Received: 13 January 2020 | Revised: 1 May 2020 | Accepted: 6 May 2020

DOI: 10.1002/ijc.33114

CANCER EPIDEMIOLOGY

IJC International Journal of Cancer

Profiling global cancer incidence and mortality by socioeconomic development

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Abstract

Economic and living conditions have improved over time in most countries, although often in association with detrimental lifestyle and environmental changes that are major determinants of cancer. In this ecological study, we assess the association between national socioeconomic levels and incidence and mortality rates for all cancers combined and 27 cancer types, in 175 countries. We obtained national level cancer incidence and mortality estimates for 2018 from GLOBOCAN and computed an index of socioeconomic development based on national education and income levels extracted from the United Nations Development Programme. Cancer incidence rates are strongly positively associated with the national socioeconomic level for all cancers combined and for a large number of cancer types, in both sexes. Conversely, the association between socioeconomic development and cancer mortality rates is less clear. The most common pattern for type-specific cancers is an increasing incidence rate with a relatively stable mortality rate as socioeconomic development increases. Despite the high incidence rates for many cancer types, mortality rates are relatively low in high-income countries, partly due to the availability of early detection and effective treatments. As socioeconomic development continues to rise, countries with currently low- and medium-development levels may experience large increases in the incidence of several cancers. Given the limited resources and lack of infrastructure, increases in incidence rates in low-income countries will likely be paralleled by increases in mortality rates. Efforts to plan, implement and evaluate prevention programs must therefore be considered as greater priorities in Low- and Middle-income countries.

KEYWORDS

cancer incidence, cancer mortality, epidemiology, socioeconomic development, socioeconomic transition

1 | INTRODUCTION

Economic and living conditions have improved over time in most countries, and, as a consequence, health outcomes (such as average life expectancy) have also been improving. Socioeconomic development is however often associated with several detrimental lifestyle

Abbreviations: EdI, Education and Income Index; GNI, Gross National Income; HDI, Human Development Index; LMICs, Low- and Middle-Income countries; UNDP, United Nations Development Programme.

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changes and environmental exposures that are major determinants of cancer and have an impact on the population-at-large,[1] Therefore, there is a complex link between the national socioeconomic level of a country and the corresponding risk of morbidity and mortality from the disease. The incidence rates of certain type-specific cancers—mainly those associated with the uptake of behaviors that are "risky", such as smoking, or are partly imposed by the built environment—appear to increase with social and economic improvement. Meanwhile, cancers associated with infections or poverty have the tendency to decline as prosperity grows.[2,3] Many exceptions to this general observation do exist however, for example, the high rates of noncardia gastric cancer in affluent countries (eg, Japan and the Republic of Korea[4]).

In this article, we systematically assess the association between average national socioeconomic levels and up-to-date estimated incidence and mortality rates for all cancers combined and for 27 common cancer types in 175 countries by using an appropriate, newly developed indicator of socioeconomic development. Our study aims to provide insight on the distribution of cancer incidence and mortality according to the country-level of socioeconomic development and to anticipate ever-changing cancer control needs nationally, regionally and globally, particularly in the context of driving support for the implementation of preventive strategies in countries undergoing very rapid socioeconomic transition.

What's new?

Socioeconomic development is often associated with detrimental lifestyle changes and environmental exposures that are major determinants of cancer. Here, the authors assess for the first time the association between national socioeconomic level and incidence and mortality rates for all cancers combined and for 27 cancer types in 175 countries. As socioeconomic development continues to grow, low- and medium-income countries may face high cancer incidence rates as already experienced by high-income countries. However, higher cancer mortality rates are likely to ensue given the limited resources and lack of infrastructure. The findings advocate for efforts to plan healthcare resources and preventive measures.

2 | MATERIALS AND METHODS

2.1 | Cancer data sources

For this ecological study, we obtained national level cancer incidence and mortality estimates (age-standardized rates) using the world standard population)[5,6] for 2018 from GLOBOCAN, for 27 cancers and all cancers combined excluding nonmelanoma skin cancer.[7] Compiled at the International Agency for Research on Cancer (part of the World Health Organization), GLOBOCAN uses a hierarchical approach to estimation, based on high-quality, timely, and representative recorded incidence data from population-based cancer registries[8] and equivalent vital registration data from the WHO mortality database, where applicable.[9] The data are presented with the Global Cancer Observatory (http://gco.iarc.fr).

2.2 | Measuring socioeconomic development

The relationship between socioeconomic development and cancer has been typically reported using indices of national income (measured by gross national income (GNI) per capita),[10] the country's status as developed vs. developing,[11] and, the Human Development Index (HDI, combining three indicators: GNI, educational level, and life expectancy).[2,12-16] HDI is a commonly used index of socioeconomic development and offers clues as to how financial resources (GNI) are allocated to education (with the national expected and observed mean years of schooling) and health (with the observed national life expectancy, a health outcome).[17] However, given that one of its dimensions, life expectancy, may be affected by common causes of death, including cancer,[18] HDI may be a less suitable regressor when assessing the association between socioeconomic level and cancer mortality. We thus created an index of socioeconomic development, named Education and Income Index (EdI), which encompasses only two dimensions of the HDI index, namely education and income levels. EdI is based on the geometric mean of normalized indices of national educational level (using expected and observed mean years of schooling) and GNI per capita, both extracted from the UNDP website for 2017.[19] All 175 countries with data for GNI and educational level were included in the analysis. Similarly to HDI, EdI is expressed as a continuous variable with a number between zero and one (the higher a country's index, the higher the level of education and income) and is employed both as a continuous and a categorical variable. Countries are then distributed into the four groups of EdI (Table S1), with cutoff points EdI < 0.55 for countries in the "low" category, 0.55 ≤ EdI < 0.70 for "medium", 0.70 ≤ EdI < 0.80 for "high", and EdI ≥ 0.80 for "very high", in accordance with the four-tier HDI cutoff points.[17]

2.3 | Statistical analysis

We plotted national age-standardized (world) cancer incidence and mortality rates estimates versus EdI, for both sexes combined (except for female breast and sex-specific cancers). To help interpret and characterize the evolution of the rates across EdI, we applied cubic spline models[20] using the MGCV package in R.[21] In modeling the splines, we gave each country equal weight, regardless of its population size. To minimize the impact of the rates of the countries at the beginning and the end of the EdI spectrum on the spline models, the five countries with the lowest EdI (2.5th percentile of countries; highest, 97.5th, respectively) were attributed an EdI of 0.35 (2.5th percentile of EdI;

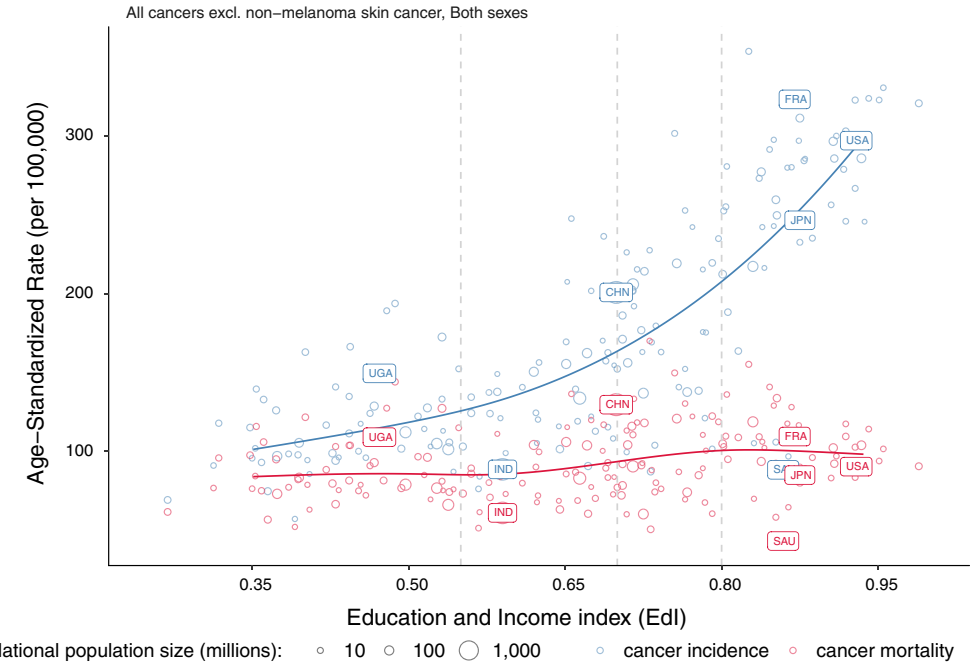

FIGURE 1 Age-standardized incidence and mortality rates estimates across Education and Income Index (EdI) for all cancers excluding nonmelanoma skin cancers, both sexes [Color figure can be viewed at wileyonlinelibrary.com]

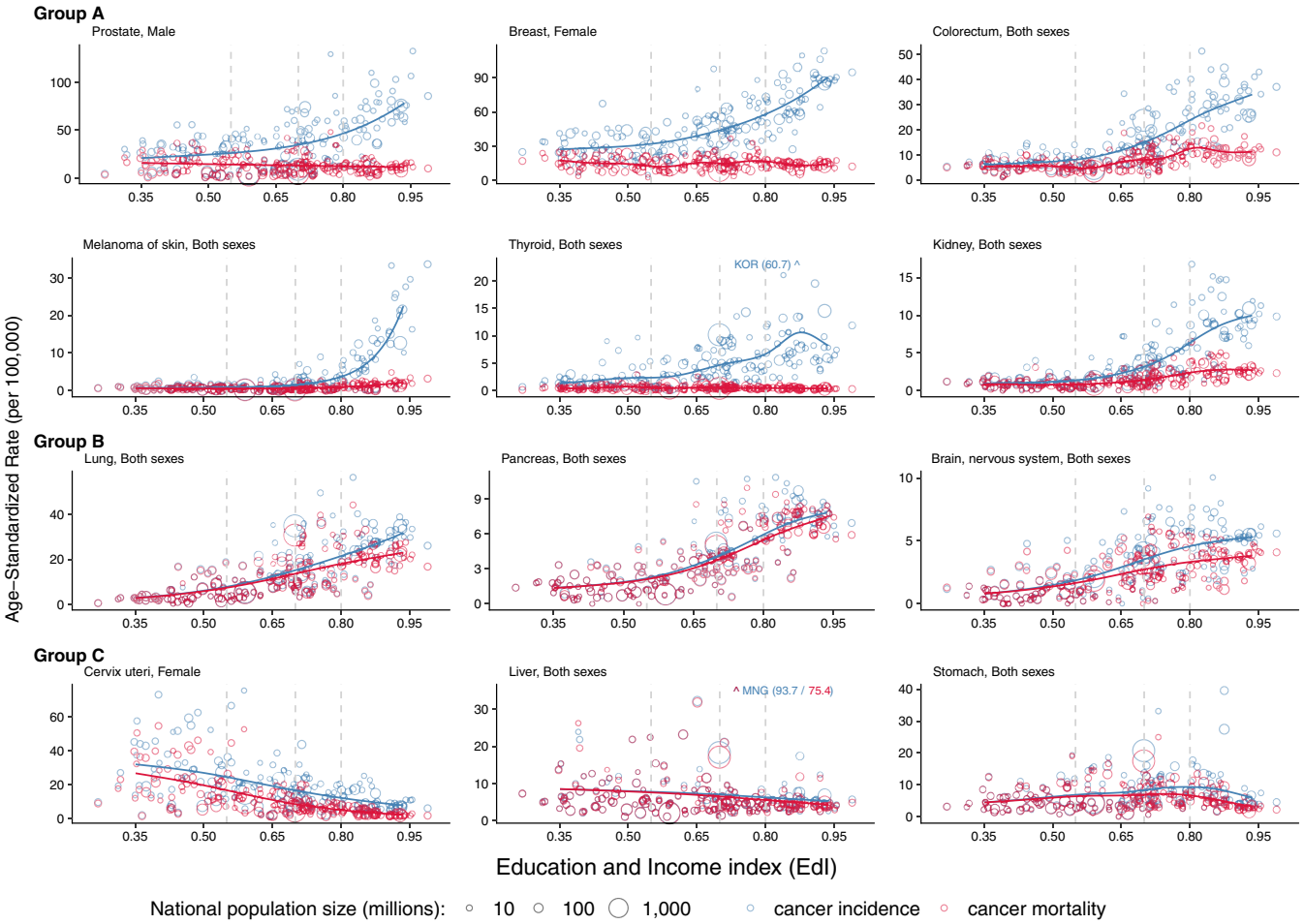

FIGURE 2 Age-standardized incidence and mortality rates estimates across Education and Income Index (EdI) for selected cancer types, both sexes or sex-specific. Group A: incidence rates increase as EdI increases, and mortality rates remain stable or increase at a low pace than incidence rates; Group B: both incidence and mortality rates increase similarly as EdI increases; Group C: both incidence and mortality rates decline as EdI increases [Color figure can be viewed at wileyonlinelibrary.com]

0.94, 97.5th, respectively). We grouped cancers together according to the relationship between EdI, rates of incidence and mortality by visual inspection.

3 | RESULTS

Figure 1 and Table S2 show that there is a strong positive relationship of EdI with incidence rates and only a weak positive relationship with mortality rates for all cancers combined, in both sexes combined. The average values of the modeled spline curves for incidence rates range from 115 to 258 cases per 100 000 from the low to the very high EdI categories—a more than twofold variation—with the largest relative differences occurring between the high and very high EdI categories (179 and 258 cases per 100 000, respectively). In contrast, the difference in average mortality rates on the spline curve in the low and very high EdI categories is less marked, ranging from around 87 to 101 deaths per 100 000, respectively.

The rates of all cancers combined in the countries with the lowest (Niger, EdI of 0.269) and the highest EdI values (Australia, EdI of 0.989) are 69 and 320 cases per 100 000, and 62 and 91 deaths per 100 000, respectively (Table S1). Nevertheless, substantial variations are observed in incidence and, to a lesser extent, mortality rates among countries with similar EdI. As examples, within the very high EdI category, incidence rates of all cancers combined in France are more than threefold higher than in Saudi Arabia (323 and 88 per 100,000, respectively) despite comparable EdI (0.870 and 0.859, respectively). In the high EdI category, China has higher incidence and mortality rates than other countries with similar EdI.

The associations of EdI with incidence and mortality rates for specific cancer types are presented in Figures 2 and S1 and S2. Four different groups of cancer types were identified based on their incidence and mortality rates patterns across EdI levels, as described below.

3.1 | Group A: incidence rates increase as EdI increases, and mortality rates remain stable or increase at a low pace than incidence rates

Almost half of cancers types (13 out of 27) belong to this group, including cancers of the prostate, breast, colorectum, thyroid, kidney, as well as melanoma of the skin. Cancers in this group exhibit a two- to 14-fold increase in the average modeled incidence rate between the low and high EdI category, combined with a more modest (onefold

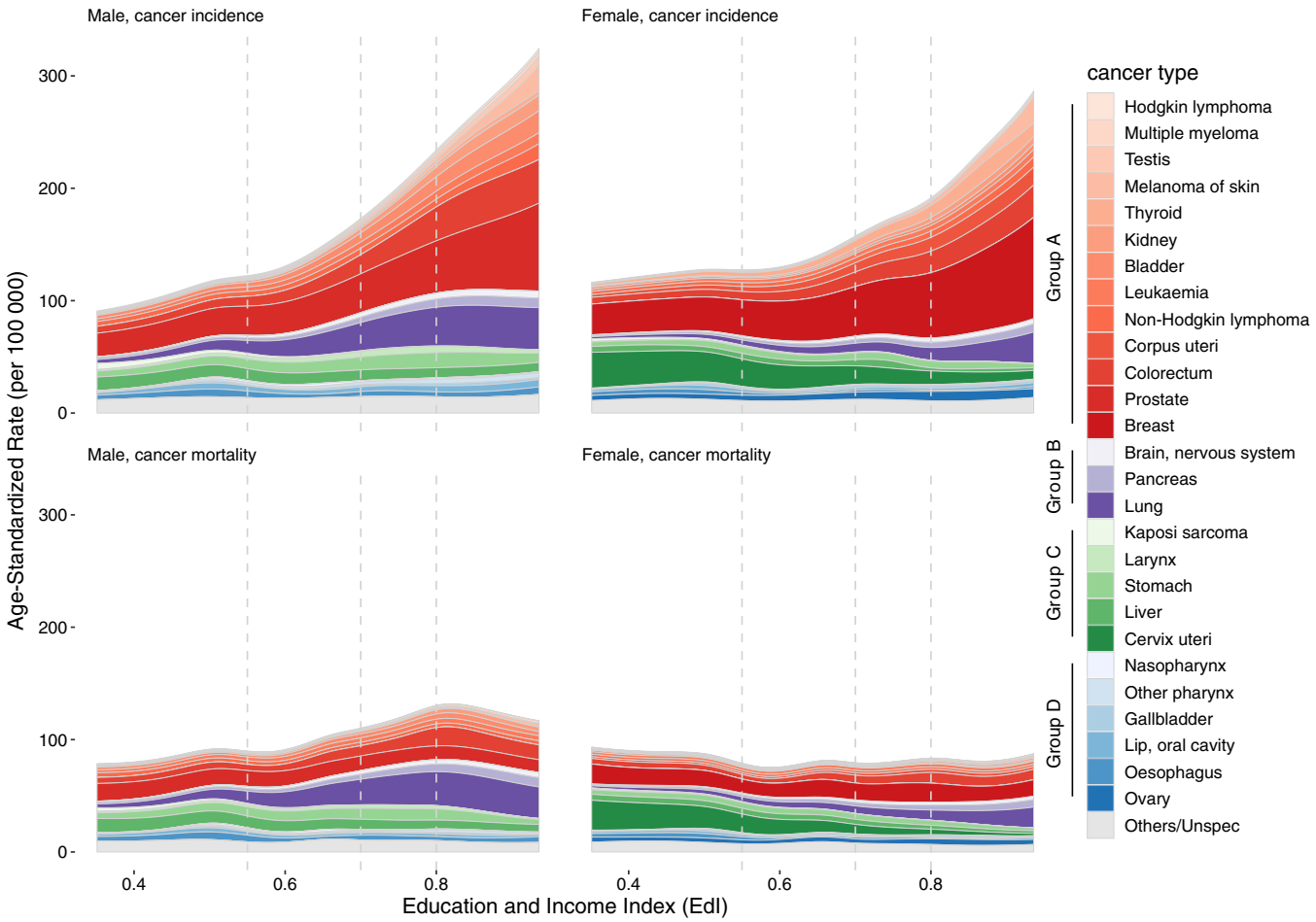

FIGURE 3 Modeled age-standardized rates across Education and Income Index (EdI), for incidence and mortality, by sex [Color figure can be viewed at wileyonlinelibrary.com]

to threefold) increase (or even a decline for female breast, prostate, and thyroid cancers as well as Hodgkin lymphoma) in mortality rates. Therefore, the gap between incidence and mortality rates increases as EdI increases and is very large in countries in the very high EdI category. It is worth noting that classification for colorectal cancer (and possibly kidney) is compatible with both Group A and Group B (see below), as these cancers show substantial increase in incidence but only moderate increase in mortality rates (only increasing from low to high EdI categories and then stabilizing in the very high EdI category).

3.2 | Group B: both incidence and mortality rates increase similarly as EdI increases

The only cancers in this group are lung, pancreatic, and brain and nervous system, all depicting similar patterns of increasing incidence and mortality rates (a fourfold to fivefold increase in average modeled incidence rates and a threefold to fourfold increase in average modeled mortality rates from the lowest to the highest EdI category, respectively) as the EdI grows.

3.3 | Group C: declining incidence and mortality rates as EdI increases

This group mainly comprises infection-related cancers (liver, stomach and cervical cancers and Kaposi sarcoma). Modeled incidence rates are on average 1.5, 3 and 17 times higher for liver and cervical cancers, and Kaposi sarcoma, respectively, in the low EdI category than in the very high EdI category. Meanwhile, modeled cancer mortality rates decrease as EdI increases (only in the very high EdI category for stomach and laryngeal cancers), for instance from 22 to three deaths per 100 000 due to cervical cancer, on average, between the low EdI and very high EdI categories, respectively.

3.4 | Group D: no clear association of incidence and mortality rates with EdI

This group includes cancers of the lip and oral cavity, ovary, esophagus, gallbladder and nasopharynx (Figure S2).

Figure 3 presents overall incidence and mortality rates across EdI disaggregated by cancer type and gender. Incidence rates for all cancers combined are increasing in both males and females (starting in the medium EdI group in females). Mortality rates for all cancers combined increase up to 0.8 EdI (the beginning of the very high EdI group) then slightly decline in males, while they remain relatively stable across EdI in females. Due to the large number of common cancer types in Group A cancers (red shading) compared to other cancer groups, the incidence and mortality rates patterns of Group A cancers across EdI drive the pattern of all cancers combined (as presented in Figure 1). The increasing contribution of Groups A and B (purple shading) cancers in all cancers combined incidence and mortality rates as EdI increases is notable. For instance, male colorectal and lung cancers represent 6%-7% of all cancers combined incidence rates in the low EdI category but 13% in the very high EdI category. Conversely, the largest contribution of Group C cancers (green shading) to all cancers combined incidence and mortality rates is observed in low EdI countries. Notably, cervical cancer incidence rates represent 23% of all cancers combined incidence rates in the low EdI group compared to about 4% in the very high EdI group. In females, the declines in incidence and mortality rates of Group C cancers as EdI rises are offset by the increases in Group B cancers. Finally, Group D (blue shading) comprises rarer cancer types at the global level.

4 | DISCUSSION

In our study, we show that cancer incidence rates are strongly positively associated with the average national socioeconomic level for all cancers combined and for a large number of cancer types, in both sexes. Conversely, a moderate positive association is observed for all cancers combined mortality rate in men and no clear association in women, whereas the association is more variable for specific cancers types.

The incidence rates of breast, prostate, and colorectal cancers are increasing with increasing level of socioeconomic development and, given their high frequency, are therefore driving the increase in incidence rate of all cancers combined. The rising incidence rate across EdI of these three cancer types and other Group A cancers can be explained by their association with risk factors increasing in prevalence as countries progress from low to very high EdI. These development-associated risks include tobacco use, alcohol consumption, overweight and obesity, lack of physical activity, low fertility and older age at first birth. Despite the relatively low overall cancer incidence rates, due to limited access to early detection and curative treatment, most of the cancer patients die from the disease in low EdI countries. Conversely, in high EdI countries, even with very high incidence rates, access to care enables mortality to be curtailed to relatively low levels. For instance, 5-year breast cancer relative survival is 59% in sub-Saharan Africa[22] as opposed to 89% in the USA.[23] Overall cancer mortality rates are thus approximately stable across levels of EdI. Over-detection practices, which become more prevalent as socioeconomic development grows, and under-diagnosis and under-reporting in countries with lower socioeconomic level, may also partly explain why incidence but not mortality rates increase together with socioeconomic development.[24-28]

The rise in cancer incidence among Group B cancers across EdI is predominantly driven by lung cancer and explained by the earlier adoption and high prevalence of tobacco smoking in high EdI countries.[29] Lung, brain and pancreatic cancers still have limited early detection and treatment options, which may explain the similarity of the patterns between incidence and mortality rates.

Group C cancers are relatively frequent in low EdI countries because of the historically higher prevalence of some infectious agents[30] (eg, Hepatitis B viruses for liver cancer, HIV in sub-Saharan

Africa for Kaposi sarcoma and *Helicobacter pylori* for stomach cancer[4]) and the lack of screening for cervical cancer.[31]

Group D appears to comprise cancers with either localized risk factors or those with a dual etiology dependent on development. As a consequence, countries with similar EdI can have very different cancer incidence and mortality rates while there seems to be no association between cancer incidence, cancer mortality, and socioeconomic level. For instance, the high Epstein-Barr virus prevalence in east and south-east Asia drives the burden of nasopharyngeal cancer[32] and tobacco chewing in Asia of lip and oral cavity cancers.[33] There are two main esophageal subtypes (each with a different set of risk factors), with varying proportions by country.

Patterns in incidence and mortality rates of some cancer types across the levels of socioeconomic development appear to mirror the trajectory of temporal trends in already-transitioned countries, as evident for instance in the United States[28,34] and Australia,[31,35-37] and in transitioning economies.[38,39] The very high incidence rates of cancer types rising with socioeconomic development in very high EdI countries could therefore possibly represent a realistic upper bound for the future cancer incidence rates in medium to high EdI countries transitioning to higher socioeconomic levels. However, as transitioning countries achieve higher socioeconomic levels and cancer incidence rates rise, cancer mortality rates will also likely rise proportionally to incidence, given that these countries may have only limited access to effective affordable treatments and cancer care. As evidence, the global shortage of health care workers was estimated to be 17.4 million in 2013 (of which 99% were in LMICs). Although the situation will improve due to the current trend in health worker training and employment, this shortage remains projected to reach 14.5 million in 2030 (of which, again, 99% will be in LMICs).[40] Hence, many LMICs will still be ill-equipped to tackle the burden of cancer in the future. Cancer prevention measures should therefore be prioritized, particularly in low and medium EdI countries, with a sustainable resource-appropriate long-term investment in preventive measures and planning of finite healthcare resources. Given that cervical cancer incidence rates represent almost a quarter of all cancers combined incidence rates in the low EdI group, HPV vaccination certainly represents a promising and cost-effective measure in low EdI countries.

Our study should be evaluated with consideration of its limitations. First, GLOBOCAN uses several methods and the validity of its estimates depends on the representativeness and quality of the data sources.[8] Incidence rates are estimated with Method 1 (short-term prediction models of national data) for 45 countries, Method 2 (short-term predictions of sub-national data or short national data span) for 50 countries, Method 3 (fitted mortality to incidence ratio) for 51 countries, Method 4 (average of age- and sex-specific rates from neighboring countries) for 7 countries, and Method 9 (average rates from neighboring countries) for 32 countries. Mortality rates are estimated with Method 1 for 81 countries, Method 2 for 20 countries, Method 3 for 81 countries and Method 9 for 3 countries. The limitations of the GLOBOCAN estimates also apply to our estimates. In addition, Method 3 incorporates the level of development (HDI) to estimate cancer incidence (in a subset of 37 countries, most of them in Latin America and the Caribbean) and mortality (81 countries, most of them in Africa and Asia) rates. As a consequence, these cancer incidences and mortality rates in the low and medium EdI categories are correlated by design. Second, by examining differences at national level, our study fails to uncover differences in the cancer burden within countries which are also important, whether at local level or between subgroups with varied levels of socioeconomic development.[41] Third, indices of socioeconomic developments, including the EdI, cannot capture all aspects of social or other conditions which could explain cancer patterns. For instance, Saudi Arabia and France have large differences in their incidence and mortality rates of all cancers combined yet similar EdI. Fourth, the cross-sectional nature of our study cannot take into account the lag time between the exposure to risk factors associated with socioeconomic development and cancer outcomes. Finally, in the absence of dependable data from the Civil Registration System, disease-specific mortality is frequently incomplete, not very reliable or are lacking in many countries particularly in Asia and Africa.[42] Consequently, cancer mortality rates may be influenced by a differential misclassification of the cause of death, and more so in lower socioeconomic level countries.

Our study has strengths. While the relationship between incidence and/or mortality of several cancers and human development has been reported before using HDI categories[16] and earlier GLOBOCAN estimates, our study analyses this relationship in 27 cancer types using a modified marker of development (EdI) and the most up-to-date data. A sensitivity analysis (data not shown) showed that using national HDI instead of EdI yielded similar spline curves and that the difference between HDI and EdI for the same country was small (0.028 on average). EdI is nevertheless more methodologically correct when assessing the link between socioeconomic development and both cancer incidence and mortality rates, as by excluding life expectancy, the EdI is free from the impact of cancer mortality rate on life expectancy that occurs using HDI.

As socioeconomic development will continue to grow in the coming years, isolating associations with specific cancer types is valuable in predicting the future burden and profile of cancer, as a means to prioritize cancer control efforts nationally and globally. Sizing the extent and the nature of the problem can give the impetus and the target to stakeholders to implement the healthcare resources needed to curtail the cancer burden.[10] This is particularly important in countries progressing toward higher levels of development, which are in addition facing the largest demographic changes. From a public health perspective, our study shows that an understanding of the drivers of, and interventions for, brain and pancreatic cancer are research priorities, given that both incidence and mortality rates tend to rise as countries transition to higher socioeconomic levels.

In conclusion, the incidence rates overall and most cancer types are strongly related to the national level of socioeconomic development, whereas, for cancer mortality rates, the associations are more variable. With national developmental gains, it is likely that countries currently at low socioeconomic development level may experience the same increases in cancer incidence rates as countries that have already transitioned to the highest levels. At the present level of

resources, it is not clear whether transitioning countries will be able to contain the increases in overall mortality rates, in the same way, many of today's more socioeconomically developed countries have been able to. Reducing the cancer burden in lower socioeconomically developed countries will thus require careful planning of finite healthcare resources, and given spiraling treatment costs, must include a long-term investment in resource-appropriate preventive measures.

ACKNOWLEDGEMENT

No dedicated funding source was involved in this project.

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

DATA ACCESSIBILITY

All data used for this project are publicly available from the United Nations Development Programme website http://hdr.undp.org/en/2018-update and the GLOBOCAN website http://gco.iarc.fr/today/home. The programs developed in R to model the incidence and mortality rates across the EdI are available at https://github.com/IARC-ICE/EdIglobocanhub under GPLv3 license.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

How to cite this article: Lortet-Tieulent J, Georges D, Bray F, Vaccarella S. Profiling global cancer incidence and mortality by socioeconomic development. *Int. J. Cancer*. 2020;147:3029–3036. https://doi.org/10.1002/ijc.33114