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European Perspectives

Expenditures on Oncology Drugs and Cancer Mortality-to-Incidence Ratio in Central and Eastern Europe

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Disclosures of potential conflicts of interest may be found at the end of this article.

Key Words. Cancer • Incidence • Mortality • Oncology • Central and Eastern Europe • Drug expenditures

Abstract

Background. There is a steady decline in cancer mortality in Western Europe (WE), but this trend is not so obvious in Central and Eastern Europe (CEE). One of the largest discrepancies between WE and CEE is the level of investment in cancer care. The objective of our analysis was to examine the correlation between mortality-to-incidence (M/I) ratio and expenditures on oncology drugs in CEE and WE.

Materials and Methods. This cross-sectional analysis was done on publicly available data. Data on expenditures for oncology drugs were obtained from QuintilesIMS, and data on M/I ratio from Globocan. The main outcome was mortality-to-incidence ratio, and the primary analysis was performed by Spearman's rank correlation.

Results. There is a large discrepancy in expenditure on oncology drugs per cancer case between WE and CEE, and within CEE. Average expenditure on oncology drugs per capita as well as per new cancer case was 2.5 times higher in WE than in CEE. Availability of oncology drugs was highest in Germany (100%), relatively similar in WE (average of 91%), but in CEE it ranged from 37% to 86%, with an average of 70%. Annual expenditures on all oncology drugs per new cancer case was significantly negatively correlated with the M/I ratio (Spearman's $\rho = -0.90$, $p < .001$).

Conclusion. There is a financial threshold for oncology drugs per cancer case needed to increase survival. Based on significantly lower expenditures for oncology drugs in CEE in comparison with WE, more investment for drugs as well as better, more organized, value- oriented consumption is needed. ***The Oncologist*** 2019;24:e30–e37

Implications for Practice: Cancer is not treated equally successfully in Western Europe (WE) and in Central and Eastern Europe (CEE). This study showed that success in treatment of cancer is associated with the amount of money invested in oncology drugs. CEE countries spend on average 2.5 times less than WE countries for oncology drugs per new cancer case. These findings should be used by health care providers and oncologists struggling for more resources and better, more organized, evidence-based allocation of these resources as well as better oncology outcomes.

Introduction

Over the last decades, cancer mortality in Europe has declined steadily [1–4], but the pace of this decline was and still is different between particular countries. Importantly, this trend is not seen in Central and Eastern Europe (CEE),

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where some countries even experienced an increase in cancer mortality [2, 4]. This discrepancy between CEE and Western Europe (WE) has complex causes, probably with unequal effects in different countries. Causes may include differences in distribution of risk factors, less primary prevention, lower access to cancer screening, later diagnosis, more deadly cancer types, lower access to quality care, fewer available treatment options, lower availability of novel drugs, shortage of radiotherapy and other equipment, lack of national cancer plans, lack of multidisciplinary teams, and absence of comprehensive cancer registries [5–7]. The discrepancy between mortality trends in CEE and WE is associated with large differences in health care budgets and the absolute investment in oncology [5, 7–9, 11]. An important part of this investment is the cost of anticancer drugs. When adjusted for inflation, expenditure on cancer care per capita increased in the European Union (EU) between 1995 and 2014 by 56%, and this increase was larger by one third in CEE than in WE [12]. However, the share of cancer care in the total health expenditure has been stable, meaning that total health expenditures increased at a similar pace. It has been documented that significant reductions in cancer mortality may be attributed to pharmaceutical innovation [13, 14]. The association of mortality-to-incidence (M/I) ratio with different socioeconomic, general health, and lifestyle factors, expenditure on health care in general, cancer-specific expenditure, and finally the expenditure on oncology drugs is different in particular cancers [5]. The association of M/I ratio with expenditure on oncology drugs is most visible in cancers for which effective treatment strategies emerged years ago; it is high and similar in breast and colorectal cancers, but it is markedly lower in lung cancer [5]. In simple words: The more investment in drugs for breast cancer, the better the outcome, but that is still not so true for lung cancer. The impact of the very recent introduction of successful, more efficient treatment modalities in the therapy of lung cancer (tyrosine kinase inhibitors and immunotherapy) in cancer registries is expected to be seen after certain lag time. At the same time, there are differences in incidence rates of certain cancers between CEE and WE, and different cancer types are associated with different financial consequences [11]. Self-evidently, high costs of novel oncology drugs and their economic burden on already overstretched health care budgets may affect patient access, especially in CEE [15]. The objective of our analysis was to examine the relationship between expenditures on oncology drugs and M/I ratio in CEE and WE, and to analyze the differences in expenditure on oncology drugs.

Materials and Methods

Study Design

This cross-sectional analysis of publicly available data was performed by a panel of oncology leaders from CEE countries. The panel was established at the 11th Central European Oncology Congress held in Croatia in 2015.

Targeted Population

The targeted populations encompasses 10 CEE countries: Bosnia and Herzegovina, Bulgaria, Croatia, the Czech Republic, Hungary, Poland, Romania, Serbia, Slovakia, and Slovenia, with a total population of 108 million. The comparator consists of seven WE countries: Austria, Germany, Italy, France, Spain, Sweden, and Switzerland, with three of them neighboring the targeted CEE region (Austria, Germany, and Italy). The total population of these seven WE countries was 277 million.

Outcome

The outcome was the M/I ratio. We obtained the mean age standardized per 100,000 inhabitants and the annual incidence and mortality rates for all cancers in each country from the study by Ferley et al. [16] and from Globocan 2012 [17]. We calculated the M/I ratio by dividing these two mean rates for all cancers in each country [18]. Higher M/I ratio indicates less favorable higher mortality. M/I ratio is a population-based indicator of survival. It is a valid approximation of the 5-year relative survival rate, but its validity is not equal in different tumors and is not validated in low-resource countries [19].

Independent Variable

The independent variable was the 2015 expenditure on ATC L01 (antineoplastic agents within Anatomical Therapeutic Chemical Classification System of World Health Organization) class drugs per new cancer case. We monitored expenses for 35 drugs. Data on annual expenditures were provided by QuintilesIMS (London, United Kingdom) [20]. QuintilesIMS sales data are based on manufacturers prices and do not represent the final sales price.

Other Explanatory and Confounding Variables

The source of data on expenditures on all prescription drugs was QuintilesIMS. Population sizes and data on gross domestic products (GDP) were obtained from the Statistical Office of the European Communities [21].

Statistical Analysis

We performed the primary analysis using Spearman's rank correlation (ρ). We had no missing data. Availability of particular drugs in each country was estimated based on the existence of any sales during the monitored time period. We treated the drugs with any sales as available, and the drugs with no sales as unavailable. Coefficients of variation of expenditures per cancer case in WE and CEE countries was calculated as standard deviation of these expenditures in the region, divided by the mean expenditure within the region. We conducted a data analysis using NCSS 12 Statistical Software (2018; NCSS, LLC, Kaysville, UT).

Results

The mean percentage of GDP per capita spent on ATC L01 class drugs was similar in WE (0.25%) and in CEE (0.28%; Table 1). However, owing to large differences in GDP, absolute expenditures on oncology drugs were markedly different between WE and CEE countries, as well as within these

Table 1. Expenditures on oncology drugs and mortality-to-incidence ratio of all cancer types in CEE and WE countries [18, 19]

Region Country	Population (million)	GDP per capita (1.000 EUR)	Expenditure on oncology (ATC L01) drugs (EUR) 2015					Share of L01 drugs in costs of all Rx drugs		New cancer cases (1.000)	Incidence (age standardized per 100,000)	Mortality (age standardized per 100,000)	M/I (2012)
			Absolute (million)	Per capita	Per new cancer case (1.000 EUR)	As percentage of GDP, %	Relative change 2013–2015, %	In 2015, %	Relative change 2013–2015, %				
WEE													
Switzerland	8.0	57.1	752	95	17.9	0.17	16	15	-5	42	287	93	0.32
Sweden	9.5	41.7	819	86	16.2	0.21	7	23	3	50	270	92	0.34
France	64.9	31.5	5.782	89	16.5	0.28	14	20	10	349	304	108	0.36
Germany	80.2	34.2	7.839	98	15.9	0.29	10	22	2	494	284	101	0.36
Italy	59.4	25.6	4.107	69	11.6	0.27	16	17	0	354	279	102	0.37
Spain	46.8	23.0	3.239	69	15.0	0.30	15	18	−3	216	249	98	0.39
Austria	8.4	36.0	646	77	15.7	0.21	−1	18	−12	41	254	104	0.41
Average WE	39.6	35.6	3.312	83	15.5	0.25	11	19	−1	221	275	100	0.36
CEE													
Czech	10.4	16.0	294	28	5.1	0.18	−7	16	−5	58	294	122	0.41
Slovenia	2.1	17.9	110	54	9.6	0.30	18	20	8	11	296	125	0.42
Slovakia	5.4	14.1	310	57	12.9	0.41	23	24	7	24	277	126	0.45
Bulgaria	7.2	5.7	199	28	6.2	0.48	48	18	22	32	235	121	0.51
Croatia	4.3	10.5	117	27	5.1	0.26	30	19	22	23	267	137	0.51
Hungary	9.9	11.0	414	42	8.2	0.38	13	19	6	50	285	152	0.53
Serbia	7.1	4.3	54	8	1.3	0.18	0	9	5	42	270	148	0.55
Poland	38.0	10.9	646	17	4.2	0.16	21	12	7	152	230	131	0.57
Romania	20.1	7.2	401	20	5.1	0.28	−6	16	−3	79	224	127	0.57
B&H	3.8	3.5	28	7	2.8	0.21	13	11	0	10	161	95	0.59
Average CEE	10.8	10.1	257	29	6.1	0.28	15	16	6	48	254	128	0.51

Data are sorted by mortality-to-incidence ratio within the region. Both incidence and mortality are age-standardized (European standard population) rates per 100,000 inhabitants.
Abbreviations: B&H, Bosnia and Herzegovina; CEE, Central and Eastern Europe; GDP, gross domestic product per capita 2015 [20]; M/I, mortality-to-incidence ratio; Rx, prescription; WEE, Western Europe.

two regions (Table 1). Average expenditure on oncology drugs per capita as well as per new cancer case was 2.5 times higher in WE than in CEE. Compared with CEE, WE was more homogeneous in regard to overall expenditure per cancer case, with coefficients of variation, calculated as standard deviation of expenditures per cancer case in all countries divided by the mean expenditure, of 56% and 13%, respectively. The expenditures per cancer case in WE ranged from €11,586 in Italy to €17,879 in Switzerland, a difference of 54%. In contrast, the difference in expenditure between Serbia (the CEE country with the smallest expenditure) and Slovakia (the one with the largest expenditure) was a staggering 907%. In CEE, the correlation between the percentage of GDP spent on oncology drugs in 2013 and relative change in expenditures from 2013 to 2015 was positive and low (Spearman's $\rho = 0.20$), and in WE, it was even smaller (Spearman's $\rho = 0.11$). Availability of oncology drugs, defined as "any sales for 35 oncology drugs" during 2015, was highest in Germany (all 35 oncology drugs were commercially available, 100%) and relatively similar in WE with an average of 91% availability (Table 2). In CEE, availability ranged from 37% in Bosnia and Herzegovina to 86% in Hungary, with an average of 70%. Overall expenditure on oncology drugs has increased from 2013 to 2015 in all CEE countries except the Czech Republic and Romania, where there has been a small decline, and in Serbia, where the expenditure has not changed. However, overall costs for all prescription drugs increased more than did the costs for oncology drugs in all countries except the Czech Republic, Romania, and Bosnia and Herzegovina. Consequently, the share of costs for oncology drugs among total costs for all prescription drugs increased in CEE from 2013 to 2015 at a slower pace than the absolute expenditure. Furthermore, differences were increased by parallel trade in several cases. We observed similar expenditures per cancer case patterns: More was spent on trastuzumab and bevacizumab than on abiraterone and imatinib. All those drugs had relatively higher sales in WE than in CEE compared with other oncology drugs, although nilotinib and sunitinib had relatively higher sales in CEE compared with other drugs. It is interesting to see that the uptake of trastuzumab emtansine was much lower in CEE compared with WE countries (Table 2).

Annual expenditures on all oncology drugs per new cancer case was significantly negatively correlated with the M/I ratio for all cancer types taken together (Spearman's $\rho = -0.90$, $p < .001$; Figure 1). The higher the annual expenditure on oncology drugs was, the better and lower the M/I ratio. Within both studied populations, the correlation was markedly lower: $\rho = -0.75$, $p = .052$ in WE, and $\rho = -0.67$, $p = .033$ in CEE.

Discussion

There are large differences in outcomes of cancer care between EU countries, especially when WE and CEE are compared [22]. Improvement in these discrepancies should be attempted via prompt action using all known anticancer strategies [7]. One of the most important measures is better access to new, innovative, often expensive but effective oncology drugs. Our study showed that absolute expenditures on oncology drugs per capita and per cancer case are markedly lower in CEE compared with WE, although the percentage of GDP spent on oncology drugs is similar. The M/I ratio correlates strongly with the expenditure on oncology drugs. The lower incidence rates and higher mortality rates in CEE compared with WE [18] results in higher total numbers of patients actively treated with curative and palliative intent (prevalence of treated patients) in WE than in CEE [23]. Thus, the CEE/WE gap in investment in oncology drugs that we observed is relatively smaller. Despite the potentially smaller prevalence of patients on therapy, higher mortality and less favorable M/I ratio suggests the need for increased investment in CEE in relation to WE. However, the percentage of GDP spent on oncology drugs is equal in CEE and in WE. The consequence of this equal spending relative to GDP is lower absolute investment in CEE because the drug prices are not lower in CEE proportionally to the difference in GDP per capita between CEE and WE. Finally, because of the aging population with associated increase of cancer incidence, the financial burden of cancer will grow in CEE relative to WE.

We have found only a small positive correlation between the percentage of GDP spent on oncology drugs in 2013 and relative change in expenditures between 2013 and 2015. In other words, countries with lower expenditure in 2013 have not been trying to invest more. This conclusion may be confounded with different factors. If countries managed to negotiate lower drugs prices, the increasing drug use will not be obvious from the relative change in total expenditure. If the use of generic or biosimilar drugs had been increased, the explained effect might be similar. On the other side, the number of patients has most likely been increasing because of population growth and aging, earlier diagnosis with consequent increase in cancer incidence, new registered indications, and more intense anticancer treatments including more treatment lines [10, 24]. This finding is consistent with the finding that the relative change of share of oncology drugs in total sales of all prescription drugs has been lower than the relative change of absolute expenditure in all monitored countries except Serbia. This may be particularly worrying in CEE countries where unfavorable mortality trends have been observed and where the M/I ratio is markedly above WE countries. An analysis of cost and burden of cancer in the European Union 1995–2014 showed that expenditures on cancer as a share of total health care expenditures are unexpectedly low considering increasing cancer incidence, and the fact that cancer is the leading cause of mortality in the working population [12].

Based on our data, the availability of oncology drugs seems to be quite high, both in CEE and even more in WE countries. However, the criterion for availability of oncology drugs that we used was imprecise. The fact that the drug has any sales does not indicate the proportion of population in need that was actually treated with the drug. A recent survey performed by the European Society for Medical Oncology highlighted important discrepancies in reimbursement, access, and availability of cancer medicines across Europe [25]. Actual availability of novel drugs in

Table 2. Oncology drug sales per new cancer cases during 2015 (EUR) [16, 17]

	Western Europe							Central and Eastern Europe									
Drug	**Switzerland**	**Sweden**	**France**	**Germany**	**Italy**	**Spain**	**Austria**	**Czech**	**Slovenia**	**Slovakia**	**Bulgaria**	**Croatia**	**Hungary**	**Serbia**	**Poland**	**Romania**	**Bosnia and Herzegovina**
Availability	86%	97%	91%	100%	89%	80%	97%	69%	80%	86%	74%	69%	80%	54%	77%	71%	37%
trastuzumab	1,061	739	677	541	714	719	1,027	136	663	527	528	532	383	240	444	359	643
bevacizumab	963	363	883	642	565	730	1,490	99	530	1,127	640	273	711	24	177	454	190
abiraterone	695	256	480	460	298	312	383	0	162	100	148	9	80	1	89	7	0
imatinib	601	514	497	516	439	549	820	357	262	351	124	150	375	14	128	231	29
ipilimumab	350	148	106	105	244	119	232	0	63	7	33	0	23	0	97	22	0
pertuzumab	303	144	158	112	124	94	399	36	69	22	30	13	16	1	1	2	0
everolimus	290	194	294	267	231	222	303	165	170	240	144	71	87	5	78	8	20
cetuximab	251	53	254	149	128	237	234	82	146	65	85	55	284	37	29	39	0
nilotinib	213	135	165	190	159	97	176	83	183	254	265	206	176	52	97	72	277
enzalutamide	213	291	262	332	48	58	392	91	144	7	57	17	16	0	1	2	0
trastuzumab.emtansine	199	77	167	78	133	43	122	0	1	1	0	0	22	2	0	1	0
dasatinib	163	136	165	136	191	124	153	19	79	92	110	66	85	0	92	279	0
crizotinib	133	58	77	46	30	32	105	14	55	49	2	0	21	0	0	2	0
pazopanib	132	104	55	111	71	74	122	75	77	180	208	37	53	2	54	1	1
cabazitaxel	111	69	90	34	45	47	93	0	51	3	75	6	0	0	0	0	0
dabrafenib	108	89	93	85	45	55	144	14	8	25	0	0	61	0	3	1	0
temozolomide	106	50	124	141	67	37	48	42	46	12	8	22	48	5	7	13	52
erlotinib	106	90	162	75	65	77	19	28	93	194	148	93	78	8	20	110	88
sorafenib	98	43	120	84	78	95	116	0	113	116	174	29	77	1	33	160	53
vemurafenib	79	20	70	32	61	24	29	59	0	57	105	116	48	3	117	37	21
panitumumab	75	102	92	62	64	82	147	19	67	53	104	16	115	1	0	0	0
sunitinib	65	119	204	181	150	145	231	166	147	306	115	125	190	63	104	188	60
axitinib	63	33	74	38	26	44	71	45	0	8	5	11	34	0	17	0	0
pembrolizumab	44	6	53	44	0	0	27	0	2	15	0	0	0	0	0	0	0
afatinib	39	16	20	35	16	13	3	5	19	22	6	4	3	0	2	0	0
gefitinib	34	23	67	37	84	46	145	16	45	109	56	16	32	27	11	0	0
lapatinib	16	8	29	22	28	31	18	12	35	60	39	27	27	15	41	9	1
cobimetinib	14	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
temsirolimus	4	1	17	9	2	10	6	10	11	2	8	3	1	0	0	25	0
nivolumab	0	40	115	56	4	0	112	0	0	0	0	0	12	0	0	0	0
cabozantinib	0	3	0	3	0	0	1	0	0	1	0	0	0	0	0	0	0
ceritinib	0	4	5	5	0	0	0	0	0	0	0	0	0	0	0	0	0
olaparib	0	13	17	16	3	0	8	0	0	0	0	0	0	0	0	0	0
trabectedin	0	22	14	32	51	59	63	0	25	27	25	16	0	0	1	16	0
trametinib	0	4	0	19	0	0	27	0	0	0	0	0	0	0	0	0	0

Drugs are sorted by sales in Switzerland.
Availability = percentage of drugs with any sales.

populations depends on reimbursement policies and was reported as much lower. Ades et al. estimated the sizes of populations in need by multiplying country population size, incidence of breast cancer, percentage of human epidermal growth receptor 2 (HER2) positive, number of new such cases, proportion of patients treated in the adjuvant or metastatic setting, and duration of adjuvant and metastatic setting treatment [26]. They found that none of the Eastern European countries achieved the total coverage of the population in need before 2006, when trastuzumab was approved only in the metastatic setting [26]. After 2006, when trastuzumab was approved in the HER2 positive adjuvant setting, only the Czech Republic and Slovenia achieved total coverage if the incidence of HER2 positive tumor was estimated to 15%. In the 20% HER2-positive scenario, no CEE country achieved total coverage.

Our analyses point toward the same direction. Availabilities of oncology drugs are different between WE and CEE, and this may affect the differences in cancer M/I ratio in these countries. High costs and economic burden of cancer therapeutics may affect patient access [15]. Because of the difference in investment in oncology drugs per cancer case shown in our study, this effect is higher in CEE than in WE. Health care payers with limited budgets make their decisions on the continuum between two extremes. One extreme option is investing in novel, more clinically beneficial and more expensive therapies. An inevitable consequence of this approach is limiting the treatment access to a relatively smaller number of patients. Another extreme option is investing more in the standard, older, generic, and less costly treatments addressed to the larger number of patients. In other words, the dilemma is whether to treat selected, limited numbers of patients with the best available treatments or to provide all patients with a less-than-state-of-the-art treatment. However, expenditures on cancer drugs are part of the total health care expenditure, and the problem of oncology drug costs should be considered in the context of other health services. We have shown that costs of oncology drugs in CEE and WE constitute 16% and 19% of the costs of all prescription drugs, respectively. At the same time, cancer has become the leading cause of death in the EU, accounting for about 25% of all mortality [27]. A significant proportion of cancer survival may be attributed to new treatments [13, 14]. Furthermore, cancer prevalence is increasing at a higher pace than share of expenditures on cancer care in total health care expenditures [28, 29]. Finally, to correctly understand the expenditure on oncology drugs, it is important to express this figure as the proportion of overall costs of cancer care. Expenditure on oncology drugs in the EU in 2009 was 27% of all direct cancer care costs [11]. When costs of informal care (unpaid care provided by relatives or friends of patients) are added, the share of expenditures on oncology drugs drops to 18%. Finally, when costs of productivity loss due to morbidity and mortality are added, the correctly calculated share of oncology drugs costs within the total cost of cancer is 11% [11]. It is somewhat higher in CEE than in WE. This should partially be attributed to several factors: the lower costs of cancer-related inpatient days, other formal treatment options, lower costs of informal care, lower costs of productivity losses, and to the interaction of differences in incidence of particular cancer types and differences in drugs and the total costs of particular cancer treatments and consequences. For example, CEE countries have higher incidences of lung cancer [1, 17], which has the highest productivity losses attributable to mortality [11].

Limitations of the Study

First, because of higher incidence and lower mortality rates, the prevalence of cancer is higher in WE than in CEE countries [23]. Throughout the study, we calculated expenditures per number of new cancer cases (incidence) or per capita, instead of per number of cancer patients actively treated with curative and palliative intent (prevalence of treated patients) when the financial costs are highest [30]. We did so because the published and available prevalence figures have lower reliability. We tried to control for the effects of this source of bias by calculating expenditures per new cancer case instead of per capita as was done in several other studies [7, 8]. However, this correction was limited because the prevalence of cases actively treated with ATC L01 class drugs may have a different correlation with the cancer incidence in WE and CEE countries. This may be caused by the differences in use and efficacy of other treatment options, differences in early diagnosis and the consequent average cancer stage at diagnosis, and differences in the adherence to clinical guidelines and the accuracy of incidence data. Second, we have not controlled for the effects of parallel trade. CEE countries have significantly more parallel export, and WE countries, particularly Germany, have more parallel import. Parallel trade is mediated by price differences and basically caused by international exchange rates and differences in patient demand and national income [31]. It affects countries in different ways and to different extents. Therefore, our results are the best-case scenario for the expenditures in CEE. Actual expenditures are most likely even lower. Third, this was a cross-sectional study, so we could not establish the temporal order of expenditures and M/I ratio. For this reason, we could not pose any causal claims. Fourth, incidence and mortality data have different reliability in different countries [6]. These differences may be associated with our key independent variable: expenditure on oncology drugs. Indeed, it was shown that accuracy of cancer registries for the total affected population is associated with the covered population's socioeconomic status [32]. Furthermore, it is possible that this effect varies between countries. This potential source of bias is common to the majority of analyses done on data based on cancer registries. This makes our analysis comparable but not necessarily valid. Fifth, we based our analysis on the overall expenditure on oncology drugs and ignored the differences in country-specific prices and/or discounts that may confound the relationship between novel drug access and use and coverage of the population in need, with the M/I ratio. The likely effect of this potential source of bias is against our null hypothesis of no association between expenditures on oncology drugs

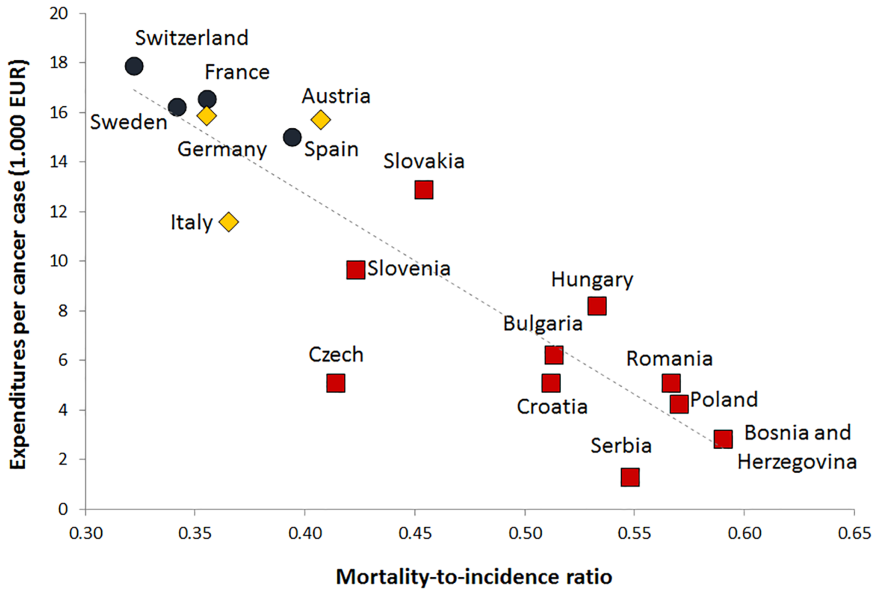

Figure 1. Correlation of annual expenditures per new cancer case for ATC L01 class drugs during 2015, and mortality-to-incidence ratio: All cancers; red squares represent Central and Eastern Europe countries, yellow rhombuses represent neighboring Western Europe (WE) countries, and blue circles represent other WE countries [17, 20].

and M/I ratio. We assumed such an effect because it is likely that drug prices are lower in lower- and middle-income countries [33, 34], and it is well documented that they have less favorable M/I ratios. Moreover, the correlation between wealth and M/I ratio is higher in CEE than in WE countries [7]. Sixth, a similar source of bias lies in the fact that we calculated the total expenditure by summing up the expenditures for particular molecules, ignoring the possibility that less-costly generic drugs or biosimilars are more often used in CEE than in WE, and consequently that the gap in drug use is smaller than what was indicated by the overall expenditure. Seventh, our key outcome was M/I ratio. Although M/I is a good approximation of the 5-year relative survival for many tumor sites, its validity varies to some extent between different tumor sites and countries [19]. Eighth, total expenditure on the oncology drugs studied may also be a surrogate marker for expenditure in total health care for cancer patients. For example, less investment in modern radiotherapy equipment or scarcer availability of appropriate multidisciplinary management, both expensive commodities in their own right, may also contribute to the observed differences in M/I ratios. Ninth, we did the analysis on the national, not the individual, patient level and so risked the ecological inference fallacy. Therefore, our study findings should be interpreted on the national rather than individual patient level. Tenth, a large number of uncontrolled, unobserved, or even unknown possible confounders of our findings may exist, and the results should be interpreted cautiously with no direct causal inferences at all. Eleventh, we calculated the M/I ratio from the age-standardized mortality and incidence rates regardless of cancer severity. However, what may be caused by the weaknesses of the secondary prevention and, consequently, more advanced stages at the detection of the same cancer may differ between different countries. The data on the cancer severity were not available to us.

Conclusion

Expenditures on oncology drugs per capita and per cancer case are markedly lower in CEE than in WE, although the spent percentage of GDP is roughly similar. The M/I ratio, which is significantly worse in CEE, is correlated with the expenditures on oncology drugs. Consequently, more investment in oncology drugs most likely will result in better M/I ratios in CEE countries. Policy makers should also be aware that expenditure on oncology drugs makes up only about 11% of total cancer costs, and that novel treatments increase survival and lower the costs associated with morbidity and mortality.

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Disclosures

Eduard Vrdoljak: Amgen, Bristol-Myers Squibb, Merck, Merck Sharp Dohme, Novartis, Roche, Sanofi (C/A); **Gyorgy Bodoky:** Amgen, Bristol-Myers Squibb, Janssen, Merck, Novartis, Merrimack, Pfizer, Roche, Servier (SAB); **Razvan Popescu:** Amgen, Bayer, Bristol-Myers Squibb, Eli Lilly, Merck, Merck Sharp & Dohme, Novartis, Roche, Sanofi (C/A), Bayer, Bristol-Myers Squibb, Merck, Merck Sharp & Dohme, Novartis, Roche, Sanofi (SAB). **Jacek Jassem:** Roche, AstraZeneca, Amgen, Boehringer Ingelheim, Merck (C/A); **Robert Pirker:** AstraZeneca, Boehringer Ingelheim, Eli Lilly, Merck, Shartp & Dohme, Syntia (C/A); **Alexandru Eniu:** Roche, AstraZeneca (R/F); **Vladimir Todorović**: Roche, Sanofi, Pfizer, Inmed (H); **Branimir I. Šikić:** Threshold (C/A), Genentech/Roche, Novartis, Sanofi, CellDex, Gilead (RF). The other authors indicated no financial relationships.

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