Smoking Associated Cancer Mortality Trends in Select Countries

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ABSTRACT: The objective of this paper was to examine potential factors contributing to smoking-related cancer mortality trends. Smoking associated cancer mortality data from 1970 to 2016 was extracted from the IARC Cancer Mortality Database and WHO Mortality Database. Data from the United States, Greece, Norway, Chile, and Colombia were analyzed due to variance in annual cigarette consumption per capita, the prevalence of current tobacco use, and geographical similarity. Norwegian males, Chilean males and females, and Colombian males and females saw decreases in cancer mortality rates during the study period; on the other hand, Greek males and females showed unchanged mortality rates, and Norwegian females showed a very slight increase in cancer mortality rates. United States age-standardized mortality rates (ASR) rose from 180.75 deaths per 100,000 persons in the year 1970 to the early 1980s before showing a steady and significant decline to 90.46 deaths per 100,000 persons in 2016. This study shows a strong correlation in developed countries (United States, Norway, and Greece) between advances in cancer therapies, early detection techniques, health screening, and public and legal health initiatives with a decrease in smoking-related cancer mortality rates. In developing countries (Chile and Colombia), widespread *H. pylori* testing, and treatment advances were found to be the main drivers of decreasing cancer mortality rates.

KEYWORDS: Translational Medical Sciences; Disease Prevention; Cancer Mortality; Smoking Related Cancer Mortality Trends; Causes of Smoking Related Cancer Mortality.

Introduction

Cancer continues to be one of the leading causes of death in the United States, being the 2nd leading cause of death in 2019 with 600,000 deaths or 21% of total deaths in the United States.[1] Cancer not only is a devastating disease, but it also carries a set of many economic burdens. In the United States alone, in 2017, cancer healthcare spending was 161.2 billion dollars, productivity loss from morbidity was 30.3 billion dollars, and the cost of premature mortality was 150.7 billion dollars.[2] Other countries such as China and South Africa face an average loss of 108,320 dollars per cancer mortality due to productivity losses.[2] These drastic economic burdens in the United States and other countries show the medical severities and economic effects of cancer.

An extreme risk factor for cancer is smoking, which results in bodily exposure to more than 70 proven carcinogenic chemicals that spread not only to the lungs but to other parts of the body.[3] The buildup of these carcinogenic chemicals can damage parts of the DNA that protect against cancer, increasing cancer risk.[3] Quitting smoking can significantly reduce one's risk of cancer by approximately 30-50% after ten years compared to smokers who continue to smoke.[4] Specifically, cancer of the lungs, trachea, and bronchus (cancers associated with smoking) was responsible for a staggering 139,682 of those deaths or roughly 5% of all deaths in the United States. The goal of this paper is to analyze certain smoking-related cancer mortality trends in select countries and their potential causes. This paper will provide better insight into the progression of cancer mortality in different countries. This research paper differs from other scientific literature as it examines potential historical, medical, and scientific factors contributing to smoking-related cancer mortality trends in several countries.

Methods

Data Source:

The data were collected from the IARC Cancer Mortality Database extracted from the WHO Mortality Database.[5] The Cancer Mortality data was sorted by type of cancer(s), sex (male or female), country, period, and age range. The database calculated yearly ASR per 100,000 persons based on the different search criteria including sex, country, and range. The periods of the data collected for all countries except Colombia were restricted from 1970 to 2016 due to inconsistencies in recorded cancer mortality data; the period for Colombia was restricted from 1984 to 2015 due to a lack of data before 1984 and after 2015. The age range for all the data from the IARC Cancer Mortality Database was restricted to ages 45 to 69 due to fully available data for that age range.[5] Data on the prevalence of current tobacco use among persons aged 15 years and older were also collected from the GHO health database.[6] The data were sorted by gender and different periods: 2000, 2005, 2010, and 2013 to 2017. Data on Annual Cigarette Consumption per person aged 15 or older were collected from *The Tobacco Atlas - 6th edition*, a report on various tobacco and smoking-related data and graphics.[7] Availability of data and statistics collected from the IARC Cancer Mortality Database, GHO Health Database, and The Tobacco Atlas were used to identify select countries.[5-7] The ICD-10 codes C00-14 (Lip, Oral Cavity, and Pharynx Cancer), C15 (Oesophagus Cancer), C16 (Stomach Cancer), and C33-34 (Lung Cancer) were extracted. Because this study used pub

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licly available deidentified data, the study was determined to be exempt from Institutional Review Board review.

Inclusion Criteria:

Countries were selected based on sufficient data availability and consistency, annual national cigarette consumption per capita rates, national tobacco usage statistics, and geographical proximity in the same continent. The five selected countries included the United States, Greece, Norway, Chile, and Colombia. Greece and Norway were selected based on the variance in prevalence of current tobacco use and geographical proximity in the same continent. Chile and Colombia were selected due to differences in annual tobacco usage and cigarette consumption per capita, and geographical proximity in the same continent. Annual mortality rates were grouped by sex (male or female), age (45 years to 69 years), and cause of death (type of cancer). Countries were generally classified by "low", "medium", and "high" smoking rates relative to the other country in the same continent in the selection process. Chile was classified as a high smoking rate country with 44.7% of its population aged above 15 years using tobacco and Colombia was classified as a low smoking rate country with 7.9% of its population aged above 15 years using tobacco. Similarly, Greece was classified as a high smoking rate country with 39.1% of its population aged above 15 years using tobacco and Norway was classified as a low smoking rate country with 18.4% of its population aged above 15 years using tobacco. Lastly, the United States was classified as a medium smoking rate country with 25.1% of its population aged above 15 years using tobacco.

Statistical Analyses:

Mortality rates were calculated by year, sex (male or female), and age (45 to 69 years). Linear regression analyses with Pearson correlation were performed to study mortality trends from 1970 to 2016 for the United States, Chile, Greece, and Norway and from 1984 to 2015 for Colombia.

Results and Discussion

Male smoking-related cancer deaths in the United States slightly increased from 180.75 ASR mortalities in 1970 to 201.34 ASR mortalities in 1986 and decreased to 90.46 ASR mortalities in 2016. A negative association was indicated by the line of best fit (Figure 1A). Female-smoking related deaths in the United States increased from 1970 to 1992 and gradually decreased from 1992 to 2016 (Figure 1B).

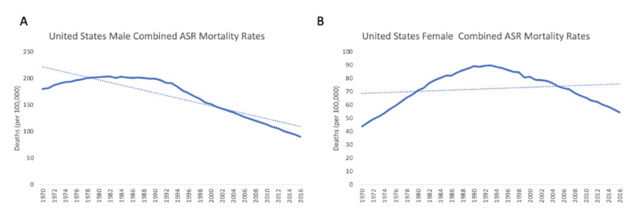

Figure 1: A) Male ASR Mortality rates per 100,000 for the United States are displayed from 1970 to 2016 (β= -2.445 ASR/year: R^2 = 0.7897). B) Female ASR Mortality rates per 100,000 for the United States are displayed from 1970 to 2016 (β= 0.1545 ASR/year: R^2 = 0.0263).

Male smoking-related cancer deaths in Greece stayed constant from 1970 to 2016, as shown by the strong association of the line of best fit (Figure 2A). Female-smoking related deaths in Greece showed a slight decline from 1970 to 2000 and an increase from 2000 to 2016 (Figure 2B). Male smoking-related cancer deaths in Norway showed a general decrease from 1970 to 2016, but female smoking-related cancer deaths in Norway showed a general increase from 1970 to 2016 (Figures 2C and 2D).

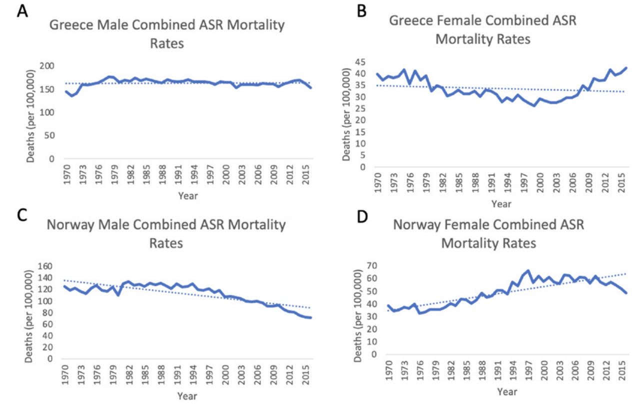

Figure 2: A) Male ASR Mortality rates per 100,000 Greece are displayed from 1970 to 2016 (β= 0.0255 ASR/year: R^2= 0.0019). B) Female ASR Mortality rates per 100,000 for Greece are displayed from 1970 to 2016 (β= -0.0585 ASR/year: R^2= 0.0298). C) Male ASR Mortality rates per 100,000 for Norway are displayed from 1970 to 2016 (β= -1.0204 ASR/year: R^2 = 0.6332). D) Female ASR Mortality Rates per 100,000 for Norway are displayed from 1970 to 2016 (β = 0.6247 ASR/year: R^2 = 0.7038).

Male and female smoking-related cancer deaths in Chile showed a general decrease from 1970 to 2016 (Figures 3A and 3B). Male and female smoking-related cancer deaths in Colombia also showed a general decrease from 1984 to 2015 (Figure 3C and 3D).

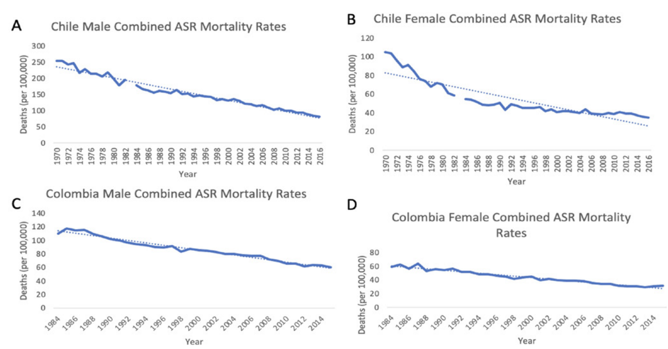

Figure 3: A) Male ASR Mortality rates per 100,000 for Chile are displayed from 1970 to 2016 (β= -3.4742 ASR/year: R^2= 0.9601). B) Female ASR Mortality rates per 100,000 for Chile are displayed from 1970 to 2016 (β= -1.2324 ASR/year: R^2= 0.7807). C) Male ASR Mortality rates per 100,000 for Colombia are displayed from 1984 to 2015 (β= -1.7672 ASR/year: R^2 = 0.9697). D) Female ASR Mortality Rates per 100,000 for Norway are displayed from 1984 to 2015 (β = -1.0636 ASR/year: R^2 = 0.9555).

The analysis of trends in the figures showed different periods of increasing and decreasing cancer mortality rates in the United States for both genders (Figure 1). The observed trends for Greece showed a steady cancer mortality rate for males and a decrease from 1970 to 2000 followed by an increase from 2000 to 2016 for females (Figure 2). The cancer mortality rate trends in Norway decreased for males and increased for females (Figure 2). Both male and female cancer mortality rate trends in Chile and Colombia showed a general decrease. Numerous factors including, but not limited to, public health initiatives, improved cancer treatment in target areas, advertisement targeting of certain groups, and the prevalence of other medical issues may have had an impact on certain trends.

Smoking Associated Cancer Mortality Rates in the United States:

In general, in the United States, male cancer mortality rates showed a slight increase from 1970 to 1986 followed by a general decrease after 1986. However, notable negative trends were observed from the mid-1990s until 2016 in both males and females. This decreasing trend could be explained through the development of smoking public health initiatives that could have contributed to the significant decline in cancer mortality rates. In 1998, California became the first US state to pass a law banning smoking in bars; combined with other laws that banned smoking in restaurants and public places, California became the first US state to pass a statewide smoke-free air law that lowered the overall risk of secondhand smoke exposure.[8] The passing of this law was controversial but approval ratings for this law significantly increased within several years. Public statewide surveys in the state of California showed that the percentage of adults who supported the law 3 months after it passed was 46% and the percentage of adults who approved the law 2.5 years after it was passed was 62%.[9] After the passing of a similar smoke-free law in New York in 2003, various surveys showed that the number of all adults in New York who supported the law increased from 64% to 80% within 2 years of its implementation.[9] The overall increased support of smoke-free laws could have contributed to the decreasing smoking-related mortality rate in the United States.

Other contributing factors for the decreasing cancer mortality rates in the United States are the improvements in pre-existing cancer treatments, the development of new cancer treatments, and the improvements in cancer diagnosis. Chimeric antigen receptor T cells (CAR T cells) are genetically designed T cells that can be used as an immunotherapy cancer treatment that supplements the immune system. The first effective CAR T cells were developed in the early 2000s and developments through the 21st century have led to the creation of "armored" CAR T cells that can produce other molecules that suppress cancerous tumors.[10] Other improved cancer treatments include certain targeted therapies like Bevacizumab which can be used to treat non-small cell lung cancer (NSCLC), which makes up approximately 85% of all lung cancers, by inhibiting angiogenesis.[11] The usage and development of CAR T cells and Bevacizumab could have significantly contributed to the decline in smoking-related cancer mortality rates in the United States (Figure 1).

Lastly, improved lung cancer screening has contributed to reduced mortality rates in the United States. Low-dose helical computed tomography (LDCT) scans were shown in the National Lung Screening Trial, from 2002 to 2004, to reduce a lung cancer patient's chance of mortality by 15% to 20%.[12] The study showed that 3 fewer deaths occurred per 1000 people screened using LDCT scans, a significant statistic.[12] This dramatic breakthrough in lung cancer screening has continued to decrease potential smoking-related cancer mortality in the United States.

Female Smoking Associated Cancer Mortality Rates in the United States:

Female smoking-related cancer mortality rates had a significant increase from the 1970s to mid-1990s compared to male smoking-related cancer mortality rates during that period (Figure 1). A potential cause of this increase is advertisement and campaign targeting of women for smoking. Starting in the 1920s, tobacco companies created women-oriented cigarettes through the promotion of cigarettes as a form of weight control and femininity.[13] Furthermore, tobacco companies created tobacco products that gained popularity through association with the Women's liberation movement, such as the Virginia slims brand. Studies have shown that during the late 1960s and early 1970s, when these products were introduced, smoking rates in females significantly increased.[13] Since then, cigarette companies have launched cigarettes with reduced levels of tar, "reduced" nicotine, and even "purse" packs that specifically targeted women. This increased level of advertising and campaign targeting have affected women throughout the 20th century and could have been a significant factor affecting the increase in smoking-related cancer mortality rates for females from 1970 to the mid-1990s (Figure 1).

Smoking Associated Cancer Mortality Rates in South America – Chile and Colombia :

In the continent of South America, countries like Chile and Colombia have seen a dramatic decrease in smoking-related cancer mortality from the 1980s to 2016 (Figure 3). These decreasing smoking-related cancer mortality rates could have been significantly influenced by the improvement of cancer treatment in rural areas and the initial prevalence of *Helicobacter pylori* bacterial infections in South American countries. *H. pylori* bacteria can live in the digestive tract for many years and when it infects the stomach, it can cause painful stomach ulcers. To treat *H. pylori* infections, proton pump inhibitors (PPIs) can be used along with antibiotics like amoxicillin, clarithromycin, or metronidazole to have a high eradication rate of the *H. pylori* infection.[14] However, a combination of high rates of *H. pylori* and high smoking rates, as in Chile and Colombia, and a lack of proper treatment in the rural areas of South America could have contributed to the high stomach cancer mortality rates. Advances in *H. pylori* infection diagnosis tests such as the urea breath test and the HpSA test could have improved *H. pylori* diagnosis and infection recurrence in patients in Chile and Colombia, leading to reductions in smoking-related cancer rates. The urea breath test and HpSA tests are simple, non-invasive tests that can be used to diagnose *H. pylori* infections as well as to manage the recurrence of such infections.[15] Both tests have been used in combination with PPIs and antibiotics to provide a safer and more manageable approach to *H. pylori* infections in Latin America.[15] These improvements in diagnostic tests reduced the risk of *H. pylori* infection and could have potentially caused a decrease in smoking-related

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cancer mortality in Chile and Colombia from the 1980s to 2016 (Figure 3).

Smoking Associated Cancer Mortality Rates in Europe - Greece and Norway:

Countries in Europe, such as Greece and Norway, seem to show varying trends in cancer mortality rates which could be due to the different public responses to smoking legislation. While Norway shows a slight mortality rate decline for males and a slight mortality rate increase for females, Greece shows a constant trend for males and a curved trend for females (Figure 2). These trends may be due to the more restrictive smoking legislation in Norway and the public criticism and disobedience of smoking legislation in Greece. In 2009, Greece banned smoking in indoor places and started to institute fines, however, this was met with criticism due to the influence of smoking culture in Greece.[16] The legislation was weakly enforced and smoking still exists in many common places such as restaurants and bars in Greece, potentially contributing to the constant and curved trends of cancer mortality rates in Greece (Figure 2).[16] Tobacco control legislation has existed in Norway for over 40 years starting with the Norwegian Tobacco Act in 1975 that banned tobacco advertising and required health warnings on tobacco packaging.[17] Since then, other strict legislation was enacted that banned retail advertising of tobacco, totally banned smoking in restaurants and bars, and increased restrictions on tobacco product advertising.[17] Such strong legislation in Norway could have potentially contributed to the decreasing smoking mortality trend in Norway and the constant and curved mortality trends in Greece (Figure 2).

Limitations:

Limitations include the varied availability of statistical cancer mortality data, internal bias, and confounding variables. The extracted cancer mortality data was based on the overall cancer mortality of a certain type of cancer, not exclusively cancer caused by smoking. For example, it is predicted that 80-90% of lung cancer mortalities are linked to smoking, so the extracted lung cancer mortality data is assumed to have been caused primarily by smoking, although it is not possible to separate the exact causes of the mortality data.[18] Lastly, confounding variables could be responsible for the presented trends in the results. While factors such as public health initiatives, smoking legislation and smoking advertisement targeting of women may be potential factors affecting cancer mortality trends, there may be other confounding variables that are not accounted for in this paper.

■ Conclusion

From 1970 to 2016, the selected countries showed declining or unchanging cancer mortality rates. This study shows a strong correlation in developed countries between advances in cancer therapies, early detection techniques, and screening and public and legal health initiatives and the decrease in smoking-related cancer mortality rates. In developing countries, widespread *H. pylori* testing, and treatment advances were found to be the main drivers of decreasing cancer mortality rates. The application of similar factors in other cancers could give clinicians and researchers insight into potential mechanisms to decrease non-smoking-related cancer mortality rates.

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■ Conclusion

Siddharth is a senior at Oyster River High School in Durham, New Hampshire. He is extremely interested in biology and biotechnology and hopes to have a career in science or medicine in the future.