

Disparities in incidence and mortality of pancreatic cancer in the world

Yousef Khani¹, Masoumeh Arabsalmani², Reza Pakzad³, Mahshid Ghoncheh⁴, Abdollah Mohammadian-Hafshejani⁵, Hamid Salehiniya^{6,7,*}

¹Alborz University of Medical Sciences, Karaj, Iran

²Health Promotion Research Center, Department of Epidemiology and Biostatistics, School of Public Health, Zahedan University of Medical Sciences, Zahedan, Iran

³Student Research committee, Ilam University of Medical Sciences, Ilam, Iran

⁴Shahid Beheshti University of Medical Sciences, Tehran, Iran

⁵Department of Epidemiology and Biostatistics, School of Public Health, Shahrekord University of Medical Sciences, Shahrekord, Iran

⁶Zabol University of Medical Sciences, Zabol, Iran

⁷Department of Epidemiology and Biostatistics, Tehran University of medical sciences, Tehran, Iran

For correspondence:

alesaleh70@yahoo.com

Competing interests: The authors declare that no competing interests exist.

Received: 17 August 2017

Accepted: 19 November 2017

Published: 26 February 2018

Copyright The Author(s) 2018. This article is published with open access by **BioMedPress**.

This article is distributed under the terms of the Creative Commons Attribution License (CC-BY 4.0) which permits any use, distribution, and reproduction in any medium, provided the original author(s) and the source are credited.

Abstract

Background: Pancreatic cancer (PC) is as the twelfth most frequent cancer and the seventh most important cause of mortality by reason of cancer in the world. Being informed about the incidence and mortality of this cancer and the potential role of development is useful in health policy. The aim of this research is investigating disparities in the incidence and mortality of PC in the world countries in the year 2012. **Methods:** This study was an ecologic study in the World for assessing the correlation between Human Development Index (HDI) and its details (Gross national income (GNI) per capita, average years of schooling and life expectancy at birth) with age-standardized incidence rate (ASIR) and age-standardized mortality rate (ASMR) of PC. **Results:** In total, 337872 new cases of PC occurred in 2012 around the world, that 178116 and 159711 cases take happen in men and women respectively, also at the same year 330391 deaths of PC occurred, that 173,827 and 156564 cases were in men and women. In assessment the relationship between HDI and ASIR and ASMR of PC there is significant positive correlation equal to 0.767 ($p < 0.001$) between HDI and ASIR of PC, and a significant positive correlation equal to 0.776 ($p < 0.001$) between HDI and ASMR of PC.

Conclusion: The incidence and mortality of PC has a significant positive correlation with the Human Development Index.

Keywords

Disparities, Incidence, Mortality, Pancreatic cancer, World

Introduction

Gastrointestinal cancers have high incidence and mortality rate worldwide (Jemal et al., 2010a; Siegel et al., 2012). pancreatic cancer (PC) is one of the cancers that is identified as the twelfth common cancer and the seventh death cause due to cancer worldwide so that its incidence was 12.2 and death due to that was 10.9 per hundred thousand people in 2014 (Howlader et al., 2011). The highest incidence of PC is observed in Northern Europe and America and the lowest incidence is seen in African countries (Altekruse et al., 2010; Curado et al., 2007; Malvezzi et al., 2013; Pakzad et al., 2016). Totally, 2/3 of PC death cases occur in world developed countries (Parkin et al., 2005). Therefore it's known as the fifth deadly cancer in developed countries in 2000 (Schwartz and Reis, 2000).

Despite the diagnosis of more than 400000 PC new cases in year, it is about 30 years that its 5-year survival remains low and less than 4 percent is reported for this cancer (Baxter et al., 2007; Jemal et al., 2010b; Stats, 2012). The global burden of PC is increasing due to aging, population growth and high-risk behaviors especially smoking and world developed countries allocated the greatest burden of the disease (Jemal et al., 2011). As the country is more advanced and has higher-income, non-communicable diseases such as cancers include more death causes (Mathers et al., 2005). However, the cause of incidence and prevalence of PC is due to its risk factors including age over 70, smoking, race, obesity, alcohol, red and processed meat consumption, chronic pancreatitis, diabetes and chronic infections (*hepatitis B*, *hepatitis C*, *Helicobacter pylori*) different distribution that is believed to be higher in developed countries (Keane et al., 2014; Lowenfels and Maisonneuve, 2006; Society, 2013). The society health is the outcome of several complex, different and constantly changing factors (Organization, 2000). So, it should be cared, intervened and managed and be in the place of social and economic development level, continuously (Organization, 2000). Therefore, one of the good public health and its related factors indicator is the Human Development Index (HDI) (Bray et al., 2012). This index is a useful classification for cancer globalization (Bray et al., 2012). The HDI was determined as a comparing index for countries in 3 fields of human dimension by the UNDP (United Nations Development Program) in 1990 (Ravallion, 1997). Three dimensions of HDI

include long and healthy life, access to knowledge and good living standards (Bray et al., 2012). Each of these factors are measured by life expectancy at birth, education and GDP per capita, respectively (Bray et al., 2012).

An estimated 5-year incidence of all cancers according to HDI regions showed that areas with high and very high HDI, have allocated highest prevalence of 21.31% to themselves despite having only 6.1% of the world's population and this ratio was 9.237% and 1.993 % for medium and low HDI regions, respectively (Bray et al., 2013).

PC among other cancers has different incidence and mortality that varies around the world and it is due to development and the diagnostic and therapeutic status of countries (Bray, 2014; Forman et al., 2014; Franceschi and Wild, 2013; Kanavos, 2006).

However, a comprehensive study that could examine the association between HDI and age-standardized incidence rate (ASIR) and age-standardized mortality rate (ASMR) of PC has not been conducted. Because of this point that knowledge about the ASIR and ASMR of cancers and the potential role of development is useful in health planning, this study conducted with the purpose of determining the ASIR and ASMR of PC and its correlation with the HDI in the world in 2012.

Materials-Methods

This study was an ecologic study in the World for assessing the correlation between HDI and its details (Gross national income (GNI) per capita, average years of schooling and life expectancy at birth) with age-standardized incidence rate (ASIR) and age-standardized mortality rate (ASMR) of PC. Detailed descriptions of the methods used in collection of data about cancer incidence and mortality in GLOBOCAN (Ferlay J et al., 2016), and HDI (Malik, 2013), and Statistical analysis of this study have been provided in previous reports (Arabsalmani et al., 2017; Ghoncheh et al., 2016; Hassanipour-Azgomi et al., 2016; Mohammadian et al., 2017; Mohammadian et al., 2016; Rafiemanesh et al., 2016; Razi et al., 2016; Shuja et al., 2017; Tiyuri et al., 2017).

Results

The frequency of incidence of PC

In total, 337872 PC cases have been occurred worldwide in 2012 that 178161 and 159711 cases were in men and women respectively (Sex Ratio = 1.11). From all occurred cases, about 174344 cases were in countries with very high HDI,

55638 cases were in countries with high HDI, 98632 cases were in countries with medium HDI, and 9108 cases occurred in countries with low HDI. Five countries with the highest sum of PC include: China (65727), America (42885), Japan (32899), Germany (16451) and Russia (14512). Five countries with highest sum of PC case in men include: China (39299), America (21713), Japan (17013), Germany (7972) and Russia (7206), and in women include: China (26428), America (21172), Japan (15886), Germany (8479), and Russia (7306).

The ASIR of PC

The ASIR of PC per hundred thousand people in the world was 4.2 (in men 4.9 and in women 3.6). The ASIR of PC in very high HDI regions was 7.2, in high HDI regions was 4.6, in medium HDI regions was 2.7, and in low HDI regions was 1.2. Five countries with the highest ASIR of PC are: Czech Republic (9.7), Slovakia (9.4), Armenia (9.3), Hungary (9.3), and Slovenia (8.8), respectively. Five countries with the highest ASIR of PC for men were: Armenia (11.9), Czech Republic (11.9), Slovakia (11.5), Hungary (11.5), and FYR Macedonia (11.5), and in women include: Czech Republic (7.9), Slovenia (7.8), Slovakia (7.8), Denmark (7.7), and Finland (7.6).

The frequency of mortality of PC

Nowadays, 330391 deaths happened because of PC around the world in 2012 that about 173827 cases were men and 156564 cases were women (Sex Ratio = 1.11). Total number of mortality from PC was 170497 cases in very high HDI region, 56474 cases in high HDI region, 94447 cases medium HDI region, and 8822 cases in low HDI region. Five countries having the highest ASMR of PC were: China (63662), America (41509), Japan (31046), Russia (16371), and Germany (16188). Five countries having the highest ASMR of PC in men were: China (37775) cases, America (21005), Japan (15809), Russia (8168), and Germany (7900), and in women include: China (25887), America (20504), Japan (15237), Germany (8288), and Russia (8203).

The ASMR of PC

The ASMR of PC per hundred thousand people in the world was 4 (in men 4.7 and in women 3.4). The ASMR of PC very high HDI regions was 6.8, in high HDI regions was 4.6, in countries with medium HDI regions was 2.6, in low HDI regions was 1.2. Five countries having the highest ASMR of PC per hundred thousand people were: Armenia (8.9), Hungary (8.8), Czech Republic (8.7), Slovakia (8.5), and French Guiana (8.1). Five countries having the highest ASMR of PC in men were: YR Macedonia (11.8), Armenia (11.6), Hungary (11.1), Estonia (10.6), and Latvia (10.4), and in women include: Slovakia (7.6), Czech Republic (7.2), Slovenia (7.2), Hungary (7), and French Guiana (7).

The association between the ASIR of PC and the HDI

In assessment the relationship between ASIR of PC and the HDI, a significant positive correlation equal to 0.767 ($p < 0.001$) was observed. There were positive correlation between ASIR of PC and components of the HDI (with the level of income equal to 0.517 ($p < 0.001$), with average years of education equal to 0.762 ($p < 0.001$) and with life expectancy at birth equal to 0.657 ($p < 0.001$) (**Fig. 1**).

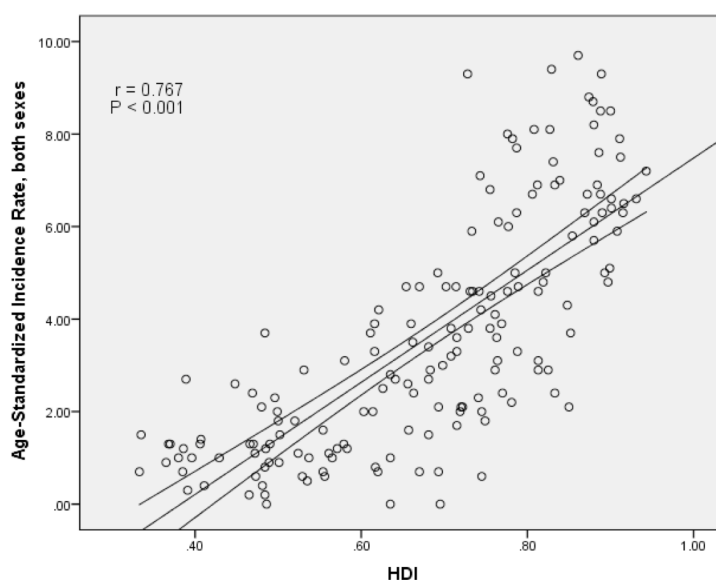


Figure 1. The relationship between standardized incidence rate and the Human Development Index.

The association between the ASMR of PC and the HDI

In topic of the relationship between ASMR of PC and the HDI, a significant positive correlation equivalent to 0.776 ($p < 0.001$) was observed. There were positive correlation between ASMR of PC and components of the HDI (with the level of income equal to 0.518 ($p < 0.001$), with average years of education equal to 0.769 ($p < 0.001$) and with life expectancy at birth equal to 0.666 ($p < 0.001$) (**Fig. 2**).

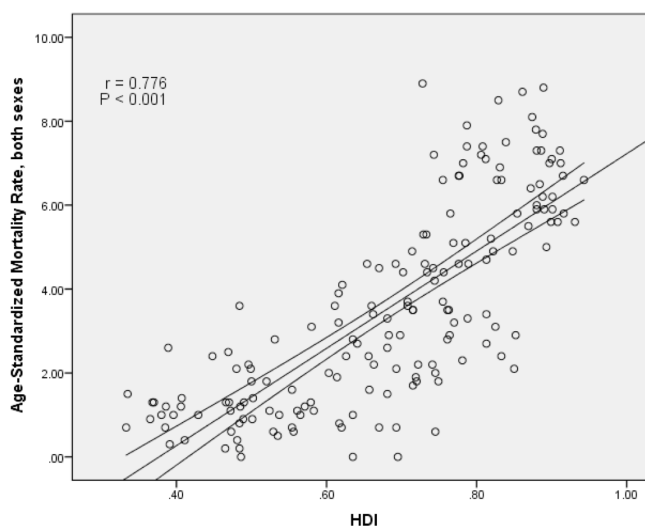


Figure 2. The relationship between standardized mortality rate and the Human Development Index.

Discussion

PC has allocated the mortality rate of 39.4 and incidence rate of 54.9 cases per 100,000 people of the population to itself in 2008 (Hu et al., 2013). Also, according to a cohort study that has been conducted in 2000-2010, incidence of PC has increased 3% annually (Keane et al., 2014).

In this study, ASIR of PC was estimated 4.2 per hundred thousand people in the world and has a positive correlation of 0.767 with the HDI that this association is statistically significant. Czech Republic, Slovakia, Armenia, Hungary and Slovenia were 5 countries that allocated the highest rate of incidence to them. This is in condition that every five country is located in group of countries with high and very high HDI.

According to studies, the incidence of PC in industrial developed countries is more than developing ones. In a systematic study which Rio conducted in 1975-2007, it's estimated that the highest incidence of PC belongs to Northern Europe and America (Altekruse et al., 2010). Estimating incidence age specified rates (ASRs) is 10.1 for both sexes per hundred thousand people based on gender in Europe in 2012 (Ferlay et al., 2013). While, the same rate is estimated to be 3.2 per hundred thousand people in Asia in 2012 (Pourhoseingholi et al., 2014).

The diseases incidence is associated with their risk factors (Ward et al., 2004). Age and smoking are strong factors that always are reported (Bonelli et al., 2003; Fuchs et al., 1996; Hassan et al., 2007; Hippisley-Cox and Coupland, 2012; Larsson et al., 2005; Muscat et al., 1997; Silverman et al., 1994; Stapley et al., 2012; Vaeian et al., 2015). So that by increasing the number of years of life that passes by smoking cigarettes, the risk to catch PC also boost per person (Keyghobadi et al., 2015). Variety diet could be mentioned that other risk factors. Also several studies have shown that the total amount of calorie and probably fat increase in the diet and obesity, may arise the risk of PC (Ghadirian et al., 1990). Finally, we can say that the high level of these factors in developed countries has led to a greater incidence of PC.

The ASMR of PC was 4 per hundred thousand people in the world in this study and a positive correlation of 0.776 was seen between ASMR of PC and the HDI that this was statistically significant. 5 countries having the highest ASMR of PC are: Armenia, Hungary, Czech Republic, Slovakia, and French Guiana. So that Armenia and French Guiana are located in group of countries with high HDI and three other ones in countries with very high HDI.

Also, due to the results of studies that have been conducted between the years 1993-95, it's estimated that PC was the sixth cause of death among cancers in the United States of America and the United Kingdom (Berman, 1995; Gold and Goldin, 1998). Also in 2002, according to cancer mortality in the world, the incidence of PC is estimated to be 6-8 per 100 thousand people in men and 4-6

per 100 thousand people in women in developed countries such as Australia and Japan (Parkin et al., 2005).

In many Asian countries such as Korea, Singapore and China that have a high HDI, PC mortality is high too (Parkin et al., 2005; Wang et al., 2003).

In this study, the incidence in men is 4.9 and in women is 3.6 per hundred thousand people and the mortality is 4.7 for men and 3.4 per hundred thousand in women.

However, in all cancer centers an association is reported between PC and gender (Bramhall et al., 1995). The prevalence of this disease in men is more than women (Bramhall et al., 1995). So that due to global estimation in 2012, the rate of mortality to incidence of cancer in both sexes is almost close (0.94 / 0.97) (Valean et al., 2015). Although the incidence in men is generally a little more than women, the high incidence and mortality of PC in men has a variety of causes such as increase in smoking (Muniraj et al., 2013), diet (high fat and protein, low fruit and vegetable consumption), consumption of coffee, alcohol and Job hazards (insecticides, aluminum, nickel and acrylamide) that these things cases are seen more in men's lifestyle (Greene et al., 2008; Lowenfels et al., 1997). While, elevated estrogen in women acts as a death cause lowering agent of PC (Greene et al., 2008).

In this study, a positive correlation was observed between the ASIR and ASMR of PC and life expectancy at birth. Also it has been seen in several studies that with increasing age, the incidence of PC dramatically raised up increases (Ferlay et al., 2015; Hartwig et al., 2009; Neesse et al., 2010; Sasson et al., 2002; Toriola et al., 2014). So that the cause for increasing incidence of this cancer in developed countries, may be a reflection of aging (Pakzad et al., 2015c; Smith et al., 2009). In this study, a significant positive correlation was seen between the ASIR and ASMR of PC with mean education level. Also in Bosetti et al study, the incidence is increased with increasing level of education (Bosetti et al., 2012). Also about the PC mortality, the mortality is increased in less educated individuals with age under 15 years (Jemal et al., 2013).

In this study, a significant positive correlation was seen between the ASIR and ASMR of PC with average income level. According to several studies, patients with high socio-economic status and PC have good chance for surgical treatment but has no significant impact on patient survival (Bakens et al., 2015; Michaud, 2004; Pakzad et al., 2015a, b). Surgery as the only treatment option for long-term survival in patients with PC as an indicator of the impact of social and economic inequality, is a good witness that socioeconomic status has the lowest effect on patient's survival (Bakens et al., 2015; Michaud, 2004). Because the average survival of PC is 3-6 months since diagnosis without treatment that has up to 23 months increase after surgery and adjunctive therapies (Neoptolemos et al., 2001; Neoptolemos et al., 2010). That's why we can say that the incidence of PC is near to its mortality rate (Michaud, 2004; Ryu et al., 2010). Although in

several studies observed that patients with higher income have more improvement than others, but this improvement is very low. Therefore, we cannot consider its protective effects very important (Neoptolemos et al., 2001; Neoptolemos et al., 2010).

Conclusion

We can say that, the incidence and mortality of PC has a significant positive correlation with the Human Development Index and its components.

Abbreviations

ASIR: Age-Standardized Incidence Rate
ASMR: Age-Standardized Mortality Rate
HDI: Human Development Index
PC: Pancreatic cancer

Author Contribution

All authors contributed to the design of the research. Y KH, M A , R P, and M GH extracted the data and summarized it. All authors drafted the first version. Y KH, A MH and HS edited the first draft. All authors reviewed, commented and approved the final draft.

References

- Altekruse, S. F., Kosary, C. L., Krapcho, M., Neyman, N., Aminou, R., Waldron, W., & Cho, H. (2010). *SEER cancer statistics review, 1975-2007* (p. 7). Bethesda, MD: National Cancer Institute.
- Arabsalmani, M., Mohammadian-Hafshejani, A., Ghoncheh, M., Hadadian, F., Towhidi, F., Vafaei, K., & Salehiniya, H. (2017). Incidence and mortality of kidney cancers, and human development index in Asia; a matter of concern. *Journal of Nephropathology*, 6(1), 30-42. <https://doi.org/10.15171/jnp.2017.06> PMID:28042551
- Bakens, M., van Gestel, Y., Bongers, M., Lemmens, V., & de Hingh, I. (2015). Socio-economic status influences chance of undergoing surgical treatment for pancreatic cancer in The Netherlands. *Pancreatology*, 15(3), S101. <https://doi.org/10.1016/j.pan.2015.05.366>

- Baxter, N. N., Whitson, B. A., & Tuttle, T. M. (2007). Trends in the treatment and outcome of pancreatic cancer in the United States. *Annals of Surgical Oncology*, 14(4), 1320-1326. <https://doi.org/10.1245/s10434-006-9249-8> PMID:17225980
- Berman, P. M. (1995). Gastroenterology: Clinical Science and Practice. *Journal of the American Medical Association*, 274(1), 79-79. <https://doi.org/10.1001/jama.1995.03530010093042> PMID:7996658
- Bonelli, L., Aste, H., Bovo, P., Cavallini, G., Felder, M., Gusmaroli, R., . . . Pugliese, V. (2003). Exocrine pancreatic cancer, cigarette smoking, and diabetes mellitus: A case-control study in northern Italy. *Pancreas*, 27(2), 143-149. <https://doi.org/10.1097/00006676-200308000-00007> PMID:12883263
- Bosetti, C., Lucenteforte, E., Silverman, D. T., Petersen, G., Bracci, P. M., Ji, B. T., . . . La Vecchia, C. (2012). Cigarette smoking and pancreatic cancer: An analysis from the International Pancreatic Cancer Case-Control Consortium (Panc4). *Annals of Oncology : Official Journal of the European Society for Medical Oncology*, 23(7), 1880-1888. <https://doi.org/10.1093/annonc/mdr541> PMID:22104574
- Bramhall, S. R., Allum, W. H., Jones, A. G., Allwood, A., Cummins, C., & Neoptolemos, J. P. (1995). Treatment and survival in 13,560 patients with pancreatic cancer, and incidence of the disease, in the West Midlands: An epidemiological study. *British Journal of Surgery*, 82(1), 111-115. <https://doi.org/10.1002/bjs.1800820137> PMID:7881926
- Bray, F. (2014). Transitions in human development and the global cancer burden. *World cancer report*, 54-68.
- Bray, F., Ren, J. S., Masuyer, E., & Ferlay, J. (2013). Global estimates of cancer prevalence for 27 sites in the adult population in 2008. *International Journal of Cancer*, 132(5), 1133-1145. <https://doi.org/10.1002/ijc.27711> PMID:22752881
- 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. *The Lancet. Oncology*, 13(8), 790-801. [https://doi.org/10.1016/S1470-2045\(12\)70211-5](https://doi.org/10.1016/S1470-2045(12)70211-5) PMID:22658655
- Curado, M.-P., Edwards, B., Shin, H. R., Storm, H., Ferlay, J., Heanue, M., & Boyle, P. (2007). *Cancer incidence in five continents* (Vol. IX). IARC Press, International Agency for Research on Cancer.
- Ferlay, J., Soerjomataram, I., Dikshit, R., Eser, S., Mathers, C., Rebelo, M., Parkin, D.M., Forman, D. and Bray, F. (2016). GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer; 2013. Available from: <http://globocan.iarc.fr>, accessed on 2/2/2016.
- Ferlay, J., Steliarova-Foucher, E., Lortet-Tieulent, J., Rosso, S., Coebergh, J.W.W., Comber, H., Forman, D. and Bray, F. (2013). Cancer incidence and mortality patterns in Europe: Estimates for 40 countries in 2012. *European Journal of Cancer*, 49(6), 1374-1403. <https://doi.org/10.1016/j.ejca.2012.12.027> PMID:23485231
- Ferlay, J., Soerjomataram, I., Dikshit, R., Eser, S., Mathers, C., Rebelo, M., Parkin, D.M., Forman, D. and Bray, F. (2015). Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012. *International Journal of Cancer*, 136(5), E359-E386. <https://doi.org/10.1002/ijc.29210> PMID:25220842
- Forman, D., Ferlay, J., Stewart, BW, & Wild, CP. (2014). The global and regional burden of cancer. *World cancer report*, 16-53.

- Franceschi, S., & Wild, C. P. (2013). Meeting the global demands of epidemiologic transition - the indispensable role of cancer prevention. *Molecular Oncology*, 7(1), 1-13. <https://doi.org/10.1016/j.molonc.2012.10.010> PMID:23218182
- Fuchs, C.S., Colditz, G.A., Stampfer, M.J., Giovannucci, E.L., Hunter, D.J., Rimm, E.B., Willett, W.C. and Speizer, F.E. (1996). A prospective study of cigarette smoking and the risk of pancreatic cancer. *Archives of Internal Medicine*, 156(19), 2255-2260. <https://doi.org/10.1001/archinte.1996.00440180119015> PMID:8885826
- Ghadirian, P., Thouez, J. P., & PetitClerc, C. (1991). International comparisons of nutrition and mortality from pancreatic cancer. *Cancer Detection and Prevention*, 15(5), 357-362. PMID:1751946
- Ghoncheh, M., Mohammadian, M., Mohammadian-Hafshejani, A., & Salehiniya, H. (2016). The Incidence and Mortality of Colorectal Cancer and Its Relationship With the Human Development Index in Asia. *Annals of Global Health*, 82(5), 726-737. <https://doi.org/10.1016/j.aogh.2016.10.004> PMID:28283123
- Gold, E. B., & Goldin, S. B. (1998). Epidemiology of and risk factors for pancreatic cancer. *Surgical Oncology Clinics of North America*, 7(1), 67-91. PMID:9443987
- Greene, Michael F, Creasy, Robert K, Resnik, Robert, Iams, Jay D, Lockwood, Charles J, & Moore, Thomas. (2008). *Creasy and Resnik's maternal-fetal medicine: principles and practice*: Elsevier Health Sciences.
- Hartwig, W., Hackert, T., Hinz, U., Hassenpflug, M., Strobel, O., Büchler, M. W., & Werner, J. (2009). Multivisceral resection for pancreatic malignancies: Risk-analysis and long-term outcome. *Annals of Surgery*, 250(1), 81-87. <https://doi.org/10.1097/SLA.0b013e3181ad657b> PMID:19561478
- Hassan, M. M., Bondy, M. L., Wolff, R. A., Abbruzzese, J. L., Vauthey, J.-N., Pisters, P. W., . . . Li, D. (2007). Risk factors for pancreatic cancer: Case-control study. *The American Journal of Gastroenterology*, 102(12), 2696-2707. <https://doi.org/10.1111/j.1572-0241.2007.01510.x> PMID:17764494
- Hassanipour-Azgomi, S., Mohammadian-Hafshejani, A., Ghoncheh, M., Towhidi, F., Jamehshorani, S., & Salehiniya, H. (2016). Incidence and mortality of prostate cancer and their relationship with the Human Development Index worldwide. *Prostate International*, 4(3), 118-124. <https://doi.org/10.1016/j.pnil.2016.07.001> PMID:27689070
- Hippisley-Cox, J., & Coupland, C. (2012). Identifying patients with suspected pancreatic cancer in primary care: Derivation and validation of an algorithm. *The British Journal of General Practice*, 62(594), e38-e45. <https://doi.org/10.3399/bjgp12X616355> PMID:22520674
- Howlader, N., Noone, A. M., Krapcho, M., Neyman, N., Aminou, R., Waldron, W., & Altekruse, S. F. (2011). *Surveillance, Epidemiology, and End Results Program*. Bethesda: National Cancer Institute.
- Hu, Q.-D., Zhang, Q., Chen, W., Bai, X.-L., & Liang, T.-B. (2013). Human development index is associated with mortality-to-incidence ratios of gastrointestinal cancers. *World Journal of Gastroenterology*, 19(32), 5261-5270. <https://doi.org/10.3748/wjg.v19.i32.5261> PMID:23983428
- Jemal, A., Bray, F., Center, M. M., Ferlay, J., Ward, E., & Forman, D. (2011). Global cancer statistics. *CA: a Cancer Journal for Clinicians*, 61(2), 69-90. <https://doi.org/10.3322/caac.20107> PMID:21296855

- Jemal, A., Center, M. M., DeSantis, C., & Ward, E. M. (2010). Global patterns of cancer incidence and mortality rates and trends. *Cancer Epidemiology, Biomarkers & Prevention*, 19(8), 1893-1907. <https://doi.org/10.1158/1055-9965.EPI-10-0437> PMID: 20647400
- Jemal, A., Siegel, R., Xu, J., & Ward, E. (2010). Cancer statistics, 2010. *CA: a Cancer Journal for Clinicians*, 60(5), 277-300. <https://doi.org/10.3322/caac.20073> PMID: 20610543
- Jemal, A., Simard, E. P., Xu, J., Ma, J., & Anderson, R. N. (2013). Selected cancers with increasing mortality rates by educational attainment in 26 states in the United States, 1993-2007. *Cancer Causes & Control*, 24(3), 559-565. <https://doi.org/10.1007/s10552-012-9993-y> PMID:22729932
- Kanavos, Panos. (2006). The rising burden of cancer in the developing world. *Annals of oncology*, 17(suppl 8), viii15-viii23. <https://doi.org/10.1093/annonc/mdl983>
- Keane, M. G., Horsfall, L. J., Rait, G., & Pereira, S. P. (2014). Sociodemographic trends in the incidence of pancreatic and biliary tract cancer in UK primary care. *PLoS One*, 9(9), e108498. <https://doi.org/10.1371/journal.pone.0108498> PMID:25268478
- Keyghobadi, N., Rafiemanesh, H., Mohammadian-Hafshejani, A., Enayatrad, M., & Salehiniya, H. (2015). Epidemiology and trend of cancers in the province of Kerman: Southeast of Iran. *Asian Pacific Journal of Cancer Prevention*, 16(4), 1409-1413. <https://doi.org/10.7314/APJCP.2015.16.4.1409> PMID:25743807
- Larsson, S. C., Permert, J., Håkansson, N., Näslund, I., Bergkvist, L., & Wolk, A. (2005). Overall obesity, abdominal adiposity, diabetes and cigarette smoking in relation to the risk of pancreatic cancer in two Swedish population-based cohorts. *British Journal of Cancer*, 93(11), 1310-1315. <https://doi.org/10.1038/sj.bjc.6602868> PMID:16288300
- Lowenfels, A. B., Maisonneuve, P., DiMaggio, E. P., Elitsur, Y., Gates, L. K., Jr., Perrault, J., & Whitcomb, D. C., & the International Hereditary Pancreatitis Study Group. (1997). Hereditary pancreatitis and the risk of pancreatic cancer. *Journal of the National Cancer Institute*, 89(6), 442-446. <https://doi.org/10.1093/jnci/89.6.442> PMID:9091646
- Lowenfels, A. B., & Maisonneuve, P. (2006). Epidemiology and risk factors for pancreatic cancer. *Best Practice & Research. Clinical Gastroenterology*, 20(2), 197-209. <https://doi.org/10.1016/j.bpg.2005.10.001> PMID:16549324
- Malik, K. (2013). Human development report 2013. The rise of the south: Human progress in a diverse world. The Rise of the South: Human Progress in a Diverse World (March 15, 2013) UNDP-HDRO Human Development Reports. 2013.
- Malvezzi, M., Bertuccio, P., Levi, F., La Vecchia, C., & Negri, E. (2013). European cancer mortality predictions for the year 2013. *Annals of Oncology : Official Journal of the European Society for Medical Oncology*, 24(3), 792-800. <https://doi.org/10.1093/annonc/mdt010> PMID:23402763
- Mathers, C. D., Fat, D. M., Inoue, M., Rao, C., & Lopez, A. D. (2005). Counting the dead and what they died from: An assessment of the global status of cause of death data. *Bulletin of the World Health Organization*, 83(3), 171-177. PMID:15798840
- Michaud, D. S. (2004). Epidemiology of pancreatic cancer. *Minerva Chirurgica*, 59(2), 99-111. PMID:15238885
- Mohammadian, M., Ghafari, M., Khosravi, B., Salehiniya, H., Aryaie, M., Bakeshei, F. A., & Mohammadian-Hafshejani, A. (2017). Variations in the Incidence and Mortality of Ovarian Cancer and Their Relationship with the Human Development Index in

European Countries in 2012. *Biomedical Research and Therapy*, 4(08), 1541-1557. <https://doi.org/10.15419/bmrat.v4i08.228>

Mohammadian, M., Soroush, A., Mohammadian-Hafshejani, A., Towhidi, F., Hadadian, F., & Salehiniya, H. (2016). Incidence and Mortality of Liver Cancer and Their Relationship with Development in Asia. *Asian Pacific Journal of Cancer Prevention*, 17(4), 2041-2047. <https://doi.org/10.7314/APJCP.2016.17.4.2041> PMID:27221893

Muniraj, T., Jamidar, P. A., & Aslanian, H. R. (2013). Pancreatic cancer: A comprehensive review and update. *Disease-a-Month*, 59(11), 368-402. <https://doi.org/10.1016/j.disamonth.2013.08.001> PMID:24183261

Muscat, J. E., Stellman, S. D., Hoffmann, D., & Wynder, E. L. (1997). Smoking and pancreatic cancer in men and women. *Cancer Epidemiology, Biomarkers & Prevention*, 6(1), 15-19. PMID:8993792

Neesse, A., Michl, P., Frese, K.K., Feig, C., Cook, N., Jacobetz, M.A., Lolkema, M.P., Buchholz, M., Olive, K.P., Gress, T.M. and Tuveson, D.A. (2011). Stromal biology and therapy in pancreatic cancer. *Gut*, 60(6), 861-868.

Neoptolemos, J.P., Stocken, D.D., Bassi, C., Ghaneh, P., Cunningham, D., Goldstein, D., Padbury, R., Moore, M.J., Gallinger, S., Mariette, C. and Wente, M.N. (2010). Adjuvant chemotherapy with fluorouracil plus folinic acid vs gemcitabine following pancreatic cancer resection: A randomized controlled trial. *Journal of the American Medical Association*, 304(10), 1073-1081. <https://doi.org/10.1001/jama.2010.1275> PMID:20823433

Neoptolemos, J. P., Dunn, J. A., Stocken, D. D., Almond, J., Link, K., Beger, H., . . . Büchler, M. W., & the European Study Group for Pancreatic Cancer. (2001). Adjuvant chemoradiotherapy and chemotherapy in resectable pancreatic cancer: A randomised controlled trial. *Lancet*, 358(9293), 1576-1585. [https://doi.org/10.1016/S0140-6736\(01\)06651-X](https://doi.org/10.1016/S0140-6736(01)06651-X) PMID:11716884

Organization, World Health. (2000). The world health report 2000: health systems: improving performance: World Health Organization.

Pakzad, R., Ghoncheh, M., Pournamdar, Z., Pakzad, I., Momenimovahed, Z., Salehiniya, H., & Makhsosi, B. R. (2016). Spatial Analysis of Skin Cancer Incidence in Iran. *Asian Pacific Journal of Cancer Prevention*, 17(sup3, S3), 33-37. <https://doi.org/10.7314/APJCP.2016.17.S3.33> PMID:27165204

Pakzad, R., Mohammadian-Hafshejani, A., Ghoncheh, M., Pakzad, I., & Salehiniya, H. (2015a). The incidence and mortality of lung cancer and their relationship to development in Asia. *Translational Lung Cancer Research*, 4(6), 763-774. <https://doi.org/10.3978/j.issn.2218-6751.2015.12.01> PMID:26798586

Pakzad, R., Mohammadian-Hafshejani, A., Ghoncheh, M., Pakzad, I., & Salehiniya, H. (2015b). The incidence and mortality of prostate cancer and its relationship with development in Asia. *Prostate International*, 3(4), 135-140. <https://doi.org/10.1016/j.pnil.2015.09.001> PMID:26779461

Pakzad, R., Mohammadian-Hafshejani, A., Mohammadian, M., Pakzad, I., Safiri, S., Khazaei, S., & Salehiniya, H. (2015). Incidence and Mortality of Bladder Cancer and their Relationship with Development in Asia. *Asian Pacific Journal of Cancer Prevention*, 16(16), 7365-7374. <https://doi.org/10.7314/APJCP.2015.16.16.7365> PMID:26514538

Parkin, D. M., Bray, F., Ferlay, J., & Pisani, P. (2005). Global cancer statistics, 2002. *CA: a Cancer Journal for Clinicians*, 55(2), 74-108. <https://doi.org/10.3322/canjclin.55.2.74> PMID:15761078

Pourhoseingholi, M. A., Vahedi, M., & Baghestani, A. R. (2014). Burden of gastrointestinal cancer in Asia; an overview. *Gastroenterology and Hepatology from Bed To Bench*, 1(1). [PMID:25584172](#)

Rafiemanesh, H., Mohammadian-Hafshejani, A., Ghoncheh, M., Sepehri, Z., Shamlou, R., Salehiniya, H., . . . Makhsosi, B. R. (2016). Incidence and mortality of colorectal cancer and relationships with the human development index across the world. *Asian Pacific journal of cancer prevention. APJCP*, 17(5), 2465-2473. [PMID:27268615](#)

Ravallion, M. (1997). Good and bad growth: The human development reports. *World Development*, 25(5), 631-638. [https://doi.org/10.1016/S0305-750X\(96\)00141-6](https://doi.org/10.1016/S0305-750X(96)00141-6)

Razi, Saeid, Ghoncheh, Mahshid, Mohammadian-Hafshejani, Abdollah, Aziznejhad, Hojjat, Mohammadian, Mahdi, & Salehiniya, Hamid. (2016). The incidence and mortality of ovarian cancer and their relationship with the Human Development Index in Asia. *ecancermedalscience*, 10.

Ryu, J. K., Hong, S. M., Karikari, C. A., Hruban, R. H., Goggins, M. G., & Maitra, A. (2010). Aberrant MicroRNA-155 expression is an early event in the multistep progression of pancreatic adenocarcinoma. *Pancreatology*, 10(1), 66-73. <https://doi.org/10.1159/000231984> [PMID:20332664](#)

Sasson, A. R., Hoffman, J. P., Ross, E. A., Kagan, S. A., Pingpank, J. F., & Eisenberg, B. L. (2002). En bloc resection for locally advanced cancer of the pancreas: Is it worthwhile? *Journal of Gastrointestinal Surgery*, 6(2), 147-157. [https://doi.org/10.1016/S1091-255X\(01\)00063-4](https://doi.org/10.1016/S1091-255X(01)00063-4) [PMID:11992799](#)

Schwartz, G. G., & Reis, I. M. (2000). Is cadmium a cause of human pancreatic cancer? *Cancer Epidemiology, Biomarkers & Prevention*, 9(2), 139-145. [PMID:10698473](#)

Shuja, M., Farsani, S. I., Salehiniya, H., Khazaei, S., Mohammadian, M., Aryaie, M., ... & Mohammadian-Hafshejani, A. (2017). Assessment the association between liver cancer incidence and mortality rate with human development index in the European countries in 2012. *Biomedical Research and Therapy*, 4(03), 1185-1197. <https://doi.org/10.15419/bmrat.v4i03.156>

Siegel, R., Naishadham, D., & Jemal, A. (2012). Cancer statistics, 2012. *CA: a Cancer Journal for Clinicians*, 62(1), 10-29. <https://doi.org/10.3322/caac.20138> [PMID:22237781](#)

Silverman, D. T., Dunn, J. A., Hoover, R. N., Schiffman, M., Lillemoe, K. D., Schoenberg, J. B., . . . (1994). Cigarette smoking and pancreas cancer: A case-control study based on direct interviews. *Journal of the National Cancer Institute*, 86(20), 1510-1516. <https://doi.org/10.1093/jnci/86.20.1510> [PMID:7932805](#)

Smith, B. D., Smith, G. L., Hurria, A., Hortobagyi, G. N., & Buchholz, T. A. (2009). Future of cancer incidence in the United States: Burdens upon an aging, changing nation. *Journal of Clinical Oncology*, 27(17), 2758-2765. <https://doi.org/10.1200/JCO.2008.20.8983> [PMID:19403886](#)

Society, American Cancer. (2013). Cancer facts and figures 2013: American Cancer Society Atlanta.

Stapley, S., Peters, T. J., Neal, R. D., Rose, P. W., Walter, F. M., & Hamilton, W. (2012). The risk of pancreatic cancer in symptomatic patients in primary care: A large case-control study using electronic records. *British Journal of Cancer*, 106(12), 1940-1944. <https://doi.org/10.1038/bjc.2012.190> [PMID:22617126](#)

Stats, F. (2012). *An interactive tool for access to SEER cancer statistics. Surveillance Research Program*. National Cancer Institute.

- Tiyuri, A., Mohammadian-Hafshejani, A., Iziy, E., Gandomani, H. S., & Salehiniya, H. (2017). The incidence and mortality of lip and oral cavity cancer and its relationship to the 2012 Human Development Index of Asia. *Biomedical Research and Therapy*, 4(02), 1147-1165. <https://doi.org/10.15419/bmrat.v4i02.151>
- Toriola, A. T., Stolzenberg-Solomon, R., Dalidowitz, L., Linehan, D., & Colditz, G. (2014). Diabetes and pancreatic cancer survival: A prospective cohort-based study. *British Journal of Cancer*, 111(1), 181-185. <https://doi.org/10.1038/bjc.2014.224> PMID: [24786605](https://pubmed.ncbi.nlm.nih.gov/24786605/)
- Valean, S., Acalovschi, M., Diculescu, M., Manuc, M., Goldis, A., Sfarti, C., & Trifan, A. (2015). Mortality in Digestive Cancers, 2012: International Data and Data from Romania. *Journal of Gastrointestinal and Liver Diseases; JGLD*, 24(4), 507-514. PMID: [26697578](https://pubmed.ncbi.nlm.nih.gov/26697578/)
- Wang, L., Yang, G.-H., Lu, X.-H., Huang, Z.-J., & Li, H. (2003). Pancreatic cancer mortality in China (1991-2000). *WJG*, 9(8), 1819-1823. <https://doi.org/10.3748/wjg.v9.i8.1819> PMID: [12918128](https://pubmed.ncbi.nlm.nih.gov/12918128/)
- Ward, E., Jemal, A., Cokkinides, V., Singh, G. K., Cardinez, C., Ghafoor, A., & Thun, M. (2004). Cancer disparities by race/ethnicity and socioeconomic status. *CA: a Cancer Journal for Clinicians*, 54(2), 78-93. <https://doi.org/10.3322/canjclin.54.2.78> PMID: [15061598](https://pubmed.ncbi.nlm.nih.gov/15061598/)