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Analysis

Economic Growth and Cancer Incidence

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ABSTRACT

Why do we observe increasing rates of new cancer cases? Is the increasing burden of cancer mainly the outcome of higher life expectancy and better life conditions brought about by economic development? To what extent do environmental degradation and changes in life-styles play a relevant role? To answer these questions, we empirically assessed the relationship between per capita income and new cancer cases (incidence) by using cross-sectional data from 122 countries.

We found that the incidence rate of all-sites cancer increases linearly with per capita income, even after controlling for population ageing, improvement in cancer detection, and omitted spatially correlated variables. If higher incidence rates in developed countries were merely due to those factors, and not also to life-styles and environmental degradation, we would have found a flat or even an inverted-U pattern between per capita income and cancer incidence.

The regression analysis was applied also to the eight most common site-specific cancers. This confirmed the existing evidence on the different patterns in rich and poor countries, explained the pattern of the estimated relationship for aggregate cancers, and gave some other interesting insights.

1. Introduction

Cancer incidence (yearly new cases of cancer) is increasing and predicted to grow fast. The term 'Cancer epidemic' has become frequently used, not only by the media (e.g. Servan-Schreiber, 2008), but also by academic journals and by the World Health Organization.[1] The problem is particularly alarming in lower- and middle-income countries (see, e.g., Boyle and Levin, 2008; GLOBOCAN, 2012; Stewart and Wild, 2014; Vineis and Wild, 2014; Ferlay et al., 2015; Torre et al., 2015). For some rich countries, incidence rates are stabilizing (or slightly decreasing), however at very high levels. In the USA, this has been the case since the mid 1990s (Siegel et al., 2016).

Although data availability on cancer has increased significantly in the last years,[2] the relationship between cancer incidence and economic development remains largely unexplored, with just a few exceptions, namely: Beaulieu et al. (2009), Bray et al. (2012), Fidler et al. (2016).[3] The first is a report by "The Economist" Intelligence Unit on the health and economic burden of cancer. As a supplementary result, in one of its appendices, the report shows the outcome of a multiple regression analysis aimed at understanding cross-country variations in both estimated cancer incidence rates for 2009, and in fatality rates for 2002. Regressors included p.c. income, per cent of population aged 65 +, and regional dummies. The authors found a positive association of higher cancer incidence rates with both age and higher per capita income countries, which they attributed to the belief of "underreporting of cancer cases in developing countries" (Beaulieu et al., 2009, 62).

Bray et al. (2012) and Fidler et al. (2016) grouped countries according to the four levels (low, medium, high, and very high) of the Human Development Index (HDI) and compared incidence and mortality rates across groups. Both articles brought support in favour of the so-called "cancer-transition", according to which the demographic transition and economic development are changing the composition of the different types of cancers, with a shift from cancers linked to infections to those associated with non-infectious risk factors and possibly associated with the "western" lifestyle.

The above-mentioned papers are in line with the health literature, briefly summarised in the next section. The general idea is that increasing cancer incidence rates might be the outcome of economic development, which delivered not only higher life expectancy and improved cancer detection and statistical reporting, but also environmental degradation and "bad" life-styles.

The aim of our research was to empirically investigate the macro

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[1] In April 2015, the Lancet Oncology and The Lancet launched a joint campaign against cancer "to inform strategies to control the global cancer epidemic" (see http://www.thelancet.com/campaigns/cancer). In 2005 the term 'epidemic' was used in the 58th resolution of the WH assembly, see http://www.who.int/mediacentre/news/releases/2005/pr_wha05/en/

[2] For an assessment of the status of population-based cancer registries worldwide see Bray et al. (2015).

[3] The differences between the present research and the previously mentioned studies will be discussed in Section 5.

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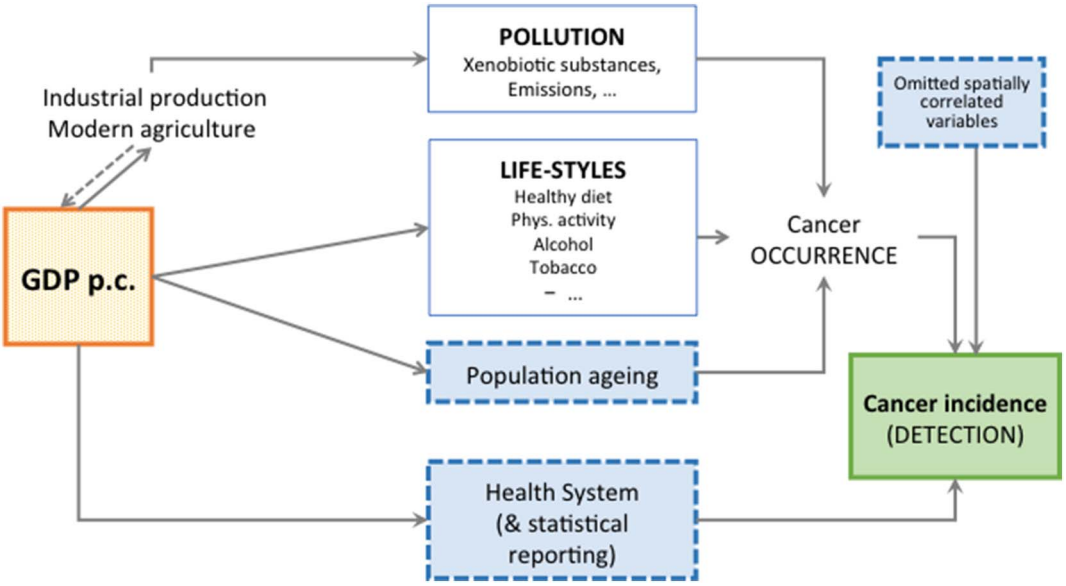

Fig. 1. From income to cancer incidence: major links.

level relationship between cancer incidence rates and per capita income. For this purpose, we tested some reduced models that looked only at the ends of the complicated causal chains. Such an approach has been followed by the so-called Environmental Kuznets Curve (EKC) literature that has been investigating the relationship between economic growth and the environment for more than 25 years (e.g., Stern, 2004; Dinda, 2004; Luzzati, 2015). While the EKC literature focused on anthropic pressures, e.g. emissions, here we focused on one possible outcome of pressures, that is, cancer occurrence.

The paper is structured as follows. The Section 2 outlines the links between cancer and economic development, from which we derived the conceptual model for our empirical analysis (Fig. 1). The Section 3 describes data and methods. In the Section 4 results are presented and discussed. The last section gives our conclusions.

2. Cancer and its Possible Links With Economic Development

This section firstly summarises what we know about cancer genesis, and then why economic development can play a major role in cancer occurrence. The dominant theory explaining cancer is the so-called Somatic Mutation Theory (SMT) (Nowell, 1976; Hanahan and Weinberg, 2000, 2011) according to which "random mutations in the genes which control proliferation or apoptosis are responsible for cancer" (Bertram, 2001, p. 170). Hence, cancer is due to stochastic (relevant) mutations that occur in oncogenes and tumour suppressor genes (Lodish et al., 2000). The older a person, the higher is the number of accumulated stochastic mutations, which ultimately leads to higher probability of cancer occurrence.

Recently, SMT has been criticised on the basis of theoretical reasons and experimental and epidemiological evidence. Hence, other theories of carcinogenesis have begun to gain ground. They shift the focus from single cells to the entire tissue and attribute a prominent role to altered environments (epigenetic signals) for regulating gene expression, rather than to stochastic mutations of DNA (see e.g. Burgio and Migliore, 2015). For instance, Tissue Organization Field Theory (TOFT) (see e.g. Baker, 2015), which is better seen as integrative rather than alternative to SMT (Bedessem and Ruphy, 2015), looks promising for understanding the role of low-dose foetal exposure to ubiquitous and long lived chemical pollutants, namely the endocrine-disrupting chemicals (EDCs).[4] These chemicals, by mimicking physiologic hormone signalling molecules, perturbate tightly regulated intercellular signalling pathways. This leads to subtle architectural changes in tissue organization that increase the risk of cancer development (Howard and Staats, 2013).

Overall, cancer is increasingly seen as the disruption of a complex equilibrium, that is, the outcome of an evolutionary process in which random genetic mutations have to face the selection of environmental pressure; moreover, intrinsic epigenetic plasticity, clonal evolution and high cellular adaptability are also crucial (Greaves, 2014). Hence, cancer is acknowledged as stemming from many interacting factors, that is, from mutations in oncogenes and tumour suppressor genes, from genetic inheritance,[5] work and living environment, and lifestyles (see e.g. Belpomme et al., 2007a, b; Stewart and Wild, 2014).

Many studies have investigated the differential contribution to cancer incidence of non-genetic risk factors (e.g. Danaei et al., 2005) and of environmental factors (e.g., Alavanja et al., 2003, Boffetta, 2006, Mannucci et al., 2015, Stare and Jozefowicz, 2008). The confluence of diverse types of evidence increasingly indicates the relevance of involuntary exposure to environmental contaminants, which affect particularly the "developing foetus, the developing child and adolescent" (Newby and Howard 2005, 57). For instance, there is evidence of decrease in the average age of cancer onset (e.g. Newby et al., 2007) and increase in childhood cancers (e.g. Steliarova-Foucher et al., 2004), which are also attributed to environmental factors (Stewart and Wild, 2014; Norman et al., 2014). Historical evidence supports the idea that cancer is a disease of industrialization/wealth since "in preindustrial societies, the death rate in infancy was high, but if adolescence was reached then […] the chances of living a reasonable life span in good health were high and unlikely to end in the development of cancer" (Howard and Staats, 2013). It is not under dispute that economic and technological progress led to the introduction of a complex mixture of persistent xeno-chemicals and other pollutants that have been recognised as carcinogenic.

Aggregate quantifications of the environmental risk factors have been proposed in a wide–ranging report by the World Health Organization that surveys the findings on the environmental risk factors (Prüss-Üstün et al., 2016). According to this report, household and

[4] A useful introduction to EDCs is Gore et al. (2014).

[5] The heritable factors have an important, but not exclusive, role. For instance, using data from Swedish, Danish and Finnish twin registries, it has been reported (Lichtenstein et al., 2000) that genetic influence on the incidence of cancer explains no more that 42% of the variance in incidence rate, depending on the cancer site.

ambient air pollution, passive tobacco smoking, radiation, chemicals, and occupational risks are responsible for at least 20% of cancer cases (in terms of disability-adjusted life years) (Prüss-Üstün et al., 2016, XVI, 50, and 86).

Of course, any estimate is highly uncertain (and incomplete) because of the complexity of the cancer-environment relationship in which polluting agents are often time persistent and pervasive, bio-accumulate and are bio-magnificated along the food chain, performing multiple biological actions as well as acting in synergy with other substances. Because of this complexity, we believe that it is also useful to tackle the issue with a very coarse grained perspective, empirically investigating to what extent economic development as a whole plays a role in cancer incidence. To this end, we performed a regression analysis in which income per capita proxies the joint effects of environmental factors and life-styles on cancer incidence. The reasons why income per capita is expected to be a significant regressor of cancer incidence come from analysing the major links of the causal chain that goes from income to cancer, which are described in what follows and summarised by Fig. 1.

Economic development started with the industrial revolution and was literally fuelled by fossil fuels (e.g., Smil, 2000). The availability of an unprecedented quantity of energy radically transformed our economy and the relationship between humans and nature, to the point that many scholars believe that we entered a new epoch, the Anthropocene (Crutzen, 2002; Steffen et al., 2011). A large amount (and number) of pollutants have populated the places where we live, resulting in prolonged and pervasive biochemical stresses that have been found to be risk factors for several diseases, including cancer. Furthermore, other new risk factors (e.g. excessive-weight and obesity) emerged as an outcome of life-style changes that have accompanied the economic development process.

At the same time, material living conditions have generally improved, thereby on the one hand bringing about an increase in cancer due to higher life expectancy and, on the other, leading to a reduction in cancers related to some infectious diseases. In other words, income growth has allowed an epidemiological transition,[6] that is, a shift "from a predominance of cancers linked to infections to cancers associated with risk factors that are mainly non-infectious and possibly related to the so-called western lifestyle" (Maule and Merletti, 2012, p. 745). The identification of this "new epidemiological age" is not only a theoretical construct, but also a relevant empirical fact. According to the World Health Organization (WHO, 2014) about 52% of worldwide deaths in 2012 were due to Non-Communicable Diseases (NCDs) and, of these, about 27% were associated with Malignant Neoplasm.

As a concluding remark, it has to be considered that part of the observed increase in cancer incidence along the economic development is the result of improved diagnostic scrutiny and statistical reporting (e.g. Li et al., 2013; Moynihan et al., 2012). In countries where health systems are not well developed, cancer statistics collection is poorly organized and the causes of death often remain undiagnosed resulting in under reporting of cancer deaths in less developed countries (e.g. Fallah and Kharazmi, 2008).

3. Material and Methods

3.1. The Empirical Model

The regression model used in this paper is visualised in Fig. 1. The items in the dashed contoured boxes have been controlled for in the regressions, so that the variability of incidence rates explained by income can be seen as coming from the joint effect of lifestyles and pollution. The design of the present analysis does not allow a distinction between lifestyles and environmental risks, the importance of which, however, can be drawn from the health literature that was briefly summarised above.

Building on the arguments put forward in the previous section, we regressed cancer incidence rates on the 20-year lagged p.c. income while controlling for (1) population ageing, (2) potential for detection and statistical reporting, and (3) omitted factors that might be related to the country's geographic location.

Lags in income were used to take into account the long genesis of cancer and its possible epigenetic nature (see, e.g., Burgio and Migliore, 2015). There are no strong theoretical reasons for taking a particular time lag. For instance, there seems to be a 30–35 years lag between the peak in tobacco consumption and the peak in the fatality cases of lung cancer attributable to tobacco smoking (Stewart and Wild, 2014, p. 82 ff.; Bilano et al., 2015). This lag is consistent with a lag of 20 years, or more, when considering cancer occurrence. We chose a 20 year lag since it was the longest available time period, due to some lack of older data for income. In any case, we also checked for different time lags (none, 5, 10, and 15 years), finding that results do not change qualitatively. This should not be surprising since income is highly autocorrelated. Hence, from an empirical point of view, the choice of the time lag has low relevance. In any case, using lagged values for income is important from a statistical point of view since it avoids potential endogeneity issues.

To control for population ageing, we used average standardized rates since they take the different age profiles of countries into account (see below). Furthermore, given that the small size of older age classes in poor countries could cause incidence rates to lose statistical significance, we did a further check by analysing the age class 40–60 separately.

Improvements in cancer detection and statistical reporting along the process of economic development were proxied by physician density (physicians per 1000 inhabitants). The reasons for choosing this variable are discussed in detail in the next section.

Many other potential factors (such as genetic risk or diet and habits) can be considered as strongly related to the geographic location of the country. Those factors have been omitted since they are either unobservable or lacking in reliable data. A spatial error model was used to take into account these omitted spatially correlated covariates.

3.2. Estimation Methods and Techniques

In order to choose the model that best fits the data, papers within the EKC literature often compare parametric estimates with different specifications of the p.c. income term, i.e., linear, quadratic or cubic (see Van Alstine and Neumayer, 2010). We followed a different approach. As in Luzzati and Orsini (2009) we preliminarily used semiparametric methods to assess whether a linear or non-linear specification better fits the data. In the case of evidence of a linear fit, we used it in the parametric estimates. If semiparametric fits suggested non-linear patterns, we chose between the quadratic and cubic specification by minimizing the corrected Akaike Information Criterion (AICc) (which also involved maximisation of the adjusted R-squared).

For the semiparametric estimates, we used the generalized additive model (GAM), in which each variable enters nonlinearly and separately. We followed the approach proposed in Wood (2006), which is based on penalized regression splines, and used the "mgcv package" in R Development Core Team (2012), with the restricted maximum likelihood (REML) option (see Wood, 2011).

For the parametric estimates, we followed the spatial econometric methodology developed by Anselin (1988) (see also LeSage and Pace, 2009). The reason behind this choice is that, differently from the inclusion of regional dummy variables (as e.g. in Beaulieu et al., 2009), this

[6] According to the theory of epidemiological transitions (Omran, 2005, pp. 737–738), three ages of mortality patterns in history are observed, namely the age of "pestilence and famine", of "receding pandemics", and of "degenerative and man-made diseases". In the first "age" life expectancy at birth is very low, but epidemic peaks then become less frequent or disappear, after which we eventually enter a phase in which mortality tends to approach stability at relatively low levels and non-communicable diseases, including malignant neoplasms, prevail.

methodology explicitly accounts for the effects of spatial correlation due to imperfections in model and measurements that exhibit a spatial structure, thereby increasing the efficiency of the parameter estimates.

The spatial correlation can be incorporated in a regression model in different ways. In the current paper, we used the spatial error model (SEM) in which the spatial correlation is modelled in the error term. This is based on the a priori grounds that cultural and genetic factors vary across space and are assumed to drive cancer incidence variability. However, due to lack and/or unreliability of data, such factors are unobserved and/or unmeasured and, therefore, omitted in the regression. If they are influential, then their impact on the explanation of cancer incidence is subsumed in the error term that shows a spatial pattern.

To check if this is the case, a spatial specification search was carried out using OLS estimation and applying a Lagrange Multiplier test. In the presence of evidence of spatial correlation, the spatial model was estimated by means of maximum likelihood.

The SEM was implemented by specifying a spatial stochastic process for the error term, which in turn yields the nonzero correlation for the units that are considered as neighbours. Consequently, the spatial error model requires the definition of a spatial matrix, which reflects the potential interactions between neighbouring units (countries in our case). Here, two different countries are considered as interacting with each other if and only if they belong to the same region. The region taxonomy was taken from the International Agency for Research on Cancer, the specialized cancer agency of the World Health Organization (WHO), and is listed in the Appendix. The spatial regressions are estimated using the "spdep package" in R Development Core Team (2012).

3.3. Variables

Data on cancer incidence are becoming increasingly reliable due to the diffusion of national cancer registries (see, e.g., Parkin, 2006). However, cross-national differences in coverage and quality of the data collected are quite pronounced, resulting in high variability of both coverage and reliability: thus the quality is often associated with the level of economic development. For a worldwide comparison, the most relevant project is GLOBOCAN, which is today incorporated in "Cancer today".[7] GLOBOCAN is a project of the International Agency for Research on Cancer of the World Health Organization. Its database contains data for 26 site-specific cancers and for all sites cancer (excluding non-melanoma skin cancer). This project produced the most recent (2012) estimates of incidence, mortality and prevalence.

In order to control for differences arising merely from differences in the age profiles of each population, the average standardized rates (weighted) - ASR(W) - have to be used. The standardization procedure (for details see, e.g., Boyle and Parkin, 1991) adjusts observed age-specific rates to a reference population, commonly referred to as the Standard Population, usually the world population. The term 'weighted' refers to standard weights taken from the population adopted as a standard. We calculated[8] ASR(W) using the population weight of the World Standard Population[9] and the population data of the United Nations database.

The p.c. income variable was the p.c. GDP, expressed in thousands of US$ PPP2011,[10] taken from the World Bank online database. Income was averaged over three years to mitigate the effect of the business cycle. As stated previously, we used a 20 year lag to consider the long genesis of cancer and tested shorter income time lags, which however left results qualitatively unchanged, as one would expect from the strong autocorrelation of p.c. income (see the Appendix, Table 2).

As regards the variable to proxy the diagnostic potential of a country, it has to be emphasised that detection and statistical reporting are very different from early detection. While the first two affect the quality of the incidence rates data, the latter is relevant for treating cancer, and hence for mortality rates. Early detection is strongly associated with the presence of screening programmes and diagnostic facilities, which are in turn associated with high levels of per capita health expenditure (and income). For mere detection and statistical reporting, however, an easy access to a doctor is a crucial variable, more important than the availability of advanced technical tools. So far, physician density has proved to be very important in cancer detection (e.g., Ananthakrishnan et al., 2010; Fleisher et al., 2008; Li et al., 2013; Sundmacher and Busse, 2011) and for many other care issues, like infant mortality (e.g., Farahani et al., 2009), and generally for health outcomes (e.g. Friedberg et al., 2010; Macinko et al., 2007; Mondal and Shitan, 2014; Shi, 2012). At the same time, physician density can be reasonably thought as having "diminishing returns" in cancer incidence reporting, that is, after some thresholds, further increases in the physician density will have increasingly smaller relevance.

For the above reasons, we took physician density as a proxy of cancer incidence reporting potential and used it in the regressions with a concave specification. This was empirically supported by the positive and decreasing marginal impact of physician density on cancer incidence in preliminary semi-parametric estimates (see, e.g., Fig. A2). Data for physician density (physicians per 1000 inhabitants) were taken from the World Bank online database. But for a few exceptions, they range from 2010 to 2012. The correlation between physician density and GDP p.c. is not strong enough to prevent the use of both variables as regressors (see Table 2).

We avoided transforming the variables into logarithms since this practice, although common, has been shown to be theoretically weak (Mayumi and Giampietro, 2010). Nonetheless, we verified that using logs does not change the results qualitatively.

3.4. Countries

The GLOBOCAN, 2012 dataset covers 184 Countries. We excluded those countries (33) for which data were estimated by merely imputing the data of neighbouring countries or registries in the same area. Of the 151 remaining countries, we excluded 5 that are not included in the World Bank online database from which we took per capita income.[11] We also excluded 18 countries for which 20 year lagged p.c. income or other data were not available. Our final list, presented in the Appendix, included 122 countries since six other countries were considered outliers and removed.

As discussed in econometrics textbooks (e.g. Damodar, 2004, 540 ff.), including or excluding outliers is a tricky issue. An outlier differs markedly from the other observations and, hence, "provides a large residual when the chosen model is fitted to the data" (Draper and John, 1981, 21). An outlier must be excluded if it is influential, that is, distorting the slope of the regression line or even forcing the researcher to change the model specification. This problem is particularly serious in semiparametric models since "GAMs can be very sensitive to the presence of a small proportion of observations that deviate from the assumed model. In other words: a few atypical observations could seriously affect the non-parametric estimates of the smooth regression function" (Azadeh and Salibian-Barrera, 2011).

A preliminary check on the dataset (see Fig. A1) shows that there

[7] See http://globocan.iarc.fr/Default.aspx

[8] The database provided by GLOBOCAN already provides ASW(R) rates. Using the data available online and implementing the procedure described by the Glossary section of GLOBOCAN, 2012 (http://globocan.iarc.fr/Pages/glossary.aspx) we obtained slightly different figures.

[9] http://seer.cancer.gov/stdpopulations/world.who.html World Standard Population is used also in GLOBOCAN, 2012.

[10] GDP was taken in Power Purchasing Parity (PPP2011) due to the cross-country nature of the analysis. PPP GDP is gross domestic product converted to international dollars using purchasing power parity rates. An international dollar has the same purchasing power over GDP as a U.S. dollar has in the United States. Data are in current international dollars based on the 2011 International Comparison Program (ICP).

[11] State of Palestine, France Guadeloupe, France La Reunion, France Martinique, and France Guyana.

are some observations that are potentially influential (due to their very high income levels) and for which one can easily imagine that they will have large regression residuals for any specification that can be conceived. One notices that the observations in question refer to two very small and atypical countries, Singapore (a city-state with a rather idiosyncratic economy) and Luxembourg (whose economy is based on financial services), and to another 5 countries whose economy is strongly based on oil exports.[12] Their special characteristics are such that other countries cannot be thought to mimic their performances. For a formal check of influential observations and outliers we followed the approach developed by Fox (2015),[13] which is based on studentized residual, hat-values and Cook's distances. Applying it to several model specifications (the linear model and those described in Section 4), we found that the 5 "oil" countries and Luxembourg should be excluded, while excluding Singapore is not statistically supported.[14]

3.5. Data Descriptive Statistics

A preliminary overview of the data is given by Table A1, which contains the main descriptive statistics for the variables. Table 2 shows the correlation matrix for all-sites cancers, both for the entire population and for the age class 40–60, p.c. income (and its lagged values), and physician density. As expected the autocorrelation of p.c. income is remarkably high.

4. Results

We start by presenting the results for all cancers, and then we move to organ site-specific cancers. The labels of the variables are as follows. *AllC* refers to incidence rates for all cancers, otherwise the name of site-specific cancer is indicated. The suffix "_40–60" indicates that the rate refers to the population in the age class 40–60. Incidence rates are measured as yearly new cases on 100,000 inhabitants. *Y_92* is the three-year average, centred on the year 1992, of GDP p.c. (thousands of $PPP2011) and *PhysD* is the physician density in 2012 (number of physicians every 1000 inhabitants).

The semiparametric analysis for all cancers is shown in Fig. 2. Regressing the incidence rate on p.c. income gives the concave curve that is shown in Fig. 2a. However, when controlling for physician density, the marginal impact of p.c. income on cancer incidence becomes linear (the straight line in Fig. 2a), while the marginal impact of physician density is non-linear (Fig. A2). Similar results (not shown) are obtained when analysing the 40–60 age class. Fig. 2b and 2c shows the confidence bands (95%) of the regression lines shown in Fig. 2a.

This preliminary evidence, as discussed in detail in Section 3.2, was helpful to specify the parametric estimates, which, in contrast to the semiparametric estimates, also allow the possible spatial correlation of errors to be taken into account.

The results of the SEM parametric regressions for all cancers are shown in Table 1. Let us start from the first three equations. Eq. (1a) and (1b) refer to the whole population, while Eq. (2) concerns the age class 40–60. In Eq. (1a) income is 20 years lagged, while in Eq. (1b) income has no lag. The two estimates are very similar. As already mentioned (see Section 3.1), this is due to the high autocorrelation of income, and also holds for estimates referring to other time lags. All estimates show that the incidence rates for all cancers are positively correlated with p.c. income even when controlling for population ageing, physician density and omitted spatially correlated covariates. Standardized incidence rates increase by 4.66 and by 0.64, respectively for all ages (Eq. (1a)) and for the age class 40–60 (Eq. (2)), per increase in p.c. income of 1000$ (1992, PPP2011). Figs. 3 and A3 show the marginal impact on standardized incidence rates of p.c. income, drawn respectively for the whole population (Eq. (1a)) and for the 40–60 age class (Eq. (2)). It should be noted that p.c. income coefficients may partially capture differences in detection/reporting capacity that cannot be accounted for in terms of physician density. However, as Fig. 2 suggests, there are no reasons for believing that including a better proxy would transform the relationship from linear to concave.

The contribution of physician density to the fitted incidence rates is measured by the corresponding terms of Eqs. (1a) and (2) and can be visualised by Figs. 4 and A4, drawn respectively for the whole population and for the 40–60 age class. For both regressions, the impact is positive and increasing only up to roughly 3.8 physicians over 1000 inhabitants. Further increases in physician density beyond this value cannot be assessed since very few countries surpass it and the confidence bands become very wide. Similar behaviour emerged in all the other regressions where physician density was significant.

Eq. (3) is shown only to illustrate the effect of not controlling for physician density, which however involves mis-specification. Given that the semiparametric fit (see Fig. 2) was non-linear, by minimizing AICc we found that in this case the best specification for income was quadratic. The fitted curve has an inverted-U shape. The reason is that the quadratic term in Eq. (3) partially captures that which in Eq. (1) is captured by physician density. The estimated relationship is increasing within almost the entire range of the observed income values since the calculated turning point (25,402$) is close to the highest p.c. income (27,352$) (see Table 1). Not controlling for physician density yields similar consequences in all the other regressions for which the estimated relationship between income and cancer was positive.

The analysis presented above was replicated for most common site-specific cancers. Tables 2 and A3 in the Appendix, referring respectively to all age classes and to the 40–60 age group, summarise the main results. They are organized as follows. Organ site-specific cancers are ordered according to their relative frequency, which is shown in the second column. The third column indicates whether, according to the health literature (see below) the cancer organ site is typical of high-income countries (H) or low/medium income (M-L) ones. Notice that the most frequent organ-site cancers are also typical of high-income countries. The fourth column gives a concise indication of the shape of the estimated relationship while the fifth column indicates whether the estimated income coefficient is positive, negative, non-significant, or follows an EKC shape. The sixth column shows whether the estimated effect of physician density is positive or concave (+), negative (−), or non-significant (n.s). The seventh and eighth columns give the values of the income coefficients and their significance level, while the ninth shows the adjusted R-squared. Full results are in the Appendix, Table A4.

The prevalence of different organ sites cancer according to the level of development is well established (e.g. Newby and Howard, 2005; Stewart and Wild, 2014). Lung, breast, colorectum and prostate cancers are the most common organ sites in developed countries, associated both with lifestyles and with environmental factors (Howard and Staats, 2013). Liver, stomach, oesophagus and cervix uteri are highly correlated to chronic infection (such as hepatitis B virus, human papillomaviruses and Helicobacter pylori), which are more common in low/medium income countries.

When regressing incidence rates on GDP p.c., the sign of the coefficient should be negative for organ-sites typical of low-income countries, and positive (or EKC shaped) for cancers typical of high income countries. This is because increase in GDP in low-income countries improves overall hygiene conditions and thus reduces cancer incidence associated with chronic infection types of cancers. In contrast, in high-income countries an increase in GDP leads to an increase of environmental pollutants and xenobiotic substances and adoption of "western" type life-styles that bring an overall increase in cancer incidence (see discussion in Section 2).

[12] Bahrain, Brunei, Oman, Saudi Arabia, United Arab Emirates.

[13] The approach is also described in Levshina (2015, 153–155). We used the *influencePlot* function in the R-Package 'car' (https://cran.r-project.org/web/packages/car/car.pdf).

[14] It is worth noticing that including the 5 "oil" countries requires changing the model specification, while Luxembourg affects only the size of the estimated coefficients.

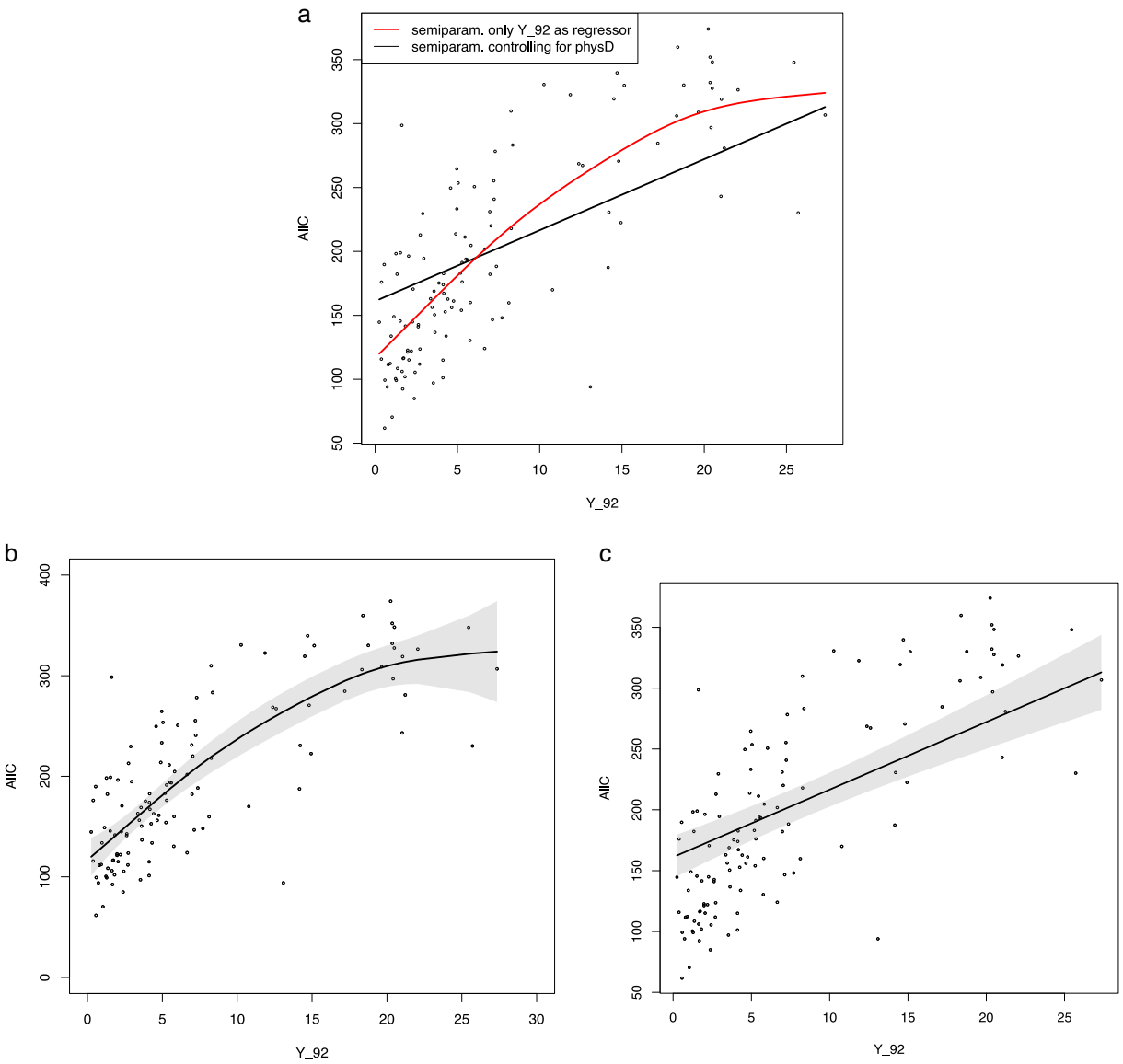

Fig. 2. a. Standardized cancer incidence rates in 2012 vs. p.c. income in 1992. Semiparametric fits when controlling (straight line) and not controlling (curve) for physician density. Age classes: whole population.
b. Standardized cancer incidence rates in 2012 vs. p.c. income in 1992. Semiparametric fits with confidence bands (5%) when not controlling (left) and controlling (right) for physician density. Age classes: whole population.

Our regressions confirmed the expected typicality for developed or LDC countries (see the signs of the income coefficients in Table 2). Results also highlighted that colorectum cancer is the only one among the most frequent organ-site cancers that follows an EKC shape, although the curve turns down only at rather high levels of p.c. income (at 22,890 1992$ GDP p.c.). The external risk factors associated with this organ cancer are mainly life-style factors, namely diets that are high in red and processed meats, habitual inactivity, alcohol use, and tobacco smoking. The latter is the most important risk factor for developing lung cancer; however, several environmental and occupational exposures have also been found to be relevant, explaining globally 36% of lung cancer (Prüss-Üstün et al., 2016, 50). The composition of smoking with other exposures could explain the linearity of the pattern for lung cancer. The environmental risks that are positively associated with income could have offset the beneficial effects of the reduction of cigarette smoking that occurred in many high-income countries (see Stewart and Wild, 2014).

The colorectum and lung cases highlight the finding that differences in relative frequency between developed and less developed countries (LDCs) do not imply that environmental factors are irrelevant in the organ-site cancers typical of LDCs. For instance, ionizing radiations, exposure in the rubber industry and to asbestos are also risk factors of stomach cancer. Among the sites that we considered, the prostate, the cervix, and the liver are likewise associated with environmental factors (Prüss-Üstün et al., 2016, 46–51), although the first is typical of high-income countries while the latter two are most frequently found in low-income areas.

In any case, disentangling the environmental effects is difficult since, for each organ site cancer, occurrence is affected by several risk factors that differ according to income. Hence, the actual shape of relationship between income and incidence depends on the relative strength of the various contrasting effects.

Two further remarks can be made. First, physician density was found to be negatively correlated with cervix uteri cancer, which is consistent with the importance of physicians in fostering prevention, and hence reducing incidence rates of this organ site cancer. Second, the estimates for the different organ-site cancers help to understand why a positive relationship with income emerges at the overall level. The reason is that the cancers for which a negative relationship with income holds are less frequent than those for which the relationship is positive.

Table 1
Summary of the spatial error model parametric estimates.[a]

Dep. Var.									
AllC	=	108.8	+	4.66 *Y_92*	+	47.94 *PhysD*	–	6.09 $PhysD^2$	[Eq. (1a)]
s.e.		9.71		0.81		8.35		1.41	
p.		<0.001		<0.001		<0.001		<0.001	
		$AdjR^2$=0.76; Spatial parameter=0.47, p<0.001							
AllC	=	107.06	+	2.20 ***Y_12***	+	46.06 *PhysD*	–	5.860 $PhysD^2$	[Eq. (1b)]
s.e.		0.60		0.34		8.06		1.36	
p.		<0.001		<0.001		<0.001		<0.001	
		$AdjR^2$=0.78; Spatial parameter=0.49, p<0.01							
AllC_40–60	=	40.05	+	0.64 *Y_92*	+	18.57 *PhysD*	–	2.47 $PhysD^2$	[Eq. (2)]
s.e.		3.30		0.29		2.97		0.50	
p.		<0.001		<0.001		<0.001		<0.001	
		$AdjR^2$=0.58; Spatial parameter=0.41, p<0.01							
AllC	=	130.93	+	11.94 *Y_92*	–	0.24 Y_92^2			[Eq. (3)]
s.e.		12.04		2.31		0.10			
p.		<0.001		<0.001		0.015			
		$AdjR^2$=0.72; Spatial parameter=0.58, p<0.01; calculated turning point *Y_92*=25.402							

Summary statistics of the observed values:		*Min*	*Mean*	*Max*
	AllC	61.8	196.3	374.1
	AllC_40–60	18.3	64.7	115.2
	Y_92	0.251	7.266	27.352
	PhysD	0.02	1.80	6.72

[a] Results are rounded to two decimal places.

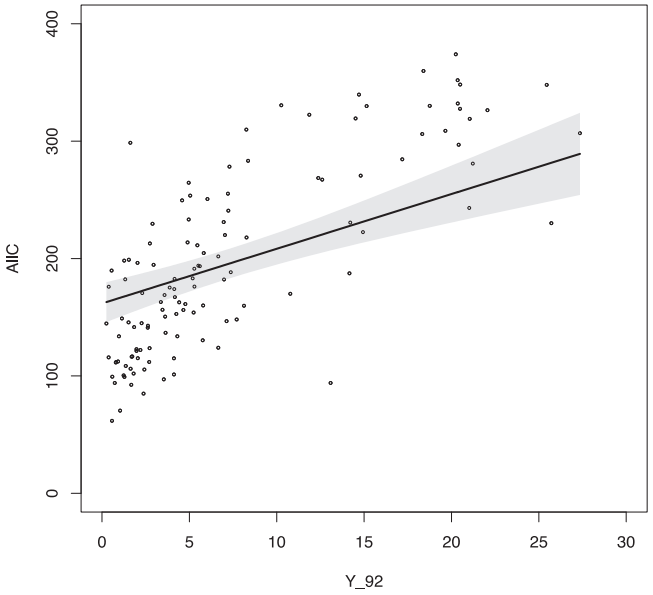

Fig. 3. Marginal impact (and 95% confidence band) of p.c. income (parametric regression of standardized incidence of all-sites cancers on p.c. income and physician density. Age class: all population).

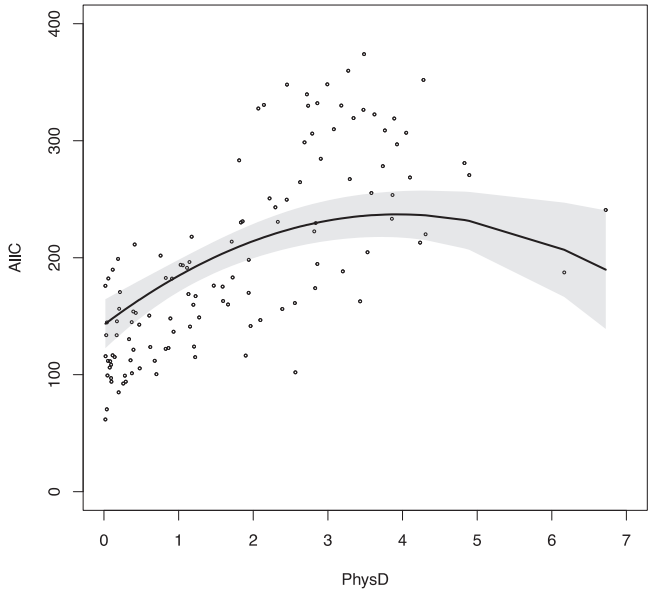

Fig. 4. Marginal impact (and 95% confidence band) of physician density (parametric regression of standardized incidence of all-sites cancers on p.c. income and physician density. Age class: all population).

Finally, the estimated coefficient of the spatial dependence in the error term was positive and significant in all regressions, confirming the relevance of omitted geographically correlated factors.

5. Conclusion

The evidence presented in this paper can be compared with the results of three previous studies, already mentioned in the introduction, the primary goal of which, however, was not to explore the relationship between cancer incidence and income growth. Beaulieu et al. (2009) used a methodology similar to ours, that is, they focused on p.c. income and performed a regression analysis. In contrast to us, they controlled for the effect of population ageing by including in the regressions the percentage of population aged 65; additionally, they used intercept dummies to control for geographical differences, but did not control for non-linear influences of income and for cancer reporting improvements. Moreover, they did not use time lags for income. Finally, they had to produce their own estimates of incidence rates in 2009, based on GLOBOCAN data for 2002, while we were able to use more reliable and recent data (2012). Hence, their results are not fully comparable with ours. Beaulieu and colleagues interpreted the positive relationship between incidence rates and income as an expected outcome of underreporting cancer cases in developing countries. We show

Table 2
Summary of the spatial error model estimates for the 8 most common organ-site cancers, all age classes.

1	2	3	4	5	6	7	8	9
Organ site	Rel. freq.	Typical of	Model	Role of *Y_92*	Role of *PhysD*	*Y_92* coeff.	Y_92^2 coeff.	Adj RSq
Lung	13.0%	H	Linear	+	+	0.41**		0.61
Breast	11.9%	H	Linear	+	+	1.89***		0.70
Colorectum	9.7%	H	EKC	§	+	2.25***	− 0.049***	0.76
Prostate	7.9%	H	Linear	+	n.s.	2.43***		0.75
Stomach	6.8%	L/M	Linear	−	+	− 0.37***		0.36
Liver	5.6%	L/M	Linear	−	n.s.	− 0.36**		0.08
Cervix uteri	3.7%	L/M	Linear	−	−	− 0.39^		0.48
Oesophagus	3.2%	L/M	None	none	n.s.	n.s.		0.28

H: High-income countries, L/M: low/medium income countries.
Significance levels: **: $p < 0.05$, ***: $p < 0.01$, ^: 0.11; n.s.: non-significant.
§ calculated turning point = 22,890 $ GDP 1992PPP.

that the positive relationship does not disappear when controlling for physician density, taken as a proxy for incidence reporting. On the contrary, our data and analysis suggest a higher effect of income on cancer incidence rates: in Beaulieu et al. (2009, 63) the income coefficient is equal to 1.457, with a 95% confidence interval of [0.50; 2.4], while ours is equal to 4.66 (see Eq. (1a)), with 95% C.I. of [3.06; 6.26].

Bray et al. (2012) and Fidler et al. (2016) did not use regression analysis or income as a key variable: rather, they compared four groups of countries pooled according to the level of HDI. This could be problematic because of ex-ante defined groups and because HDI also includes life expectancy, which should, instead, be a control variable. In any case, their design is too different to allow for a close comparison of the results. Nonetheless, it can be noticed that their papers likewise found both a positive relationship of incidence with levels of development, and different patterns for different cancer sites when comparing less developed and developed countries.

Overall, our results are in line with previous evidence, which is not only updated but also strengthened because of the use of a different methodology. Our regressions, which explain a substantial part of the variability (in most cases adjusted R-squared values are higher than 0.6), showed that the relationship between income and cancer incidence rate remains positive (and significant) even after controlling both for favourable effects of economic development - namely population ageing and improvements in cancer detection and statistical reporting - and for spatially correlated omitted variables.

Another result of this work is that underreporting can be proxied by a concave function of physician density, the contribution of which is positive and increasing up to roughly 3.8 physicians over 1000 inhabitants, while further increases do not seem to be relevant. Only for cervix uteri cancer did physician density result to be negatively correlated. This should not be surprising since prevention is particularly important for cervix uteri cancer and physicians play a key role in prevention. Finally, omitting to control for physician density would produce in some cases inverted-U patterns, with turning points at the very end (or beyond) of the income range of the sample. Such an omission, however, was regarded here as a misspecification.

To sum up, our analysis shows that the cancer epidemic cannot be explained solely by higher life expectancy, by better statistics and by regional peculiarities: rather, a significant role must also be attributed to environmental degradation and life-styles. Unfortunately, our regressions are unable to distinguish between the two. Some clues can be drawn from the case of lung cancer, which, despite the decrease in smokers in high-income countries, still exhibits a positive relationship with income rather than a Kuznets curve. This could be interpreted as arising from environmental exposure. In any case, due to the presence of so many confounding factors, separating the environmental effects from the life-style aspects would require either using micro data or restricting the analysis to units for which a considerable range of statistics is available.

However, the relevance of environmental risk factors can be inferred from the increasing evidence available from the health literature according to which “environmental factors play a more important role in cancer genesis than it is usually agreed” (Irigaray et al., 2007, 640). Our findings are consistent with this literature, namely, that both social change (e.g. lifestyles) and “the involuntary exposure to many carcinogens in the environment contributes to the rising trend in cancer incidence” (Belpomme et al., 2007a, 1037).

The policy message that can be drawn from our work is that only by becoming aware of the negative side effects of economic development will we also be able to implement policies to tackle them. This is the message of one of the most important recent reports on cancer, according to which “the realization of just how much disease and ill health can be prevented by focusing on environmental risk factors should add impetus to global efforts to encourage preventive health measures” (Prüss-Üstün et al., 2016, VII).

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The paper is the outcome of the joint work of the authors. Nonetheless, Sections 1, 3.1, 3.2, and 5 are attributable to Luzzati, Sections 3.2, 3.4 to Parenti, Sections 2 and 3.5 to Rughi. The latter also prepared the dataset (including standardization) and performed a preliminary OLS analysis.

Appendix A

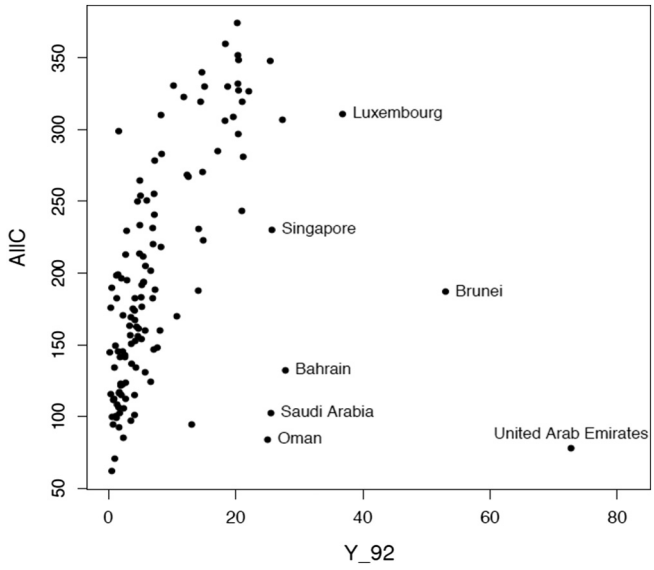

Fig. A1. Scatter plot of standardized incidence of all-sites cancers vs. p.c. income in 1992: outliers.

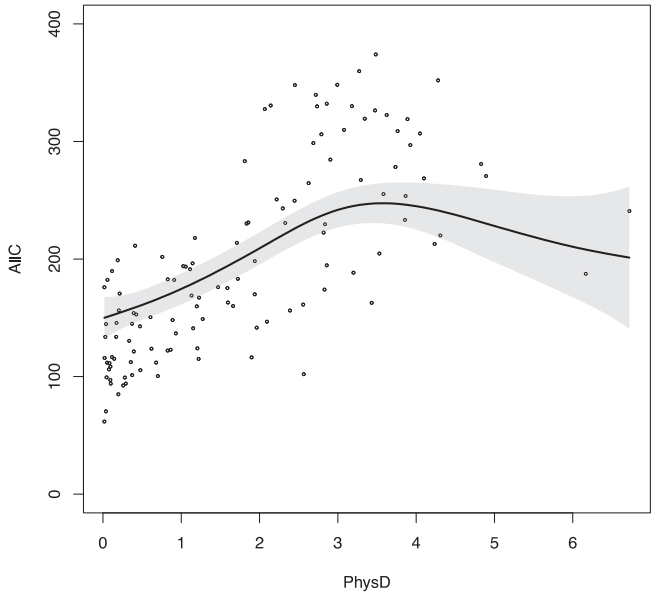

Fig. A2. Marginal impact of Physician density in the semi-parametric regression of standardized incidence of all-sites cancers on p.c. income and physician density. Age class: all population.

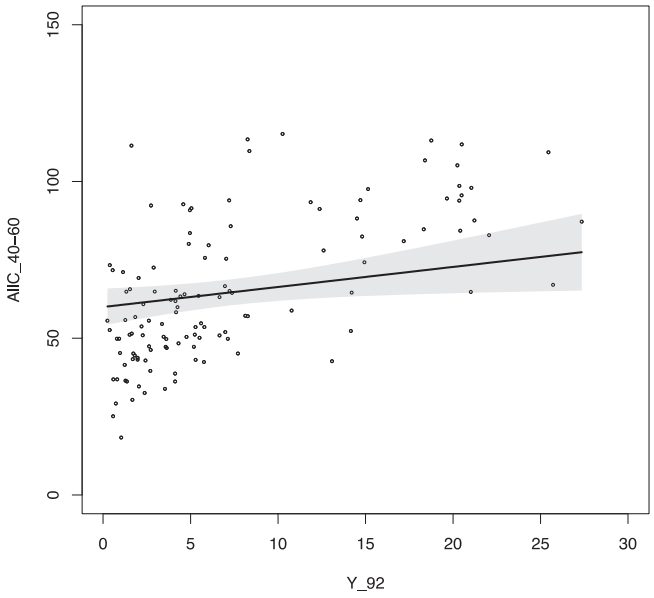

Fig. A3. Marginal impact (and 95% confidence band) of p.c. income in the parametric regression of standardized incidence of all-sites cancers on p.c. income and physician density. Age class: 40–60 yrs.

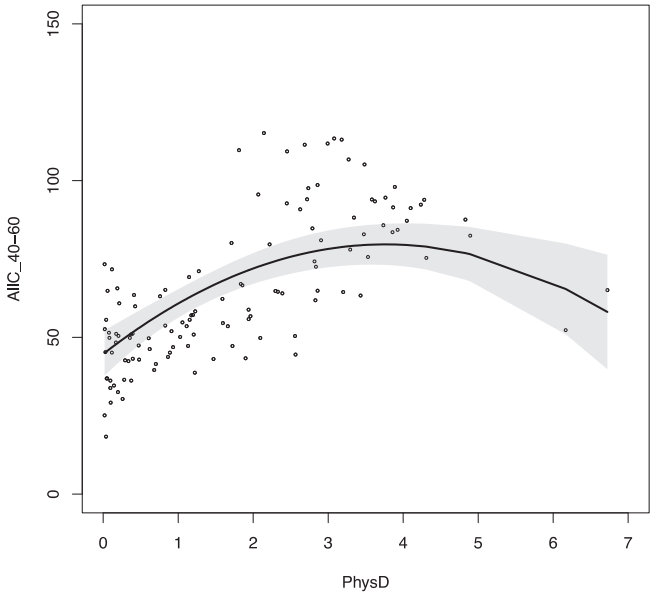

Fig. A4. Marginal impact (and 95% confidence band) of physician density in the parametric regression of standardized incidence of all-sites cancers on p.c. income and physician density. Age class: 40–60 yrs.

Table A1
Descriptive statistics of the variables.

	Min	Max	Median	Average	Stand err.
AllC	61.8	374.1	182.2	196.3	78.9
AllC_40_60	18.3	115.2	60.4	64.7	22.7
Lung	0.2	55.5	15.6	17.8	13.2
Lung_40_60	0.1	22.8	4.2	5.1	4.2
Breast	5.4	118.5	45.1	51.4	27.4
Breast_40_60	2.7	57.7	23	25.3	12.8
Colorectum	1.2	48.8	13.1	18.1	13.4
Colorectum_40_60	0.3	16.6	3.9	5.1	3.2
Prostate	1.3	144.4	31.6	44.4	37
Prostate_40_60	0	67.5	4	7.5	9.2
Stomach	0.8	45.4	7.3	9.8	7.6
Stomach_40_60	0.3	15.4	2	2.8	2.4
Liver	1.1	89	5.2	7.7	9.5
Liver_40_60	0.2	29.7	1.4	2.5	3.4
Cervix	2.3	86.7	16.9	20.8	15.4
Cervix_40_60	1.2	49	8.4	9.9	7.7
Oesophagus	0	28	2.6	4.3	4.9
Oesophagus_40_60	0	10.3	0.8	1.3	1.5
Y_92	251	27,352	4833	7266	6858
PhysD	0.02	6.72	1.59	1.80	1.50

Table 2
Correlation matrix of all-sites incidence rates and regressors.

	AllC	*AllC 40–60*	*Y_92*	*Y_97*	*Y_02*	*Y_07*	*Y_12*	*Phys*
AllC	1							
AllC 40–60	0.93	1						
Y_92	0.78	0.64	1					
Y_97	0.78	0.63	0.99	1				
Y_02	0.80	0.65	0.98	0.99	1			
Y_07	0.80	0.65	0.96	0.98	0.99	1		
Y_12	0.80	0.66	0.95	0.97	0.98	0.99	1	
Phys	0.71	0.67	0.61	0.58	0.60	0.62	0.63	1

Table A3
Summary of the spatial error model estimates for the 8 most common organ-sites cancer, 40_60 age classes.

1	2	3	4	5	6	7	8	9
Organ site	Rel. freq.	Typical of	Model	Role of *Y_92*	Role of *PhysD*	*Y_92* coeff.	Y_92^2 coeff.	Adj RSq
Lung	13.0%	H	Linear	None	+	n.s.		0.61
Breast	11.9%	H	Linear	+	+	0.80***		0.64
Colorectum	9.7%	H	EKC	§	+	0.51***	− 0.012**	0.67
Prostate	7.9%	H	Linear	+	n.s.	0.42***		0.47
Stomach	6.8%	M-L	Linear	−	+	− 0.17***		0.35
Liver	5.6%	M-L	Linear	−	n.s.	− 0.15**		0.11
Cervix uteri	3.7%	M-L	Linear	−	−	− 0.26**		0.47
Oesophagus	3.2%	M-L	None	None	n.s.			

Significance p levels: ** < 0.05, *** < 0.01, ^=0.11; n.s. = non-significant.
§ calculated turning point = 21,450 $ GDP 1992PPP.

Table A4
Regressions for the most frequent organ-site cancers.

		Lung	
All	Coeff.	Std. error	p
Intercept	5.34	1.86	0.00
Y_92	0.41	0.17	0.01
PhysD	7.40	1.73	0.00
$PhysD^2$	− 0.71	0.30	0.02
Spatial parameter = 0.36*; AdjRsq = 0.61			
40–60	Coeff.	Std. error	p
Intercept	2.07	0.72	0.00
Y_92	− 0.04	0.06	0.55
PhysD	2.62	0.62	0.00
$PhysD^2$	− 0.26	0.10	0.01
Spatial parameter = 0.47***; AdjRsq = 0.61			

		Breast	
All	Coeff.	Std. error	p
Intercept	22.67	3.87	0.00
Y_92	1.89	0.32	0.00
PhysD	16.23	3.27	0.00
$PhysD^2$	− 2.62	0.55	0.00
Spatial parameter = 0.49***; AdjRsq = 0.70			
40–60	Coeff.	Std. error	p
Intercept	11.57	1.89	0.00
Y_92	0.80	0.16	0.00
PhysD	8.93	1.65	0.00
$PhysD^2$	− 1.49	0.28	0.00
Spatial parameter = 0.45***; AdjRsq = 0.64			

		Colorectum	
All	Coeff.	Std. error	p
Intercept	0.51	1.66	0.76
Y_92	2.25	0.39	0.00
Y_92^2	− 0.05	0.02	0.00
PhysD	5.96	1.42	0.00
$PhysD^2$	− 0.84	0.24	0.00
Spatial parameter = 0.39***; AdjRsq = 0.76			
40–60	Coeff.	Std. error	p
Intercept	0.82	0.46	0.07
Y_92	0.51	0.11	0.00
Y_92^2	− 0.01	0.00	0.01
PhysD	1.77	0.40	0.00
$PhysD^2$	− 0.27	0.07	0.00
Spatial parameter = 0.36***; AdjRsq = 0.67			

		Prostate	
All	Coeff.	Std. error	p
Intercept	21.45	6.53	0.00

Y_92	2.43	0.42	0.00
PhysD	4.32	4.24	0.31
$PhysD^2$	− 0.68	0.69	0.32
Spatial parameter = 0.70***; AdjRsq = 0.75			
40–60	Coeff.	Std. error	p
Intercept	3.80	1.71	0.03
Y_92	0.42	0.14	0.00
PhysD	0.32	0.59	0.59
Spatial parameter = 0.56***; AdjRsq = 0.47			

	Stomach		
All	Coeff.	Std. error	p
Intercept	5.37	1.53	0.00
Y_92	− 0.37	0.13	0.00
PhysD	6.93	1.32	0.00
$PhysD^2$	− 0.98	0.22	0.00
Spatial parameter = 0.46***; AdjRsq = 0.36			
40–60	Coeff.	Std. error	p
Intercept	1.87	0.47	0.00
Y_92	− 0.17	0.04	0.00
PhysD	2.15	0.41	0.00
$PhysD^2$	− 0.29	0.07	0.00
Spatial parameter = 0.45***; AdjRsq = 0.35			

	Liver		
All	Coeff.	Std. error	p
Intercept	8.45	1.80	0.00
Y_92	− 0.36	0.18	0.04
PhysD	0.99	0.77	0.20
Spatial parameter = 0.36**; AdjRsq = 0.08			
40–60	Coeff.	Std. error	p
Intercept	2.89	0.65	0.00
Y_92	− 0.15	0.06	0.01
PhysD	0.38	0.27	0.17
Spatial parameter = 0.38***; AdjRsq = 0.11			

	Cervix		
All	Coeff.	Std. error	p
Intercept	31.11	2.99	0.00
Y_92	− 0.39	0.24	0.10
PhysD	− 7.03	2.44	0.00
$PhysD^2$	0.90	0.41	0.03
Spatial parameter = 0.53***; AdjRsq = 0.48			
40–60	Coeff.	Std. error	p
Intercept	15.81	1.44	0.00

Y_92	− 0.26	0.12	0.03
PhysD	− 3.65	1.21	0.00
$PhysD^2$	0.48	0.20	0.02
Spatial parameter = 0.49***; AdjRsq = 0.47			

	Oesophagus		
All	Coeff.	Std. error	p
Intercept	4.51	1.20	0.00
Y_92	− 0.21	0.24	0.38
Y_92^2	0.003	0.01	0.77
PhysD	0.50	0.37	0.18
Spatial parameter = 0.57***; AdjRsq = 0.28			
40–60	Coeff.	Std. error	p
Intercept	1.49	0.37	0.00
Y_92	− 0.08	0.08	0.28
Y_92^2	0.002	0.003	0.58
PhysD	0.10	0.12	0.39
Spatial parameter = 0.54***; AdjRsq = 0.26			

List of Countries and Regions

Countries			
Albania	Ecuador	Kenya	Samoa
Algeria	Egypt	Korea, Republic of	Singapore
Armenia	El Salvador	Kyrgyzstan	South African Rep.
Australia	Ethiopia	Lebanon	Spain
Austria	Fiji	Malawi	Sri Lanka
Azerbaijan	Finland	Malaysia	Sudan
Bahamas	France (metrop.).	Mali	Suriname
Bangladesh	FYR Macedonia	Malta	Swaziland
Barbados	Gabon	Mauritius	Sweden
Belarus	Gambia	Mexico	Switzerland
Belgium	Georgia	Moldova, rep. of	Tajikistan
Belize	Germany	Mongolia	Tanzania
Bhutan	Ghana	Morocco	Thailand
Bolivia	Greece	Mozambique	Togo
Botswana	Guatemala	Namibia	Trin. and Tobago
Brazil	Guinea	New Zealand	Tunisia
Bulgaria	Guyana	Nicaragua	Turkey
Burkina Faso	Honduras	Niger	Turkmenistan
Cameroon	Hungary	Nigeria	Uganda
Canada	Iceland	Netherlands, the	Ukraine
Chile	India	Norway	United Kingdom
China	Indonesia	Pakistan	USA
Colombia	Iran, Islamic Rep. of	Panama	Uruguay
Congo, Rep. of	Iraq	Papua New Guinea	Uzbekistan
Costa Rica	Ireland	Paraguay	Vanuatu
Cote d'Ivoire	Israel	Peru	Venezuela
Cuba	Italy	Philippines	Vietnam

Cyprus	Jamaica	Poland	Yemen
Czech Republic	Japan	Portugal	Zambia
Denmark	Jordan	Romania	
Dominican Rep.	Kazakhstan	Russian Federation	

Regions
Australia/New Zealand
Caribbean
Central America
Eastern Africa
Eastern Asia
Eastern Europe
Mela/Micro/Polynesia
Middle Africa
Northern Africa
Northern America
Northern Europe
South America
South Central Asia
South Eastern Asia
Southern Africa
Southern Europe
Western Africa
Western Asia
Western Europe

References

Alavanja, M.C., Samanic, C., Dosemeci, M., Lubin, J., Tarone, R., Lynch, C.F., Knott, C., Thomas, K., Hoppin, J.A., Barker, J., Coble, J., Sandler, D.P., Blair, A., 2003. Use of agricultural pesticides and prostate cancer risk in the Agricultural Health Study cohort. Am. J. Epidemiol. 157 (9), 800–814.

Ananthakrishnan, A.N., Hoffmann, R.G., Saeian, K., 2010. Higher physician density is associated with lower incidence of late-stage colorectal cancer. J. Gen. Intern. Med. 25 (11), 1164–1171.

Anselin, L., 1988. Spatial Econometrics: Methods and Models. Kluwer, Dordrecht.

Azadeh, A., Salibian-Barrera, M., 2011. An outlier-robust fit for generalized additive models with applications to disease outbreak detection. J. Am. Stat. Assoc. 106 (494), 719–731.

Baker, S.G., 2015. A cancer theory kerfuffle can lead to new lines of research. J. Natl. Cancer Inst. 107 (2), 1–8.

Beaulieu, N., Bloom, D., Bloom, R., Stein, R., 2009. Breakaway: the global burden of cancer—challenges and opportunities. In: The Economist Intelligence Unit.

Bedessem, B., Ruphy, S., 2015. SMT or TOFT? How the two main theories of carcinogenesis are made (artificially) incompatible. Acta Biotheor. 63 (3), 257–267.

Belpomme, D., Irigaray, P., Hardell, L., Clapp, R., Montagnier, L., Epstein, S., Sasco, A.J., 2007a. The multitude and diversity of environmental carcinogens. Environ. Res. 105 (3), 414–429.

Belpomme, D., Irigaray, P., Sasco, A.J., Newby, J.A., Howard, V., Clapp, R., Hardell, L., 2007b. The growing incidence of cancer: role of lifestyle and screening detection. Int. J. Oncol. 30, 1037–1049.

Bertram, J.S., 2001. The molecular biology of cancer. Mol. Asp. Med. 21 (6), 167–223.

Bilano, V., Gilmour, S., Moffiet, T., d'Espaignet, E.T., Stevens, G.A., Commar, A., Tuyl, F., Hudson, I., Shibuya, K., 2015. Global trends and projections for tobacco use, 1990–2025: an analysis of smoking indicators from the WHO Comprehensive information Systems for Tobacco Control. Lancet 385 (9972), 966–976.

Boffetta, P., 2006. Human cancer from environmental pollutants: the epidemiological evidence. Mutat. Res. Genet. Toxicol. Environ. Mutagen. 608 (2), 157–162.

Boyle, P., Levin, B., 2008. World Cancer Report 2008. (World Health Organisation).

Boyle, P., Parkin, D.M., 1991. Statistical methods for registries. In: Cancer Registration: Principles and Methods. 95. pp. 126–158.

Bray, F., Jemal, A., Grey, N., Ferlay, J., Forman, D., 2012. Global cancer transitions according to the human development index (2008–2030): a population-based study. Lancet Oncol. 13 (8), 790–801.

Bray, F., Ferlay, J., Laversanne, M., Brewster, D.H., Gombe Mbalawa, C., Kohler, B., Piñeros, M., Steliarova-Foucher, E., Swaminathan, R., Antoni, S., Soerjomataram, I., 2015. Cancer incidence in five continents: inclusion criteria, highlights from volume X and the global status of cancer registration. Int. J. Cancer 137 (9), 2060–2071.

Burgio, E., Migliore, L., 2015. Towards a systemic paradigm in carcinogenesis: linking epigenetics and genetics. Mol. Biol. Rep. 42 (4), 777–790.

Crutzen, P.J., 2002. Geology of mankind. Nature 415 (6867) (23-23).

Damodar, N., 2004. Basic Econometrics. The Mc-Graw Hill.

Danaei, G., Vander Hoorn, S., Lopez, A.D., Murray, C.J., Ezzati, M., Comparative Risk Assessment collaborating group (Cancers), 2005. Causes of cancer in the world: comparative risk assessment of nine behavioural and environmental risk factors. Lancet 366 (9499), 1784–1793.

Dinda, S., 2004. Environmental Kuznets curve hypothesis: a survey. Ecol. Econ. 49 (4), 431–455.

Draper, N.R., John, J.A., 1981. Influential observations and outliers in regression. Technometrics 23 (1), 21–26.

Fallah, M., Kharazmi, E., 2008. Substantial under-estimation in cancer incidence estimates for developing countries due to under-ascertainment in elderly cancer cases. Cancer Lett. 264 (2008), 250–255.

Farahani, M., Subramanian, S.V., Canning, D., 2009. The effect of changes in health sector resources on infant mortality in the short-run and the long-run: a longitudinal econometric analysis. Soc. Sci. Med. 68 (11), 1918–1925.

Ferlay, J., Soerjomataram, I., Dikshit, R., Eser, S., Mathers, C., Rebelo, M., Parkin, D.M., Forman, D., Bray, F., 2015. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. Int. J. Cancer 136, E359–E386. http://dx.doi.org/10.1002/ijc.29210.

Fidler, M.M., Soerjomataram, I., Bray, F., 2016. A global view on cancer incidence and national levels of the human development index. Int. J. Cancer 139, 2436–2446.

Fleisher, J.M., Lou, J.Q., Farrell, M., 2008. Relationship between physician supply and breast cancer survival: a geographic approach. J. Community Health 33 (4), 179–182.

Fox, J., 2015. Applied regression analysis and generalized linear models 3rd edition. Sage Publications Inc, Thousand Oaks, California.

Friedberg, M.W., Hussey, P.S., Schneider, E.C., 2010. Primary care: a critical review of the evidence on quality and costs of health care. Health Aff. 29 (5), 766–772.

GLOBOCAN, 2012. Estimated Cancer Incidence, Mortality and Prevalence Worldwide in 2012, WHO. http://globocan.iarc.fr/Default.aspx.

Gore, A.C., Crews, D., Doan, L.L., La Merrill, M., Patisaul, H., Zota, A., 2014. Introduction to Endocrine Disrupting Chemicals (EDCs), Endocrine Society and Ipen (available on line at). https://saludsindanio.org/sites/default/files/documents-files/2999/Introduction%20to%20Endocrine%20Disrupting%20Chemicals.pdf.

Greaves, M., 2014. "An Evolutionary Foundation for Cancer Control" in Stewart BW and Wild CP (2014).

Hanahan, D., Weinberg, R.A., 2000. The hallmarks of cancer. Cell 7 (100), 57–70.

Hanahan, D., Weinberg, R.A., 2011. Hallmarks of cancer: the next generation. Cell 4 (144), 646–674.

Howard, C.V., Staats, G., 2013. Cancer and environmental influences. In: Dubitzky, W., Wolkenhauer, O., Cho, K., Yokota, H. (Eds.), Encyclopedia of Systems Biology. Springer Science + Business Media, LLC. http://dx.doi.org/10.1007/978-1-4419-9863-7.

Irigaray, P., Newby, J.A., Clapp, R., Hardell, L., Howard, V., Montagnier, L., Epstein, S., Belpomme, D., 2007. Lifestyle-related factors and environmental agents causing cancer: an overview. Biomed Pharmacother 61 (10), 640–658.

LeSage, J., Pace, R.K., 2009. Introduction to Spatial Econometrics. CRC Press, Taylor & Francis Group, Boca Raton, Florida.

Levshina, N., 2015. How to Do Linguistics with R: Data Exploration and Statistical Analysis. John Benjamins Publishing Company.

Li, N., Du, X.L., Reitzel, L.R., Xu, L., Sturgis, E.M., 2013. Impact of enhanced detection on the increase in thyroid cancer incidence in the United States: review of incidence trends by socioeconomic status within the surveillance, epidemiology, and end results registry, 1980–2008. Thyroid 23 (1), 103–110.
Lichtenstein, P., Holm, N.V., Verkasalo, P.K., Iliadou, A., Kaprio, J., Koskenvuo, M., Pukkala, E., Skytthe, A., Hemminki, K., 2000. Environmental and heritable factors in the causation of cancer—analyses of cohorts of twins from Sweden, Denmark, and Finland. N. Engl. J. Med. 343 (2), 78–85.
Lodish, H., Berk, A., Zipursky, S.L., Matsudaira, P., Baltimore, D., Darnell, J., 2000. Molecular Cell Biology WH Freeman (New York, Available at). http://www.ncbi.nlm.nih.gov/books/NBK21662/.
Luzzati, T., 2015. Kuznets curves. In: Wright, J.D. (Ed.), International Encyclopedia of the Social & Behavioral Sciences, 2nd edition. Vol 13. Elsevier, pp. 144–149.
Luzzati, T., Orsini, M., 2009. Investigating the energy-environmental Kuznets curve. Energy 34 (3), 291–300.
Macinko, J., Starfield, B., Shi, L., 2007. Quantifying the health benefits of primary care physician supply in the United States. Int. J. Health Serv. 37 (1), 111–126.
Mannucci, P.M., Harari, S., Martinelli, I., Franchini, M., 2015. Effects on health of air pollution: a narrative review. Intern. Emerg. Med. 10 (6), 657–662.
Maule, M., Merletti, F., 2012. Cancer transition and priorities for cancer control. Lancet Oncol. 13 (8), 745–746.
Mayumi, K., Giampietro, M., 2010. Dimensions and logarithmic function in economics: a short critical analysis. Ecol. Econ. 69 (8), 1604–1609.
Mondal, M.N.I., Shitan, M., 2014. Relative importance of demographic, socioeconomic and health factors on life expectancy in low-and lower-middle-income countries. J. Epidemiol. 24 (2), 117–124.
Moynihan, R., Doust, J., Henry, D., 2012. Preventing overdiagnosis: how to stop harming the healthy. BMJ e3502.
Newby, J.A., Howard, C.V., 2005. Environmental influences in cancer aetiology. J. Nutr. Environ. Med. 5 (2–3), 56–114.
Newby, J.A., Busby, C.C., Howard, C.V., Platt, M.J., 2007. The cancer incidence temporality index: an index to show temporal changes in the age of onset of overall and specific cancer (England and Wales, 1971–1999). Biomed Pharmacother 61 (10), 623–630.
Norman, R.E., Ryan, A., Grant, K., Sitas, F., Scott, J.G., 2014. Environmental contributors to childhood cancers. J. Environ. Immunol. Toxicol. 1 (4), 12.
Nowell, P.C., 1976. The clonal evolution of tumor cell populations. Science 194 (4260), 23–28.
Omran, A.R., 2005. The epidemiologic transition: a theory of the epidemiology of population change. Milbank Q. 83 (4), 731–757.
Parkin, D.M., 2006. The evolution of the population-based cancer registry. Nat. Rev. Cancer 6 (8), 603–612.
Prüss-Üstün, A., Wolf, J., Cor Prüss Alán, C., Bos, R., Neira, M., 2016. Preventing Disease Through Healthy Environments. World Health Organization, Geneva, Switzerland.
R Development Core Team, 2012. R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna, Austria (URL). http://www.R-project.org/ (ISBN 3-900051-07-0).
Servan-Schreiber, D., 2008. We can Stop the Cancer Epidemic, The New York Times, Sept. 19, 2008 (available at). http://www.nytimes.com/2008/09/19/opinion/19iht-edservan.1.16308287.html.
Shi, L., 2012. The impact of primary care: a focused review. Scientifica 2012.
Siegel, R.L., Miller, K.D., Jemal, A., 2016. Cancer statistics, 2016. CA Cancer J. Clin. 66 (1), 7–30.
Smil, V., 2000. Energy in the twentieth century: resources, conversions, costs, uses, and consequences. Annu. Rev. Energy Environ. 25 (1), 21–51.
Stare, S.M., Jozefowicz, J.J., 2008. The effects of environmental factors on cancer prevalence rates and specific cancer mortality rates in a sample of OECD developed countries. Int. J. Appl. Econ. 5 (2), 24.
Steffen, W., Grinevald, J., Crutzen, P., McNeill, J., 2011. The Anthropocene: conceptual and historical perspectives. Philos. Trans. R. Soc. Lond. A 4 (369), 842–867 (1938).
Steliarova-Foucher, E., Stiller, C., Kaatsch, P., Berrino, F., Coebergh, J.W., Lacour, B., Perkin, M., 2004. Geographical patterns and time trends of cancer incidence and survival among children and adolescents in Europe since the 1970s (the ACCIS project): an epidemiological study. Lancet 364 (9451), 2097–2105.
Stern, D.I., 2004. The rise and fall of the environmental Kuznets curve. World Dev. 32 (8), 1419–1439.
Stewart, B., Wild, C.P. (Eds.), 2014. World Cancer Report 2014. World Health Organisation, Geneva Switzerland.
Sundmacher, L., Busse, R., 2011. The impact of physician supply on avoidable cancer deaths in Germany. A spatial analysis. Health Policy 103 (1), 53–62.
Torre, L.A., Bray, F., Siegel, R.L., Ferlay, J., Lortet-Tieulent, J., Jemal, A., 2015. Global cancer statistics, 2012. CA Cancer J. Clin. 65, 87–108.
Van Alstine, J., Neumayer, E., 2010. The environmental Kuznets curve. In: Gallagher, K.P. (Ed.), Handbook on Trade and the Environment. E Elgar.
Vineis, P., Wild, C.P., 2014. Global cancer patterns: causes and prevention. Lancet 383 (9916), 549–557.
WHO, 2014. Global Status Report on Noncommunicable Diseases 2014. World Health Organization, Geneva, Switzerland.
Wood, S.N., 2006. Generalized Additive Models. An Introduction With R. Chapman and Hall, London.
Wood, S.N., 2011. Fast stable restricted maximum likelihood and marginal likelihood estimation of semiparametric generalized linear models. J. R. Stat. Soc. Ser. B 1 (73), 3–36.