World Journal of Gastroenterology

Online Submissions: http://www.wjgnet.com/esps/
wjg@wjgnet.com
doi:10.3748/wjg.v19.i32.5261

World J Gastroenterol 2013 August 28; 19(32): 5261-5270
ISSN 1007-9327 (print) ISSN 2219-2840 (online)

ORIGINAL ARTICLE

Human development index is associated with mortality-to-incidence ratios of gastrointestinal cancers

Qi-Da Hu, Qi Zhang, Wei Chen, Xue-Li Bai, Ting-Bo Liang

Qi-Da Hu, Qi Zhang, Wei Chen, Xue-Li Bai, Ting-Bo Liang, Department of Surgery, the Second Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou 310009, Zhejiang Province, China

Author contributions: Hu QD and Liang TB conceived the study; Hu QD and Zhang Q, Liang TB designed the study; Hu QD collected data; Hu QD, Zhang Q, Chen W and Bai XL analyzed the data; Hu QD, Zhang Q and Chen W drafted the manuscript; Liang TB finalized the manuscript, and took responsibility for the integrity of the data and the accuracy of the data analysis; all authors have read and approved the final manuscript.

Supported by The National Natural Science Funds for Distinguished Young Scholars, No. 30925033; and the Innovation and High-Level Talent Training Program of Department of Health of Zhejiang Province, China

Correspondence to: Ting-Bo Liang, MD, PhD, Department of Surgery, the Second Affiliated Hospital, School of Medicine, Zhejiang University, 88 Jiefang Road, Hangzhou 310009, Zhejiang Province, China. liangtingbo@zju.edu.cn
Telephone: +86-571-87315006 Fax: +86-571-87315006
Received: May 18, 2013 Revised: July 7, 2013
Accepted: July 17, 2013
Published online: August 28, 2013

Abstract

AIM: To identify the role of human development in the incidence and mortality rates of gastrointestinal cancers worldwide.

METHODS: The age-standardized incidence and mortality rates for gastrointestinal cancers, including cancers of the esophagus, stomach, pancreas, liver, gallbladder, and colorectum, were obtained from the GLOBOCAN 2008 database and United States Cancer Statistics (USCS) report. The human development index (HDI) data were calculated according to the 2011 Human Development Report. We estimated the mortality-to-incidence ratios (MIRs) at the regional and national levels, and explored the association of the MIR with development levels as measured by the HDI using a modified "drug dose to inhibition response" model. Furthermore, countries were divided into four groups according to the HDI distribution, and the MIRs of the four HDI groups were compared by one-way ANOVA followed by the Tukey-Kramer *post-hoc* test. State-specific MIRs in the United States were predicted from the estimated HDI using the fitted non-linear model, and were compared with the actual MIRs calculated from data in the USCS report.

RESULTS: The worldwide incidence and mortality rates of gastrointestinal cancers were as high as 39.4 and 54.9 cases per 100000 individuals, respectively. Linear and non-linear regression analyses revealed an inverse correlation between the MIR of gastrointestinal cancers and the HDI at the regional and national levels ($\beta < 0$; $P = 0.0028$ for regional level and < 0.0001 for national level, ANOVA). The MIR differed significantly among the four HDI areas (very high HDI, 0.620 ± 0.033; high HDI, 0.807 ± 0.018; medium HDI, 0.857 ± 0.021; low HDI, 0.953 ± 0.011; $P < 0.001$, one-way ANOVA). Prediction of the MIRs for individual United States states using best-fitted non-linear models showed little deviation from the actual MIRs in the United States. Except for 28 data points (9.93% of 282), the actual MIRs of all gastrointestinal cancers were mostly located in the prediction intervals *via* the best-fit non-linear regression models.

CONCLUSION: The inverse correlation between HDI and MIR demonstrates that more developed areas have a relatively efficacious healthcare system, resulting in low MIRs, and HDI can be used to estimate the MIR.

Key words: Gastrointestinal neoplasms; Mortality-to-incidence ratio; Human development index; Healthcare disparities; Socioeconomic factors

Core tip: This study is the first to explore the exact re-

lationship between the epidemiology of gastrointestinal cancers and area-specific development disparities. We showed the association between the mortality-to-incidence ratios (MIRs) and the human development index at the regional and national levels using a modified "drug dose to inhibition response" model. Further prediction of the MIRs for individual United States states on the basis of best-fitted non-linear models showed little deviation from the actual MIRs in the United States.

Hu QD, Zhang Q, Chen W, Bai XL, Liang TB. Human development index is associated with mortality-to-incidence ratios of gastrointestinal cancers. *World J Gastroenterol* 2013; 19(32): 5261-5270 Available from: URL: http://www.wjgnet.com/1007-9327/full/v19/i32/5261.htm DOI: http://dx.doi.org/10.3748/wjg.v19.i32.5261

INTRODUCTION

The digestive system includes multiple organs within or alongside the alimentary tract and is of vital importance in the proper functioning of the body. Currently, gastrointestinal cancer is a leading cause of cancer-related deaths in many developed countries, and it has been predicted to have the highest incidence and mortality rates worldwide, irrespective of the level of a country's resources[1-3]. Gastrointestinal cancers are known to notably affect the pathophysiological condition and functioning of the digestive system. Both cancer incidence and mortality in highly developed countries such as the United States peaked in the early 1990s and have since declined because of enhanced awareness, preventive measures, earlier detection and the availability of new and more effective treatment regimens, although very little progress has been made in the treatment of some cancers such as pancreatic cancer[4]. In contrast, limited or inaccessible healthcare resources in developing areas remain barriers to the effective control of future changes in incidence and mortality rates[5,6]. The expected cancer burden will continue to be a serious public health problem in the coming decade, particularly in developing countries[3,7,8].

Disparities in healthcare have received considerable attention from international organizations and national governments[9,10]. The socioeconomic determinants of the inequality reflect regional imbalances in human development. A previous study found that 35% of the cancer deaths may be attributable to nine modifiable risk factors: alcohol, smoking, low fruit and vegetable intake, overweight and obesity, physical inactivity, urban air pollution, unsafe sex, contaminated injections in health care settings, and indoor smoke from household activities such as cooking or indoor heating[11]. Most of these risk factors vary widely among populations in areas with different levels of development[12,13]. However, there is little knowledge about the healthcare disparities in the individuals suffering from gastrointestinal cancers. This study is the first to explore the exact relationship between the epidemiology of gastrointestinal cancers and area-specific development disparities. We aimed to identify the role of human development in the incidence and mortality rates of gastrointestinal cancers worldwide.

MATERIALS AND METHODS

Incidence and mortality data

The global incidence and mortality estimates for gastrointestinal cancers in 184 countries were obtained from the GLOBOCAN 2008 database (http://globocan.iarc.fr/) maintained by the WHO International Agency for Research on Cancer[14,15]. GLOBOCAN also provided regional estimates for each continent.

United States Cancer Statistics (USCS) reported the incidence and mortality rates associated with cancers in United States states[16]. State-specific incidence data were collected from the National Program of Cancer Registries and the Surveillance, Epidemiology, and End Results Program. Mortality information was collected by the National Vital Statistics System, National Center for Health Statistics and United States Centers for Disease Control and Prevention (United States-CDC).

We obtained the data of the incidence and mortality rates of gastrointestinal cancers in six major sites, namely, the esophagus, stomach, pancreas, liver, gallbladder, and colorectum. The USCS did not provide gallbladder cancer data. The overall rates of gastrointestinal cancers were estimated by addition of the rates of the six cancers. The rates were age-standardized using the world standard population and a previously proposed method[17], and presented as age-standardized rates (ASR). ASR is a summary measure of the rate that a population distribution would have if it had a standard age structure. Since age has a powerful influence on the risk of cancer, standardization is necessary when comparing several populations that differ with respect to age[14].

Mortality-to-incidence ratio

The mortality-to-incidence ratios (MIRs) were calculated from the obtained incidence and mortality rates provided by the GLOBOCAN database[14] and USCS report[16]. Extreme MIRs (0, 1, or > 1) were considered abnormal because of (1) illogical data (zero mortality or mortality more than incidence); and (2) zero incidence, and these results were excluded from the regression fit and further analysis. Respectively, 25, 13, 62, 82, 46, and 0 extreme MIR results were excluded in the analysis for cancers of the esophagus, stomach, pancreas, liver, gallbladder, and colorectum.

Estimated human development index

The human development index (HDI) data of Union Nation members in 1980-2011 were available in the United Nations Development Programme (UNDP) database (http://hdr.undp.org/en/statistics). The HDI was calculated according to the 2011 Human Development Report (HDR 2011)[18]. The HDI of Taiwan was

obtained from the National Statistics (Taiwan) website (http://www.stat.gov.tw), and subsequently verified.

We further estimated the state-specific HDI in the United States on the basis of data provided by various data agencies. Information on life expectancy at birth provided by the CDC was adapted by the American HDI Project[19]. The gross domestic product (GDP) per capita was acquired from the Bureau of Economic Analysis at the United States Department of Commerce, and compiled by the Bureau of Business and Economic Research, University of New Mexico[20]. The GDP values were converted to international dollars using purchasing power parity rates. The mean duration of education was estimated from the 2009 American Community Survey data provided by the United States Census Bureau[21], according to the method of Barro and Lee[22]. The expected duration of education in the United States was defined as 12 years; this value was adapted from the United Nations Educational, Scientific and Cultural Organization Institute for Statistics[23].

Statistical analysis

Only the countries with both epidemiologic data from the GLOBOCAN database and HDI from the UNDP program were included in the analysis. Taiwan was not excluded because its HDI value was available at the National Statistics (Taiwan) website. The number of countries included in our research was 165. Patterns in the MIR of gastrointestinal cancers with respect to the levels of socioeconomic development were investigated by correlating the MIRs to the corresponding HDIs *via* linear or non-linear regression. Linear regression fit was conducted to determine the existence of correlations. Derivation of the slope parameter β from 0 was defined by ANOVA. Correlation existence referred to the significantly non-zero β value. Non-linear regression fit was based on a modified "drug dose to inhibition response" model using the formula:

$$\mathrm{MIR} = \frac{1}{1+10^{(\mathrm{HDI}_{50}-\mathrm{HDI})\times\mathrm{Slope}}},$$

where "HDI_{50}" was the HDI value at half maximal MIR and "slope" was a parameter that indicated the steepness of the slope. The MIRs of the four HDI groups were compared by one-way ANOVA followed by the Tukey-Kramer *post-hoc* test. A P value of less than 0.05 was considered statistically significant. Statistical analysis and plotting were performed using Prism 5 (GraphPad, San Diego, CA, United States). The geographical map showing MIR was created using the open source software TileMill (a GitHub project maintained by MapBox, Washington, WI, United States), with map data sources from the Natural Earth database rendered by the Mapnik Library.

RESULTS

Global incidence and mortality of gastrointestinal cancers

In 2008, gastrointestinal cancers were estimated to have affected a total of 3878986 individuals and caused 2824985 deaths worldwide. The global mortality and incidence rates were as high as 39.4 and 54.9 cases per 100000 individuals, respectively. Colorectal cancer was the third most common cancer with 1235108 incidences among the 27 cancers included in the GLOBOCAN database, and it was the most common cancer among the six gastrointestinal cancers included in the current study. Other prevalent cancers according to the incidences reported in the database included stomach cancer (ranked 4th, with 988602 incidences), liver cancer (6th, 749744 incidences), esophageal cancer (8th, 481645 incidences), pancreatic cancer (13th, 278684 incidences), and gallbladder cancer (21st, 145203 incidences). However, stomach cancer had the highest mortality rate (26.1%, 737419 deaths) among all gastrointestinal cancers. In terms of the mortality rate, liver cancer (ranked 3rd with 695726 deaths), colorectal cancer (4th, 609051 deaths), esophageal cancer (6th, 406533 deaths), pancreatic cancer (8th, 266669 deaths) and gallbladder cancer (17th, 109587 deaths) contributed to 24.6%, 21.6%, 14.4%, 9.4% and 3.9% of all deaths caused by gastrointestinal cancers, respectively.

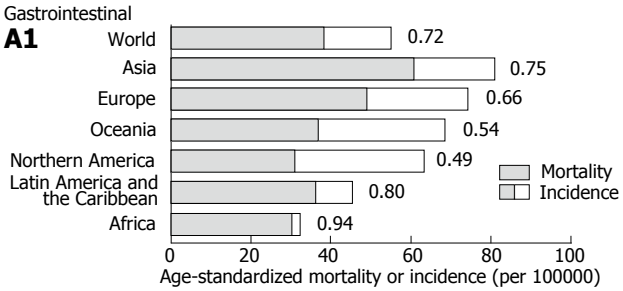
Differences in the regional incidence and mortality

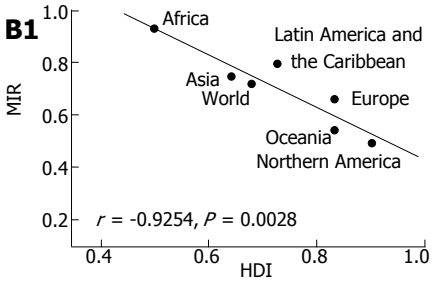
The regional incidence and mortality rates varied among different continents and regions (Figure 1A). Asia had the highest incidence rates of esophageal, stomach and liver cancers, as well as gastrointestinal cancers overall. Interestingly, the MIRs for gastrointestinal cancers, except for pancreatic cancer, were higher in Africa compared with other continents. Linear regression analysis revealed a significant inverse correlation between the regional HDI and MIR of stomach, gallbladder and colorectal cancers and gastrointestinal cancer overall ($P < 0.05$, ANOVA) (Figure 1B).

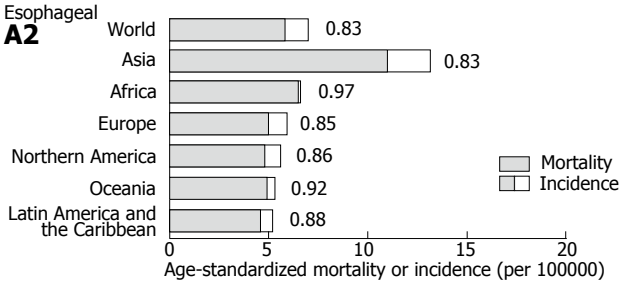
Association between national HDI and MIR

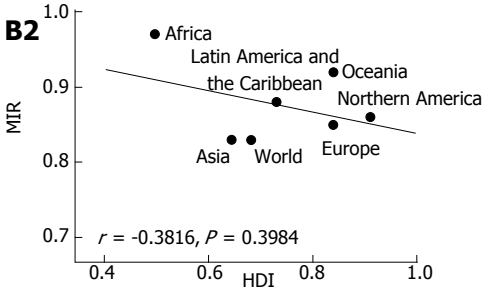
The national MIR varied across different countries with different levels of development, as measured by HDI (Figure 2). Countries with high HDI tended to have relatively low MIR. Cross-national analysis demonstrated that the MIRs of gastrointestinal cancers consistently showed an inverse correlation with the national HDI values *via* linear regression ($\beta < 0$; $P < 0.05$, ANOVA; Table 1, Figure 3A). Furthermore, non-linear regression based on the "drug dose to inhibition response" model was used to analyze this correlation, and a more satisfactory fitting result with larger R square values was achieved for all gastrointestinal cancers (Table 1, Figure 3B). The HDI values at half-maximal MIR (HDI_{50}) in gastrointestinal cancers overall and colorectal cancer were 0.946 and 0.825, respectively. Five other cancers had an HDI_{50} of more than 1.

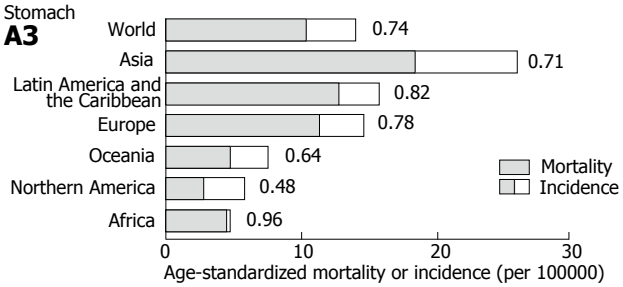
Countries were divided into four groups according to the HDI distribution reported in HDR 2011[18]. The MIR of gastrointestinal cancers differed significantly among these four groups ($P < 0.001$, one-way ANOVA). The mean MIR of countries with very high HDI was

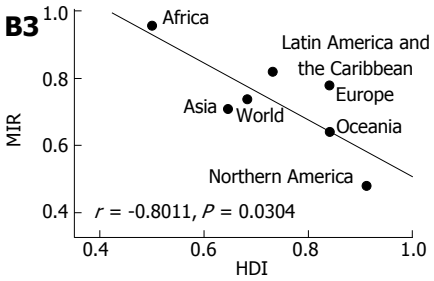

Gastrointestinal
A1
World
Asia
Europe
Oceania
Northern America
Latin America and the Caribbean
Africa
0.72
0.75
0.66
0.54
0.49
0.80
0.94
Mortality
Incidence
0
20
40
60
80
100
Age-standardized mortality or incidence (per 100000)

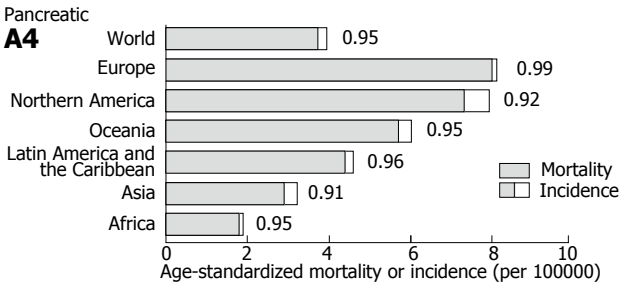

B1
MIR
HDI
Africa
Latin America and the Caribbean
Asia
World
Europe
Oceania
Northern America
r = -0.9254, P = 0.0028

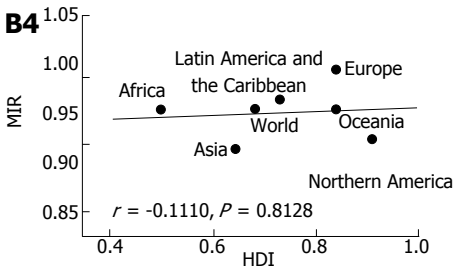

Esophageal
A2
World
Asia
Africa
Europe
Northern America
Oceania
Latin America and the Caribbean
0.83
0.83
0.97
0.85
0.86
0.92
0.88
Mortality
Incidence
0
5
10
15
20
Age-standardized mortality or incidence (per 100000)

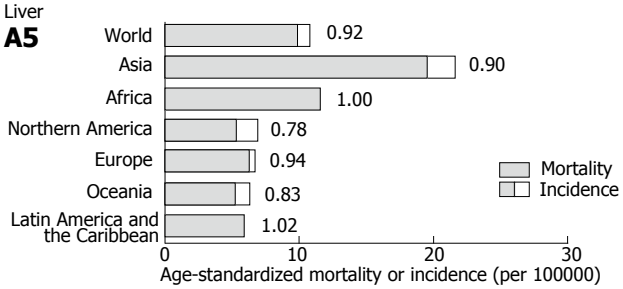

B2
MIR
HDI
Africa
Latin America and the Caribbean
Oceania
Northern America
Asia
World
Europe
r = -0.3816, P = 0.3984

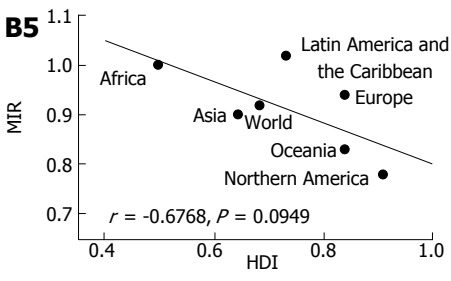

Stomach
A3
World
Asia
Latin America and the Caribbean
Europe
Oceania
Northern America
Africa
0.74
0.71
0.82
0.78
0.64
0.48
0.96
Mortality
Incidence
0
10
20
30
Age-standardized mortality or incidence (per 100000)

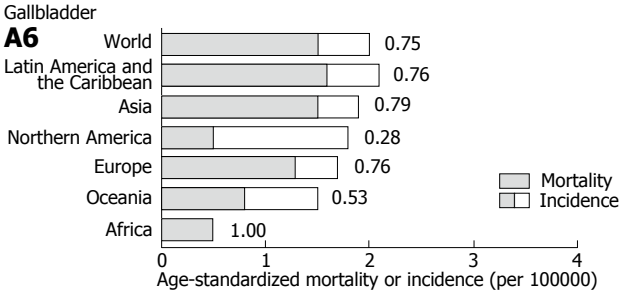

B3
MIR
HDI
Africa
Latin America and the Caribbean
Europe
Asia
World
Oceania
Northern America
r = -0.8011, P = 0.0304

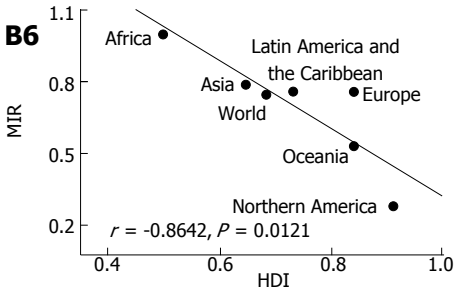

Pancreatic
A4
World
Europe
Northern America
Oceania
Latin America and the Caribbean
Asia
Africa
0.95
0.99
0.92
0.95
0.96
0.91
0.95
Mortality
Incidence
0
2
4
6
8
10
Age-standardized mortality or incidence (per 100000)


B4
MIR
HDI
Latin America and the Caribbean
Europe
Africa
World
Oceania
Asia
Northern America
r = -0.1110, P = 0.8128


Liver
A5
World
Asia
Africa
Northern America
Europe
Oceania
Latin America and the Caribbean
0.92
0.90
1.00
0.78
0.94
0.83
1.02
Mortality
Incidence
0
10
20
30
Age-standardized mortality or incidence (per 100000)


B5
MIR
HDI
Latin America and the Caribbean
Africa
Europe
Asia
World
Oceania
Northern America
r = -0.6768, P = 0.0949


Gallbladder
A6
World
Latin America and the Caribbean
Asia
Northern America
Europe
Oceania
Africa
0.75
0.76
0.79
0.28
0.76
0.53
1.00
Mortality
Incidence
0
1
2
3
4
Age-standardized mortality or incidence (per 100000)


B6
MIR
HDI
Africa
Latin America and the Caribbean
Asia
Europe
World
Oceania
Northern America
r = -0.8642, P = 0.0121

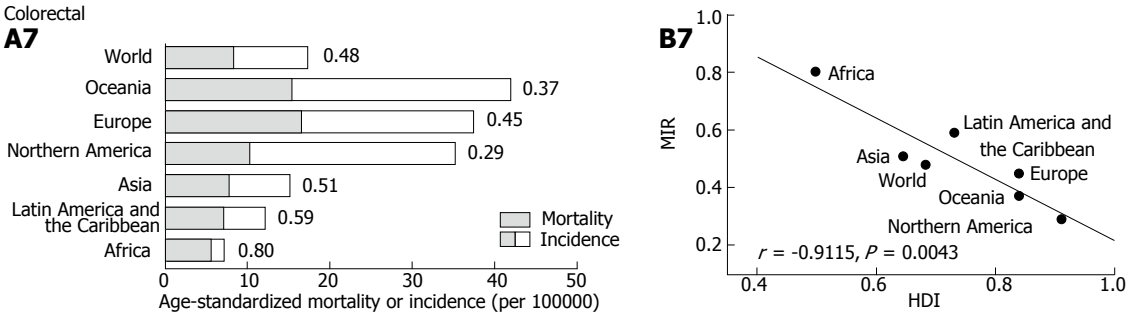


Figure 1 Association between the mortality-to-incidence ratio and human development at the regional level. A: Regional age-standardized mortality (grey) and incidence (white and grey) rates per 100000 individuals for gastrointestinal cancers. The mortality-to-incidence ratios (MIRs) are denoted; B: The regional MIRs of gastrointestinal cancers overall and stomach, liver and colorectal cancers correlate with the human development index (HDI). Best-fit lines by linear regression (solid) are indicated.

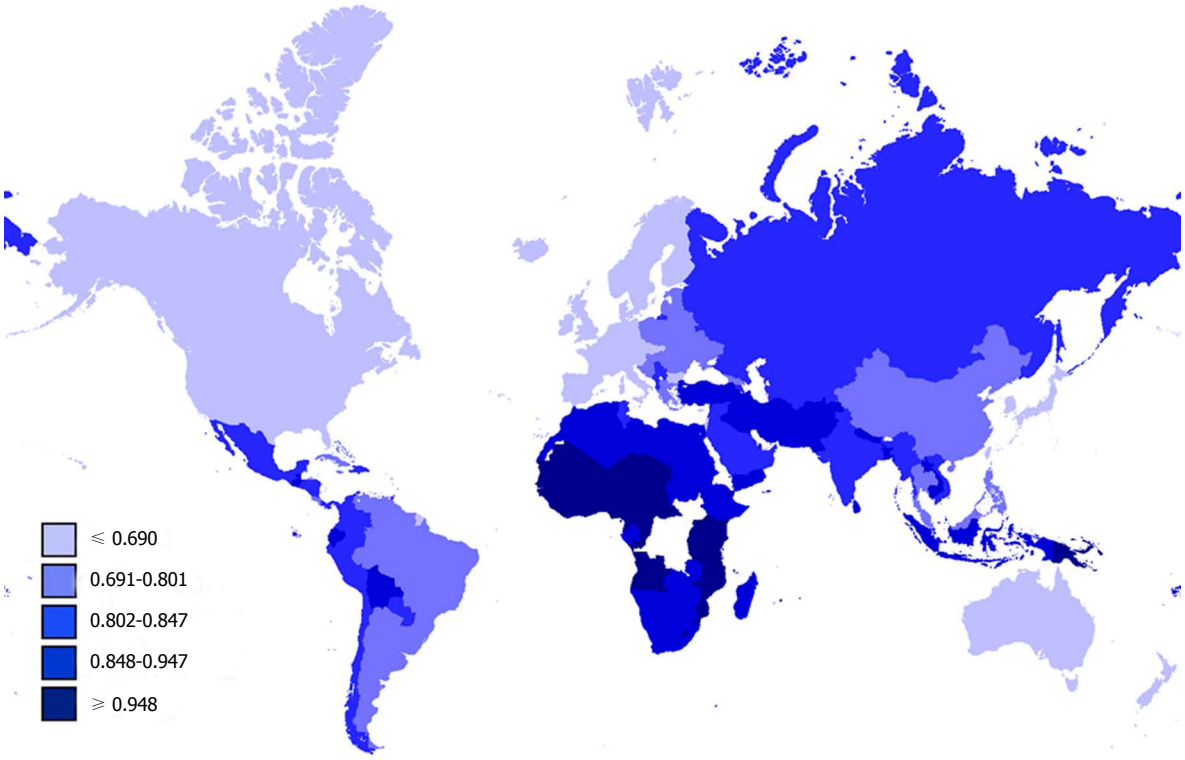


Figure 2 Global mortality-to-incidence ratios of gastrointestinal cancers. Mortality-to-incidence ratios (MIRs) varied across different countries.

0.620 ± 0.033 (95%CI), which was significantly lower than the corresponding values of countries with high, medium, and low HDIs (0.807 ± 0.018, 0.857 ± 0.021, and 0.953 ± 0.011, respectively; $P < 0.05$, Tukey-Kramer *post-hoc* test; Figure 4). Furthermore, there was a significant difference among the four groups in each specific cancer ($P < 0.001$, one-way ANOVA).

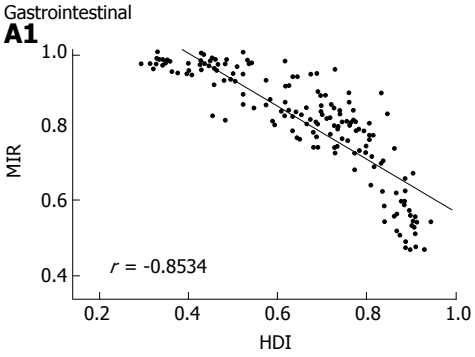
Prediction of MIR in individual United States states

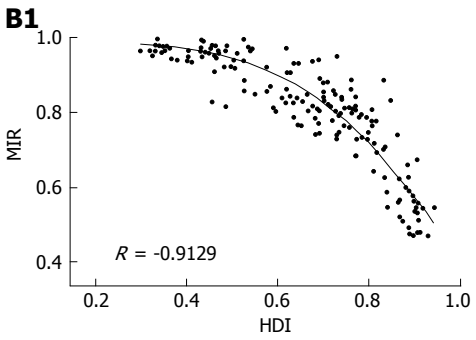
The individual HDIs of 51 United States states were calculated as previously described in HDR 2011. The HDI values in each state ranged from 0.847 to 0.962. To verify the effectiveness of the fitted models, the MIRs of gastrointestinal cancers in each of the United States states were predicted using respective best-fit equations. Except for 28 data points (9.93% of 282), the actual MIRs of all gastrointestinal cancers were mostly located in the prediction intervals *via* the best-fit non-linear regression models. In California, for example, the estimated HDI was 0.907 and the predicted MIR of gastrointestinal cancers was 0.560 ± 0.118 (95% prediction interval, 95%PI). The actual MIR calculated from the reported incidence and mortality was 0.533, and the difference between the actual and predicted MIRs (Δ_{MIR}) was -0.027 (23.1% of 95%PI). The actual MIRs of the six cancers were also in the 95%PI predicted by the respective regression fitting equations (Table 2).

DISCUSSION

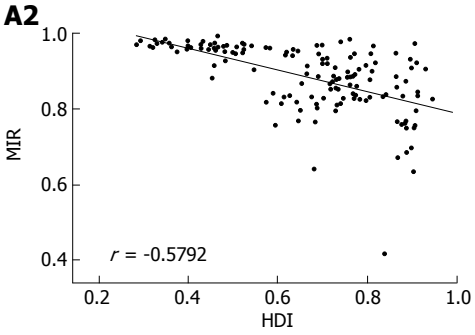
Gastrointestinal cancers have high incidence and mor-

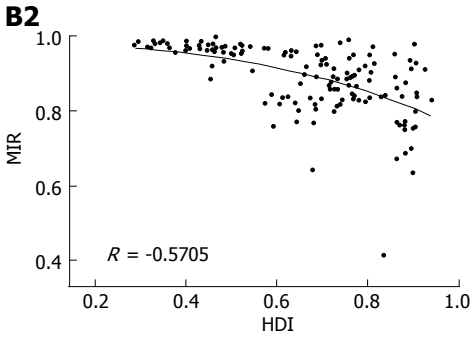
Gastrointestinal



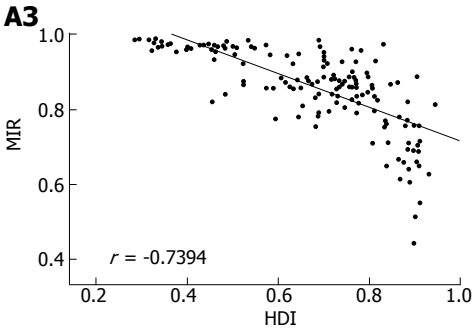


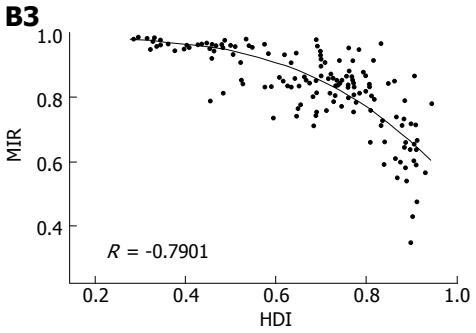
Esophageal



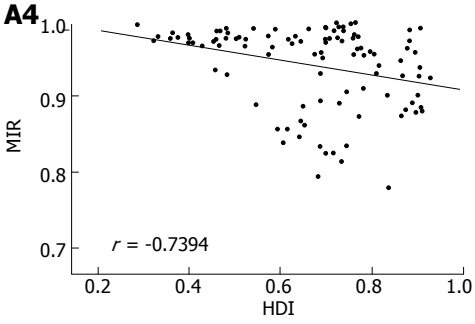


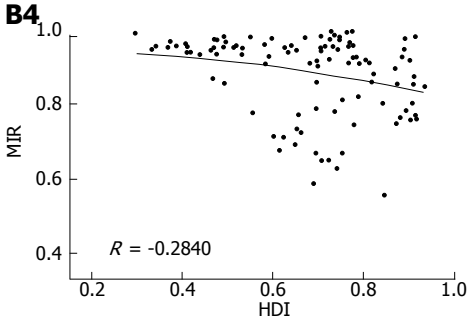
Stomach



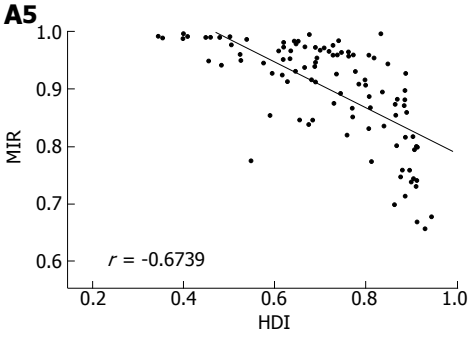


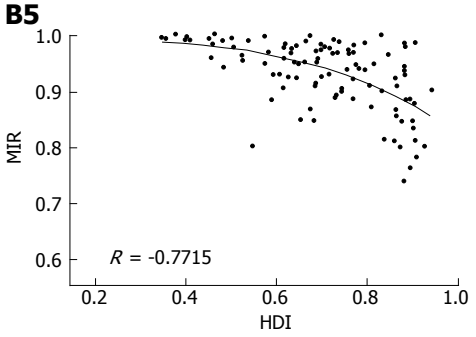
Pancreatic





Liver, gallbladder and pancreatic





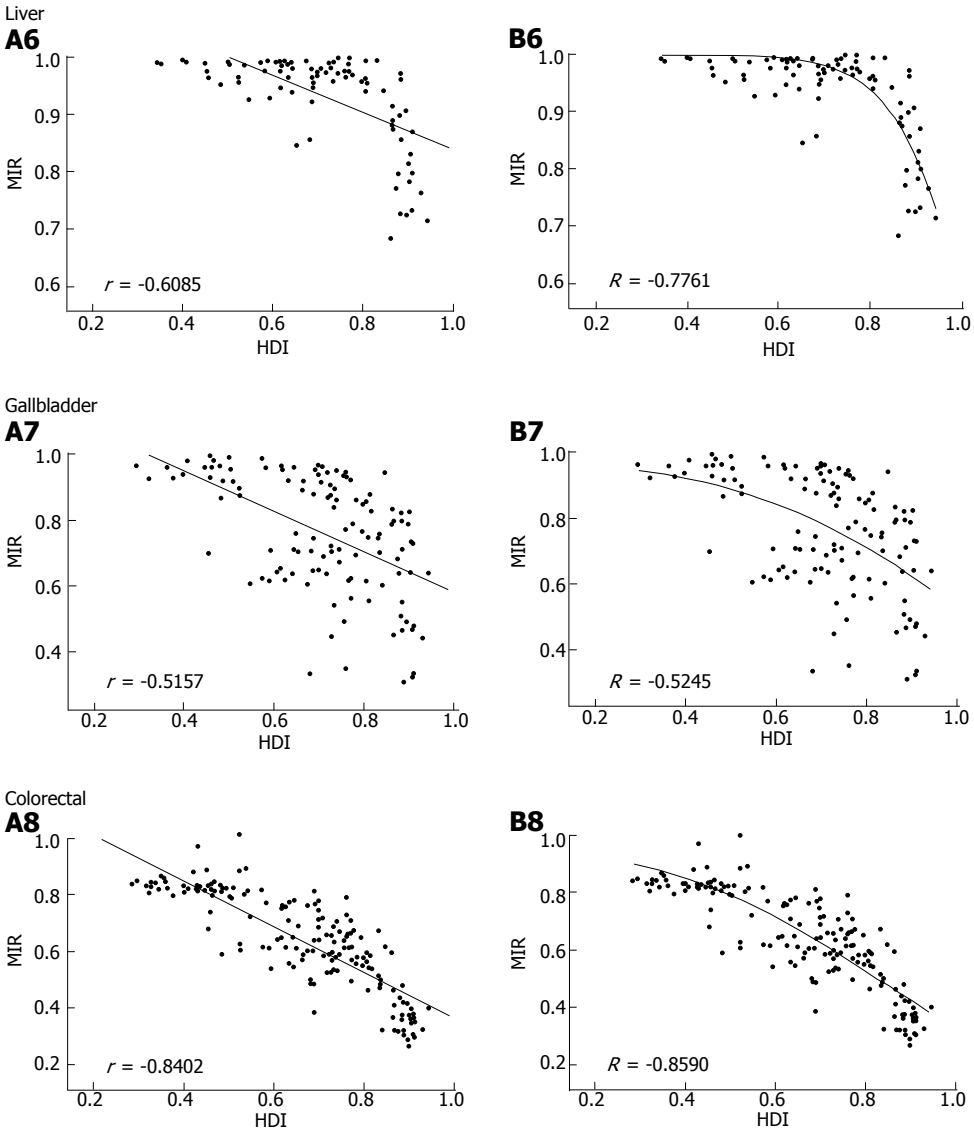


Figure 3 Correlation between national human development index and mortality-to-incidence ratio of gastrointestinal cancers *via* (A) linear or (B) non-linear regression. Best-fit line by regression (solid) is indicated, with *r* or *R* values denoted.

tality rates worldwide[1,24]. We found that both the incidence and mortality rates differed greatly from region to region. Interestingly, the ratio of the mortality rate to the incidence rate, *i.e.*, the MIR, appeared to be higher in less developed regions such as Africa. The development level was quantified by HDI, which is a composite measure of human development. Estimation of national HDI is based on the following parameters: a long and healthy life, access to knowledge, and a decent standard of living[18]. As an indicator of the socioeconomic factor of health, the HDI may serve as the gold standard for international comparisons of development.

MIR is derived as a surrogate indicator of the effectiveness of the health system. It has been proposed as an indirect measure of true biological differences in disease phenotypes or health system-related attributes such as screening, diagnostic modalities, treatment and follow-up[25,26]. An MIR-associated derivative form was identified as a good approximation of the 5-year relative survival for most, but not all, cancers[27]. The MIR is computed from age-standardized rates, and it also reflects a population-based approximation of survival[25]. Accordingly, it could be used to assess the diagnosis proficiency and treatment effectiveness in gastrointestinal cancers.

Africa, which had a relatively low HDI, showed a high MIR for most gastrointestinal cancers, whereas Northern America, which had a higher HDI, showed a low MIR. Furthermore, we found a significant inverse correlation between the regional MIR and corresponding HDIs in some, but not all, gastrointestinal cancers. However, only seven data points were included in the region-specific linear regression analysis. Insufficient sample size for regression analysis might cause fitting inaccuracy[28]. To avoid such inaccuracies, country-specific regression was performed. Linear regression analysis in this study revealed a correlation between the national HDI and MIR in all gastrointestinal cancers. The impact of hu-

Table 1 Results of regression in a cross-national analysis of human development index and mortality-to-incidence ratio

Cancer	Linear regression			Non-linear regression[1]		
	β	*P*	*r*	HDI_{50}	Slope	*R*
All gastrointestinal	-0.703	< 0.001	-0.853	0.946	2.746	-0.9129
Esophageal	-0.295	< 0.001	-0.579	1.362	1.344	-0.5705
Stomach	-0.536	< 0.001	-0.739	1.023	2.372	-0.7901
Pancreatic	-0.097	0.0019	-0.301	2.391	0.706	-0.2840
Liver	-0.322	< 0.001	-0.609	1.026	5.247	-0.7761
Gallbladder	-0.611	< 0.001	-0.516	1.027	1.697	-0.5245
Liver, gallbladder and pancreas	-0.216	< 0.001	-0.543	1.386	1.726	-0.5704
Colorectal	-0.808	< 0.001	-0.840	0.825	1.785	-0.8590

[1]Non-linear regression based on the "drug dose to inhibitory response" model, and human development index $(HDI)_{50}$ and slope were the two parameters used. $P < 0.01$ was defined as significantly non-zero β; ANOVA.

Table 2 Actual and predicted mortality-to-incidence ratio values of gastrointestinal cancers in California

Cancer	Incidence (ASR, per 100000)	Mortality (ASR, per 100000)	Actual MIR	Predicted MIR (95%PI)[1]	Δ_{MIR}
All gastrointestinal	74.3	39.6	0.533	0.560 ± 0.118	-0.027
Esophageal	3.8	3.4	0.895	0.803 ± 0.148	0.091
Stomach	7.4	4.3	0.581	0.653 ± 0.158	-0.072
Pancreatic	11.3	10.3	0.912	0.918 ± 0.104	-0.006
Liver	8.4	6.8	0.810	0.807 ± 0.101	0.002
Colorectal	43.4	14.8	0.341	0.416 ± 0.173	-0.075

[1]MIR values were predicted using California's human development index (HDI) (0.907) and the best-fit regression models. Δ_{MIR} = actual MIR-predicted MIR. ASR: Age-standardized rate; MIR: Age-standardized mortality-to-incidence ratio; PI: Prediction interval.

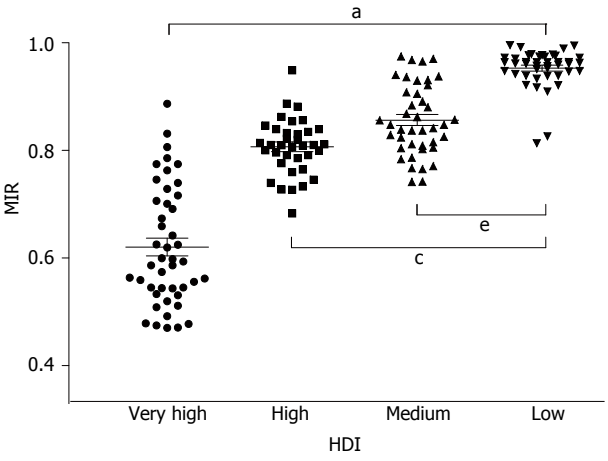


Figure 4 Overall mortality-to-incidence ratio of gastrointestinal cancers in four human development index groups. The mortality-to-incidence ratio (MIR) differs significantly among areas having very high, high, medium and low human development index (HDI); [a]$P < 0.05$ *vs* very high HDI areas; [c]$P < 0.05$ *vs* high HDI areas; and [e]$P < 0.05$ *vs* medium HDI areas; one-way ANOVA followed by the Tukey-Kramer *post-hoc* test.

man development on the effectiveness of healthcare for gastrointestinal cancers, as reflected by the relationship between HDI and MIR, was assumed to bear a similarity to the dose-dependent inhibitory response by anticancer drugs. HDI-to-MIR and dose-to-response patterns both have several characteristics in common, such as (1) MIR or response approaches 1 as HDI or dose approaches 0; (2) MIR or response decreases as HDI or dose increases; and (3) MIR or response approaches 0 as HDI or dose approaches infinity. Non-linear regression using the modified "drug dose to inhibition response" model confirmed the assumption and provided the HDI_{50} value, which was found to be a potential estimate of healthcare effectiveness on gastrointestinal cancers. The progress in screening, diagnostic and therapeutic techniques for colorectal cancer in recent decades[1,29] has resulted in an HDI_{50} of 0.825, which is the lowest value among all the gastrointestinal cancers investigated in this study.

Inequality in healthcare has been regarded as a major cause of variation in the effectiveness of cancer care[30], reflected by the inverse correlation between MIR and HDI. Although eliminating such disparities in healthcare has become the focus of an initiative of healthcare reform in many countries, quality improvement in medical care is not yet obvious[9]. Region- or country-specific disparities in cancer care still exist, even in highly developed countries[7]. Apart from healthcare inequality, the inverse correlation between HDI and MIR is also influenced by the factors such as socioeconomic conditions, lifestyle (particularly diet and tobacco use), and genetic variances among individuals or races[7,9]. Infection with *Helicobacter pylori*, hepatitis virus or other cancer-inducing micro-organisms is another risk factor for gastrointestinal cancers[31-33]. A very recent study analyzed world cancer burden by HDI groups and suggested disparities in cancer distributions[3]. We further demonstrated that HDI influenced cancer MIRs on a country level, which resembled the effect of drug dose on inhibitory response. Therefore, relatively high MIRs indicate the premature mortality from cancer in lower HDI areas. Healthcare disparities emphasize the need for efforts in cancer control in low human development settings.

Cancer health disparities occur not only between countries, but also within a single country[7,34,35]. The health outcomes in the United States were related to socioeconomic factors and racial diversity[9,36]. Health inequality between different socioeconomic levels also contributed to the health disparities observed in the United States. Therefore, we supposed that the observed association between HDI and MIR could be applied to United States states. Prediction based on the modified "drug dose to inhibition response" model turned out to be relatively satisfactory.

The methods used to estimate cancer-specific incidence and mortality rates at the national level in the GLOBOCAN database depend on the availability and accuracy of local data sources[3]. Despite the various provisos concerning data quality and methods of estimation, the estimates in GLOBOCAN are the most accurate that can be made at present, and may be used in the setting of priorities for cancer control actions in different regions and countries of the world[14]. Countries

without high quality data are usually those countries with lower development levels. Limiting analysis to high quality data could eliminate biases due to data inaccuracy, but would lead to excessive absence of epidemiological data in the less developed countries. Since our study aimed to show the disparities of cancer MIRs between low and high HDI countries, the data with relatively low quality were essential to this study and therefore remained in our analysis.

In conclusion, the results of this study obtained by collating excellent data resources revealed an inverse correlation between HDI and MIR at the regional and national levels. This association illustrated that more developed areas tend to have relatively more effective healthcare systems, resulting in low MIRs. Further prediction of the state-specific MIR of gastrointestinal cancers obtained using a fitted non-linear regression model revealed the potential application of HDI for estimation of the MIR.

COMMENTS

Background

Gastrointestinal cancer is a common, highly fatal disease. The expected cancer burden will be a serious public health problem in the coming decade, particularly in developing countries. However, little is known about healthcare disparities in individuals suffering from gastrointestinal cancers.

Research frontiers

There is little knowledge about the healthcare disparities in individuals suffering from gastrointestinal cancers. Inequality in healthcare has been regarded as a major cause of variation in the effectiveness of cancer care. Region- or country-specific disparities in cancer care still exist, even in highly developed countries.

Innovations and breakthroughs

According to the authors of this study, this study is the first to explore the exact relationship between the epidemiology of gastrointestinal cancers and area-specific development disparities. The authors showed the association between the mortality-to-incidence ratios (MIRs) and the human development index (HDI) at the regional and national levels using a modified "drug dose to inhibition response" model. Further prediction of the MIRs for individual United States states on the basis of best-fitted non-linear models showed little deviation from the actual MIRs in the United States.

Applications

Based on the modified "drug dose to inhibition response" model, more developed areas have relatively more effective healthcare systems, resulting in low MIRs. Prediction of the state-specific MIR of gastrointestinal cancers obtained using a fitted non-linear regression model revealed the potential application of HDI for estimation of the MIR.

Terminology

MIR is derived as a surrogate indicator of the effectiveness of the health system, and is proposed as an indirect measure of true biological differences in disease phenotypes or health system-related attributes such as screening, diagnostic modalities, treatment and follow-up. HDI is a composite measure of human development based on the following parameters: a long and healthy life, access to knowledge, and a decent standard of living.

Peer review

The authors, using the GLOBOCAN 2008 database, obtained age-standardized incidence and mortality rates for gastrointestinal cancers. They estimated the MIRs at the regional and national levels, and explored the association between the MIR and development levels as measured by the HDI. Furthermore, they have predicted state-specific MIRs in the United States from the estimated HDI using the fitted non-linear model. Finally, the authors have managed to show an inverse correlation between HDI and MIR at the regional and national levels and that more developed areas tend to have relatively more effective healthcare systems, resulting in low MIRs. Overall, the manuscript is very well written and well organized. The language is satisfactory and the tables along with the figures are well structured.

REFERENCES

1 **Siegel R**, Naishadham D, Jemal A. Cancer statistics, 2012. *CA Cancer J Clin* 2012; **62**: 10-29 [PMID: 22237781 DOI: 10.3322/caac.20138]

2 **Keighley MR**. Gastrointestinal cancers in Europe. *Aliment Pharmacol Ther* 2003; **18** Suppl 3: 7-30 [PMID: 14531737 DOI: 10.1046/j.0953-0673.2003.01722.x]

3 **Bray F**, Jemal A, Grey N, Ferlay J, Forman D. Global cancer transitions according to the Human Development Index (2008-2030): a population-based study. *Lancet Oncol* 2012; **13**: 790-801 [PMID: 22658655 DOI: 10.1016/S1470-2045(12)70211-5]

4 **Jemal A**, Thun MJ, Ries LA, Howe HL, Weir HK, Center MM, Ward E, Wu XC, Eheman C, Anderson R, Ajani UA, Kohler B, Edwards BK. Annual report to the nation on the status of cancer, 1975-2005, featuring trends in lung cancer, tobacco use, and tobacco control. *J Natl Cancer Inst* 2008; **100**: 1672-1694 [PMID: 19033571 DOI: 10.1093/jnci/djn389]

5 **Farmer P**, Frenk J, Knaul FM, Shulman LN, Alleyne G, Armstrong L, Atun R, Blayney D, Chen L, Feachem R, Gospodarowicz M, Gralow J, Gupta S, Langer A, Lob-Levyt J, Neal C, Mbewu A, Mired D, Piot P, Reddy KS, Sachs JD, Sarhan M, Seffrin JR. Expansion of cancer care and control in countries of low and middle income: a call to action. *Lancet* 2010; **376**: 1186-1193 [PMID: 20709386 DOI: 10.1016/S0140-6736(10)61152-X]

6 **Kapiriri L**. How effective has the essential health package been in improving priority setting in low income countries? *Soc Sci Med* 2013; **85**: 38-42 [PMID: 23540364 DOI: 10.1016/j.socscimed.2013.02.024]

7 **Jones LA**, Chilton JA, Hajek RA, Iammarino NK, Laufman L. Between and within: international perspectives on cancer and health disparities. *J Clin Oncol* 2006; **24**: 2204-2208 [PMID: 16682740 DOI: 10.1200/JCO.2005.05.1813]

8 **Kulendran M**, Leff DR, Kerr K, Tekkis PP, Athanasiou T, Darzi A. Global cancer burden and sustainable health development. *Lancet* 2013; **381**: 427-429 [PMID: 23388076 DOI: 10.1016/S0140-6736(13)60138-5]

9 **Fiscella K**, Franks P, Gold MR, Clancy CM. Inequality in quality: addressing socioeconomic, racial, and ethnic disparities in health care. *JAMA* 2000; **283**: 2579-2584 [PMID: 10815125 DOI: 10.1001/jama.283.19.2579]

10 **Betancourt JR**, Green AR, Carrillo JE, Ananeh-Firempong O. Defining cultural competence: a practical framework for addressing racial/ethnic disparities in health and health care. *Public Health Rep* 2003; **118**: 293-302 [PMID: 12815076]

11 **Danaei G**, Vander Hoorn S, Lopez AD, Murray CJ, Ezzati M. Causes of cancer in the world: comparative risk assessment of nine behavioural and environmental risk factors. *Lancet* 2005; **366**: 1784-1793 [PMID: 16298215 DOI: 10.1016/S0140-6736(05)67725-2]

12 **Baker EA**, Metzler MM, Galea S. Addressing social determinants of health inequities: learning from doing. *Am J Public Health* 2005; **95**: 553-555 [PMID: 15798106 DOI: 10.2105/AJPH.2005.061812]

13 **Braveman P**, Egerter S, Williams DR. The social determinants of health: coming of age. *Annu Rev Public Health* 2011; **32**: 381-398 [PMID: 21091195 DOI: 10.1146/annurev-publhealth-031210-101218]

14 **Ferlay J**, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer* 2010; **127**: 2893-2917 [PMID: 21351269 DOI: 10.1002/ijc.25516]

15 **Ferlay J**, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. GLOBOCAN 2008 v2.0, Cancer Incidence and Mortality

Worldwide: IARC CancerBase No. 10. Lyon: International Agency for Research on Cancer, 2010. Available: http: //globocan.iarc.fr
16 **US Cancer Statistics Working Group**. United States Cancer Statistics: 1999-2008 Incidence and Mortality Web-based Report. Atlanta: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute, 2012. Available: http: //www.cdc.gov/uscs
17 **Curado MP**, Edwards B, Shin HR, Storm H, Ferlay J, Heanue M, Boyle P. Cancer Incidence in Five Continents, Vol. IX. Lyon, IARC: IARC Scientific Publications, 2007: 160
18 **United Nations Development Programme**. Human Development Report 2011: Sustainability and Equity: A Better Future for All, 2012. Available: http: //hdr.undp.org
19 **Lewis K**, Burd-Sharps S. The Measure of America, 2010-2011: Mapping Risks and Resilience. New York: NYU Press, 2010
20 **US Department of Commerce, Bureau of Economic Analysis**. Real Per Capita Gross Domestic Product by State, 2012. Available: http: //bber.unm.edu/econ/st-gdp5.htm
21 **US Census Bureau**. Educational Attainment by State. 2009 American Community Survey. Available: http://www.census.gov/acs
22 **Barro RJ**, Lee JW. A new data set of educational attainment in the world, 1950-2010. National Bureau of Economic Research Working Paper Series No. 15902, 2010. Available: http://www.nber.org/papers/w15902
23 **United Nations Educational, Scientific and Cultural Organization (UNESCO)**. UNESCO Institute for Statistics: Data Centre. Available: http: //stats.uis.unesco.org
24 **Jemal A**, Center MM, DeSantis C, Ward EM. Global patterns of cancer incidence and mortality rates and trends. *Cancer Epidemiol Biomarkers Prev* 2010; **19**: 1893-1907 [PMID: 20647400 DOI: 10.1158/1055-9965.EPI-10-0437]
25 **Hébert JR**, Daguise VG, Hurley DM, Wilkerson RC, Mosley CM, Adams SA, Puett R, Burch JB, Steck SE, Bolick-Aldrich SW. Mapping cancer mortality-to-incidence ratios to illustrate racial and sex disparities in a high-risk population. *Cancer* 2009; **115**: 2539-2552 [PMID: 19296515 DOI: 10.1002/cncr.24270]
26 **Patel AR**, Prasad SM, Shih YC, Eggener SE. The association of the human development index with global kidney cancer incidence and mortality. *J Urol* 2012; **187**: 1978-1983 [PMID: 22498216 DOI: 10.1016/j.juro.2012.01.121]
27 **Asadzadeh Vostakolaei F**, Karim-Kos HE, Janssen-Heijnen ML, Visser O, Verbeek AL, Kiemeney LA. The validity of the mortality to incidence ratio as a proxy for site-specific cancer survival. *Eur J Public Health* 2011; **21**: 573-577 [PMID: 20813895 DOI: 10.1093/eurpub/ckq120]
28 **Dupont WD**, Plummer WD. Power and sample size calculations for studies involving linear regression. *Control Clin Trials* 1998; **19**: 589-601 [PMID: 9875838 DOI: 10.1016/S0197-2456(98)00037-3]
29 **Lieberman D**. Progress and challenges in colorectal cancer screening and surveillance. *Gastroenterology* 2010; **138**: 2115-2126 [PMID: 20167216 DOI: 10.1053/j.gastro.2010.02.006]
30 **Murray SA**, Grant E, Grant A, Kendall M. Dying from cancer in developed and developing countries: lessons from two qualitative interview studies of patients and their carers. *BMJ* 2003; **326**: 368 [PMID: 12586671 DOI: 10.1136/bmj.326.7385.368]
31 **Perz JF**, Armstrong GL, Farrington LA, Hutin YJ, Bell BP. The contributions of hepatitis B virus and hepatitis C virus infections to cirrhosis and primary liver cancer worldwide. *J Hepatol* 2006; **45**: 529-538 [PMID: 16879891 DOI: 10.1016/j.jhep.2006.05.013]
32 **Uemura N**, Okamoto S, Yamamoto S, Matsumura N, Yamaguchi S, Yamakido M, Taniyama K, Sasaki N, Schlemper RJ. Helicobacter pylori infection and the development of gastric cancer. *N Engl J Med* 2001; **345**: 784-789 [PMID: 11556297 DOI: 10.1056/NEJMoa001999]
33 **Yan TL**, Hu QD, Zhang Q, Li YM, Liang TB. National rates of Helicobacter pylori recurrence are significantly and inversely correlated with human development index. *Aliment Pharmacol Ther* 2013; **37**: 963-968 [PMID: 23550618 DOI: 10.1111/apt.12293]
34 **Gouws L**, Eedes D, Marais E, Valodia P, De Villiers M. Revolutionising cancer care in South Africa. *Lancet Oncol* 2012; **13**: 447-448 [PMID: 22554538 DOI: 10.1016/S1470-2045(12)70159-6]
35 **Fiscella K**, Franks P, Doescher MP, Saver BG. Disparities in health care by race, ethnicity, and language among the insured: findings from a national sample. *Med Care* 2002; **40**: 52-59 [PMID: 11748426]
36 **Braveman PA**, Cubbin C, Egerter S, Williams DR, Pamuk E. Socioeconomic disparities in health in the United States: what the patterns tell us. *Am J Public Health* 2010; **100** Suppl 1: S186-S196 [PMID: 20147693 DOI: 10.2105/AJPH.2009.166082]

P- Reviewers Akbulut S, Koukourakis GV, Motoo Y
S- Editor Gou SX **L- Editor** A **E- Editor** Zhang DN

百世登

Baishideng®

Published by **Baishideng Publishing Group Co., Limited**
Flat C, 23/F., Lucky Plaza,
315-321 Lockhart Road, Wan Chai, Hong Kong, China
Fax: +852-65557188
Telephone: +852-31779906
E-mail: bpgoffice@wjgnet.com
http://www.wjgnet.com

ISSN 1007-9327

Baishideng Publishing Group Co., Limited