U.S. Men Melanoma Incidences by State explained by the UV Index and Air Toxics

Patrick Ryan, Ph.D.
Stanley Consultants, Inc., Coralville, IA, USA

Abstract

The biggest risk factors to developing melanoma are race (the paler your skin, the higher your chances), sun exposure, and air toxics. Melanoma skin cancer incidences occur 5-20 times more frequently in light skinned individuals when compared with darker skinned races. A linear regression model with components the annual solar UV index, two air toxics, and the % of adult smokers by state explained male melanoma incidence rate variation by state at the 95% confidence level with a data fit correlation coefficient squared (r^2) of 0.79. The annual solar UV index explained 80% and two air toxics explained the other 20% of the melanoma incidence rate data. Smoking acted to suppress melanoma incidences, which is consistent with findings from epidemiological studies.

Implications

Air toxics significantly explain melanoma incidence data given that the air toxic trichloroethylene (TCE) atmospheric variation explained 20% of the melanoma incidence rate data. A qualitative explanation for the increase seen in melanoma incidences over the last 30 years is offered by the regression model. The regression model identifies that smoking suppressed melanoma incidences, which is consistent with the factor of two drop in the % of adult smokers from 37% in 1975 to 21% in 2005 that occurred while the melanoma incidence rate increased by about the same factor of two. For a continued decline in the % of adult smokers future increases in the melanoma rate are predicted.

Introduction

A continuous increase of melanoma incidence rates have been observed in the United States over the last four decades (Purdue et al., 2008). The underlying causes of the rising melanoma trend is widely debated. Most authors attribute the increase to environmental risk factors and changes in sun exposure behavior. Top-down and bottom-up strategies process data in different ways to better understand the cause and effect relationship of variables. In this study, the top-down strategy was followed that began with downloading men melanoma cancer incidence rate data by state for each state in the United States. The melanoma incidence data by state were fitted to data of known or suspected causes of melanoma cancer. Epidemiological studies were used as a source of information on possible causes of melanoma. The purpose of this study is to learn whether air toxics might help explain melanoma incidences.

The availability of nationwide ambient monitoring for the criteria air pollutants (carbon monoxide, lead, nitrogen dioxide, ozone, particulate matter, and sulfur dioxide) makes assessment of exposure and risk for these chemicals feasible. Considerably less is known about the distribution of exposure to and risk from the wide range of hazardous air pollutants (HAPs; also known as "air toxics") identified by Congress in the Clean Air Act Amendments. Less information is known because nationwide ambient monitoring is impractical given the number of air toxics and their diverse chemical monitoring needs (Caldwell et al., 1998; Morello-Frosch et al., 2001; Woodruff et al., 1998). To analyze whether a data relationship exists between melanoma cancer incidences and air toxics, this study used the U.S. EPA (2015) 2011 National-scale Air Toxics Assessment (NATA) to estimate air toxic levels in the atmosphere. The NATA estimates aggregated at the State level were used. The NATA air toxic concentration estimates by state were fitted to melanoma cancer incidence rate data across the fifty United States.

In the early 1990s, the U.S. EPA undertook the Cumulative Exposure Project (CEP) with the goal of modeling annual ambient air concentrations of 148 air toxics and predicting their associated cancer risk (Rosenbaum et al., 1999; Woodruff et al., 1998). Historical modeled national estimates suggested that ambient concentrations of HAPs exceeded benchmark risk levels for cancer and non-cancer end points in many areas of the country (Caldwell, 1998; Woodruff et al., 1998 & 2000). Boffetta and Nyberg (2003) examined the contribution of environmental factors to cancer risk and concluded just the opposite that there was insufficient data to estimate the

cancer risk posed by outdoor air pollution. Ten years after Bofetta and Nyberg in 2013, the specialized cancer agency of the World Health Organization, the International Agency of Research on cancer (IARC), announced that it had classified outdoor air pollution as carcinogenic to humans.

Materials and Methods

Epidemiological studies were reviewed to identify causes of melanoma cancer incidence rates in men. Sunlight and air toxics are two identified causes of melanoma. The U.S. EPA (2015) National Air Toxics Assessment estimates of air toxics cancer risk for each of the fifty United States were used. The National Cancer Institute (2016) latest 5-year average (2008-2012) melanoma cancer incidence rate data for men for each of the fifty United States were the observed data.

A simple regression analysis was conducted to identify those air toxics with a positive correlation (r) compared with the melanoma cancer incident rate variation across the fifty United States. Those air toxics with a positive correlation to melanoma cancer incidence rates variations by state were reviewed for confirmation of causality by epidemiological studies. Only positively correlated air toxics with epidemiological support were considered for data fit using a multiple linear regression program. This study used a multiple linear regression program to determine whether the EPA NATA 2011 predicted cancer risk by air toxic could help explain the variation in melanoma cancer incidence rates across the fifty United States.

Epidemiological studies and melanoma cancer

The ATDSR (2016) cites trichloroethylene (TCE) as a carcinogenic source of skin cancer.

Melanoma cancer incidence rate data

The most recent five-year average male melanoma incidence rates available for each of the fifty United States were downloaded from the National Cancer Institute (2016) and reviewed. Melanoma incidence data for the United States do not include incidence data for Nevada but

does include data for the District of Columbia. The highest rates of melanoma are in some of the cloudiest states, like Washington, Oregon, and Vermont. Melanoma rates are higher in the cloudiest states because of a higher percentage of light skinned adults in the cloudiest states. The adult race composition by state varies significantly (e.g., Vermont is 94% white, the District of Columbia is 47% black, and New Mexico is 43% Hispanic) (Henry J. Kaiser Foundation, 2016) and light skinned adults are 5 to 20 times more frequently diagnosed with melanoma than American Natives, Asians, Blacks, and Hispanics (CDC, 2016a). The male melanoma incidence data by state was normalized to remove the varying race composition confounding effect using the following equation:

$$\text{Race Normalized Melanoma Incidence by State} = \text{Melanoma Incidence by State} / (Pop_{f\text{-White}} + 0.53\ Pop_{f\text{-2orMoreRaces}} + 0.033\ Pop_{f\text{-Black+Hispanic}} + 0.03\ Pop_{f\text{-Asian}} + 0.06\ Pop_{f\text{-AI/AN}}) \quad (1)$$

Where Pop_f denotes the population fraction by state of White, Two or More Races, Blacks and Hispanics, Asians and American Indian/Alaska Native (AI/AN). The population fraction by race by state were taken from the Henry J. Kaiser Foundation (2016) web site. The adjustment factors of 0.53, 0.033, 0.03 and 0.06 denote the relative melanoma incidence rates for Two or more races, Black + Hispanics, Asian and American Indian/Alaska Native compared with those of Whites as reported for California by the National Cancer Institute (2016). California data were used as California data provides reasonably accurate melanoma incidence data for each race. For diseases like melanoma where the incidence data primarily results from one race (white) over all others, race normalization offers a way to seek information on the underlying causes of the disease.

U.S. EPA's NATA.

The NATA and its predecessor the Cumulative Exposure Project established a means for using source emission data to derive estimates of human exposure to air toxics (Rosenbaum et al., 1999) and human cancer risk (Caldwell, 1998; Woodruff et al., 1998 & 2000). This study downloaded the NATA 2011 cancer risk estimates by air toxic aggregated at the State level. The U.S. EPA (2015) most recent national-scale air toxics assessment was conducted using the 2011

air toxic emissions inventory. This NATA calendar year 2011 study offers a snapshot in time of the predicted health risks associated with 179 air toxic chemicals. NATA combines source emission data (i.e., TRI data, databases from the U.S. EPA's Maximum Achievable Control Technology program, and emissions estimates for mobile and area sources) with meteorology (wind speed and direction) in a Gaussian dispersion model called the Human Exposure Model version 1.3.1 (HEM-3) for the 179 HAPs and diesel PM. A photo-chemical grid model, Community Multi-Scale Air Quality Modeling System (CMAQ), is then used for a subset of 40 HAPs and diesel PM to improve mass conservation. The air toxic annual ambient concentrations are input into the Hazardous Air Pollution Exposure Model 7 (HAPEM7) that incorporates activity patterns influence on personal exposure to ambient air toxic concentrations.

From the HAPEM7 human concentration exposure estimates, air toxic concentrations from the NATA 2011 study were converted to cancer risk by applying inhalation unit risk factors following the U.S. EPA standard methods. For cancer, even though the type (e.g., liver, blood, melanoma) and weight of evidence (e.g., known, suspected, or possible) varied by chemical, aggregate risk was estimated as the sum of individual chemical risks. The cancer risk estimates are considered by the U.S. EPA to be "upper-bound" estimates" that are a plausible upper limit to the true probability that an individual will contract cancer over a 70 year lifetime as a result of a given hazard (such as exposure to a toxic chemical)".

The following emission source categories are included in the inventory and subsequent assessment. Major emissions sources were "stationary facilities that emit or have the potential to emit 10 tons of any one toxic air pollutant or 25 tons of more than one toxic air pollutant per year" (e.g., electric utility power plants, oil refineries). Area and other emissions sources were "sources that generally have smaller emissions on an individual basis than 'major sources' and are often too small or ubiquitous in nature to be inventoried as individual sources"; this may include smaller facilities (e.g., dry cleaning facilities, gas station/automobile repair) or other sources such as wildfires. On-road mobile sources were "vehicles found on roads or highways." Nonroad mobile sources were "mobile sources not found on roads and highways (e.g., airplanes, trains, lawn mowers, construction vehicles, farm machinery)." In addition, background concentrations are estimated, which represent exposure from "natural sources, persistence in the environment of past years' emissions and long-range transport from distant sources." NATA cancer risk estimates were calculated for the year 2011 and use 2010 census tracts.

Annual Solar UV index

The National Oceanic and Atmospheric Administration (NOAA, 2016) reports a daily solar UV index for major cities in the United States. The 2015 daily solar UV index with cloud cover accounted for were downloaded and the annual average by major city was calculated and used for that State. Alaska had the lowest and Hawaii the highest annual solar UV indexes at 1.94 and 9.63, respectively. The difference between the highest and lowest annual solar UV indexes is 7.69, which is 396% of the lowest annual UV index for Alaska.

Smoking

The Center for Disease Control and Prevention (CDC, 2016b) report data on the percentage of adult smokers for calendar year 2012 for each of the fifty United States. These data were downloaded and used in this study's analysis. Utah has the lowest and Kentucky the highest percentage of adult smokers at 10.6 percent and 28.3 percent for 2012. The difference between the highest and lowest percentage of smokers by state is 17.6 %, which is 166% of the lowest smoking percentage that is in Utah.

Results

The normalized melanoma cancer incidence rate data at the State level were the observed or y-variables. The NATA 2011 predicted cancer risk estimates by air toxic for each of fifty United States areas (Nevada omitted and the District of Columbia included) were initially assigned as the independent variables. A linear regression program was run to identify those air toxics with a significant positive correlation compared with the melanoma cancer incidence variation by state. Trichloroethylene (0.48) showed a high positive data correlation with the race normalized melanoma cancer incidence variations across the United States and is an identified carcinogen for melanoma. Adult smoking percentages and the annual solar UV index developed by state for each of the fifty United States areas were added as independent variables. Two multiple regression equations with all terms statistically significant at the 95% confidence interval explained the race normalized melanoma cancer incidence rate variations across the fifty United

States. The two data fit multiple regression equations that have data fit correlation coefficients squared (r^2) values of 0.71 and 0.79 are as follows:

Race Normalized Melanoma Cancer Incidence Rate (per 100 k) =

$$28 - 1.4 \times \%\ \text{Adult Smokers} + 125\ CR_{TCE} + 6.5 \times \text{Annual UV Index} \quad (r^2=0.71) \quad (2)$$

Race Normalized Melanoma Cancer Incidence Rate (per 100 k) =

$$26 - 1.3 \times \%\ \text{Adult Smokers} + 250\ CR_{TCE}\ (1 - 22\ CR_{Styrene}) + 6.3 \times \text{Annual UV Index} \quad (r^2=0.79) \quad (3)$$

Where CR_{TCE} and $CR_{Styrene}$ denote the TCE and Styrene NATA calendar year 2011 modeled cancer risks reported for the 50 United States. The Annual UV Index represents the annual averaged solar UV index by State. The % Adult Smokers denotes the percentage of adult smokers by state that varies across the 50 United States. In equation (3), styrene acts as an inhibitor to the TCE contribution to melanoma formation. The annual solar UV index explains 80% of the men melanoma cancer incidence rate data. The air toxic(s) TCE with or without styrene explain 20% of the race normalized melanoma cancer incidence rate data. Smoking acts as a suppressor of melanoma incidences. **Figure 1** graphically shows the multiple regression equation (3) data fit to the race normalized male melanoma incidence rate data for the fifty United States.

Figure 1 here

Discussion

This study identified two regression equations that can explain the variation in the race normalized men melanoma incidence rate data (2008-2012) across the fifty United States. Both equations explain the melanoma cancer incidence data using the annual solar UV index, NATA 2011 cancer risk estimates for one or two air toxics, and the adult smoking % by state. The annual solar UV index explains 80% and air toxic(s) explain 20% of melanoma cancer incidence variations by state across the United States.

For comparison to this study's estimate that the solar UV index explains 80% of melanoma incidences, this study offer up two other estimates. The Canadian Cancer Society (2014) reports the solar UV index is responsible for 90% of Canadian melanoma incidences. On the other hand, the Hispanic melanoma rate is ~20% that of whites and the most common sites of melanoma in non-whites are sun-protected (Rouhani et al., 2008), which would lead to the conclusion that 20% of white melanoma incidences can be attributed to something other than the solar UV index.

The two air toxics TCE and styrene have a combined predicted effect less than the summation of the toxicity of the components. A large number of chemical interactions have been described in animal studies by administering high doses of chemicals by routes and scenarios often different from anticipated human exposures. Though limited, these studies provide evidence to support this predicted occurrence of infra-additive (the combined effects are smaller than the simple summation of the individual effects) chemical interactions in humans (Krishnan and Brodeur, 1994). This study also found that benzene could replace styrene as an interaction term and the data fit data would achieve an almost equivalent correlation.

The regression models predict smoking suppresses melanoma incidence consistent with epidemiological study findings (DeLancey et al., 2011). The prediction that smoking suppresses melanoma incidences does (help) explain a thirty year (1975 to 2005) time trend of higher cutaneous melanoma incidences. From 1975 to 2005, the trend of increasing melanoma incidences in white females (from 5.5 to 13.9 per 100 k; a factor of 2.5) and males (from 4.6 to 7.7 per 100 k; a factor of 1.7) age 15-39 (Purdue et al., 2008) has occurred simultaneously with the % of adults who smoked falling by almost the same factor of 2 from 37% to 21% (CDC, 2016c).

These findings may be used to prioritize research, monitoring, and regulatory intervention activities that reduce potential cancer risks to the United States population.

References

Agency of Toxic Substances & Disease Registry. 2016. Toxic Substances Portal – Trichloroethylene (TCE). Web page: http://www.atsdr.cdc.gov/toxprofiles/tp.asp?id=173&tid=30 ; last accessed 20 May 2016.

Boffeta, P.; and Nyberg, F. 2003. Contribution of environmental factors to cancer risk. British Medical Bulletin. 68, 1, 71-94.

Caldwell, J.C.; Woodruff, T.J.; Morello-Frosch, R.; and Axelrad, D.A. 1998. Application of health information to hazardous air pollutants modeled in EPA's Cumulative Exposure Project. Toxicol Ind Health. 14, 429–454.

Canadian Cancer Society (2014). Melanoma: deadliest type of skin cancer is on the rise. Web page: https://www.cancer.ca/en/about-us/for-media/media-releases/national/2014/2014-canadian-cancer-statistics/?region=on ; last accessed 1 July 2015.

CDC. 2016a. Center for Disease Control and Prevention. Skin Cancer Incidence Rates by Race and Ethnicity. Web site: http://www.cdc.gov/cancer/skin/statistics/race.htm ; last accessed 20 May 2016.

CDC. 2016b. Center for Disease Control and Prevention. Chronic Disease and Health Promotion Data & Indicators. Adult smoker percentages by state for 2012. Web site: https://chronicdata.cdc.gov/health-area/tobacco-use ; last accessed 12 April 2016.

CDC. 2016c. Center for Disease Control and Prevention. Smoking and Tobacco Use. Trends in Current Cigarette Soming Among High School Students and Adults, United States, 1965-2014. Web site: http://www.cdc.gov/tobacco/data_statistics/tables/trends/cig_smoking/ ; last accessed 1 July 2016.

DeLancey, J.O.; Hannan, L.; Gapstur, S.M.; and Thun, M.J. 2011. Cigarette smoking and the risk of incident and fatal melanoma in a large prospective cohort study. Cancer Causes and Control. 22(6):937-42.

Henry J. Kaiser Foundation (2016). Population Distribution by Race/Ethnicity. Web site: http://kff.org/other/state-indicator/distribution-by-raceethnicity/ ; last accessed 20 May 2016.

Krishnan, K. and Brodeur, J.. 1994. Toxic Interactions among Environmental Pollutants: Corroborating Laboratory Observations with Human Experience. Environmental Health Perspectives. Volume 102, Supplement 9, November.

Morello-Frosch, R.; Manuel, P.; and James, S. 2001. Environmental Justice and Southern 'Riskscape': The Distribution of Air Toxics Exposures and Health Risks among Diverse Communities. Urban Affairs Review. 36, 551–78.

National Cancer Institute. 2016. State Cancer Profiles. Web site: http://www.statecancerprofiles.cancer.gov/incidencerates/ ; last accessed 5 May 2016.

NOAA. 2016. UV Index Data with cloud effects. Web site: ftp://ftp.cpc.ncep.noaa.gov/long/uv/cities/ ; last accessed May, 20, 2016.

Purdue, M.P.; Freeman, L.B.; Anderson, W.F.; and Tucker, M.A. (2008). Recent trends in incidence of cutaneous melanoma among U.S. Caucasian young adults. J Invest Dermatol. 128(12): 2905–2908.

Rosenbaum, A.S.; Axelrad, D.A.; Woodruff, T.J.; Wei, Y.H.; Ligocki, M.P.; and Cohen, J.P. 1999. National estimates of outdoor air toxics concentrations; J. Air Waste Manag. Assoc. 49, 1138–1152.

Rouhani, P.; Hu, S.; and Kirsner, R.S. (2008). Melanoma in Hispanic and Black Americans. Cancer Control. 15, 3.

U.S. EPA. 2015. EPA's 2011 National-scale Air Toxics Assessment. Technical Support Document. 2011 NATA TSD. Washington, DC: U.S. Environmental Protection Agency. Web site: https://www.epa.gov/national-air-toxics-assessment/2011-nata-technical-support-document ; last accessed 11 April 2016.

Woodruff, T.J.; Axelrad, D.A. ; Caldwell, J.; Morello-Frosch, R.; and Rosenbaum, A. 1998. Public health implications of 1990 air toxics concentrations across the United States. Environ Health Perspect. 106, 245–251.

Woodruff, T.J.; Caldwell, J.; Cogliano, V.J.; and Axelrad, D.A. 2000. Estimating cancer risk from outdoor concentrations of hazardous air pollutants in 1990. Environ Res. 82, 194–206.

About the Author

Patrick Ryan is a Senior Scientist at Stanley Consultants in Coralville, IA.

Corresponding Author Phone: 1-319-626-5342; e-mail: RyanPatrick@stanleygroup.com

Figure Captions

Figure 1. Five term regression equation (3).

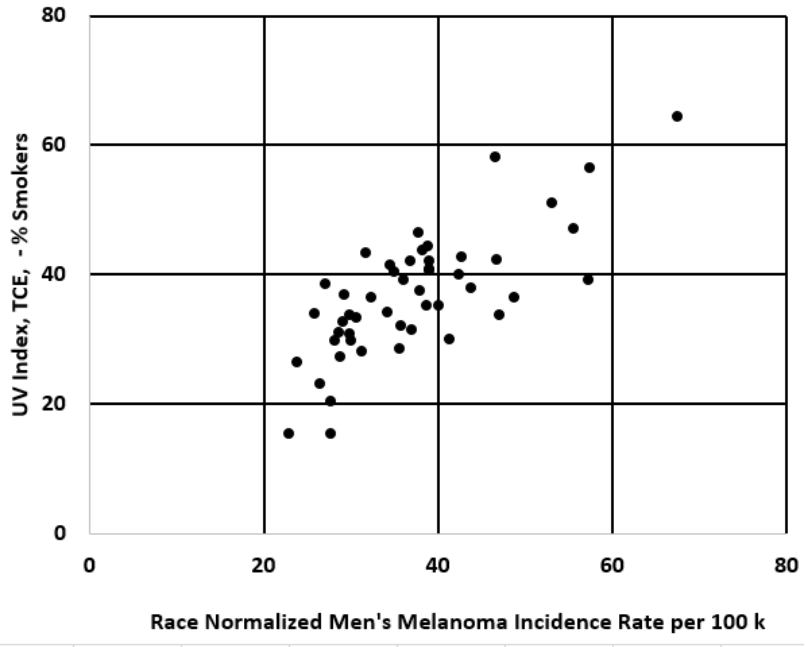

Figure 1. Five term regression equation (3).