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Patient survival for all cancers combined as indicator of cancer control in Europe

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Background: EUROCARE found marked differences in cancer survival across European populations, provoking extensive discussion as to the cause. We investigated the influence of socioeconomic indicators on survival, making use of the indicator population-based age-standardized and cancer site-standardized relative survival for all cancers combined (*all cancer survival*). **Methods:** Bivariate correlation and multivariate regression analyses investigated relations between 1995 socioeconomic variables and *all cancer survival* in EUROCARE-3 patients from 19 European countries diagnosed 1990–94 and followed to 1999. **Results:** Gross domestic product (GDP) and total national expenditure on health (TNEH) correlated highly with *all cancer survival*. Wealthy northern and western European countries had high survival; eastern European countries had low *all cancer survival*. GDP, TNEH, and number of computed tomography scanners per million—proxy of technological investment in cancer care—explained most survival differences. Low *all cancer survival* in the UK and Denmark compared to countries of similar wealth was closely related to fewer computed tomography scanners. Low *all cancer survival* in Poland compared to countries of similar wealth was also related to low TNEH. **Conclusions:** *All cancer survival* appears a useful and important indicator for monitoring countries' performance in cancer control. The most direct way for poorer European countries to improve *all cancer survival* would be to get richer; for richer countries more investment in health technology is important. However the sharply increasing costs of cancer care may render this impossible suggesting the need to radically rethink cancer control strategies.

Keywords: cancer survival, cancer indicator, cancer control, EUROCARE, EUROCHIP

Introduction

Cancer is of increasing importance as cause of death in developing countries where life expectancy at birth (LE) is increasing. In the European Union, 2.1 million new cancer cases were estimated in 2002[1] and cancer control is a major health care priority.[2] The EUROCARE studies[3–5]—the largest yet population-based investigations on cancer patient survival—showed that for most cancer sites there were marked differences in cancer survival between European countries. The wealthier countries of northern Europe generally had high cancer survival, other western European countries—at intermediate levels of socioeconomic development—had intermediate survival, and the poorer countries of eastern Europe had worst survival. The EUROCARE-4 study, whose initial results have been published recently,[6–7] supported this overall picture although only two eastern European countries (the Czech Republic and Poland) participated, compared to four (Estonia, Poland, Slovakia and the Czech Republic) in EUROCARE-3[5] severely limiting possibilities for comparing eastern Europe with the rest of the continent. The ITACARE study,[8] and its update[9] revealed a similar pattern within Italy, where the more affluent central and northern areas of the country had higher cancer survival than the south. In England and Wales, cancer survival has been shown to be closely related to level of deprivation for which it can serve as a proxy.[10]

Unlike survival in clinical series, population-based cancer survival is estimated from all incident cases in a cancer registry area over a defined period, and provides an average measure of cancer care performance. In fact it has been shown that survival for just two of the commonest treatable cancers—breast and colon—correlates with per-capita health expenditure, LE at birth, infant mortality and other socioeconomic indicators,[11] suggesting that survival for these major cancers is, by itself, an indicator of health system performance.

In contrast, for rare cancers that can be treated effectively (e.g. several leukaemias and testicular cancer) geographic differences in survival are low.[12] This is likely to be due to the wide dissemination of effective evidence-based treatments, that because of the rarity of the diseases do not require major investments to implement. Similarly, for rapidly fatal cancers for which no effective treatments are available—such as those of liver, oesophagus and pancreas—geographic variations in survival are also low, and do not provide any information of the performance of a national health system.[12]

In this article, we introduce the indicator *population-based age-standardized and cancer site-standardized relative survival* (ASRS) *for all cancers*, also referred to as *all cancer survival*, as a means of summarizing a country's performance in cancer care. We analysed relations between *all cancer survival* and socio-economic variables and identified those that predict survival. We made use of EUROCARE-3 survival data covering the diagnosis period 1990–94 of patients followed to 1999, because between-country survival differences are more marked than for the more recent EUROCARE-4 period, and also because

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socioeconomic variables for the more recent period are missing for some countries, yet are available for all countries participating in EUROCARE-3.

Methods and data sources

We started with *relative survival*—the ratio of observed cancer survival to survival in the age and sex-matched general population—to eliminate the effect of mortality from competing (non-cancer) causes. Relative survival data were extracted from the publicly available EUROCARE-3 database.[13] We then *age-standardized* the relative survival data (ARS) to take into account the different age distributions of patients at diagnosis in different countries.[14] Finally, we adjusted survival for the *differing mix of cancers in different countries* (ASRS), to eliminate the confounding effect that arises if, for example, the incidence of highly lethal cancers is higher in one country than another. More formally, given the ARS^i_{ck} for a given cancer c in each country or population k, for follow-up period i, we obtained the ASRS for all cancers ASRS^i_k from ARS^i_{ck} by applying the weighting W_{ck} defined by

$$W_{ck} = \frac{n_{ck}}{\sum_c n_{ck}}$$

where n_{ck} is the cancer site-specific number of cases at the beginning of follow-up in the country or population k.

Thus, ASRS^i_k is given by

$$\mathrm{ASRS}^i_k = \sum_c W_{ck}\mathrm{ARS}^i_{ck} \text{ with } W_{ck} = \frac{n_{ck}}{\sum_c n_{ck}}$$

When ARS^i_{ck} is not available for a cancer site c and population k, as may occur for rare cancers particularly in small populations, we used information from larger populations (Nordic countries, central European countries, Mediterranean countries, eastern European countries or the UK, as appropriate) that contained the population k.

The resulting measures—1- and 5-year ASRS—are suitable for international survival comparisons. We estimated ASRS with standard errors for patients diagnosed in 1990–94 in 19 European countries participating in EUROCARE-3. For nine of these countries (Norway, Denmark, Sweden, Finland, Wales, Scotland, Slovenia, Slovakia and Estonia) cancer registration covers the entire nation, while for the other 10 countries (England, The Netherlands, the Czech Republic, Poland, Switzerland, France, Germany, Austria, Spain and Italy) data are available for only part of the country. For the purposes of this study we assumed that the partial data were representative of the country as a whole.

We first performed bivariate Pearson's correlation analyses (r correlation index) to study relations between socioeconomic variables and *all cancer survival* in the 19 European countries, and separately in 10 countries with GDP above, and nine countries with GDP below the median. We next performed multivariate ecological regression analyses of ASRS data for these countries in relation to country-specific macroeconomic variables. Let sc_{nk} ($n = 1, 2, \ldots, N$) be N socioeconomic variables for country k. ASRS^i_k is related to these variables by the regression model:

$$\log(-\log(\mathrm{ASRS}^i_k)) = \sum_{n=1}^{N} b_n sc_{nk} + \varepsilon$$

The multivariate regression analyses were performed with SPSS[15] using backward stepwise selection of the variables according to the significance of their contribution to explaining differences in the excess risk of death of cancer patients 1 year and 5 years after diagnosis, rejecting variables with $P \geq 0.03$ and adding those with $P \leq 0.01$; outcomes were presented by corrected R^2—the adjusted form of R^2 (the coefficient of determination)—associated to the final model.

We considered the following socioeconomic variables: infant mortality (INFMORT), expressed as deaths/1000 live births; LE at birth, expressed per years; GDP, expressed in US dollars ($) per capita adjusted for purchasing power parity (PPP); proportion of total population unemployed (UNEMPL), expressed in percentage; TNEH and public expenditure on health (PEH) both expressed in US dollars ($) per capita adjusted for PPP and computer tomography scanners (CTS), per million people.

INFMORT, LE, GDP and UNEMPL were considered because they are indicators of countries' health and economic performance used by the WHO (LE)[16] or EUROSTAT (GDP, UNEMPL),[17] or had been shown important in ecological studies (UNEMPL, INFMORT).[11,18–20] TNEH, PEH and CTS had been proposed as important cancer control indicators by EUROCHIP.[21–22] CTS was proposed because it is available for all countries, rich and poor alike and was viewed a proxy for direct investment in technology for cancer. We considered socioeconomic indicators for 1995; most were obtained from the Organization for Economic Co-operation and Development (OECD) database.[23] However, data for Estonia, Slovenia, Scotland and Wales were not present in OECD and were obtained from ELDCARE.[18–19] Because CTS did not satisfactorily reflect technological investment in cancer when GDP was high in comparison when GDP was low, we introduced a new variable: CTS° divided by GDP (CTS°/GDP). CTS° is CTS divided by a million and hence gives the fraction of CT scanners per person. We subsequently multiplied (CTS°/GDP) by 10^{10} to render the fraction visually manageable. CTS°/GDP may be interpreted as an index of technological investment in cancer, considering GDP.

Results

Table 1 shows *all cancer survival* (ASRS) 1 year and 5 years after diagnosis in the 19 European countries. Five-year ASRS ranged from 25.2% (Poland) to 47.5% (Austria) for men, and from 40.5% (Poland) to 57.9% (France and Austria) for women. The bivariate analyses (table 2) showed that INFMORT and LE correlated strongly (inversely for the former, directly for the latter) with ASRS and also with other socioeconomic variables (data not shown). When all 19 countries were considered, these correlations were all significant. Although these associations reinforced ASRS as an important indicator of cancer control, INFMORT and LE cannot be modified by cancer control policies, and were not therefore included in the multivariate analyses. PEH also correlated with *all cancer survival*: the correlations were significant for all countries and for those below median GDP (except 1-year ASRS in women), but because of the major structural changes that have occurred in European national health systems in recent years,[24] generally in the direction of reducing the role of the public sector and facilitating the private sector, PEH had unintelligible effects on *all cancer survival*, and was also excluded from the multivariate analysis.

TNEH correlated significantly with ASRS in all countries and in the poorer countries (except 1-year ASRS in women), but less strongly in the richer countries. GDP behaved very similar to TNEH. CTS correlated strongly and significantly with ASRS in all countries, and also in the poorer countries; the significant correlation remained in the rich countries but was less strong. UNEMPL correlated inversely and weakly with ASRS when all countries were considered and when those with GDP above the median were considered; it correlated directly with ASRS in the poorer countries.

Based on these findings and considerations we therefore investigated the explanatory roles on ASRS of TNEH, the most intelligible variable in terms of public health action, the new variable CTS°/GDP, and also UNEMPL, in the multivariate analyses.

Multivariate analyses were performed for all countries, for countries with GDPs above and below the median, and for men and women separately. When all 19 countries were considered, TNEH and CTS°/GDP emerged as significant ASRS descriptors, except for 5-year ASRS in women where UNEMPL also played a role. In all models with GDP above the median, CTS°/GDP emerged as the main variable related to ASRS. Except of 1-year ASRS in women where no variable had the criteria for inclusion in the final model, for the poorer countries, the main explanatory variable was TNEH. Corrected R^2 associated to final models ranged from 47% to 84%.

Figure 1 shows the distributions of GDP, TNEH and CTS in the countries ranked by GDP in 1995. As is evident from the figure, the wealth difference between western and eastern European countries was large. TNEH had a distribution very similar to that of GDP except that TNEH was higher than suggested by GDP for Switzerland, Germany and France. The CTS histogram shows that for Denmark, England, Wales, Slovenia and Poland, the number of CT scanners in 1995 was lower than expected in relation to GDP and TNEH of the other countries.

Figure 2 shows ASRS ranked by TNEH, for male cancer patients 1 year and 5 years after diagnosis and, on the right, CTS°/GDP—the factor that best explained the between-country *all cancer survival* differences according to our models, when TNEH was already considered. The first point to note from figure 2 is that it indicates a clearer relation of male *all cancer survival* to TNEH for the less rich countries—in the lower portions of the graphs—compared to rich countries. Further inspection shows that some countries have ASRS distant from the smoothed superimposed curve (indicating expected survival). Considering for example, 1-year ASRS, this was lower than expected in relation to TNEH in Germany, Denmark, England, Wales and to a lesser extent in Poland. The survival deficit in these countries was partially explained—in our multivariate modelling—by the CTS°/GDP distribution by country: this is illustrated in the right histogram which shows the CTS°/GDP profile for the countries ranked by TNEH. The right histogram shows for example that in Denmark, with low survival in comparison to countries of similar wealth, CTS°/GDP was low. A similar situation is evident for England, Wales and Poland. Slovenia, which also had low CTS°/GDP, had lower 5-year ASRS than the countries with similar TNEH.

Table 1 One- and 5-year age- and cancer site-standardized all cancer relative survival (%) – *ASRS*[a] with standard errors (SE), for cancer patients[b] diagnosed 1990–94 in 19 European countries

Country	Men		Women	
	1-year (SE)	5-year (SE)	1-year (SE)	5-year (SE)
Austria	67.9 (0.6)	47.5 (0.7)	76.7 (0.5)	57.9 (0.7)
France	67.6 (0.4)	44.5 (0.5)	77.2 (0.3)	57.9 (0.4)
Germany	63.1 (0.5)	44.1 (0.6)	73.3 (0.4)	55.6 (0.5)
Spain	62.0 (0.3)	43.9 (0.3)	73.9 (0.3)	57.1 (0.3)
Switzerland	66.7 (0.6)	43.5 (0.7)	76.8 (0.5)	56.7 (0.6)
The Netherlands	65.0 (0.3)	42.7 (0.3)	75.1 (0.2)	55.7 (0.3)
Sweden	64.4 (0.2)	42.5 (0.2)	75.3 (0.2)	57.6 (0.2)
Finland	63.3 (0.3)	41.4 (0.3)	74.3 (0.2)	55.8 (0.3)
Italy	63.8 (0.1)	41.2 (0.2)	75.2 (0.1)	55.6 (0.2)
Norway	62.2 (0.2)	40.0 (0.3)	74.0 (0.2)	54.9 (0.3)
England	56.2 (0.1)	37.1 (0.1)	68.1 (0.1)	50.8 (0.1)
Scotland	56.4 (0.2)	35.6 (0.3)	67.7 (0.2)	49.5 (0.2)
Wales	50.5 (0.3)	34.8 (0.3)	61.4 (0.2)	47.3 (0.3)
Denmark	57.7 (0.2)	33.5 (0.3)	70.9 (0.2)	51.3 (0.2)
The Czech Republic	54.3 (0.6)	32.3 (0.8)	66.9 (0.5)	46.0 (0.7)
Slovenia	55.6 (0.5)	31.2 (0.6)	68.4 (0.4)	47.0 (0.5)
Estonia	50.9 (0.6)	29.9 (0.8)	64.6 (0.5)	43.1 (0.6)
Slovakia	53.4 (0.3)	29.7 (0.4)	66.3 (0.3)	43.6 (0.4)
Poland	48.1 (0.4)	25.2 (0.5)	62.4 (0.3)	40.5 (0.4)

The data are ordered by decreasing 5-year *ASRS* in men

a: Estimated from unadjusted relative survival data extracted from the publicly available EUROCARE-3 database[13]

b: All cancers excluded non-melanoma skin cancer, i.e. ICD-9 codes 140 to 208 excluding 173[16]

Table 2 Pearson correlations (*r*) between 1995 socioeconomic indicators and 1- and 5-year ASRS for cancer patients diagnosed in 1990–94 in all 19 European countries, and separately for the 10 countries with GDP above and nine countries with GDP below the median

	INFMORT	LE	GDP	PEH	TNEH	CTS	UNEMPL
All 19 European countries							
1-year W	−0.681***	0.745***	0.801***	0.738***	0.817***	0.812***	−0.261
1-year M	−0.714***	0.778***	0.830***	0.766***	0.848***	0.851***	−0.268
5-year W	−0.806***	0.871***	0.874***	0.811***	0.854***	0.825***	−0.124
5-year M	−0.728***	0.811***	0.815***	0.753***	0.816***	0.841***	−0.120
GDP above median							
1-year W	−0.337	0.620	0.414	0.087	0.503	0.692*	−0.231
1-year M	−0.247	0.566	0.356	0.079	0.506	0.698*	−0.240
5-year W	−0.362	0.644*	0.243	0.167	0.428	0.674*	−0.115
5-year M	−0.100	0.453	0.173	0.104	0.413	0.659*	−0.217
GDP below median							
1-year W	−0.611	0.547	0.599	0.566	0.665	0.734*	0.406
1-year M	−0.732*	0.661	0.738*	0.705*	0.791*	0.841**	0.440
5-year W	−0.797**	0.806**	0.861**	0.780*	0.885**	0.868**	0.593
5-year M	−0.754*	0.777*	0.839**	0.753*	0.855**	0.887***	0.622

Men (M) and Women (W)

*Correlation significant at $P < 0.05$

**Correlation significant at $P < 0.01$

***Correlation significant at $P < 0.001$

INFMORT, infant mortality; LE, life expectancy at birth (men and women combined); GDP, gross domestic product; PEH, public expenditure on health; TNEH, total national expenditure on health; CTS, computer tomography scanners frequency; UNEMPL, unemployed as proportion of total population

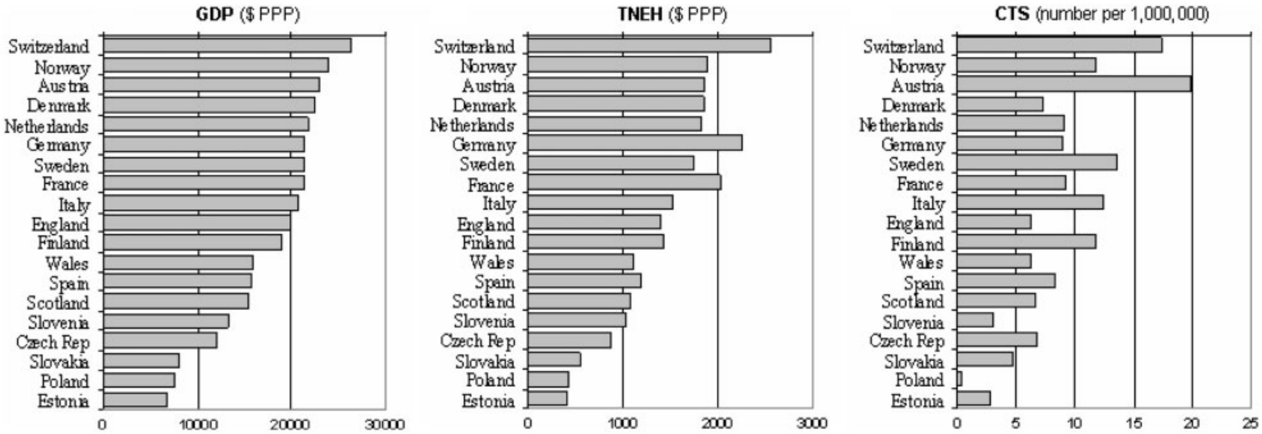

Figure 1 Distribution of GDP (left), TNEH (middle) and CTS (right) in 19 European countries, ranked by GDP in 1995

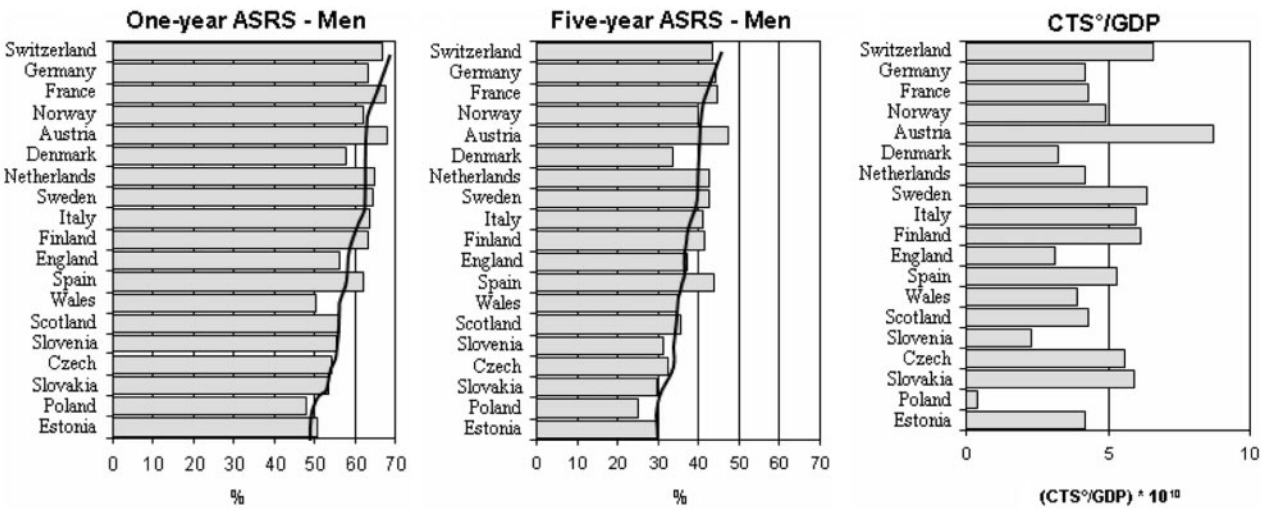

Figure 2 ASRS 1 (left) and 5 (centre) years after diagnosis and CTS°/GDP (right) for 19 European countries ranked by 1995 TNEH, in men. The superimposed curves (left and centre) are smoothed trends expected when TNEH alone is considered the explicatory variable of survival

When 1- and 5-year ASRS in women were ranked by TNEH, CTS°/GDP again helped to explain survival deficits (data not shown). One-year survival was lower than expected, in relation to TNEH, in Denmark, England, Wales and Poland and again these countries had lower investment in technology for cancer (low CTS°/GDP) than countries of comparable wealth. High female cancer survival for Austria, Sweden, Italy and Finland was explained by the model in terms of high CTS°/GDP, corresponding to greater investment in technology for cancer than other countries of similar wealth (data not shown).

Discussion

We have shown that our *all cancer survival* indicator (ASRS) is informatively related to several common macroeconomic indicators. In particular ASRS strongly and significantly correlated with wealth (GDP) and national investment in health (TNEH) for all 19 European countries considered and for the nine poorer countries; but only weakly among the richer countries. ASRS also correlated with number of CT scanners (CTS)—proxy of technological investment for cancer—both in the poorer and richer countries.

To further investigate ASRS behaviour, we performed multivariate analyses. These analyses indicated that *all cancer survival* differences between richer countries mainly depend on CTS°/GDP (index of technological investment in cancer in relation to available prosperity). In contrast, survival differences between poorer countries mainly depend on TNEH—general level of health investment. ASRS therefore emerges as a highly informative measure of a country's performance in cancer control. It is noteworthy, however, that the indicator has little meaning from the clinical point of view.

Several international ecological studies have examined cancer survival in comparison to socioeconomic indicators. In the US, cancer registry-derived relative survival for individual cancer sites was used in models with socioeconomic indicators to estimate survival in areas not covered by cancer registration. This study showed that breast, prostate and, to a lesser degree, colorectal cancer survival were strongly associated with demographic and socioeconomic indicators (including percentage unemployed, median family income, percentage with high school diploma, etc) at the county level.[20] The ELDCARE project studied between-country differences in cancer survival in the elderly, taking account of socioeconomic conditions and the characteristics, finding that cancer survival for various cancer sites in the elderly was strongly related with GDP, TNEH and CTS.[18–19] Furthermore, ranking of *all cancer survival* by TNEH, the recent EUROCARE-4 study found that wealthy countries with high TNEH generally had good cancer outcomes, and suggested that countries with conspicuously worse outcomes than those with similar TNEH were allocating health resources inefficiently.[6]

Our analysis concerned the survival of patients diagnosed in the early 1990s. We used EUROCARE-3 data because the more recent EUROCARE-4 data[6,7] show reduced cancer survival differences across Europe, in part because fewer eastern European countries participated. Furthermore, up-to-date macroeconomic information is not available for all EUROCARE-4 countries.

We used the macroeconomic indicators suggested by EUROCHIP, a European Commission project to propose cancer control indicators for Europe.[21,22] INFMORT and LE were significantly associated with ASRS reinforcing role of the latter as an indicator. CTS was suggested, by a consensus of experts convened by EUROCHIP, as the best proxy for technological investment in cancer as it was available for countries irrespective of wealth. Countries with high GDP use more modern technologies such as magnetic resonance imaging (MRI) and positron emission tomography scanners (PET) but these were not widely in many European countries in 1995.

A possible limitation of the study is that, for 10 countries *all cancer survival* was estimated from survival data covering only a fraction of the population. However this does not appear as a major limitation: *all cancer survival* variance within a country is likely to be lower than that between countries and thus a given country's survival should be well estimated for our purposes.

Another limitation is that the analysis was performed on data that are at least 13 years old. Certainly an analysis on more recent data is desirable but unfortunately more recent data are not available.

An important implication of our analysis is that for some European countries, ASRS for cancers diagnosed in the early 1990s was unacceptably low in comparison to that of other countries of similar wealth and health investment. This was the case for England, Wales and Poland, and also for Denmark. The first EUROCARE study[3] on cancers diagnosed 1978–85, brought to light unexpectedly low survival for common cancers in the UK compared to continental Europe. The *all cancer survival* data presented here for cases diagnosed in 1990–94 continue to indicate low survival in the UK and suggest that inadequate health investment contributed to this. In fact an audit of cancer care in England and Wales[25] showed that in 1993 the ratio of hospital patients to CT and MRI scanners varied 5-fold between hospitals. Some patients waited for over 3 months for scans. Some hospitals scanned more patients with a single MRI scanner than other hospitals did with three or four scanners.[26] The audit concluded that imaging resources were often not used optimally. More recent ASRS figures for 1995–99 indicate that the survival gap between the UK and continental Europe was closing although difficulties remain;[6] projections suggest that for major cancer sites UK survival will improve in the future to approach that of other countries of comparable wealth.[7] This anticipated improvement may be in part attributable to the implementation, in 2000, of a plan to increase investment and improve the organization of cancer services in England.[27]

Our findings have several possible implications for the future of cancer control in Europe. They suggest that the most direct way for poorer European countries to close the 15 percentage point survival gap[5] between them and the richest countries would be to get richer! This aim is no doubt being pursued by all countries, but cannot be part of a cancer control policy. Improving *all cancer survival* is also problematic for the richer countries. The last 30 years have seen major advances in the application of technology to medicine. The cancer field has been characterized by the introduction of high-cost diagnostic technologies such as CT, MRI, PET and others. New anticancer drugs are also extremely expensive. It seems likely that only the richest countries will be able to continue offering the latest diagnostic and therapeutic modalities to their citizens so as improve cancer survival.[21] A likely longer term trend, as costs continue to escalate, is that the best treatments will only be available to individuals who can afford them, as even wealthy countries decide they cannot allocate the resources necessary to provide optimal cancer care for all citizens. These considerations suggest the need for a radical evaluation of cancer control strategies in general and their costs in particular. Cancer research is a major consumer of resources in developed countries[28] but appears largely immune from cost considerations. Clinical trials on new diagnostic or therapeutic methods almost never include costs among their assessment criteria. Yet costs must be a central concern if the intention is to improve cancer survival for all, and not just the privileged few. Whatever direction future cancer control strategies take in Europe our *all cancer survival* indicator appears eminently suited to monitoring their outcomes.

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Conflicts of interest: None declared.

Key points

- Population-based age-standardized and cancer site-standardized relative survival for all cancers, referred to as *all cancer survival*, is introduced as an indicator for monitoring countries' performance in cancer control.
- By regression analysis of macroeconomic variables in 19 European countries of variable wealth, *all cancer survival* emerged as closely related to a country's wealth (GDP) and also its overall investment in health. Among richer countries, those with best *all cancer survival* had significantly more computed tomography scanners indicating greater investment in *technology* for cancer care.
- Improving cancer care principally requires greater wealth. Poorer countries must invest adequately in health infrastructure; richer countries with adequate infrastructure need to invest in technology for cancer. However, since cancer incidence and costs are increasing, even rich countries may not have the resources for adequate cancer control. A radical rethink of cancer control strategies is therefore imperative.
- There has been extensive discussion of the reasons for the marked differences in survival for several major cancer malignancies across European populations revealed by the EUROCARE studies. Macroeconomic analyses with *all cancer survival* can contribute to explaining these differences.

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