RT treatment courses of 16% was estimated with variations across European countries from less than 5% to more than 30% [22].

These data point to significant shortages of both equipment and qualified manpower with a lack of strategic attention to RT at the policy level. Globally, more that 40% of high-income countries have national cancer control or general health care plans that do not address RT as an option [46]. In many European countries RT is not even included in the general oncology curriculum [47].

LACK OF PRIMARY PREVENTION AND SCREENING PROGRAMS IN CENTRAL AND SOUTH-EASTERN EUROPE

Around 40% of cancer cases are caused by potentially modifiable cancer risk factors, including tobacco use, high alcohol intake, poor diet, lack of physical activity, obesity as well as infections and environmental factors, which can be prevented through lifestyle changes and actions at the individual and societal levels [48-52].

While primary prevention is the most cost-effective long-term public health strategy in cancer control early detection and diagnosis of cancer through population-based screening programmes should be prioritized since treatment at early cancer stages is generally more effective, less complex and less expensive than in the advanced setting [53-55]. In 2003, the EU Council published a series of recommendations urging Member States to introduce or scale up breast, cervical and colorectal cancer screening through systematic population-based approaches with quality assurance at all levels [56].

While the first report, prepared by the International Agency for Research on Cancer (IARC), highlighted the adoption of the Council recommendations it also concluded that the number of individuals having access to population-based screening in the year 2007 was much lower than the desired level [57, 58]. According to the second report (2017), substantial improvement in screening efforts across most of the EU Member States has been achieve in 2016 with the exception of Bulgaria, Greece and the Slovak Republic [59]. On-going rollout was reported for Slovenia and Lithuania. Romania had a small-scale pilot project on-going in 2016; thus, the majority of the target population was subjected to non-population-based screening. Bulgaria completed a pilot project ("Stop and Get Screened") in 2014 to provide breast, cervical and colorectal cancer screening using a population-based approach, though there was no scaling up.

Rollout of population-based *cervical cancer* screening programmes was complete in 4 CEE countries (Slovenia, Poland, Latvia and Estonia) whereas rollout was on-going in another six (Czech Republic, Hungary, Romania, Croatia, Lithuania).

Population-based *colorectal cancer* screening programmes were being rolled out in Slovenia, Czech Republic and Croatia, with rollout on-going in Poland and Lithuania. While Hungary and Estonia were piloting population-based colorectal cancer screening programmes, Slovakia, Romania and Bulgaria had no such programmes [57].

The European expert group EUPS recommended a European *lung cancer* screening policy and the implementation of a lung cancer screening program by 2019/2020 [60]. Currently several national screening programmes are established in Europe ranging from the Nordic countries, to Switzerland and Poland [61-63]. While Poland and Hungary are piloting lung cancer screening programmes in the Central and Southern Europe region, no programmes have been implemented or published in the other countries [63, 64].

With regard to invitation coverage, all screening programmes showed a high variation across the EU, ranging from 0.2-111% for breast cancer, 7.6-105% for cervical cancer and 1.8-127% for colorectal cancer in the target populations [58].

To improve implementation, monitoring and evaluation of breast, cervical and colorectal cancer screening programmes, the European project EUROCOURSE called for a collaboration between cancer registries and screening programmes since monitoring and evaluation are essential to quality assurance of population-based cancer screening programmes [65].

SCARCITY OF NATIONAL CANCER REGISTRIES

The earliest population-based cancer registries (PCR) in Europe have been established more than 70 years ago (e.g. Denmark 1942; Slovenia 1950; Sweden and Norway 1951; Finland 1952) but still one third of the European population lacks quality cancer registration [66-68].

Currently, nearly 200 PCR are members of the European Network of Cancer Registries (ENCR) covering about 60% of the European population, with an increasing trend [68-71]. High quality registration of 10-60% of the population is available in France, Germany, Italy, Poland, Serbia, Switzerland and Spain, which all have national plans and legislation to reach complete coverage [1, 71]. For nine European countries (Albania, Bosnia-Herzegovina, Northern Macedonia, Greece, Luxembourg, Hungary, Romania, Portugal, Moldova, Montenegro, Serbia) the latest national incidence data publicly available for 2014/15 represented only estimates, which were calculated based on data available from partial registration and registries in neighbouring countries [1].

To reduce the disparities in terms of CRs population coverage, data quality, and data output across Europe and to reach a harmonised, collaborative, and effective system of cancer surveillance in Europe, engagement of all stakeholders on national and pan-European levels are needed [68, 71].

CLOSING THE GAP OF CANCER CARE IN EUROPE – INITIATIVES AND CROSS-COUNTRY ACTIONS

Initiatives by the European Union

In 1985, the Heads of State and Government of the then twelve Member States of the European Community decided to launch the first "Europe Against Cancer" (EAC) programme which became operational in 1987. This initiative of the European Commission (EC) was the first of many to follow with the aim to reduce the burden of cancer in the EU, often in close collaboration with the WHO and the IARC (see Supplement, Table S1) [56, 72, 73].

INITIATIVES BY MEDICAL SOCIETIES, HEALTH-RELATED ORGANISATIONS AND PATIENT ADVOCACY GROUPS

To reduce cancer mortality in Europe, medical societies and health-related organisations as well as patient advocacy groups regularly engage in public policy and European affairs (Table 2). The most prolific organisations are the European Society for Medical Oncology (ESMO) [74, 75], the WHO Regional Office for Europe (WHO/Europe) [54, 76, 77], the European CanCer organisation (ECCO) [78, 79] as well as the European Cancer Patient Coalition (ECPC) [80-83] and the All. Can group [84]. The International Atomic Energy Agency (IAEA) [85-89] has implemented extensive capaci-

TABLE 2. Main initiatives by medical societies and health-related organisations

Acronym	Society/Organisation	Aims
ESMO [74, 75]	European Society for Medical Oncology	To reduce healthcare inequalities To publish cancer policy briefings and statements (e.g. in case of the new EU Clinical Trials Regulation) To advocate for EU recognition of the specialty of medical oncology To collaborate with EU Presidencies
WHO/Europe [76, 77]	World Health Organisation Regional Office for Europe	To coordinate and conduct research on causes and develop scientific strategies for cancer prevention and control, e.g. WHO Framework Convention on Tobacco Control, Action Plan for the Prevention and Control of Noncommunicable Diseases in the WHO European Region 2016-2025
IAEA [86-90]	International Atomic Energy Agency	To enhance capacity in Member States to safely and effectively detect and treat cancer using nuclear techniques: Programme of Action for Cancer Therapy (PACT), Technical Cooperation projects in human health, Coordinated Research Projects (CRPs) in human health/radiotherapy worldwide
ECCO [79, 80]	European CanCer Organisation	To improve outcomes for all cancer patients in Europe through multidisciplinarity To improve access to innovation To address disparities in cancer outcomes across Europe To address financial discrimination encountered by cancer patients To promote cancer research at an European level

ty building activities in all of its Member States in the region provided through their Technical Cooperation (TC) programme in cancer and radiation medicine. The IAEA and the European Society for Radiotherapy and Oncology (ESTRO) collaborate and provide sponsored training courses to increase the efficiency of technical cooperation activities, and facilitate networking among Member States, professional associations and partner organizations, such as the World Health Organization (WHO). The All.Can group comprises leading representatives from patient organisations, policymakers, healthcare professionals, research and industry from across Europe and Canada and was set up in 2016 to optimise the efficiency of cancer care by focusing on improving outcomes for cancer patients [84].

NATIONAL CANCER CONTROL PROGRAMMES

The concept for National Cancer Control Programmes (NCCP) was developed by the WHO in 1995 to provide the framework for national policies on cancer control with the aim of reducing cancer morbidity and mortality, and improving the quality of life of cancer patients [90, 91].

In order to support national efforts in preparation of services and actions related to cancer control, the EU has initiated the "European Guide for Quality National Cancer Control Programmes" to serve as a guide to Member States [92]. The IAEA also offers its Member States a planning tool, known as an integrated review of comprehensive cancer control needs and capacities (imPACT) [93]. This review is being organized at the request of the national authorities, i.e. the Ministry of Health, and is conducted in close collaboration with relevant national and international health authorities, such as WHO and the International Agency for Research on Cancer (IARC). It assesses the status of national capacities for the implementation of cancer control plans and the readiness to establish long-term radiation medicine infrastructure projects [93]. Since 2005, over 100 IAEA Member States have benefited from imPACT reviews, including several CEE countries, i.e. Albania, Serbia, Montenegro, Moldova, Armenia, Romania, Tajikistan, Uzbekistan, Georgia, Croatia, Kyrgyzstan, Bosnia-Herzegovina, Belarus, Kazakhstan, Ukraine and North Macedonia.

IMPROVING PATIENT CARE PATHWAYS

Delays in diagnosing symptomatic cancer, leading to more advanced stage at diagnosis are one of the factors contributing to poor cancer outcomes [94]. Intervals between referral for suspicion of cancer, confirmation of diagnosis and beginning of treatment are indicators of quality in cancer care [95]. Systematic efforts to enhance the delivery of cancer services have been introduced in several health systems in Europe, such as the UK, Sweden, Denmark and Hungary. All these programmes aim to reduce waiting times via special care pathways, specifying time frames for different diagnostic steps [96-101]. The psychological burden faced by Eastern European cancer patients and their carers is addressed by providing access to psycho-oncological therapy. Psycho-oncology and palliative care should be included in the national cancer guidelines.

ACCESS TO TREATMENT AND VALUE ASSESSMENT

Marketing authorisation by the European Medicines Agency (EMA) is generally based on a benefit-risk assessment, in which a benefit clearly outweighs the risks of a drug. To satisfy unmet medical demands of patients or overall public health priorities, EMA has introduced the conditional approval pathway that allows marketing authorisations to be granted on the basis of limited evidence [102]. However, reducing premarketing development procedures may increase the risk of approving ineffective and/or unsafe drugs [103, 104].

Since the trend towards faster access to medicines with uncertain benefit is increasing rather than declining, systematic and transparent post-approval monitoring mechanisms are of high relevance to assure a clinically relevant patient benefit [104]. Countries like the UK or France have established mechanisms such as the Cancer Drugs Fund (CDF) or the temporary authorisation for use (ATU; authorisation temporaire d' utilisation), which allow early access while evidence is further developed [105, 106]. Other countries, like Belgium, have developed a longer-term medicines strategy, securing timely access while setting financial resources aside to finance innovation ("Pact of the Future").

To stratify the potential clinical benefit that may be anticipated from a novel anticancer treatment, ESMO developed the Magnitude of Clinical Benefit Scale (ESMO-MCBS), a standardized, generic, validated approach to stratify the magnitude of clinical benefit from anticancer therapies [107, 108]. The costs of treatments are not integrated in view of significant heterogeneity across Europe. The ESMO-MCBS is an important first step to the critical public policy issue of value in cancer care, supports treatment decisions based on the clinical benefit to be expected from a novel approach and might also support decision-making within socioeconomic questions.

FUNDING FOR CANCER MEDICINES – A COLLABORATIVE POLICY-MIX NEEDED

Efficient procurement of medicines means that products of good quality are available at affordable prices on a sustainable basis and at the right time [109]. In most European countries, citizens benefit from comprehensive coverage of healthcare costs and a major part of spending on medicines comes from public programmes [110]. However, there is considerable variation in public

funding on medicines between countries, especially with regard to high-priced innovative medicines.

To achieve affordable access while securing sufficient incentives for future innovation various strategies have been proposed, such as cross-country collaboration, in-market competition, tiered or differential pricing or managed entry agreements (MEAs) [35, 55, 109, 111-113]. The European Federation of Pharmaceutical Industries and Associations (EFPIA) has put forward five guiding principles for cross-border collaboration, including relevance for patients, acceleration of access, similarity of collaborating countries, voluntariness and the protection of commercial information [114].

Several EU-wide as well as more localized initiatives have been established and reflect the growing interest in voluntary collaboration on access to new medicines and other medical products [56, 111]. Although joint procurement collaboration seems promising, the evidence is still missing in terms of whether such deals are actually working to reach lower prices and broadened access to medicine in Europe [115].

Many countries increasingly use managed entry agreements (MEAs), i.e. either financial agreements to obtain discounts on list prices or performance-based agreements, which link coverage conditions or prices to health outcomes in real life, either on each patient or on the whole patient population [111, 116]. The type of MEA for a single product/indication may vary across countries [117]. Although MEAs, in particular outcomes-based agreements, may involve some complexities – data infrastructure, time to negotiate and administer agreements – they allow for timely access while ensuring predictable budget impact as the CDF example in the UK shows [118].

CONCLUSIONS OF THE CECOG MEETING TO IMPROVE ACCESS TO BETTER CANCER CARE IN CEE COUNTRIES

Disparities in cancer care between Western/Central Europe and Eastern/South-Eastern Europe are highly related to differences of the general economic situation as well as the organisation of the respective health care systems.

There is not only a discrepancy in access to novel cancer medicines and upgraded technologies, but also with regard to the quality of cancer care, especially concerning prevention programmes, supportive and palliative care as well as cancer care provision.

The data presented here indicate that solutions to these disparities in outcome might mainly be reached by increasing expenditures on health in general, and cancer services in particular, in countries with survival figures significantly below the average [16]. If disparities are to be eliminated, it is not enough to concentrate all attention on one area such as drug costs as part of general country-specific health care systems. To this end, a systems-based approach is required which engages all involved stakeholders – patients, physicians and politicians. Good examples are the CDF in the UK or the "Pact of the Future" in Belgium.

Accordingly, the panel discussions of the CECOG meeting included suggestions for improvement of oncology care in CEE countries:

- In light of limited healthcare resources in most CEE countries, an efficient allocation in a more structured cancer patient management with less inpatient/hospital-based care and more ambulatory and day care treatment to contain costs should be pursued to reduce costs and to improve patients' quality of life.
- In countries with substantial out-of-pocket payments health system financing needs to be revisited.
- Access is a joint responsibility. All stakeholders should work together on an access to cancer care strategy.
- In the majority of CEE countries more rapid reimbursement decisions and introduction of novel drugs in routine clinical practice, along with better access to clinical trials, are needed. To achieve this, higher investments into cancer care and more organized, value-oriented application of novel diagnostic and treatment approaches are necessary.
- The implementation, as well as the up-to-date revision of national cancer control plans must involve all stakeholders – policy makers, academia, patients.
- With regard to epidemiologic data on preventable cancer risk factors, CEE countries should widely implement national prevention programs targeting tobacco smoking, obesity, HPV vaccination and alcohol consumption.
- Patients advocacy groups should be much more involved in cancer research, approval processes as well as decision-making with regard to prioritise cancer treatment reimbursement.
- Screening programmes should be universally available, implemented and attract as much persons as possible.
- Molecular cancer testing is mostly available; however, more structured and sustainable policies of molecular testing and reimbursement are needed to ensure testing to all patients in the majority of countries.
- Population-based cancer registries containing also information on treatment are highly needed.
- "Clinical benefit" from and "value" of treatment modalities that include quality and consistency of evidence for effectiveness, toxicity, and cost of cancer medicines should be considered.
- Pressure should be put on registration agencies (FDA, EMA) to use a criterion of value for approval such as the ESMO-Magnitude of Clinical Benefit Scale (ESMO-MCBS) rather than statistical significance of an outcome measure. Simultaneously, it should be considered whether treatments with a low clinical benefit should not be abandoned in favour of more effective ones.

- In many countries social education is needed to change the attitude of the society towards cancer ("cancer = death"), and to advocate that cancer is to a large part a preventable chronic disease.
- Patients advocacy groups should be much more involved in clinical trials development on the regional level, and increasing access to clinical trials, in collaboration with the pharmaceutical industry, academia and healthcare professionals.
- Every country of the CEE region should develop a clear cancer patient pathway and record treatment outcomes. This should be a joint endeavour of healthcare professionals and patient advocacy groups. The final outcome should be the development and implementation of national systems of comprehensive cancer care from primary prevention to palliative care.

DISCLOSURE

The authors report no conflict of interest.

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AUTHORS' CONTRIBUTIONS

CT, IB, AC, TC, JJ, BK, LEM, BP, RR, RS, NW and CZ generated data and made the analyzes of the data, CT, TC, JJ, RO, AR, NW and CZ worked on the concept and design of the publication, CT, AR and CZ wrote and revised the publication. All authors have given their final approval to the final version of the paper.

SUPPLEMENTARY MATERIAL

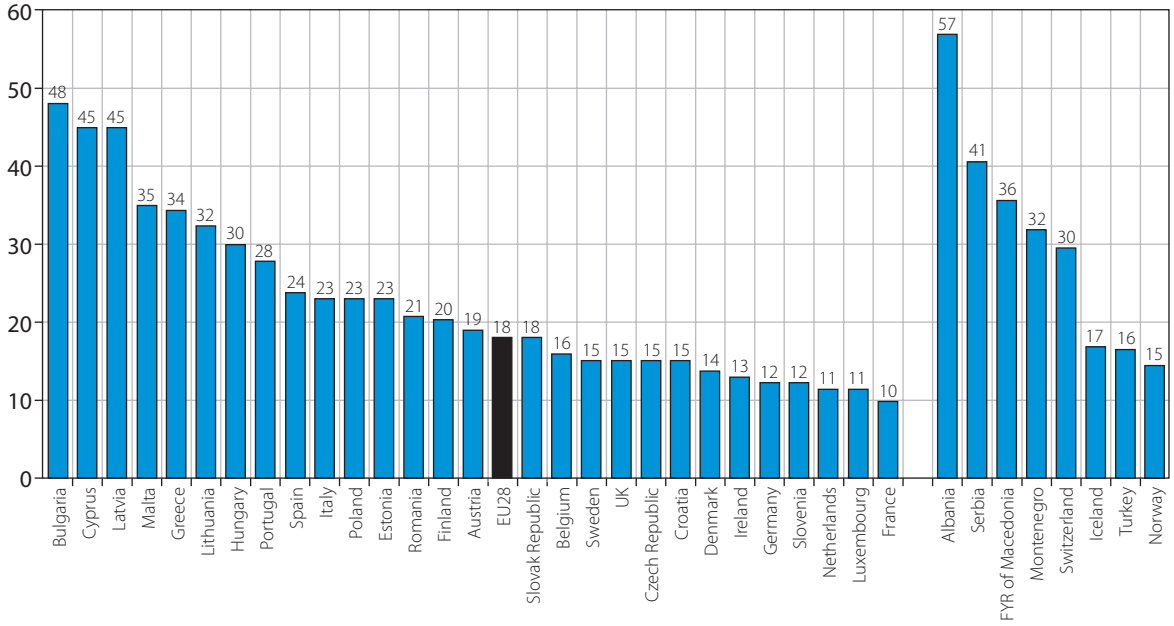

FIG. S1. Out-of-pocket payments for health services (% of current health expenditure) in Europe in 2016 (or latest year) [25]. Statlink: http://dx.doi.org/10.1787/888933836276

TABLE S1. Initiatives by the European Union

Acronym	Initiative	Aims
EAC	Europe against Cancer	To accelerate primary prevention, health promotion, education for the public and health professionals and scientific research
EPAAC	European Partnership for Action Against Cancer	To bring together the efforts of different stakeholders into a joint response to prevent and control cancer
CANCON	Comprehensive cancer control	To contribute in different ways to reducing the cancer burden in the EU by creating a European Guide on Quality Improvement in Comprehensive Cancer Control
JARC	Joint Action on Rare Cancers	To advance quality of care and research on rare cancers
iPAAC	Innovative Partnership on Action against Cancer	To implement innovative approaches to cancer control, e.g. Work Package 7 to enhance population-based cancer information systems to better support evidence-based comprehensive cancer care
ECIBC	European Commission Initiative on Breast Cancer	To improve breast cancer care and develop evidence -based recommendations on screening and diagnosis
ENCR	European Network of Cancer Registries	To promote collaboration between cancer registries, to define data collection standards, to provide training for cancer registry personnel and to regularly disseminate information on incidence and mortality from cancer in the EU and Europe
ECIS	European Cancer Information System	To enable comparisons of cancer burdens across Europe using the most recent information from national cancer registries

Source: The authors from publicly available European Commission reports and data