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Age and Sex as Risk Factors for Lung Cancer in Setif Region - Algeria: Fuzzy Inference Modeling

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Authors' contributions

This work was carried out in collaboration between all authors. Author S. Bouaoud designed the study. Author KB performed the statistical analysis. Author AM wrote the protocol. Author LK wrote the first draft of the manuscript. Author NB managed the analyses of the study. Author S. Bouharati performed intelligent analysis. Author MHC managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Aims: The risk factors for lung cancer are multiple. Smoking, Exposure to secondhand smoke, Exposure to radon gas, Exposure to asbestos and other carcinogens, Family history of lung cancer. However, what characterizes these factors is uncertainty and vagueness. Several analytical studies have been devoted to this domain, but the complexity of the environment makes it very difficult to model those using conventional mathematical or statistical tools. Also, the classical tools of analysis characterized by the vagueness. This insufficiency is compensated in our method by the fuzzyfication of the variables. In this study, age and sex are analyzed over a period from 2006 to 2014 according with the incidences recorded. Given the characteristic of the variables analyzed, a fuzzy logic system is proposed.
Methods: The input variables (age and sex) are fuzzyfied as well as the output variable which

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expresses the corresponding lung cancer incidence. By referring to the values recorded over the entire period, a rule base is established. The basis of the rules encompasses all possible combinations.

Results: The result is an algorithmic application which makes it possible to instantly read the expected incidence as a function of the values introduced randomly at the input of the system. The result at the output takes into consideration the collaboration of all the parameters at the input.

Conclusion: As these factors are considered fuzzy. This makes it possible to have the most precise result possible. The presentation is symbolic and numerical and expressed instantaneously.

Keywords: Lung cancer; risk factors; fuzzy logic.

1. INTRODUCTION

Despite major advances in understanding and treating cancer, the relative survival rate in North Africa is 5 years. With the exception of Algeria, where squamous cell carcinomas are more frequent, and are approximately in the same proportion in males, adenocarcinomas tend to predominate in females. An obvious risk is found in the prevalence of tobacco and the incidence of lung cancer in Algeria in men than in women. The overall incidence and mortality rate of lung cancer in Algeria is (15.4%). The incidence rates observed in Algeria (Setif) is low compared to those of the Western countries and even Tunisia. These data are provided by state and territory, remoteness, socio-economic status [1]. Lung cancer accounts for 19% of all cancer deaths [2]. About 27% of the global cancer deaths in the United States by about 2015 and 20% by 2016 in the European Union [3]. The incidence of lung cancer is low in both sexes in people under the age of 40 and increases until the age of 75 to 80 years. In several countries, the peak of the tobacco-related lung cancer epidemic was reached by the generation born in the years 1930-1940 [4]. The analysis by the classical mathematical tool mainly the differential equations are very complex. A differential equation cannot include several variables. Also the statistical tool, its results always remain in the probable, the significant or the not significant.

The use of artificial intelligence techniques have found application in many fields, including in the field of medicine such as diagnosis, treatment of disease, patient follow-up, disease risk prediction and so on. Artificial intelligence techniques make it possible to design systems that allow the construction of intelligent models to predict patients' response to treatment and to determine the prediction of disease risk. Fuzzy logic as a domain of artificial intelligence finds its application very adequate in this field [5]. Data deficiencies may be related to the phenomenon itself. This is generally the case in medicine, when the factors that intervene are characterized by their vagueness and far from being accurate and can be interpreted in the same way for all patients. Conditions vary in a given situation.

In this analysis we try to give a basic introduction to the basic notions of fuzzy logic in order to facilitate the understanding of its application. The risk factors analyzed (age, sex, years) are considered as fuzzy variables and as such they must be fuzzyfied. A rule base is established based on the real values recorded over the entire study period. The result is an application to predict the onset of lung cancer just by randomly introducing variables to the input of the system. This will give physicians and public health officials the opportunity to predict the occurrence of this type of cancer and to make the necessary arrangements. This tool can then constitute help and support in this field.

2. RISK FACTORS

There are several types of lung cancer risk factors, some may be changed and others may not. Although the cause of lung cancer is not fully understood, it is known that people with certain risk factors are more likely than others to develop this disease. Age for example can be a risk factor. The most obvious cause of lung cancer is tobacco. Lung cancer among non-smokers, which accounts for up to 15% of cases, is often attributed to other factors such as genetics, radon gas, and asbestos and air pollution [1].

Smoking, age, occupational exposure (asbestos, radon), air pollution, genetic predisposition and low consumption of fruits and vegetables all increase the chances of developing lung cancer [6]. However, cancers occurring in a given year, related to specific risk factors, are likely to be linked to cumulative exposures to the relevant factor over a period of several years since their joint effects are multiplicative [7].

2.1 Age

At a middle age, the risk factors for lung cancer multiply. This increases with age. As the number of elderly people increases, the number of cancer patients increases accordingly. These arguments make it necessary to take the necessary preventive measures at an earlier age. Also human metabolism varies according to age. Vulnerability is also increasing. Among others, predisposition to lung cancer.

2.2 Sex

Studies show that lung cancer is less pronounced in women than in men. While a number of results predict the increase in women with breast cancer, this is still below the male sex. Even with respect to the risk of death, males remain higher than females regardless of age of diagnosis.

2.3 Tobacco

Tobacco is the most frequently modifiable risk factor for cancers [8]. Smoking accounts is nearly 90% of all cases of lung cancer. Smoking is the most common cause of death in the world. The vast majority of lung cancers occurs in smokers could be prevented by smoking cessation [9]. Smoking is the leading cause of all major histological types of lung cancer. A carcinogenic effect of tobacco smoke on the lung has been demonstrated in epidemiological studies conducted since the early 1950s and has been recognized by public health and regulatory authorities since the mid-1960s [10]. The geographic and temporal profiles of the disease largely reflect the consumption of tobacco accumulated in previous decades [11,12]. The excess risk in smokers compared to non-smokers is in the order of 20 to 50 times. The duration of smoking is considered the most important risk of lung cancer in smokers [13]. In the case of new smokers, at a reduced dose, a displacement of the site of the disease is therefore found in the lung cancer histology, from the squamous cell, Adenocarcinoma. Their impact on the overall risk of lung cancer, compared to older tar cigarettes, is still quantifying [14]. Lung cancer in non-smokers represents a distinct clinical entity with unique epidemiological, clinical and molecular characteristics. A high level of suspicion leading to a rapid diagnosis and treatment with targeted agents in appropriate cases should be the primary focus for clinicians. Future collaborative efforts should focus on conducting studies in this part of the globe to further delineate underlying biological differences, identify potential non-tobacco risk factors, molecular differences and further refine treatment strategies for these groups of patients [15].

2.4 Asbestos

All the different forms of asbestos (chrysotile and amphiboles, including crocidolite, amosite and tremolite) are carcinogenic to human lung ([16]. Asbestos can cause a variety of lung diseases, including lung cancer. Exposure to asbestos is strongly associated with the cause of lung cancer. Exposure to asbestos increases the risk of developing respiratory cancer up to five times. Tobacco smoke and asbestos exposure work synergistically and the risk of developing lung cancer among people who smoke tobacco and have a history of exposure to asbestos is 80 to 90 times higher to the population [17].

2.5 Viruses

Viruses are known to be a cause of lung cancer in animals, and recent evidence suggests a similar potential in humans. The viruses involved include human papillomavirus, JC virus, simian virus (SV40), BK virus and cytomegalovirus. These viruses can inhibit apoptosis, allowing control of cell division [1].

2.6 Family History of Lung Cancer

The effects of family history on the risk of lung cancer by histological types suggest that family aggregation of lung cancer is independent of those associated with smoking. The association between a family's history of lung cancer in a parent and lung cancer varies according to ethnicity. Family history is an approximation of the genetic risk and varies with environmental exposures. The association between lung cancer and a family history of lung cancer remains significant [18].

2.7 Other Environmental Agents

2.7.1 Air pollution

Air pollution, including exposure to nitrogen oxides and hydrocarbons from the exhaust gases of transport vehicles, constitutes a risk of lung cancer [19]. Air pollution that contains gases, dust or fumes in amounts considered harmful to the health or comfort of humans and animals may increase the risk of lung cancer. It involves many components such as carbon monoxide, nitrogen dioxide, sulfur dioxide, ozone and particulate matter [20]. Indoor air pollution is considered an important risk factor for lung cancer among non-smokers in several parts of Asia. In Europe, an association between indoor air pollution and the risk of lung cancer has been reported [21].

2.7.2 Dietary

Fruits and vegetables rich in dietary fiber are considered protective against lung cancer. Diets rich in fruits and vegetables appear to be associated with lower rates of lung cancer [22].

3. TYPES OF LUNG CANCER

There are several types of lung cancer. Types are classified into two main groups: small cell carcinoma and non-small cell carcinoma. They are classified in this way because their histological characteristics are distinct and also because their treatment is different. Lung cancer consists of a heterogeneous set of invasive tumors that have as origin the different types of cells in the lung. The type of cancer depends on risk factors, history of natural behavior and responsiveness to therapeutic interventions [20]. We can classify lung cancers according to the cell type in question. Small cell carcinoma which usually arises from epithelial cells that line the surface of the centrally located bronchi [23], non-small cell carcinoma which consists of a heterogeneous set of invasive tumors that tend to grow and spread more slowly than small cell lung cancer. Also, Squamous cell carcinoma begins in the squamous cells that cover the airways in the larger and more central part of the lungs. Adenocarcinoma develops from the epithelium or glandular cells (that is, mucus producing cells) in the peripherally located bronchioles and alveoli and the large cell carcinoma can form in any part of the lung and tends to grow and spread quickly [20].

4. DATA ANALYSIS

The use of massive quantities of information and relatively simple learning algorithms makes it possible to solve problems that have recently been considered inaccessible. The possibility of predicting a phenomenon from past observations presupposes the existence of a causal mechanism. To predict a phenomenon, two possibilities arise. The first, that used, will consist in understanding this causal mechanism by elaborating an explanatory model. The second, without being as ambitious remains very useful. It seeks only to discover significant correlations in a set of observations, that is, to find a predictive model. In both cases, we need exact measured values; however, most recorded data are characterized by their uncertainty and their imprecision. As noted above, several risk factors are involved in the development of lung cancer. It becomes impossible to analyze with precision the weight of the effect of each meter. The fuzzy logic treats the information as linguistic variables. In this mode of reasoning emanates human reasoning. Reasoning by the approximate can fill in the deficiencies related to the measured values and the complexity of the system of factors that intervene in lung cancer. Fuzzy logic analysis becomes a necessity. To avoid this handicap, we propose in this study the data analysis using fuzzy logic inference system.

4.1 Data Sources

In our study, a key data source was the Setif (Algeria) Cancer Registry. The Registry is a database that holds information on population incidence per 100,000 by age group (Period) Male and Female cancer cases diagnosed between 2006 and 2014. Table 1 presents the age-standardized rates of lung cancer in men and women (at all ages) in Setif region –Algeria- as a whole, in 2006–2014, with the corresponding percent change.

4.2 Fuzzy Inference System

Medicine and epidemiology are the area where the need for a tool dealing with the uncertain is most pressing. Any disease whatsoever may manifest itself in different ways from one person to another with different pathological states. Different diseases can be manifested by a single symptom. Whereas in one person, several diseases coexist, it becomes even more complicated and imprecise [24]. Nowadays, fuzzy logic is considerate as a tool for modeling and processing in natural language. Fuzzy logic can be considered as a qualitative computational approach. Since uncertainty is inherent in areas such as medicine, it takes this uncertainty into account. The theory of fuzzy sets can be considered as an appropriate formalism in intrinsic processing in the biomedical field [24].

The fuzzy variables in medical terms are imprecise: truth is expressed by degrees. A fuzzy proposition may be true to some extent. The standard examples of fuzzy propositions use linguistic variables with possible true, such as race black or white values. The phrase "patient is African" is true to some extent – more the darker of patient color more the sentence is true. The truth of a proposition is expressed by its degree. In fuzzy logic, if we assume X is a set serving as the universe of discourse, a fuzzy subset A of X is associated with a function: µA: X → [0 , 1] which is generally called membership function. The idea is that for each x, µA(X) indicates the degree to which X is a member of the fuzzy set A [25].

4.2.1 Fuzzy variables

Unlike the binary variables that are defined by the two states "true" or "false", in binary the (1 and 0), the fuzzy variables present a gradation between the value "true" and the value "false". Two remarks are necessary about this representation: On the one hand, it is preferable to represent the state of the variable using its degree of truth by associating the value 1 (degree of truth of 100%) with the value "true" and the degree of truth zero at "False" value. On the other hand, we see that this way of doing things is very far from the reality and what the human being does when he solves this kind of problem.

4.2.2 Fuzzy intervals

These intervals define the number of fuzzy variables associated with an input variable. In the case of people's ages, for example, fuzzy intervals are used: "Adult" and "Old". Moreover, each interval refers to a membership function which allows defining the degree of truth of the corresponding fuzzy variable according to the age of the person and therefore his belonging.

4.2.3 Fuzzyfication of the membership function

Every fuzzy subset A of U can be defined by a particular mathematical function which gives a weighting to each element X∈U. This function is called membership function, it is denoted by $\mu_A : x \in U \rightarrow \mu_A(x) \in [0,1]$

4.2.4 Inferences rules

A fuzzy implication between two elementary propositions is a relation R between the two sets U1 and U2, quantifying the degree of truth of the proposition: If (X is A) Than (Y is B).

4.2.5 Fuzzification

In order to make fuzzyfication, the linguistic expressions below are used. The proposed fuzzy logic factors impact control system consists of five inputs variables.

- Fuzzy variable “Age” has the linguistic values young; old; very old
- Fuzzy variable “Years” has the linguistic values from 2006 to 2014 by creating fuzzy intervals between two neighboring years.
- Fuzzy variable “Incidence” has the linguistic values; Small, Mean, High
- Sex variable is not fuzzyfied, we attribute (1 for male; 2 for female).

The mapping values of input variable through the membership function are the linguistic values. The linguistic values of inputs are shown as a result (Age, Sex, and Years). The number of recorded cases expresses the output variable of the system. A bloc system is constructed (Fig. 1) with three inputs and one output.

4.2.5.1 Fuzzyfication of the input variable "Age"

The input that represents the age is expressed by three fuzzy intervals and membership functions defining the young; old; very old. Fig. 2.

The variable 'Sex' is not fuzzyfied, we attribute numerical values for each sex, (1 for Male and 2 for Female)

4.2.5.2 Fuzzyfication of the input variable "Years"

The input that represents the age is expressed by three fuzzy intervals and membership functions defining the years from 2006 to 2014. Fig. 3.

4.2.5.3 Fuzzyfication of the output variable "Incidence"

In the same way, the output variable that represents the incidence of the lung cancer according input variables is expressed by three fuzzy intervals and membership functions defining the: Low risk, Mean and High. Fig. 4.

The (Table 1) includes the 2006 - 2014 incidences of lung cancer patients by age and sex. These cases are recorded from the cancer registry of the Setif region in Algeria.

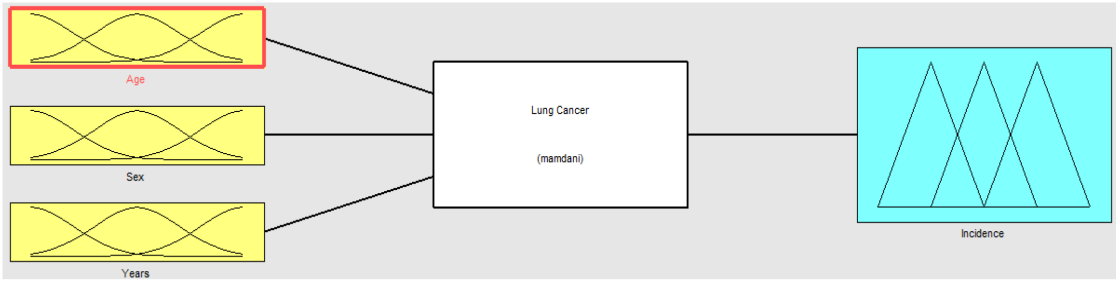

Fig. 1. Block diagram

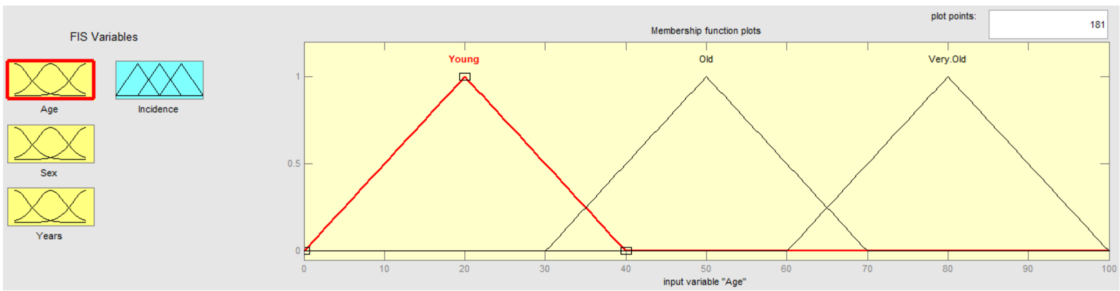

Fig. 2. Values attributed to the 'Age' variable

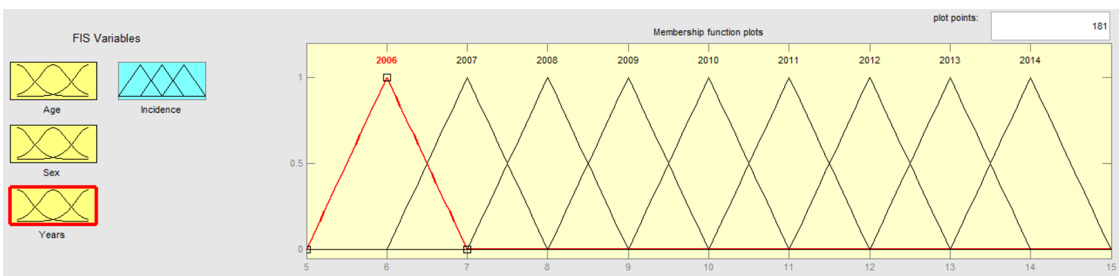

Fig. 3. Values attributed to the 'Years' variable

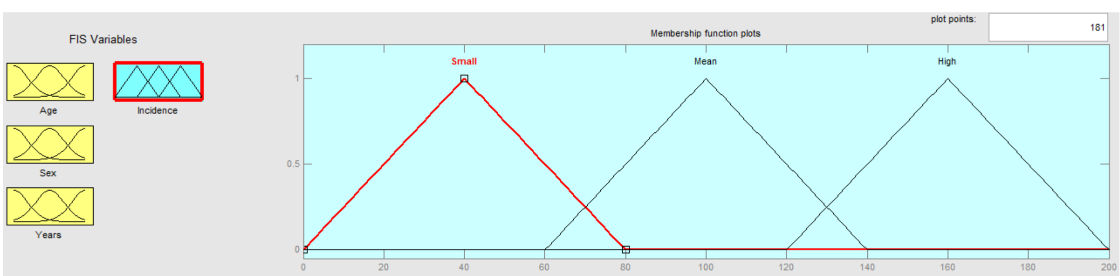

Fig. 4. Values attributed to the 'Incidence' variable

In according with the recorded values, the fuzzy rules are established. Referring to the table, we establish the sets of combinations connecting incidence to input factors in the form (IF ... THAN). These rules are in the form for example:

IF 'Age' is 63.4, AND 'Sex' is Female, AND 'Year' is 2007 THAN 'Incidence is 63,2.

The basis of the established rules must take into account all possibilities and all possible combinations according to the values recorded.

Table 1. Incidence per 100.000 by age group (period) of trachea bronchus and lung cancer (2006-2014). Setif cancer registry – Algeria

Age / Sex / Years			All ages	-15	-20	-25	-30	-35	-40	-45	-50	-55	-60	-65	-70	-75	-80	+85
Male	Years	2006	100	-	2.2	-	1.7	6.4	10	26.6	26	63.6	144.1	101.8	214.9	74.2	128.3	205.1
		2007	144	-	1.1	1.3	-	12.2	17.2	19.9	50.5	57.0	122.1	159.7	193.5	112.3	100.1	200.1
		2008	104	1.1	1.1	2.5	9.1	17.4	9.5	13.6	35.5	56.5	121.1	113.8	173.8	40.1	116.8	46.8
		2009	94	-	-	-	1.5	3.7	4.6	15.9	59.6	53.5	122.7	106.0	112.8	103.3	90.2	45.0
		2010	105	-	-	-	1.4	1.8	2.2	23.4	41.1	43.5	114.1	176.5	145.1	138.8	126.1	84.0
		2011	74	1.2	-	-	4.0	8.5	4.3	10.2	18.1	26.8	94.5	98.2	84.5	75.4	79.4	39.7
		2012	85	-	1.1	-	-	11.7	12.7	12.5	20.8	30.3	65.9	96.7	135.2	111.3	117.2	39.1
		2013	70	-	-	-	-	-	10.5	17.3	16.3	18.7	32.6	114.5	82.1	122.1	173.5	38.6
		2014	12	-	-	6.8	-	-	-	-	11.1	15.4	21.3	-	-	-	68.6	34.3
Fem.	Years	2006	16	-	-	1.4	1.7	2.2	-	3.0	-	5.4	-	47.2	-	55.1	24.9	-
		2007	24	-	-	-	-	4.1	2.5	11.4	7.4	4.9	22.8	39.5	26.9	38.9	-	-
		2008	24	-	-	-	-	2.0	-	5.5	10.7	13.8	21.9	48.2	17.6	12.3	65.3	-
		2009	32	-	-	-	1.5	3.8	4.7	2.7	10.2	8.7	40.8	48.7	43.5	46.7	-	-
		2010	24	1.3	-	-	1.4	5.5	2.3	2.6	12.9	8.3	18.6	24.6	17.4	22.3	-	37.9
		2011	19	-	-	-	1.4	1.7	4.4	5.2	3.1	12.0	22.4	-	-	21.4	17.8	71.4
		2012	18	-	1.1	-	-	-	2.2	9.0	3.0	15.8	16.6	16.3	17.1	-	17.6	-
		2013	16	1.3	-	-	-	-	-	7.5	-	15.6	-	40.1	16.9	-	17.3	-
		2014	12	-	-	3.4	-	-	-	-	5.9	7.7	10.8	-	-	-	34.3	-

The result at output is calculated after defuzzyfication. This allows switching between linguistic variables and numeric variables. We have chosen the center of area method, which the crisp output y is found by:

$$Y = \frac{\int yF(y)dy}{\int F(y)dy}$$

5. RESULTS AND DISCUSSION

The proposed system consists of three input variables and one output variable that represents the incidence of lung cancer (Fig. 1). This system remains extensible to other factors that are not supported in this study and will also be input variables.

The 'Age' factor is a determining factor in the onset of lung cancer. However, this variable is far from accurate. It varies from one person to another according to other such uncertain parameters. By considering this variable as a fuzzy variable by the creation of fuzzy intervals between different age groups, this makes it possible to overcome this uncertainty (Fig. 2).

Also, the 'sex' factor is far from accurate in its influence on lung cancer. By introducing this variable into the system (although it is not fuzzyfied), this allows us to take into account the uncertainty associated with this factor.

The incidence of cancer varies from year to year. Here too several parameters come into play and they are far from being precise. By fuzzyfying these years throughout the study period, it compensates for the inaccuracy (Fig. 3).

From what threshold we can decide on the importance of the incidence of lung cancer? Again, we found it useful to consider this variable as a fuzzy variable. In fuzzyfication, we come closer to human reasoning (Fig. 4).

6. CONCLUSION

Once the rule base is established, it becomes possible to instantly read the degree of lung cancer incidence (Fig. 5). The result is the collaboration of the set of rules that support all input variables. Since the input variables are considered as fuzzy variables by expressing them by linguistic variables, this gives an analysis as precise as possible. Also the output variable is expressed in linguistic terms concerning the incidence of lung cancer. This also gives the possibility of reading a result in a wide numerical and symbolic range.

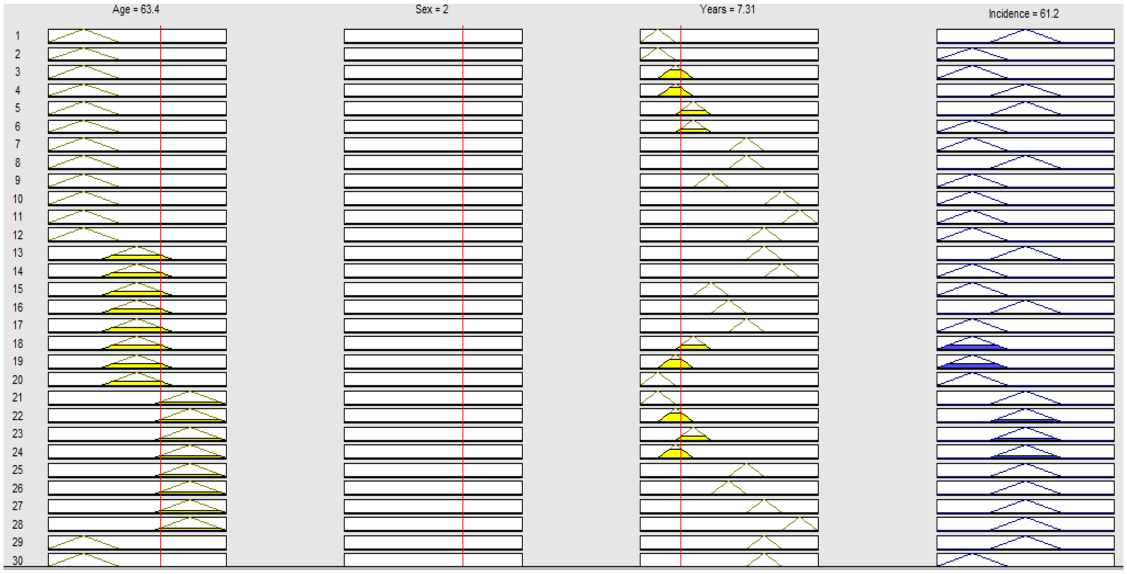

Fig. 5. Instantaneous reading of the incidence by the random introduction of input variables

At the end, the resulting application makes it possible to randomly display values at the input to read the result at the output. If all of the factors are taken in a precise manner and the rules are established correctly and encompassing all possibilities, it becomes possible to predict the onset of lung cancer without making appropriate diagnoses. This tool can be considered as an aid to doctors in their diagnosis, prevention and treatment of lung cancer patients.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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