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Examination of Malignant Neoplasm and Revealing Relationships with Cigarette Consumption

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ABSTRACT

Tobacco smoking is overwhelmingly the most significant risk factor for cancer and across the board for chronic diseases. Cigarette smoking is causally related to several cancers with inconsistent associations. In this study, malignant neoplasms of larynx and trachea/bronchus/lung, liver and the intrahepatic bile ducts and cervix uteri, other parts of uterus, ovary, and prostate are examined according to their statistics of total death by gender. The aim of this study is to reveal the relationship between cigarette consumption and the number of deaths of malignant neoplasms. Moreover, forecasting for cigarette consumption is performed. According to the predicted values of cigarette consumption, the number of deaths of malignant neoplasms is predicted. Interpretations are provided based on statistical data analyses. This study can act as a guideline for healthcare decision makers for policy making to decrease the risk factors for cancer and other chronic diseases.

Keywords: Forecasting, Statistical data analyses, Regression, Trend projection

INTRODUCTION

In 2010s' Turkey, approximately 20% of deaths are caused by neoplasms and malignant neoplasms constitute almost all of this percentile. There are several main reasons for carcinoma such as biological, environmental, behav-

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ioural factors, etc. According to gender, age, hormones, genetic heritage, mutation of DNA, etc. are considered in biological factors. Environmental factors change with respect to living environment, lifestyle, working place. Behavioural factors depend on individuals' habits.

Tobacco smoking is overwhelmingly the most significant risk factor for cancer and across the board for chronic diseases. (Gelband and Sloan, 2007) Cigarette smoking is causally related to several cancers, particularly lung cancer, yet for some cancers, there are inconsistent associations. (Ray et al., 2010)

In this study, malignant neoplasms of larynx and trachea/bronchus/lung, liver, and the intrahepatic bile ducts and cervix uteri, other parts of uterus, ovary and prostate are examined according to their statistics of total death. These three groups of data are obtained from Turkish Statistical Institute (TUIK) years between 2009-2016. They are described with descriptive statistics like bar chart, pie chart, box plot, and line chart. Their similarities and dissimilarities are interpreted via these charts.

In the other section, these three groups of malignant neoplasms are analysed with trend projection and simple linear regression analysis. The aim of this part was to observe the relationship between cigarette consumption and the number of deaths of malignant neoplasms and to predict future values. Firstly, with the method of trend projection, the future values of cigarette consumption are predicted. Then, according to these future values cigarette consumptions, the number of deaths of malignant neoplasms is predicted, too. The strength of these associations is interpreted.

Literature Review

Pesch et al. (2012) mentioned that maintaining gas exchange in the lung requires tight coordination of functional components, including neural regulation of breathing, plasticity, and permeability of the lung surface and protection from inhaled toxicants. This is reflected in a number of different cell populations that, in case of malignant transformation, can result in a variety of tumours as described in the WHO's histological classification of lung cancer. (World Health Organisation, 1999) Smoking is a strong risk factor for all forms of lung cancer, and among male smokers, squamous cell carcinoma (SqCC) is the predominant subtype. Smoking is also closely associated with small cell

lung carcinoma (SCLC) (Khuder et al, 1998). Adenocarcinoma (AdCa) is the most common subtype in never smokers and women, with increasing incidence rates over time.

Asbestos exposure and cigarette smoking are recognized risk factors for lung cancer mortality, but the exact nature of the interaction between the two remains uncertain. Frost et al. (2011) examined the effect of smoking and smoking cessation among asbestos workers in Great Britain (GB) and investigated the interaction between asbestos exposure and smoking. They performed Poisson regression to estimate relative risks of lung cancer mortality associated with smoking habits of the asbestos workers and to assess whether these effects differed within various categories of asbestos exposure. Also, they estimated the proportion of lung cancers among smokers attributable to the interaction of asbestos and smoking. As a result, the risk of lung cancer mortality increased with packs smoked per day, smoking duration, and total smoke exposure (pack-years). For those asbestos workers who smoked, an estimated 26% (95% CI 14–38%) of lung cancer deaths were attributable to the interaction of asbestos and smoking.

Mihaela et al. (2012) performed artificial intelligence techniques to determine a multivariate model which is able to identify tumour stage and of the histopathological type for lung cancer patients based on predictive environmental and behavioural factors. They indicated that tobacco use and the environmental factors related to the workplace (e.g. metallurgical industry) are the best predictive risk factors for the incidence of lung cancer.

Smoking is the greatest risk factor for lung cancer, being the most probable cause for the great majority of lung cancers for both men and women. The patient working environment is also an important factor influencing the chances of developing lung cancer. (Peto et al., 1994)

According to Doll et al. (2005), a smoker would die from lung cancer with a probability 15 times higher than a non-smoking patient. They examined 50 years observations on British doctors for cancers liability to be caused by smoking showing the mortality rates in relation to smoking habits of 13 types of cancer in men. They inspected eight of the specified types of cancer and cancers of unspecified type but the most notably lung cancer were all clearly related to smoking, in that there were statistically significant positive trends in the mortality rates from lifelong non-smokers through light and moderate

cigarette smokers to heavy cigarette smokers and from non-smokers through ex-smokers to continuing smokers.

Cigarette smoking is causally related to several cancers, particularly lung cancer, yet for some cancers, there are inconsistent associations. Ray et al (2010) investigated the association of smoking with other cancers by correlating them with the regional incidence rates for lung cancer, which was used as a proxy for cigarette smoking.

METHODOLOGY

Descriptive Statistics

It is always beneficial to describe a problem or a model visually. This helps to focus on the important points of an entire system. Well-constructed data summaries and displays are essential to good statistical thinking because they can focus the engineer on important features of the data or provide insight about the type of model that should be used in solving the problem. (Montgomery and Runger, 2012: 190)

There are many types of descriptive statistics to display data. A researcher would choose which one is he going to use according to his data set and his points to consider. Box plot, bar chart, line chart and pie chart were more suitable with respect to data which was obtained from different sources for this study.

a. Box Plot

Exploratory data analysis involves the use of statistical techniques to identify patterns that may be hidden in a group of numbers. One of these techniques is the "box plot," which is used to visually summarize and compare groups of data. The box plot uses the median, the approximate quartiles, and the lowest and highest data points to convey the level, spread, and symmetry of a distribution of data values. It can also be easily refined to identify outlier data values and can be easily constructed by hand. We apply box plots to tabular data from two recently published articles to show how readers can use box plots to improve the interpretation of data in complex tables. The box plot, like other visual methods, is more than a substitute for a table: It is a tool that can improve our reasoning about quantitative information. We recommend that the box plot be used more frequently. (Williamson et al, 1989)

b. Bar Chart

A bar chart similarly looks like a histogram but what is different on a bar chart is, it is to display categorical data sets. Each column's height or length is proportional to categories. Usually, x-axis is for categories and y-axis is for the value of its category.

This is a very useful way to compare groups between each other. Peak areas, minimum and maximum values are able to be seen clearly.

One of the most important points for a bar chart is that it is for discrete variables and on the chart, the columns for each group should be separated from each of them.

c. Line Chart

When a quantitative variable is recorded over time at equally spaced intervals (such as daily, weekly, monthly, quarterly, or yearly), the data set forms a time series. Time series data are most effectively presented on a line chart with time as the horizontal axis. The idea is to try to discern a pattern or trend that will likely continue into the future, and then to use that pattern to make accurate predictions for the immediate future. (Mendenhall, 2012)

d. Pie Chart

Pie chart is a circular chart to represent one unit. All of its slices are proportional to this unit. It is easy to observe a category's percentile in a whole.

Simple Linear Regression Analysis & Trend Projection

Many problems in engineering and science involve exploring the relationships between two or more variables. Regression analysis is a statistical technique that is very useful for these types of problems. For example, in a chemical process, suppose that the yield of the product is related to the process-operating temperature. Regression analysis can be used to build a model to predict the yield at a given temperature level. This model can also be used for process optimization, such as finding the level of temperature that maximizes yield, or for process control purposes. (Montgomery and Runger, 2012: 373)

Regression analysis is used to predict the value of the dependent variable based on the value of at least one independent variable. Dependent variable(y)

is the variable we wish to explain. Independent variable(y) is the variable used to explain the dependent variable.

There are two types of regression analysis; simple linear regression and logistic regression. If there is only one independent variable in the analysis, it is simple linear regression but if there are more than one independent variable, then it is logistic regression analysis.

In simple linear regression model, there is only one independent variable. The model shows us the relationship between x and y which is described by a linear function. Changes in y variable are assumed to be caused by changes in x variable.

General formula for simple linear regression model is;

$$y = \beta_0 + \beta_1 x + \varepsilon \qquad (1)$$

β_0 represents the population y-intercept coefficient of this model. β_1 represents the population slope coefficient of this model's line. ε represents the random error term or residual. For the forecasting model, the equations become;

$$= b_0 + b_1 x \qquad (2)$$

b_0 and b_1 values are for predicted values of β_0 and β_1. Sample regression line provides prediction of population regression line.

There are several assumptions for linear regression. Error values (ε) are statistically independent and they are normally distributed for any given x value. The underlying relationship between x and y variables are linear. The probability distribution of errors is normal and it has constant variance.

To interpret b_0 and b_1, we can say that b0 is the predicted average value of y when the value of x is equal to zero and b1 is the predicted change in the average value of y as a result of one-unit change in x.

Trend projection is similar to simple linear regression but the difference is that its independent variable(t) is time. This analysis is to predict future values according to the time passed. Numerical data should be obtained at regular time intervals. Time intervals can be annual, quarterly, daily, hourly distributed. Trend projection can be summarized as predicting trend line using regression analysis. The general formula for trend projection is;

$$= b_0 + b_1 t \qquad (3)$$

Correlation Analysis

Correlation analysis is used to evaluate the strength of association between two variables. There may be a non-linear relationship between variables, but correlation analysis does not detect this. Also, this analysis is not related to the causal effect of these two variables.

Scatter plot is used to show the relationship between two variables. We can see the linearity from the shape of the distribution of dots on the plot.

The strength of this association is measured with a correlation coefficient. It is shown as r for sample, ρ for population. Sample correlation coefficient r is the estimate of population correlation coefficient ρ and is used to measure the strength of association in sample observations.

ρ or r is a unit free coefficient. Its range is between -1 and 1. If its value is closer to the -1, we can say there is a stronger negative linear relationship. If its value is closer to the 1, we can say there is a stronger positive linear relationship. If its value is closer to the 0, we can say there is a weaker linear relationship.

RESULTS

Data Extraction

Data of neoplasms of death is obtained from Turkish Statistical Institute (TUIK) years between 2009-2016. The data is extracted from the data of the distribution of causes of death by gender 2009-2016 that is published at TUIK.

Data for domestic sales for cigarette consumption is taken by years. Annual data on cigarette sales were obtained from the Tobacco and Alcohol Market Regulatory Authority (TAPDK). Data were available from 1925 until 2016. Cigarette sales numbers which they are the numbers to show domestic sales years between 1925-2016 were displayed as billion units. The data has obviously continuous variables.

Descriptive Statistics

When we look at the box plots that are given below, we can compare males and females in themselves basically. Male_1, Male_2, Male_3, and Male_4 represents the number of deaths because of malignant neoplasms of larynx and trachea/bronchus/lung, malignant neoplasms of liver and intrahepatic bile

ducts, malignant neoplasms of cervix uteri, other parts of uterus, ovary, and prostate and malignant neoplasms of others for males, respectively. Female_1, Female_2, Female_3, and Female_4 represents the number of deaths because of malignant neoplasms of larynx and trachea/bronchus/lung, malignant neoplasms of liver and intrahepatic bile ducts, malignant neoplasms of cervix uteri, other parts of uterus, ovary and prostate, and malignant neoplasms of others for females, respectively.

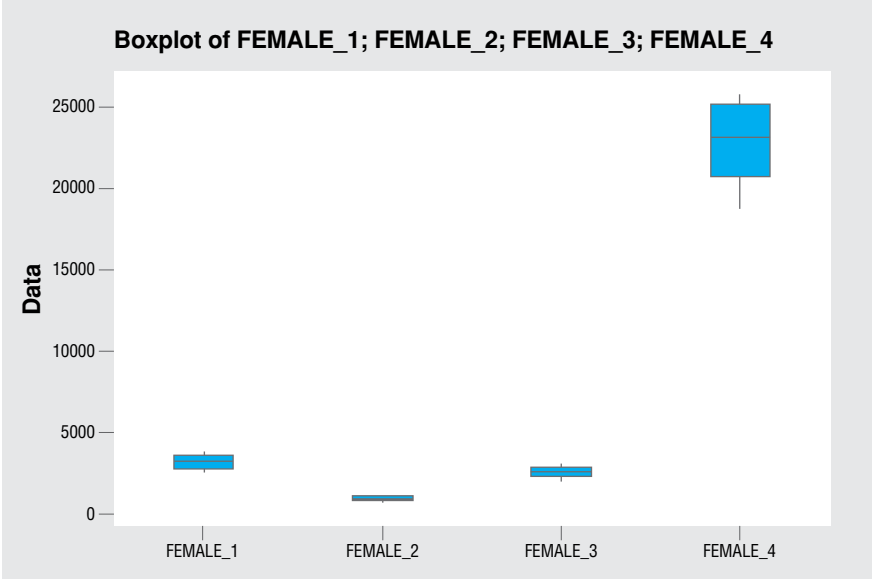

Figure 1: Boxplot of Females

As we can see from the figure 1, Female_1, Female_2 and Female_3's medians are close to each other and their variabilities are less than Female_4. Female_4 has higher median and larger variability.

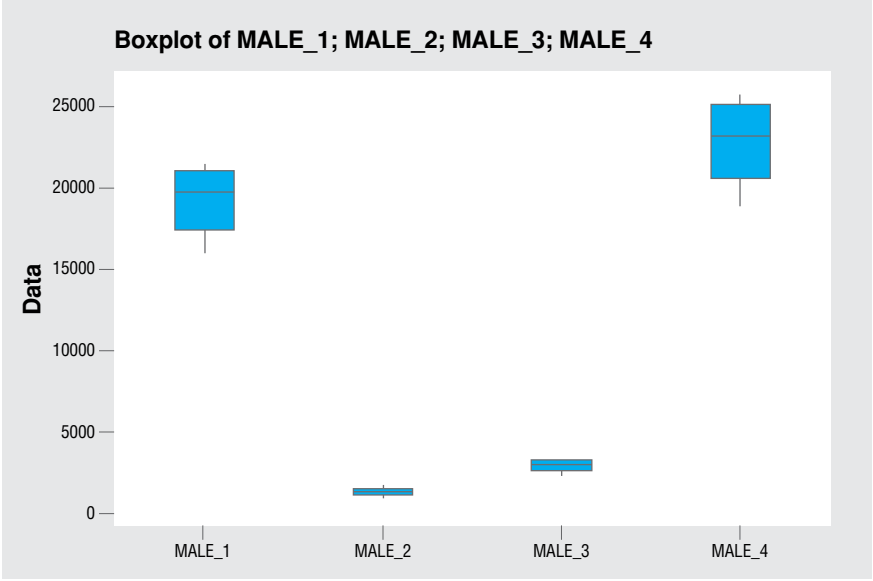

Figure 2: Boxplot of Males

In the figure 2, we can see that Male_2 has the smallest median when we compare to others and Male_4 has the largest median. Male_2 and Male_3 have smaller variabilities rather that Male_1 and Male_4. Male_1 and Male_4's plots are left skewed.

The biggest difference between boxplot for males and females is in the malignant neoplasms of larynx and trachea/bronchus/lung. There is a noticeable change between Male_1 and Female_1. We can conclude that males have bigger proportion rather than females. (Mihaela et al.,2012)

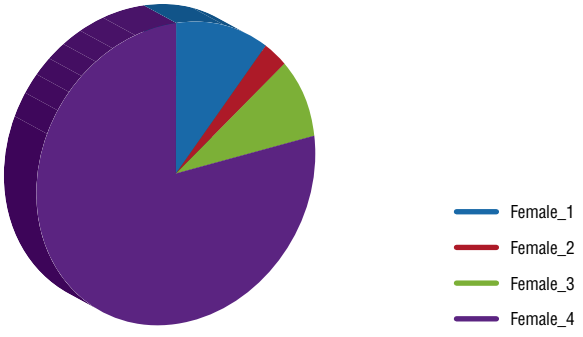

Figure 3: Pie Chart for Females

To interpret figure 3, except the malignant neoplasms of others, malignant neoplasms of larynx and trachea/bronchus/lung has greater percentile. Malignant neoplasms of liver and intrahepatic bile ducts have the smallest percentile in the total.

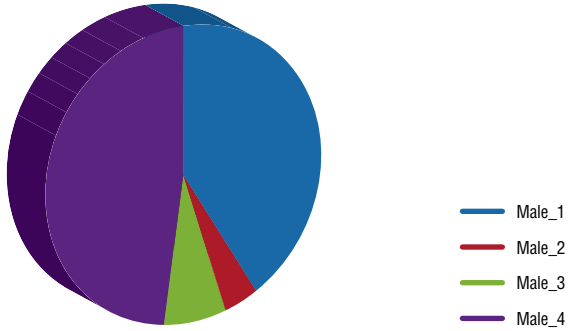

Figure 4: Pie Chart for Males

As we can see from the figure 4, malignant neoplasms of larynx and trachea/bronchus/lung have a great percentile rather than the malignant neoplasms of liver and intrahepatic bile ducts and malignant neoplasms of cervix uteri other parts of uterus, ovary, and prostate. Malignant neoplasms of liver and intrahepatic bile ducts have the smallest slice in the chart.

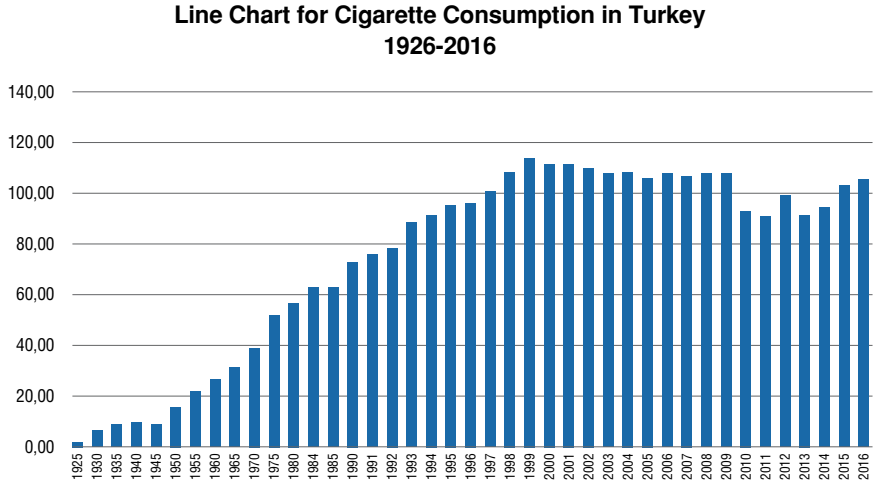

Figure 5: Line Chart of Cigarette Consumption in Turkey, 1925-2016

We can see from figure 5 that cigarette consumption is mainly increasing year after year. When we look at this graph carefully, we can face a strong slump after 2009. It is possible to comment on this slump that it caused by ban on smoking in the closed areas of the Turkish Republic Ministry of Health. This is the most probable reason for this situation. The other significant point is there is a peak area in 1999. We can interpret this peak is caused by the psychological influences of the earthquake and economic crisis in 1999.

Regression Analysis & Trend Projection

Trend projection model for cigarette consumption is;

$$\hat{y} = 96{,}29 + 0{,}45t \qquad (4)$$

Predictions until 2023 for cigarette consumption are given in Table 1.

Table 1: Computations for Trend Projection of Cigarette Consumption

years	t=integer for years	y=cigarette consumption
2017	9	100.33
2018	10	100.78
2019	11	101.23
2020	12	101.68
2021	13	102.13
2022	14	102.58
2023	15	103.03

Next future values for the types of malignant neoplasms will be predicted according to the predictions in Table 1.

Simple linear regression model for malignant neoplasms of larynx and trachea/bronchus/lung is;

$$\hat{y} = 20830.28 + 3.8x \qquad (5)$$

Predictions until 2023 for malignant neoplasms of larynx and trachea/bronchus/lung are given in Table 4.3.2.

Table 2: Computation for Simple Linear Regression Analysis of Malignant Neoplasms of Larynx and Trachea/Bronchus/Lung

years	x=cigarette consumption	y=number of m.n. of larynx and trachea/bronchus/lung	y=cigarette consumption
2017	100.33	21211	100.33
2018	100.78	21213	100.78
2019	101.23	21215	101.23
2020	101.68	21216	101.68
2021	102.13	21218	102.13
2022	102.58	21220	102.58
2023	103.03	21221	103.03

Simple linear regression model for malignant neoplasms of malignant neoplasms of liver and the intrahepatic bile ducts is;

$$\hat{y} = 2391.29 + 2.67x \quad (6)$$

Predictions until 2023 for malignant neoplasms of liver and the intrahepatic bile ducts are given in Table 3.

Table 3: Computation for Simple Linear Regression Analysis of Malignant Neoplasms of Liver and the Intrahepatic Bile Ducts

years	x=cigarette consumption	y =number of m.n. of liver and the intrahepatic bile ducts
2017	100.33	2660
2018	100.78	2661
2019	101.23	2662
2020	101.68	2663
2021	102.13	2664
2022	102.58	2666
2023	103.03	2667

Simple linear regression model for malignant neoplasms of Simple linear regression model for malignant neoplasms of cervix uteri, other parts of uterus, ovary & prostate is;

$$\hat{y} = 6788.38 - 10.557x \quad (7)$$

Predictions until 2023 for malignant neoplasms of cervix uteri, other parts of uterus, ovary & prostate are given in Table 4.

Table 4: Computation for Simple Linear Regression Analysis of Malignant Neoplasms of Cervix Uteri, Other Parts of Uterus, Ovary & Prostate

years	x=cigarette consumption	y =number of m.n. of cervix uteri, other parts of uterus, ovary & prostate
2017	100.33	5730
2018	100.78	5725
2019	101.23	5721
2020	101.68	5716
2021	102.13	5711
2022	102.58	5706
2023	103.03	5702

Correlation Analysis

In the figure 6, there is scatter plot for regression model of malignant neoplasms of larynx and trachea/bronchus/lung.

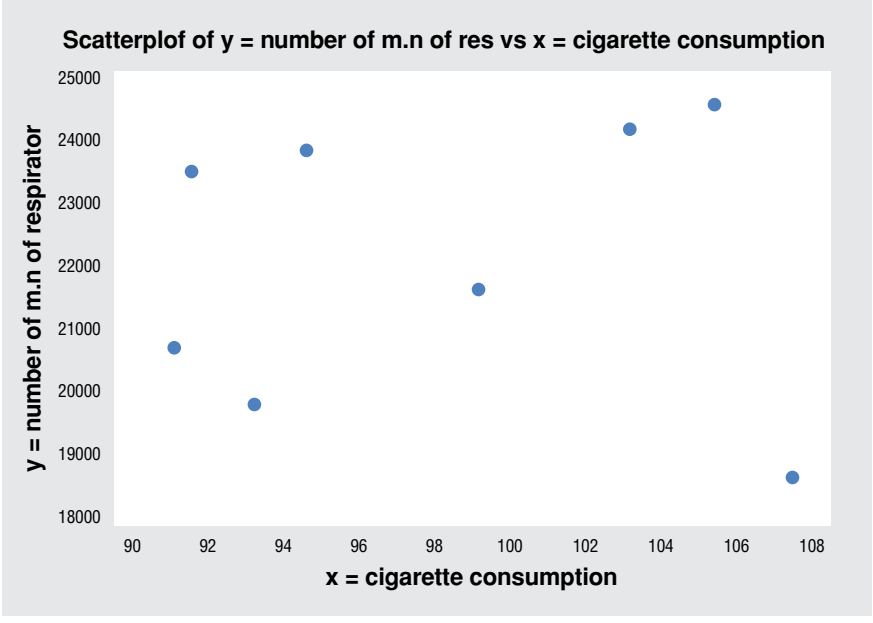

Figure 6: Scatter Plot for Malignant Neoplasms of Larynx and Trachea/Bronchus/Lung

In the figure 6, there is scatter plot for regression model of malignant neoplasms of liver and the intrahepatic bile ducts.

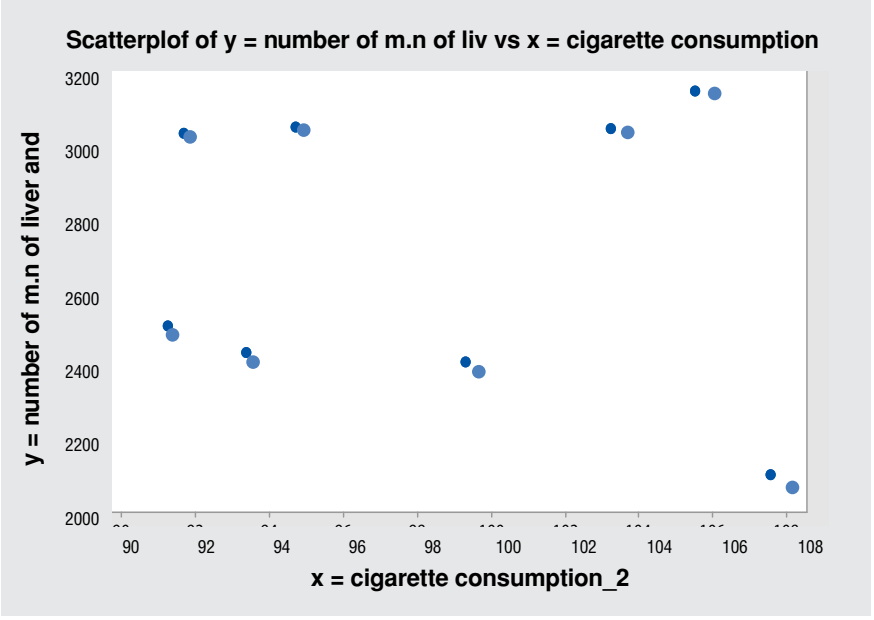

Figure 7: Scatter Plot for Malignant Neoplasms of Liver and the Intrahepatic Bile Ducts

In the figure 7, there is scatter plot for regression model of cervix uteri, other parts of uterus, ovary & prostate.

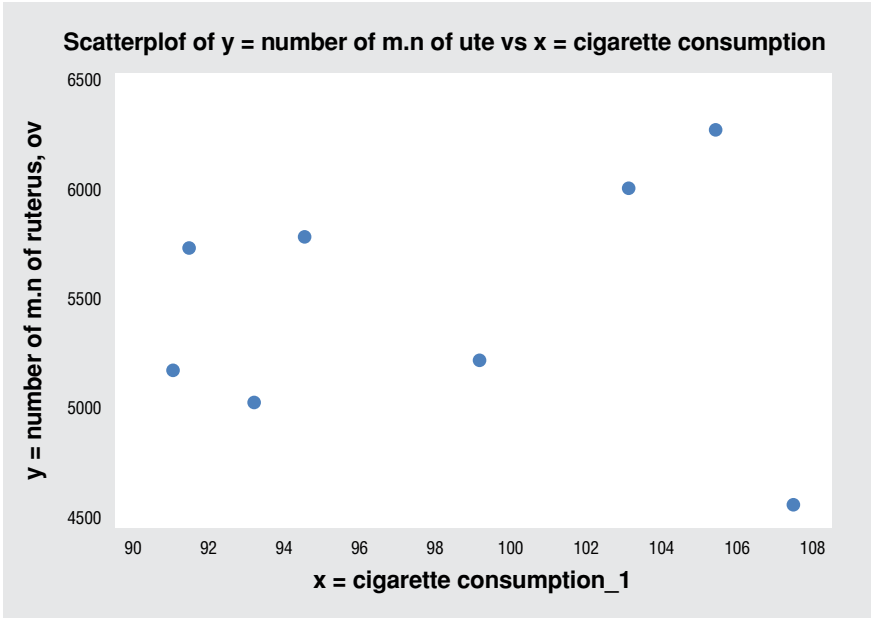

Figure 8: Scatter Plot for Malignant Neoplasms of Cervix Uteri, Other Parts of Uterus, Ovary & Prostate

Table 4: Values of r and R2 for Each Three Groups

	r	R^2
Malignant Neoplasms of Larynx and Trachea/Bronchus/Lung	0.01	0.0001
Malignant Neoplasms of Liver and the Intrahepatic Bile Duct	-0.09	0.009
Malignant Neoplasms of Cervix Uteri, Other Parts of Uterus, Ovary & Prostate	0.04	0.001

As it is shown in the Table 4.4.1, r values imply there are weak linear relationships between cigarette consumption and these three types of malignant neoplasms, R2 values implies that linear trend models cannot be fitted adequately for the data.

DISCUSSION S AND CONCLUSION

In this study, the numbers of four groups of malignant neoplasms are examined. Their similarities and dissimilarities are identified. The aim of this study is to reveal the relationship between cigarette consumption and the number of deaths of malignant neoplasms and to predict future values. Firstly, with the method of trend projection, the future values of cigarette consumption are predicted. Then, according to these future values cigarette consumptions, the number of deaths of malignant neoplasms is predicted, too.

When we compare malignant neoplasms of larynx and trachea/bronchus/lung, malignant neoplasms of liver and intrahepatic bile ducts and malignant neoplasms of cervix uteri, other parts of uterus, ovary, and prostate in the female deaths, there is no significant difference between proportions of these types of neoplasms having the same median approximately.

When we look at the malignant neoplasms of larynx and trachea/bronchus/lung, malignant neoplasms of liver and intrahepatic bile ducts and malignant neoplasms of cervix uteri, other parts of uterus, ovary and prostate in the male deaths, malignant neoplasms of larynx and trachea/bronchus/lung have such a big slice, larger median and more variability rather than others.

Predicted values are obtained; the number of cigarette consumption is expected to reach 103.03 billion units in 2023. For malignant neoplasms of larynx and trachea/bronchus/lung, according to the predicted cigarette consumptions values, the number of deaths because of malignant neoplasms of larynx and trachea/bronchus/lung is increasing. For malignant neoplasms of liver and the intrahepatic bile ducts, according to the predicted cigarette consumptions values, the number of deaths because of malignant neoplasms of larynx and trachea/bronchus/lung is increasing. For malignant neoplasms of cervix uteri, other parts of uterus, ovary, and prostate, according to the predicted cigarette consumptions values, the number of deaths because of malignant neoplasms of larynx and trachea/bronchus/lung is decreasing. According to the examinations and comparisons that are given above, cigarette consumption affects malignant neoplasms of larynx and trachea/bronchus/lung more than the others. The coefficient of independent variable is the greatest in its model, which means a change in cigarette consumption effects more malignant neoplasms of larynx and trachea/bronchus/lung.

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Results. This section could include preparation, isolation, synthetic schemes and tables of data.

Discussion and Conclusions. The discussions should be descriptive. Authors should discuss the analysis of the data together with the significance of results and conclusions. An optional conclusions section is not required.

Sections above (Methodology, Results, Discussion and Conclusions) are not required for review articles.

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PDB ID Codes: Include the PDB ID codes with assigned compound Arabic number. Include the statement "Authors will release the atomic coordinates and experimental data upon article publication."

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Specialized Data

Biological Data. Quantitative biological data are required for all tested compounds. Biological test methods must be referenced or described in sufficient detail to permit the experiments to be repeated by others. Detailed descriptions of biological methods should be placed in the experimental section. Standard compounds or established drugs should be tested in the same system for comparison. Data may be presented as numerical expressions or in graphical form; biological data for extensive series of compounds should be presented in tabular form.

Active compounds obtained from combinatorial syntheses should be resynthesized and retested to verify that the biology conforms to the initial observation. Statistical limits (statistical significance) for the biological data are usually required. If statistical limits cannot be provided, the number of determinations and some indication of the variability and reliability of the results should be given. References to statistical methods of calculation should be included.

Doses and concentrations should be expressed as molar quantities (e.g., mol/kg, μmol/kg, M, mM). The routes of administration of test compounds and vehicles used should be indicated, and any salt forms used (hydrochlorides, sulfates, etc.) should be noted. The physical state of the compound dosed (crystalline, amorphous; solution, suspension) and the formulation for dosing (micronized, jet-milled, nanoparticles) should be indicated. For those compounds found to be inactive, the highest concentration (in vitro) or dose level (in vivo) tested should be indicated.

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Confirmation of Structure. Adequate evidence to establish structural identity must accompany all new compounds that appear in the experimental section. Sufficient spectral data should be presented in the experimental section to allow for the identification of the same compound by comparison.

List only infrared absorptions that are diagnostic for key functional groups. If a series contains very closely related compounds, it may be appropriate merely to list the spectral data for a single representative member when they share a common major structural component that has identical or very similar spectral features.

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