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Causality in Medicine and Its Relationship with the Role of Statistics

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Abstract: The general goal of this work is the clarification of the use of concepts of causality in medicine and its relationship with the role of statistics. The value of an association is the evidence of causality. The Bradford Hill considerations on causality are the criteria commonly used to infer causality. Statistics help to know the role of chance in the working medical hypotheses but does not prevent other common mistakes made during clinical research, such as biases. Man has found a procedure that removes the most of all subjectivities and external factors: the scientific method, this does not mean that scientific studies are infallible. There are many factors influencing the cure or improvement of a disease that would be take in account: spontaneous resolution, regression to the mean, the Forer effect, placebo effect and other. The subjective observation of these phenomena is often insufficient when it comes to analyzing the effectiveness of therapies, medications, diets, homeopathy, cosmetics and natural therapies. It is very difficult to establish causality in health sciences but not impossible, the principles of this establishement can be resumed as Temporality, Strength, Consistency, Biology, Plausibility, Specificity, Analogy, Experiment and Coherence.

Keywords: Statistics, Causality, Medicine, Mathematics, Epidemiology

1. Background

Scientific evidence in medicine and health sciences is related with the basic concepts of causality and statistics, which are sometimes confused and that have appeared in history since Aristoteles. Such coincidence between two elements is essential to establish scientific evidence; in turn, it provides statistical knowledge without which it is difficult to argue causalities. It's difficult but not impossible. If we also consider the phenomena of a medical nature, biomedical and biological-social is unavoidable to discuss the current situation and explain its components.

The concept of causality is important in medicine and science in general because it is precisely through causality can be inferred that the behavior of a variable (cure from the behavior of another (treatment). The purpose of the causality analysis is to explain the operation of a system from the causal relationships of the same, considering that the establishment of such relations requires theoretical constructions, that is, behind all causal relationship must have a theory. Nevertheless this concept is not clear to many clinicians, some think that "correlation implies causation" when it is not always true. That is why we proposed in this work to review and clarify it again.

The idea behind this article is to approach causality, its actual bases and the role of statisics. It is essential the importance of deterministic and probabilistic thinking in the development of the idea of causality and the methods on it is founded, errors that originate in chance, bias and quantify certainty. Finally the implications of the failure of the causality as with the use of homeopathy.

1.1. Causality and Their Criteria

There are many references about the meaning of causality in medicine and especially in the epidemiological field [1], which indicates that the value of an association (statistical correlation) are evidence of causality if they possess certain traits that increase the value of this partnership. It is based on

various historical and philosophical currents of deterministic thought and probabilistic thinking, such as those provided by Aristotle, Hippocrates, Galileo, Hume, Fermat, Pascal, contributions of Snow, Smemelwies, Pasteur, Koch and the most recent of Bergson as so the importance of causality criteria Hill. Of paramount importance are the seven features that are called criteria Bradford Hill [2] and have been studied in numerous works as "The Bradford Hill considerations on causality: a counterfactual perspective?" [3]. These criteria are commonly used by epidemiologists and clinicians to infer causality, and are reproduced below:

a. *Temporal relationship*: Exposure always precedes outcome. If factor "A" is believed to cause a disease, then it is clear that factor "A" must necessarily always precede the occurrence of the disease. This is the only essential criterion. It requires that the risk factor precedes the onset effect that it causes. For example, AIDS can occur to individuals but only those who have been exposed to the HIV virus. So, in order to be infected by AIDS individuals must be exposed to the HIV virus.

b. *Strength*: This is defined by the size of the association measured by appropriate statistical tests. The stronger the association, the more likely the relation "A" to "B" is causal. Correlation or the evidence must be clear, for example a moderate to high correlation. If the association were an indication of relative risk (RR), odds ratio (OR) or Hazard Ratio (HR), it would be interesting that this was 2 or higher [4]. For example, the more highly correlated hypertension is with a high sodium diet the stronger is the relation between sodium and hypertension.

c. *Dose-Response Relationship*: An increasing amount of exposure increases risk. If a dose-response relationship is present, it is a strong evidence for causal relationship. However, as with specificity, the absence of a dose-response relationship does not rule out a causal relationship. A threshold may exist above which a relationship may be developed. At the same time, if a specific factor is the cause of a disease, the incidence of the disease should be declined when its exposure to the factor is reduced or eliminated. The causal interpretation is more plausible if the frequency of appearance of the disease increases with the dose level and time of exposure to the disease. An example of this section could be the chronic exposure to ionizing radiation causes leukemia and other cancers; there is a link between the disease and dose level and time of exposure.

d. *Consistency*: The association is consistent when results are replicated in studies in different settings using different methods. That is, if a relationship were causal, we would expect to find it consistently in different studies and among different populations. This is why numerous experiments have to be done before meaningful statements can be made about the causal relationship between two or more factors. It is a good indication of causality consistency and reproducibility of the association. If there are different populations studies, methods and different periods come to the same conclusion is a good indication of causality. A reference book on causality and meta-analysis can be found in [5]. For example, they have required thousands of rigorous technical studies of the relationship between cigarette smoking and cancer before a definitive conclusion that cigarette smoking increases the risk of (but does not cause) cancer.

e. *Plausibility*: The association agrees with currently accepted understanding of pathological processes. In other words, there needs to be some theoretical basis for positing an association between a vector and disease, or one social phenomenon and another. The association between phenomena must have an empirical clear base and supported by previous studies on current scientific and biological knowledge. It may be that at the present time there is no scientific knowledge to support the observations made, although it must exist deductions based on the existence of a plausible biological mechanism to explain the cause-effect relationship. For example, HIV was not identified until 1984 as the causative agent of AIDS, a disease described years earlier, although from the outset it was suggested that it was caused by an infectious agent.

f. *Consideration of Alternate Explanations*: When judging whether a reported association is causal it is necessary to determine the extent to which researchers have considered other possible explanations and have effectively ruled out such alternate explanations. In other words, it is always necessary to consider multiple hypotheses before making conclusions about the causal relationship between any two items under investigation.

g. *Experiment*: The condition can be altered (prevented or ameliorated) by an appropriate experimental regimen. This is the causal proof par excellence, although it is difficult to prove the ethical implications. It is normally tested in animals or laboratory, for example cells or tissues inside.

h. *Specificity*: This is established when a single putative cause produces a specific effect. This is considered by some to be the weakest of all the criteria. If the factor studied is associated with a disease, so that the introduction of this factor follows from the onset of the disease and its withdrawal from removing it, the interpretation is easier. Causality is most often multiple. Therefore, it is necessary to examine specific causal relationships within a larger systemic perspective. A disease such as heart valves disease has multiple risk factors, such as advanced age and heart problems, infections and untreated strep throat, which can cause rheumatic fever, among other. The diseases attributed to cigarette smoking, for example, do not meet this criterion. When specificity of an association is found it provides additional support for a causal relationship. However, absence of specificity in no way negates a causal relationship.

i. *Coherence*: The association should be compatible with existing theory and knowledge. In other words, it is necessary to evaluate claims of causality within the context of the current state of knowledge in a given field and in related fields. All currently accepted theories including genetics, biochemistry, and biology were at one time new ideas that challenged orthodoxy [6].

1.2. Cause-Effect Relationship

The biology and clinical practice indicate that no two equal subjects and pharmacology demonstrates that the same dose of drug causes different response intensity in different patients. This variability is due in part to the pharmacokinetics (differential absorption, metabolism and excretion of the drug) or pharmacodynamic type (drug-receptor interaction), for reasons of genetic, environmental or clinical course of the disease type (acute or chronic). You can see a review of work in "Clinical Epidemiology & Evidence-Based Medicine: Fundamental Principles of Clinical Reasoning & Research" in [7] and recently at [8].

Inter and individual variability intra effects of drugs on people require addressing the problem of demonstrating efficacy of a treatment and especially drugs from a group perspective rather than individuals. But there are also studies of one patient and the effects of different treatments (n = 1 study).

Currently several methods are used to establish the cause-effect relationship between drug and disease using the so-called probabilistic method. The observation in a single patient may suggest the possibility of a new property of a drug, or an adverse effect on him. In case-control studies, the association between a factor (for example drug, narcotics, and toxic) and the emergence of a new clinical condition may point to the causal link described. These criteria do not ensure that these observations are due to causality but can help rule out the possibility of coincidence between exposure to a factor and clinical events.

Clinical studies where the clinical status of a patient population is compared before and after drug administration do not allow causal relationships because most diseases have an unpredictable course. Many serious diseases can cause outbreaks with spontaneous remissions. People tend to change their behavior to be subject to interest and eventually respond according to the care they are given, regardless of the nature of the intervention. Another reason for the ineffectiveness of uncontrolled trials is the regression to the mean: patients with extreme values of a (sick) through distribution tend to have less extreme values in the following term measurements.

From the point of view of the classification of scientific evidence according to the study designed, studies can be sorted (Fig. 1.) in which produce weak evidence of causality, as studies of a case to the more controlled studies with more evidence as randomized controlled trials [9, 10, 11]. In them, the drug is administered to a large number of people and the results are analyzed to ensure that the effect is due to the action of the drug and not random, spontaneous remission or the placebo effect or otherwise.

Controlled clinical trials are those experimental trials which a control or reference group is given. Are the types of studies par excellence, the "summum" of experimental design? In experimental studies, subjects who participate are selected from a population and randomly distributed into, as many groups as required, will generally be 2, the patients treated with the experimental drug and patients with control drug (placebo or drug known effects). Randomization of patients enables taken a sufficient sample patients, are distributed randomly also variables forecast study (age, degree of progression of the disease, other diseases and other drugs taken by the patient), this will constitute part of the randomization of the groups. Any difference that is detected between the treatment groups should be to pharmacological treatments and not to other variables, which may influence, giving causality to treatment.

There are other clinical studies with treatments such as observational, which are made when they cannot be performed by the experimental organizational or ethical reasons, and where reality is observed. In these studies, it cannot assure that factors other than treatment or study variable, do not affect one group or another differently. When you cannot perform a random assignment of patients to treatments, you can opt for 2-way: study cohort and case-control studies.

An example of non-causality is the use of homeopathy. None homeopathic product has achieved to date must undergo an assessment of these characteristics, and therefore none has shown a higher efficacy of the placebo effect. The prestigious medical journal The Lancet published in 2005 [12] an article makes clear that no medical value of homeopathy, with the unequivocal conclusion that the clinical effects of homeopathy were due solely to the placebo effect.

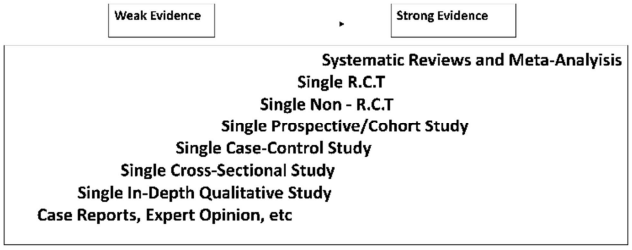

Figure 1. *Scale of various types of research according to their relation to the evidence of causality (RCT: Regular Clinical Trials).*

1.3. Other Factors Influencing the Cure or Improvement of a Disease and the Effectiveness of Treatment

There are many other factors [13, 14] influencing the cure or improvement of a disease and the effectiveness of treatment. Some of the most importants are spontaneous resolution, regression to the mean, the Forer effect, placebo effect and other that will be commented on the anexe comments. 1) Correlation is not sufficient for causation: We must also emphasize the role of statistics to know the role of chance in the working hypotheses, but that does not prevent other common mistakes made during clinical research, such as biases confusion and bias selection. Remember that "correlation does not imply causation", although the correlation between phenomena is r = 1 does not mean that one is the cause of another [1]. It is important to understand that the existence of correlation does not imply causation in

the sense that the correlation indicates a mathematical relationship between the variables but does not indicate that one variable causes the other. 2) Remission of a disease or regression to the mean: Regression to the mean is a biological phenomenon well studied and described long ago, which is that values are observed frequently apparently unusual in measurements, that repeat the measurement value returns to normal limits. 3) Placebo Effect. Any substance, even without therapeutic action, that is capable of producing a curative effect that is given to an individual that believes that has beneficial properties for its body. 4) The Forer effect or Barnum effect. In addition, there are psychological components clouding our perceptions of reality of the effect of treatment, making us think that it is an effective treatment as it works to a large number of people, it is known as the Barnum Effect Barnum or Forer effect: People tend to accept treatments about themselves in proportion to their desire that the treatments be effective rather than in proportion to the empirical accuracy of the treatments as measured by some non-subjective standard.

2. Main Discussion

Researcher's tenacity have found a procedure that removes the most of all subjectivities and external factors: the scientific method. To test the effect of a drug beyond placebo: for example, two experimental groups. One treated with sugar pills and another with the drug to be tested. After the statistical study is conducted, if patients taking the experimental drug cured significantly more than the others that who do not want to say that its composition has properties that go beyond the placebo effect, remission or subjectivity of the individual treated. This does not mean that scientific studies are infallible. Often there are many factors that can influence the improvement of a person; you may only bring us some clues about where that river runs.

The human brain tends to show that correlate phenomena are causal. It is a very valuable instinct: "If I touch the fire I burn, so I do not do it again." However, it also misleads us in understanding the nature of the phenomenon, to rationalize. An example: a person has a seasonal allergy, you are advised a cure, the test and the symptoms subside. The association is usually automatic: "What I took healed me and I will advise". But it's just an observation, a tree from the thousands that exist in a forest. The typical response when questioned is: "Well, it works for me." Nevertheless, many other factors could have influenced in that case. The subjective observation of these phenomena is often insufficient when it comes to analyzing the effectiveness of therapies, medications, diets, homeopathy, cosmetics and natural therapies.

3. Conclusions

The causality principles can be resumed as: a) Temporality, b) Strength, c) Consistency, d) Biological gradient, e) Plausibility, f) Specificity, g) Analogy, h) Experiment, i) Coherence. The scientific method removes all subjectivities: hence the importance of 'scientifically proven'. The need to complete three elementary to prove causality steps clearly appears today: first designing the type of study to avoid bias and reduce as much as possible to chance, second completing it with epidemiological criteria for causality and third keeping in mind that the error may come at any time, at the beginning, during the process or at the end of our task.

There are many factors that influence the cure or improvement of a disease and the effectiveness of treatment: the spontaneous resolution, regression to the mean, the Forer effect, placebo effect and other. We analysed some of them, adding the fallacies that carry from a patient's perspective. We think that the patient has feelings and sometimes must be corrected or not, since the intention is to promote healing not only with treatment. It is very difficult to establish causality in health sciences but not impossible.

4. Comments

4.1. Comment: What Is the Role of Statistics? Cum Hoc Ergo Propter Hoc

Statistics, science derived from the theory of probability, help to know the role of chance in the working hypotheses, but does not prevent other common mistakes made during clinical research, such as biases confusion and bias selection. It must be made studies with groups of patients and should not be performed with a single patient since there is a wide variability in the response with similar characteristics. The assessment of the effect of treatment should be carried out in a sample of patients to further extrapolate the results to the rest of the population [15]. See "Clinical Epidemiology: Principles, Methods, and Applications for Clinical Research" [11].

Sometimes one has to generalize in medicine. A statistical generalization is a claim that is usually true, but not always be so [16]. He often uses the expression "most", as in "most doctors believe that is abusing antibiotics." Other times he uses the word "generally", as in "doctors usually are in favor of reducing the use of antibiotics." At other times, you do not use a specific word, as in "doctors prefer to reduce the use of antibiotics." Fallacies based on statistical generalizations occur because the generalization is not always true. When a scientist is a statistical generalization as though it were always real, is fallacious and one of the most popular and generates more confusion among clinicians is the "fallacy of causation".

Cum hoc ergo propter hoc ("With this, therefore because of this'). It is a fallacy, which is perpetrated to infer that two or more events are causally connected because they occur together. That is, the fallacy is to infer a causal relationship between two or more events for a statistical correlation (r) have been observed between them. In general, the fallacy is that given two events, A and B, to find a statistical correlation between the two, it is a mistake to infer that A causes B because it could be that B causes A, or could also

be a third event causes both a and B, thus explaining the correlation. At least four possibilities:

- Let B be the cause of A.
- Let there be the third unknown factor that is really the cause of the relationship between A and B.
- That the relationship is so complex and numerous that the facts are mere coincidences.
- B is the cause of A while A is the B, ie, they agree, that is a synergistic or symbiotic relationship where the union catalyzes the effects observed.

Let us remember that if we have a sample of quantitative paired data

$\{(X_1, Y_1), (X_2, Y_2), \ldots, (X_n, Y_n)\}$, to establish statistical correlation we estimate the sample covariance as:

$$S_{XY} = \frac{1}{n}\sum_{i=1}^{n}(X_i - \bar{X})(Y_i - \bar{Y}) \quad (1)$$

The representation of such pairs of numbers (X: weight Y: height) can be done by a scatter plot as in Fig. 2.

A measure of correlation of two variables X, Y represents the degree of quantitative relationship between the variables and their degree is defined as:

$$r_{XY} = \frac{\sum_{i=1}^{n}(X_i-\bar{X})(Y_i-\bar{Y})}{\sqrt{\sum_{i=1}^{n}(X_i-\bar{X})^2 \sum_{i=1}^{n}(Y_i-\bar{Y})^2}} \quad (2)$$

The correlation takes values in the range $[-1, 1]$: $-1 \leq r \leq +1$ and it is actually a measure normalized of the covariance between two variables measured sample:

$$r_{XY}\frac{S_{XY}}{S_X S_Y} \quad (3)$$

To facilitate interpretation, it is normal to interpret the degree of correlation between X, Y using the following scale: (See Table num.1)

This fallacy is often refuted by the phrase "correlation does not imply causation", although the correlation between phenomena is r = 1 does not mean that one is the cause of another. It is important to understand that the existence of correlation does not imply causation in the sense that the correlation indicates a mathematical relationship between the variables but does not indicate that one variable causes the other.

Table 1. *Interpretation of the values of a correlation.*

Value of correlation	Meaning
-1	Large and perfect negative correlation
-0.9 a -0.99	Very high negative correlation
-0.7 a -0.89	High negative correlation
-0.4 a -0.69	Moderate negative correlation
-0.2 a -0.39	Low negative correlation
-0.01 a -0.19	Very low negative correlation
0	No correlation
0.01 a 0.19	Very low positive correlation
0.2 a 0.39	Low positive correlation
0.4 a 0.69	Moderate positive correlation
0.7 a 0.89	High positive correlation
0.9 a 0.99	Very high positive correlation
1	Large and perfect positive correlation

4.2. Comment: Remission of a Disease or Regression to the Mean

We must be clear that many diseases are cured alone independently of what we do and therefore the mere improvement or cure is not synonymous with treatment efficacy. Has been attributed to Voltaire the phrase *"The art of medicine consists of amusing the patient while nature cures the disease"*, which clearly reflects what spontaneous improvement of a disease in its natural history or natural course. A sore back it comes and goes, like the symptoms of hay fever or flu without complications spontaneously heals with or without medication. Often gotten with any treatment when symptoms are at their highest peak, so that decline is normal, whether we are taking something or not [17].

Take for example the case of pain. It usually ranges: often individuals begin treatment when it is at its peak and then a decrease is normal, taking medication or not. The natural course of the disease causes that the disease is cured and to attribute/relate this cure to a drug or treatment is wrong. Homeopathy has taken advantage of this phenomenon we will try to justify: Imagine a person suffering a disease. It is treated with homeopathy and improving the course of their disease. Then the homeopathy "works." This pseudoterapia has not shown any effectiveness beyond placebo, so it is very likely that the improvement is due to this effect. They can also be determining factors, such as spontaneous remission: many ailments are cured alone, so it does not matter that we take something or not, finally, they disappear. Finally, due to symptomatic disease oscillation can occur naturally remission of symptoms or phenomenon of regression to the mean

Regression to the mean is a biological phenomenon well studied and described long ago, which is that values are observed frequently apparently unusual in measurements, that repeat the measurement value returns to normal limits. Therefore, an example studied in [18] on the relationship between height of parents and children, Pearson made the comparison between 10 measures of parents and children at random (Fig. 2). [19]

A statistical explanation to the phenomenon of regression to the mean and the mathematical formulation of regression and correlation, as it developed historically, would be: If x_1, x_2,..., x_n is a first set of measures (eg. Height of parents, numerical measure of symptoms at first) and (eg. Height of children, numerical measure of symptoms in a second time) a second set, regression to the mean indicates that for all i values, the expected value (height of children) is closer to the value (mean value x_i) that x_i (height of parents), as shown in Fig. 2. This can be written mathematically as:

$$E(|y_i - \bar{x}|) < E(|x_i - \bar{x}|) \quad (4)$$

Where E() denotes the mathematical expectation. So the relationship is proposed:

$$0 \leq E\left(\left|\frac{y_i - \bar{x}}{x_i - \bar{x}}\right|\right) < 1 \quad (5)$$

[3] it is more restrictive than in the first inequality proposal [4] as it needs the expected value is expressed in the same way as the average. To check this, if $t = E(\left|\frac{y_i - \bar{x}}{x_i - \bar{x}}\right|)$ and for n values can be calculated:

$$\varphi = \sum_{i=1}^{n} (\left|\frac{y_i - \bar{x}}{x_i - \bar{x}}\right|) \quad (6)$$

There is a problem of calculation (6), as taking an arithmetic mean can be seen that it is not a good statistic, as it tends to 0. Even if it is close to 0, these points can dominate the calculation, so the ratio t it is not adequate and should be corrected using

$$(x_i - \bar{x})^2 : \varphi^* = \frac{\sum_{i=1}^{n} (x_i - \bar{x})(x_i - \bar{x})}{\sum_{i=1}^{n} (y_i - \bar{x})^2} \quad (7)$$

Can be written as,

$$\hat{\beta} = \frac{\sum_{i=1}^{n} y_i x_i - \bar{x}\sum_{i=1}^{n} y_i - \bar{x}\sum_{i=1}^{n} x_i + n\bar{x}^2}{\sum_{i=1}^{n} (x_i - \bar{x})^2} \text{ or } \hat{\beta} = \frac{\sum_{i=1}^{n} y_i x_i - n\bar{x}\bar{y}}{\sum_{i=1}^{n} (x_i - \bar{x})^2} \quad (8)$$

In the formula (7), it can be seen that the slope of the regression model formula. Then, you can ensure that the phenomenon of regression toward the mean can be interpreted as:

$$0 \le \beta_{x,y} < 1 \quad (9)$$

What is true for two sets of measurements on the same sample (eg..: height of parent and child). It is expected that if the standard deviations s_x and s_y two sets of measurements related are equal, the regression coefficient β It will be equal to the coefficient r correlation. It is sufficient to say that if you notice $\beta \le 1$ will notice $r \le 1$. If the linear relationship between measures is not perfect, we expect a coefficient $\beta <$ 1. However, if the measures have some relevant information, r > 0, so $\beta > 0$. r = 1 It corresponds to the case of perfect relationship while corresponds to the case of connection with full error. It is to be noted that $\hat{\beta} = r$ when $s_x = s_y$ as $\hat{\beta} = r\frac{s_y}{s_x}$.

As seen in Fig. 2 the regression to the mean occurs when $0 \le \beta_{x,y} < 1$. For small values of x $\beta x + \alpha > x$ and for large values of x of $\beta x + \alpha < x$. If a linear regression model between the characteristic of the ascendancy "Y" of parents and descendants X is assumed, regression to the mean will occur when $0 \le \beta_{x,y} < 1$ consequently, $E(Y) = \beta x + \alpha$.

In the example of Fig. 2 are represented the lines $y = \beta x + \alpha$ e $y = x$, it has been determined that $\hat{\beta} = 0.464$ and how $0 \le \beta_{x,y} < 1$, the line $y = \beta x + \alpha$ it is above of $y = x$ for small values of x, and is below the high values for x. So the evidence suggests that taller parents tend to have taller children, also they indicate that children of parents who are extremely high or extremely low tend to approximate the average, more than their parents, which is known as regression toward the mean [20, 21].

Galton, the discoverer of this statistical phenomenon [18, 19] believed that the regression toward the mean was simply a legacy of the genetic characteristics of the ancestors that are not expressed in the parents. He did not understand the regression to the mean as a statistical phenomenon. In contrast to this view, it is now known that regression to the mathematical average is inevitable in biological data: if there is a random variation between the height of an individual and parents - if the correlation is not exactly equal to 1, the predictions tend toward the mean, regardless of the underlying mechanisms of heredity, race or culture. According to [20] Ross (2006) a modern explanation of the phenomenon of regression toward the mean is based on the consideration that a descendant (the son) gets a random selection of half of the genes from each parent, a descendant of one of the very tall parents tend to have less higher than those of the parent genes.

This phenomenon has also been observed in situations where you have two sets of data on the same variables (eg.: deaths from traffic accidents occurred in the US in 2 consecutive years [20]. Other reference works regression to the mean are those of [22, 23] may be an application of this phenomenon to the design of clinical studies where there is no comparison control group.

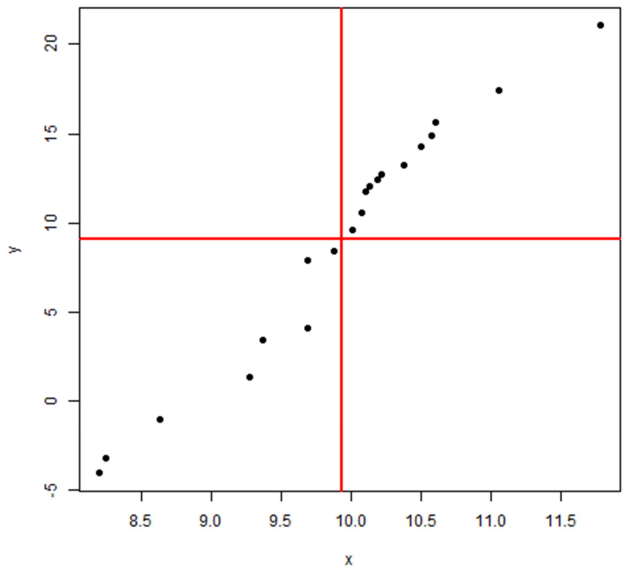

Figure 2. *Statistical regression between weight and height of different people.*

4.3. Comment: Placebo Effect

Any substance, even without therapeutic actions that are capable of producing a curative effect that individuals ingest

and believe that has beneficial properties for their body. This is proved and known for some time even though the reason of why this happens has mot been understood yet. Humans tend to do what they are expected to do and so do patients. To demonstrate efficacy of treatment is necessary for the patient and the investigator ignorant of the treatment being given to patient because the researcher may think that a treatment may be more beneficial than another or in detriment of another treatment.

So how do we know that the effect of a drug is due to the drug itself and not to the placebo effect? Thanks to clinical trials and statistical analysis of the results. They called "masking" is performed. The way of carrying out masking, usually double-blind, so both the patient and the investigator unaware of the assigned treatment. It is necessary that the administration form, color, taste and appearance is the same in the two treatments. So in trials in different routes of administration are compared, you can give a correct performance problems masking, and can be solved by giving placebo patients. For example, if patients in-group A are receiving the drug orally and group B patients intravenously, patients in-group A are supplied placebo orally and patients in-group B intravenously. Tests should not always be performed in double blind system: if there is an unnecessary risk to the patient, it is not possible to have a suitable dosage formula, if pharmacological effects of drugs detect another treatment or you can damage the medical relationship patient. Diseases that are most likely to improve to a placebo are those psychological (eg.: depression, pain, anxiety).

It is well known that homeopathy uses and maximize the placebo effect: in the famous studio where homeopathic treatments and drug treatments were compared in different clinical trials concluded that the main effect of homeopathy is the placebo effect: “This finding is compatible with the notion that the clinical effects of homoeopathy are placebo effects” [12].

4.4. Comment: The Forer Effect or Barnum Effect

In addition, there are psychological components clouding our perceptions of reality of the effect of treatment, making us think that it is an effective treatment as it works to a large number of people, it is known as the Barnum Effect Barnum or Forer effect. Bertram Forer, proved in 1949 [24] in an experiment with his students made them a personality test. Days later he returned their results that was supposedly described how each. The average identification was 4.26 on 5, a success. However, in reality they all received the same text, generic and copied from an astrological text [24] phrases. This fallacy of subjective validation is the same that can occur when we feel within us the effects of treatments without efficacy or when someone hits a seer (works for me). Other authors who most recently studied this paradox are cognitive [25] in his work "The 'Barnum Effect' in Personality Assessment: A Review of the Literature".

According to Kammann [26] in his book "The Psychology of the psychic" when a person finds a belief or expectation that resolves the uncertainty (uncomfortable definition for humans), the individual will attend more likely to new information confirms the belief and discard the evidence to the contrary (confirmation bias). This self-perpetuating mechanism consolidates the original error and overconfidence in which the arguments against are seen as too fragmentary or disjointed as to undo the adopted belief accumulates.

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