Discrepancies in cancer incidence and mortality and its relationship to health expenditure in the 27 European Union member states

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Background: The European Union (EU) is a confederation of 27 member states, the institutions of which work according to negotiated decisions. The EU has implemented similar legislation and a common market, and has adopted the same currency in most of its member states. Although financing health systems is a responsibility of the national governments, the EU has enacted the Charter of Fundamental Rights to standardize public health policies. However, for historical reasons, health policy and health expenditure is not uniform across the 27 EU member states (EU-27).

Material and methods: We hypothesized that increased health expenditure would be associated with better cancer outcome and that this would be most apparent in breast cancer, because of the availability of effective screening methods and treatments. Using publically available data from the World Health Organization, the International Monetary Fund, and the World Bank, we assessed associations between cancer indicators and wealth and health indicators. To do so, we constructed scatter plots and used the Spearman’s rank correlation coefficient.

Results: A marked difference in wealth and health expenditure indicators was observed between Eastern and Western European countries, with Western European being the higher. Higher wealth and higher health expenditures were associated both with increased cancer incidence and decreased cancer mortality. In breast cancer, the association with incidence was stronger. We created mortality/incidence ratios and observed that the more spent on health, the fewer the deaths after a cancer diagnosis.

Conclusion: Despite the initiatives to standardize public health policies of the EU-27, health expenditure continues to be higher in Western European countries and this is associated with better cancer outcome in these countries.

Key words: cancer indicators, health expenditure, health policy, breast cancer, European Union, health and wealth indicators

introduction

The European Union (EU) is a political and economic confederation of 27 member states, the territories of which are primarily located on Europe [1]. The EU institutions work according to negotiated decisions made by the member states [2]. The EU has established a common market with standardized legal systems, and the same currency has been adopted by 17 out of its 27 members [3]. To facilitate the circulation of people, goods, services, and capital, the EU maintains common policies on trade, and similar legislation in justice and home affairs [4]. The Schengen area was created with the same objectives, abolishing passport control in 22 EU and 4 non-EU states [5].

The health systems of the EU countries are primarily funded by the national governments, with private funding and health insurance companies playing an accessory role.
socioeconomic factors are important variables in determining how the health systems of EU member states are financed and organized. They influence the priority given to the allocation of resources to match social objectives such as equity, efficiency, and affordability [6]. The EU is not in charge of promoting health care for its citizens; this is responsibility of the national governments, and the health care systems differ from country to country. However, the Charter of Fundamental Rights of the EU stipulates in article 35 that ‘everyone has the right of access to preventive health care and the right to benefit from medical treatment under the conditions established by national laws and practices. A high level of human health protection shall be ensured in the definition and implementation of all the Union’s policies and activities’ [7].

The EU promotes several initiatives to standardize public health policies in its member states. The Directorate General for Health and Consumers is a section of the European Commission responsible for creating regulations and laws for safety in food, drugs, and other products, and for the protection of people’s health and consumer’s rights [8]. The European Commission also created the European Health Insurance Card, which allows European citizens covered by social security to use the health care systems of all EU member states for free or at a reduced cost when travelling or during temporary stays [9].

A shared characteristic of all EU health system funding is the use of a three-party model. The first party is the patient, the second party is the provider of the medical service, and the third party is the healthy individual insured by the system. Money is transferred to the second party when a health service is provided. In EU member states, this transfer of money is shared between the first and third parties and is adjusted by the individual’s ability to pay. This solidarity mechanism highlights an EU consensus that health care should be regulated by the state and not simply by free market rules [6].

With the ageing of the European population, an extra burden on the European health systems is expected. The World Health Organization (WHO) predicts an increase in the number of new cases of cancer worldwide, from 10 million in 2000 to 15 million in 2020. Ageing, smoking and unhealthy lifestyles are considered to account for most of the increase in incidence [10]. To face this challenge, it is not only necessary to find ways to fund health systems, but also identify strategies to develop more effective treatments.

For historical reasons, health policy and health expenditure is not uniform across the 27 EU member states [11]. We hypothesized that lower expenditures would be related to an increase in cancer mortality and that this difference should be greater in malignancies where there are effective treatments and available screening methods, as in the case of breast cancer. To test the hypothesis, we analyzed demographic and cancer registry data from the 27 EU member states, checking for correlations.

### Material and Methods

#### Definition of Western and Eastern European Countries

The EU comprises 27 sovereign member states. To perform the analyses, we divided the countries into two blocks: western European countries (EU-15, OECD definition), composed of Austria (AT), Belgium (BE), Denmark (DK), Finland (FI), France (FR), Germany (DE), Greece (EL), Ireland (IE), Italy (IT), Luxembourg (LU), The Netherlands (NL), Portugal (PT), Spain (ES), Sweden (SE), and United Kingdom (UK); and Eastern European countries (10 EU members joining on 1 May 2004 and 2 members joining on January 2007), composed of Bulgaria (BG), Cyprus (CY), Czech Republic (CZ), Estonia (EE), Hungary (HU), Latvia (LV), Lithuania (LT), Malta (MT), Poland (PL), Romania (RO), Slovakia (SK), and Slovenia (SI) [12]. For the presentation of the results, we use the ISO 3166 norm, the International Standard codes for country names.

#### Data Extraction

Demographic and cancer registry data were extracted from the publicly available databases of the World Health Organization (GLOBOCAN 2008 [13] and WHO World Health Statistics 2012 [14]), the International Monetary Fund Report 2009 [15], and the World Bank Report 2011 [16]. To compare health expenditure with cancer indicators, we examined the countries’ populations, total and per capita gross domestic product (GDP), percentage of GDP invested in health care, health expenditure per capita, and percentage of government health expenditure. Table 1 shows the OECD’s and World Bank’s definitions of these indicators [17].

### Table 1. OECD and World Bank definitions of indicators

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Definition</th>
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<tbody>
<tr>
<td>Gross domestic product, GDP (current US$)</td>
<td>Gross domestic product is an aggregate measure of production equal to the sum of the gross values added of all resident institutional units engaged in production (plus any taxes, and minus any subsidies, on products not included in the value of their outputs). The sum of the final uses of goods and services (all uses except intermediate consumption) measured in purchasers’ prices, less the value of imports of goods and services, or the sum of primary incomes distributed by resident producer units.</td>
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<tr>
<td>GDP per capita (current US$)</td>
<td>Gross domestic product divided by midyear population.</td>
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<tr>
<td>Health expenditure as % of GDP</td>
<td>Percentage of total general government expenditure that is spent on health.</td>
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<td>Health expenditure per capita (current US$)</td>
<td>Total health expenditure is the sum of public and private health expenditures as a ratio of total population. It covers the provision of health services (preventive and curative), family planning activities, nutrition activities, and emergency aid designated for health but does not include provision of water and sanitation.</td>
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<tr>
<td>Health expenditure, public (% of total health expenditure)</td>
<td>Public health expenditure consists of recurrent and capital spending from government (central and local) budgets, external borrowings and grants (including donations from international agencies and nongovernmental organizations), and social (or compulsory) health insurance funds.</td>
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data analysis
We evaluated total cancer incidence and mortality in the 27 EU member states. We performed a separate analysis for breast cancer because of the availability of effective screening programs and available treatments. Scatter plots were generated to assess the relationship between wealth and health expense indicators (GDP per capita, GDP % allocated to health, and health expenditure per capita) and cancer demographics. We also created mortality/incidence ratios for all cancers and for breast cancer as a way to estimate the proportion of patients dying after a cancer diagnosis and compared them to wealth and health expense indicators.

To assess the strength of the associations among these variables, we calculated the Spearman’s rank correlation coefficient. The following rule was used to characterize the strength of the association: a coefficient under 0.20 was classified as ‘very weak’; between 0.20 and 0.40 ‘weak’; between 0.40 and 0.60 ‘moderate’; between 0.60 and 0.80 ‘strong’; and between 0.80 and 1.00 ‘very strong’. For the direction of the association, we used the terms ‘positive’ when the two variables went in the same direction or ‘negative’ when the variables went in opposite directions. All coefficients are presented with their respective P-values, and an association was considered to be statistically significant when the P-value was < 0.05.

results
population, GDP, and allocation of resources to health care
With ~400 million inhabitants, Western Europe holds most of the European Union’s population, while Eastern Europe has around 100 million inhabitants. There is a marked difference in the respective GDPs of these regions: Western Europe GDP is around 16.1 trillion dollars, while for Eastern Europe, it is 1.3 trillion dollars. While the population of Western Europe is around four times larger than Eastern Europe, its GDP exceeds that of Eastern Europe more than 10-fold.

We then evaluated the total health expenditure for the 27 EU member states (Supplementary Table, available at Annals of Oncology online). A clear division between the two geographic blocks can be made according to this parameter. Western European countries have higher health expenditure than their Eastern counterparts, with the West–East ‘cutoff’ being around US$ 2600 per person per year. Not surprisingly, health expenditure per capita strongly correlated with the GDP per capita and with the percentage of GDP in health care, as shown in Figure 1. Eastern European countries have lower per capita GDPs when compared with Western countries and allocate a lower percentage of their GDP to health.

Interestingly, and despite the differences in health expenditure among the 27 EU member states, most health related expenses are reimbursed by the national governments in both blocks (Supplementary Figure, available at Annals of Oncology online). There are still differences between them regarding the percentage of health expenses reimbursed; however, this is much less marked than the differences in percentage of GDP allocated to health and total health expenditure.

incidence versus mortality analyses
Figure 2A shows that there is a weak, positive (Spearman’s $\rho = 0.227$), and nonsignificant ($P = 0.253$) association between
cancer incidence and mortality. However, it is evident that all the Eastern European countries, except Cyprus, have higher mortality rates than the Western European countries for approximately the same range of incidence. This indicates that, proportionally, more patients die after a diagnosis of cancer in Eastern Europe than in Western Europe. When the same analysis is performed for breast cancer, a slightly different result is observed (Figure 2B). The association is also positive and weak (Spearman’s $\rho = 0.381$), but nearly significant ($P = 0.050$). Although the West–East separation is still noticeable (high incidence–low mortality versus low incidence–high mortality), a third group of countries with high incidence and high mortality stands out. This third group comprises four Western European countries: Belgium, Denmark, the Netherlands, and Ireland. Three of them are located close together geographically, raising the question of a possible genetic or environmental predisposition to breast cancer in those populations.

association between health and wealth and cancer indicators
We analyzed the association between the incidence of all cancers and breast cancers, and the wealth and health expenditure indicators. There was a positive and moderate correlation between all cancer incidence and all three health and wealth expenditure indicators. These associations are all statistically significant, except for the relationship between mortality and health expenditure as a percentage of GDP ($P = 0.255$). When the same analysis was done for breast cancer, strong, positive, and significant associations were observed.

On the contrary, mortality revealed a different pattern of correlation with wealth and health expenditure indicators. In regard to all cancers, it had a moderate inverse correlation with GDP and health expenditure per capita, meaning the higher the expenditure, the lower overall cancer mortality. However, only very weak and nonsignificant associations between wealth and health expenditure indicators and breast cancer mortality were observed (Table 2).

effectiveness of cancer care and health resources allocation
We then calculated mortality/incidence ratios, representing the fraction of patients dying after cancer diagnosis, and compared these to wealth and health expenditure indicators. An inverse and strong correlation was seen in both the ratio for all cancers and the ratio for breast cancer (Table 3). This means that the more resources are allocated to health, the fewer patients diagnosed with cancer die from it. Figure 3A and B shows the association of the ratio and health expenditure per capita.

discussion
The Western and Eastern blocks of countries composing the EU have marked differences in regard to population size (∼400 million versus ∼100 million citizens, respectively) and GDP (∼16 trillion versus ∼1.3 trillion dollars, respectively). As a consequence, Western Europe has higher GDP per capita and allocates more resources to health care. However, the member states seem to be compliant with the Charter of Fundamental Rights of the EU, as the European national health systems are responsible for most health expenditure. Twenty-five of the 27 states are responsible for funding 60% or more of the health costs of their citizens (Supplementary Figure, available at *Annals of Oncology* online). This evidences a common policy to keep health in control of the national governments, independently of the amount of resources allocated to health funding.

The differences between Eastern and Western Europe are also evident with respect to cancer incidence and mortality. Not surprisingly, we showed a lack of correlation between these parameters among the EU-27. Instead, we observed two rather distinctive patterns: proportionally Eastern Europe has lower

| Table 2. Association (Spearman’s $\rho$ coefficient) between wealth and health and cancer indicators |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
|                                 | All cancers                     |                                 | Breast cancer                   |
|                                 | Incidence                       | Mortality                       | Incidence                       | Mortality                       |
| Indicator                       | Correlation P-value             | Correlation P-value             | Correlation P-value             | Correlation P-value             |
| GDP per capita                  | 0.588                            | -0.467                           | 0.014                            | 0.7855                             | <0.001                            | 0.1139                             | 0.572                             |
| % GDP                           | 0.5041                            | -0.2271                           | 0.255                            | 0.6139                             | <0.001                            | 0.2376                             | 0.233                             |
| Health expenditure per capita   | 0.6265                            | -0.4145                           | 0.032                            | 0.7941                             | <0.001                            | 0.1582                             | 0.431                             |

| Table 3. Association between the cancer mortality/incidence ratio and wealth and health expenditure indicators |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
|                                 | All cancers                     |                                 | Breast cancer                   |
|                                 | Correlation (Spearman’s $\rho$) | P-value                         | Correlation (Spearman’s $\rho$) | P-value                         |
| Indicator                       |                                 |                                 |                                 |                                 |
| GDP per capita                  | -0.7961                          | <0.001                          | -0.7436                          | <0.001                          |
| % GDP                           | -0.4726                          | 0.013                           | -0.5147                          | <0.001                          |
| Health expenditure per capita   | -0.757                           | <0.001                          | -0.7411                          | <0.001                          |
cancer incidence and higher cancer mortality, while the opposite happens in Western Europe. We did see moderate and strong correlations between the allocation of resources to health and cancer incidence, this correlation being even stronger when the analysis was restricted to breast cancer. Mortality, however, was correlated to wealth and health expenditure indicators in all types of cancers, but not in breast cancer. Using the mortality/incidence ratio to identify the fraction of diagnosed patients who die from cancer, we found a strong and consistent relationship between wealth and health expenditure indicators in the full range of cancers and in the breast cancer comparisons.

The variances in cancer indicators among different countries are multifactorial. Cancer incidence and mortality may be influenced by genetic characteristics, life style factors, environmental exposure to carcinogenic agents, and infections [18]. Tobacco [19] and alcohol consumption [20] as well as dietary habits and obesity [21] are also known to be related to increased cancer incidence. Our hypothesis is that the high level of cancer diagnosis in Western Europe is related to the previous described risk factors and also to screening and that the low mortality/incidence ratio is related to diagnosis at earlier stages, when the chance of cure is higher.

The results of this analysis must be interpreted with caution. Our analyses were based on data extracted from trustworthy databases; however, we cannot ensure that the data were collected in a similar way across all countries. Similarly, we cannot infer that there is a relationship between data precision and health investment. In that regard, an important point to be considered is the difference in data collection between mortality and incidence. Mortality information is more precise, given that it is directly related to the disease outcome; by contrast, incidence can be influenced by external factors such as screening programs, and access to health care systems. Thus, cancer incidence could be underestimated in countries that allocate fewer resources to health care or, in the contrary, overestimated in countries with higher allocation of resources to health care.

Another point to stress is that, through this data, we cannot assess the influence of genetic and environmental factors and its relation to cancer incidence and mortality across the European populations. However, one would expect that ‘real’ versus ‘screening’-increased incidences theoretically have different impacts in cancer mortality rates. While a ‘real increase’ in cancer incidence would lead to increased mortality, a ‘screening increase’ incidence would lead to mortality decrease because of disease diagnosis at an early stage. Our data suggest that the second scenario is probably the true in the EU-27.

Breast cancer mortality is decreasing in Europe as a result of a multidisciplinary treatment approach involving improvements in breast surgery, radiotherapy, clinical oncology, and screening. Breast cancer is the best example of an oncologic disease with effective screening methods [22, 23]. In European populations, it has been shown that breast cancer screening reduces mortality in comparison to nonscreening [24–26]. Breast cancer is also a disease for which there are a range of targeted therapies available. Tamoxifen has been in use for more than 30 years [27]. More recently, aromatase inhibitors have been developed to deprive breast tumors of stimulation by endogenous estrogens [28]. Since 1998 anti-HER2 treatments such as trastuzumab are available [29–32] followed, more recently, by other effective anti-HER2 targeted agents like lapatinib [33], pertuzumab [34], and TDM1 [35]. Therefore, the availability of these drugs in different countries may play an important role in breast cancer mortality.

In conclusion, our results show that higher expenditure in health is correlated to better cancer outcome. Although no direct correlation can be made from our results, they suggest that the part of the excess incidence of cancer in Western Europe may be related to the screening programs in place since mortality does not increase in the same proportion. The availability of effective treatments and diagnosis at earlier stages could be the cause of the proportionally lower mortality in observed in Western Europe. To further explore these issues, we are developing a research project to assess how quickly and to what extent the health care systems and health care providers of the respective member states approve and start using a life-saving drug, using HER2-positive breast cancer and an anti-HER2 drug as study case.

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disclosure

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references