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Conditio sine qua non

Research article

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Abstract:
Background:
Human knowledge might come from experiments, experience, et cetera. This standard can be applied rigorously to conditions and causation too. Instead of taking necessary conditions for granted, human beings are challenged to consider what allows us to know about this relationship.
Methods:
The usual mathematical rules were used. Examples are presented to illustrate the methods developed in detail.
Results:
Of two events, A and B, we say that A is a necessary condition for B when an event B cannot occur without an event A.
Conclusion:
It is possible to detect necessary condition relationships (within a dataset).

Keywords: Binomial distribution; Variance; Refuted

1. Introduction

Nature or objective reality as such is sometimes determined by changes, by processes or by events et cetera which occur **independently and outside of human mind and consciousness** too. In this context, there are events (i. e. A_t) at a certain Bernoulli trial (or period or point in space-time) t which must be present, which must be given in order for another event (i. e. B_t) to occur at the same Bernoulli trial (or period or point in space-time) t. To put it in exaggerated terms, there are objective and real necessary conditions which exist independently and outside any human mind and consciousness. In simple terms, necessary conditions have traditionally been discussed especially by philosopher's. Bluntly said, let us now consider a simple example. At most, it is appropriate to make it clear again that sufficient amounts of gaseous oxygen or air as such at these days is a necessary condition for humans being alive. In other words, human beings require air to live or having air to breathe is a necessary condition for survival. Broadly speaking, **without** air (i. e. gaseous oxygen) **no** human life. The relationship between air and human survival is *independent of human mind and consciousness*, it is independent of the fact whether a single human being knows something about this relationship et cetera. Thus far, in order for human beings to stay alive, it is necessary that there is enough gaseous oxygen or air given. In this context it doesn't matter whether a single human being is healthy or sick, young or old, tiny or small, rich or poor et cetera. Every single human being require sufficient amounts of air to survive. However, even if air or gaseous oxygen given at certain amounts is a necessary condition for human life, air is by no means a sufficient condition, i.e. it does not, by itself, i.e. alone, suffice for human life. Theoretically, relating such a basic natural processes with mathematical reasoning is more than meaningful, it is necessary under different aspects. It is imperative to consider that the use of mathematics does not produce the relationship of a necessary condition, such a relationship is already given in nature. Still, how can we express mathematically the relationship of a necessary condition? In order to obtain a logically consistent and more adequate mathematical picture of a necessary condition, it is appropriate to consider several points of view. The (scientific) concept of a necessary condition appears to be as old as human mankind itself. Historically, *Aristotle* himself was one of the first forerunners of a theoretical concept of a necessary condition. *Anicius Manlius Torquatus Severinus Boetius* (ca. 477–524 AD), a Roman senator and philosopher of the early 6th century, elaborated among other authors, in his book *De consolatione philosophiae* on the necessary condition too. What, then, from the standpoint of classical logic, mathematics and probability theory or bio-statistics, is a necessary condition?

2. Material and methods

Scientific knowledge and objective reality are deeply interrelated. Seen by light, grey is never merely simply grey, and many paths may lead to climb up a certain mountain. In the following of this paper, we will reanalyse the relationship between oxygen and human survival in many ways and under different circumstances to reach the main goal.

2.1. Methods

Definitions should help us to provide and assure a systematic approach to a mathematical formulation of the relationship of a necessary condition. It also goes without the need of further saying that a definition must be logically consistent and correct.

2.1.1. Random variables

Let a **random variable**(Gosset, 1914) X denote something like a function defined on a probability space, which itself maps from the sample space(Neyman and Pearson, 1933) to the real numbers.

2.1.2. Expectation of a Random Variable

Definition 2.1 (**The First Moment Expectation of a Random Variable**). *Summaries of an entire distribution of a random variable(see Kolmogorov, 1950, p. 22) X, such as the expected value, or average value, are useful in order to identify where X is expected to be without describing the entire distribution. For practical and other reasons, we shall limit ourselves here to discrete random variables, while the basic properties of the expectation value of a random variable X will not be investigated. Thus far, let X be a discrete random variable with the probability p(X). The first moment expectation value (see Huygens and van Schooten, 1657, Kolmogorov, 1950, LaPlace, 1812, Whitworth, 1901) of X, denoted by E(X), is a number defined as follows:*

$$E(X) \equiv p(X) \times X \tag{1}$$

The first moment expectation value squared of a random variable X follows as

$$\begin{aligned} E(X)^2 &\equiv p(X) \times X \times p(X) \times X \\ &\equiv p(X) \times p(X) \times X \times X \\ &\equiv (p(X) \times X)^2 \end{aligned} \tag{2}$$

Definition 2.2 (**The Second Moment Expectation of a Random Variable**). *The second(see Kolmogorov, 1950, p. 42) moment expectation value (or more or less arithmetic mean) of a (large)*

number of independent realizations of a random variable X follows as:

$$\begin{aligned} E\left(X^2\right) &\equiv p\left(X\right) \times X^2 \\ &\equiv \left(p\left(X\right) \times X\right) \times X \\ &\equiv E\left(X\right) \times X \\ &\equiv X \times E\left(X\right) \end{aligned} \tag{3}$$

Definition 2.3 (**The n-th Moment Expectation of a Random Variable**). *The n-th(see Barukčić, 2020a, 2021c) moment expectation value of a (large) number of independent realizations of a random variable X follows as:*

$$\begin{aligned} E\left(X^n\right) &\equiv p\left(X\right) \times X^n \\ &\equiv \left(p\left(X\right) \times X\right) \times X^{n\text{-}1} \\ &\equiv E\left(X\right) \times X^{n\text{-}1} \end{aligned} \tag{4}$$

2.1.3. Probability of a Random Variable

The probability p(X) of a random variable X follows as (see equation 1)

$$\begin{aligned} p\left(X\right) &\equiv \frac{E\left(X\right)}{X} \\ &\equiv \frac{E\left(X\right) \times E\left(X\right)}{E\left(X\right) \times X} \equiv \frac{E\left(X\right)^2}{E\left(X^2\right)} \end{aligned} \tag{5}$$

2.1.4. Variance of a Random Variable

Definition 2.4 (**The Variance of a Random Variable**). *Johann Carl Friedrich Gauß (1777-1855) introduced the normal distribution and the error of mean squared in his 1809 monograph(see Gauß, Carl Friedrich, 1809). In the following, Karl Pearson (1857-1936) coined the term "standard deviation"in 1893. Pearson is writing: "Then σ will be termed its standard-deviation (error of mean square)."(see Pearson, 1894, p. 80). Finally, the term variance was introduced by Sir Ronald Aylmer Fisher (1890-1962) in the year 1918.*

> *"The ... deviations of a ... measurement from its mean ... may be ... measured by the standard deviation corresponding to the square root of the mean square error ... It is ... desirable* ***in analysing the causes*** *... to deal with the square of the standard deviation as the measure of variability. We shall term this quantity the Variance... "*
>
> *(see Fisher, Ronald Aylmer, 1919, p. 399)*

The deviation of a random variable X from its population mean or sample mean E(X) has a central role in statistics and is one important measure of dispersion. The variance (see Kolmogorov, 1950, p.

42), the second central moment of a distribution, is the expectation value of the squared deviation of a random variable X from its own expectation value E(X) and follows as (see equation 3):

$$\begin{aligned} \sigma(X)^2 &\equiv E\left(X^2\right) - E(X)^2 \\ &\equiv (X \times E(X)) - E(X)^2 \end{aligned} \tag{6}$$

Based on equation 6, it is

$$E\left(X^2\right) \equiv E(X)^2 + \sigma(X)^2 \tag{7}$$

2.1.5. Bernoulli distribution

A single event distribution is more or less a discrete probability distribution of any random variable X which takes a certain (observer independent) single value X_t at a **Bernoulli trial**(Uspensky, 1937, p. 45) (period of time) t with the probability $p(X_t)$. The same random variable X takes a certain single anti value $\underline{X}_t$ at a Bernoulli trial (period of time) t with the probability 1-$p(X_t)$. There are conditions in nature where a random variable X can take only the values either +0 or +1. Under these conditions, the random variable X takes the value 1 with probability $p(X_t = +1)$ and the value 0 with probability $q(X_t = +0) = 1 - p(X_t = +1)$ while the single event distribution passes over into the **Bernoulli distribution**, named after Swiss mathematician Jacob Bernoulli(Bernoulli, 1713). Less formally, many times, the Bernoulli distribution is represented by a (possibly not biased) coin toss where 1 and 0 would represent 'heads'and 'tails'(or vice versa), respectively. However, the relationship between random variables (Gosset, 1914) can be investigated by many (Gosset, 1908) methods, including the tools of probability theory, too.

Definition 2.5 (Two by two table of single event random variables).

The two by two or contingency table which has been introduced by Karl Pearson(Pearson, 1904b) in 1904 harbours still a large variety of topics and debates. Central to this is the problem to apply the laws of classical logic on data sets, which concerns the justification of inferences which extrapolate from sample data to general facts. Nevertheless, a contingency table is still an appropriate theoretical model too for studying the relationships between random variables, including *Bernoulli(Bernoulli, 1713) (i.e. +0/+1) distributed random variables* existing or occurring at the same *Bernoulli trial* (Uspensky, 1937) (period of time) t.

In this context, let a random variable A at the *Bernoulli trial* (Uspensky, 1937) (period of time) t, denoted by A_t, indicate a risk factor, a condition, a cause et cetera and occur or exist with the probability $p(A_t)$ at the *Bernoulli trial* (Uspensky, 1937) (period of time) t. Let $E(A_t)$ denote the expectation value of A_t. In general it is

$$p(A_t) \equiv p(a_t) + p(b_t) \tag{8}$$

The expectation value $E(A_t)$ follows as

$$\begin{aligned} E(A_t) &\equiv A_t \times p(A_t) \\ &\equiv A_t \times (p(a_t) + p(b_t)) \\ &\equiv (A_t \times p(a_t)) + (A_t \times p(b_t)) \\ &\equiv E(a_t) + E(b_t) \end{aligned} \tag{9}$$

Under conditions of +0/+1 distributed Bernoulli random variables it is

$$\begin{aligned} E(A_t) &\equiv A_t \times p(A_t) \\ &\equiv (+0+1) \times p(A_t) \\ &\equiv p(A_t) \\ &\equiv p(a_t) + p(b_t) \end{aligned} \tag{10}$$

Furthermore, it is

$$p(\underline{A}_t) \equiv p(c_t) + p(d_t) \equiv (1 - p(A_t)) \tag{11}$$

The expectation value E($\underline{A}_t$) is given as

$$\begin{aligned} E(\underline{A}_t) &\equiv A_t \times (1 - p(A_t)) \\ &\equiv A_t \times (p(c_t) + p(d_t)) \\ &\equiv (A_t \times p(c_t)) + (A_t \times p(d_t)) \\ &\equiv E(c_t) + E(d_t) \end{aligned} \tag{12}$$

Under conditions of +0/+1 distributed Bernoulli random variables we obtain

$$\begin{aligned} E(\underline{A}_t) &\equiv A_t \times (1 - p(A_t)) \\ &\equiv (+0 + 1) \times (1 - p(A_t)) \\ &\equiv (1 - p(A_t)) \\ &\equiv p(c_t) + p(d_t) \end{aligned} \tag{13}$$

Let a random variable B at the *Bernoulli trial* (Uspensky, 1937) (period of time) t, denoted by B_t, indicate an outcome, a conditioned, an effect et cetera and occur or exist with the probability p(B_t) at the *Bernoulli trial* (Uspensky, 1937) (period of time) t. Let E(B_t) denote the expectation value of B_t. In general it is

$$p(B_t) \equiv p(a_t) + p(c_t) \tag{14}$$

The expectation value E(B_t) is given by the equation

$$\begin{aligned} E(B_t) &\equiv B_t \times p(B_t) \\ &\equiv B_t \times (p(a_t) + p(c_t)) \\ &\equiv (B_t \times p(a_t)) + (B_t \times p(c_t)) \\ &\equiv E(a_t) + E(c_t) \end{aligned} \tag{15}$$

Under conditions of +0/+1 distributed Bernoulli random variables it is

$$\begin{aligned} E(B_t) &\equiv B_t \times p(B_t) \\ &\equiv (+0 + 1) \times p(B_t) \\ &\equiv p(B_t) \\ &\equiv p(a_t) + p(c_t) \end{aligned} \tag{16}$$

Furthermore, it is

$$p(\underline{B}_t) \equiv p(b_t) + p(d_t) \equiv (1 - p(B_t)) \tag{17}$$

The expectation value E($\underline{B}_t$) is given by the equation

$$\begin{aligned} E(\underline{B}_t) &\equiv B_t \times (1 - p(B_t)) \\ &\equiv B_t \times (p(b_t) + p(d_t)) \\ &\equiv (B_t \times p(b_t)) + (B_t \times p(d_t)) \\ &\equiv E(b_t) + E(d_t) \end{aligned} \tag{18}$$

Under conditions of +0/+1 distributed Bernoulli random variables it is

$$\begin{aligned} E\left(\underline{B}_t\right) &\equiv B_t \times \left(1 - p\left(B_t\right)\right) \\ &\equiv (+0+1) \times \left(1 - p\left(B_t\right)\right) \\ &\equiv \left(1 - p\left(B_t\right)\right) \\ &\equiv p\left(b_t\right) + p\left(d_t\right) \end{aligned} \tag{19}$$

Let $p(a_t)= p(A_t \wedge B_t)$ denote the joint probability distribution of A_t and B_t at the same Bernoulli trial (period of time) t. In general, it is

$$\begin{aligned} E\left(a_t\right) &\equiv E\left(A_t \wedge B_t\right) \\ &\equiv \left(A_t \times B_t\right) \times p(A_t \wedge B_t) \\ &\equiv \left(A_t \times B_t\right) \times p(a_t) \end{aligned} \tag{20}$$

Under conditions of +0/+1 distributed Bernoulli random variables, it is

$$\begin{aligned} E\left(a_t\right) &\equiv E\left(A_t \wedge B_t\right) \\ &\equiv \left(A_t \times B_t\right) \times p(A_t \wedge B_t) \\ &\equiv ((+0+1) \times (+0+1)) \times p(A_t \wedge B_t) \\ &\equiv p(A_t \wedge B_t) \\ &\equiv p\left(a_t\right) \end{aligned} \tag{21}$$

Let $p(b_t)= p(A_t \wedge \neg B_t)$ denote the joint probability distribution of A_t and not B_t at the same Bernoulli trial (period of time) t. In general, it is

$$\begin{aligned} E\left(b_t\right) &\equiv E\left(A_t \wedge \neg B_t\right) \\ &\equiv \left(A_t \times \neg B_t\right) \times p(A_t \wedge \neg B_t) \\ &\equiv \left(A_t \times \neg B_t\right) \times p(b_t) \end{aligned} \tag{22}$$

Under conditions of +0/+1 distributed Bernoulli random variables, it is

$$\begin{aligned} E\left(b_t\right) &\equiv E\left(A_t \wedge \neg B_t\right) \\ &\equiv \left(A_t \times \neg B_t\right) \times p(A_t \wedge \neg B_t) \\ &\equiv ((+0+1) \times (+0+1)) \times p(A_t \wedge \neg B_t) \\ &\equiv p(A_t \wedge \neg B_t) \\ &\equiv p\left(b_t\right) \end{aligned} \tag{23}$$

Let $p(c_t)= p(\neg A_t \wedge B_t)$ denote the joint probability distribution of not A_t and B_t at the same Bernoulli trial (period of time) t. In general, it is

$$\begin{aligned} E\left(c_t\right) &\equiv E\left(\neg A_t \wedge B_t\right) \\ &\equiv \left(\neg A_t \wedge B_t\right) \times p\left(\neg A_t \wedge B_t\right) \\ &\equiv \left(\neg A_t \wedge B_t\right) \times p(c_t) \end{aligned} \tag{24}$$

Under conditions of +0/+1 distributed Bernoulli random variables, it is

$$\begin{aligned} E(c_t) &\equiv E(\neg A_t \wedge B_t) \\ &\equiv (\neg A_t \times B_t) \times p(\neg A_t \wedge B_t) \\ &\equiv ((+0+1) \times (+0+1)) \times p(\neg A_t \wedge B_t) \\ &\equiv p(\neg A_t \wedge B_t) \\ &\equiv p(c_t) \end{aligned} \tag{25}$$

Let $p(d_t) = p(\neg A_t \wedge \neg B_t)$ denote the joint probability distribution of not A_t and not B_t at the same Bernoulli trial (period of time) t. In general, it is

$$\begin{aligned} E(d_t) &\equiv E(\neg A_t \times \neg B_t) \\ &\equiv (\neg A_t \times \neg B_t) \times p(\neg A_t \wedge \neg B_t) \\ &\equiv (\neg A_t \times \neg B_t) \times p(d_t) \end{aligned} \tag{26}$$

Under conditions of +0/+1 distributed Bernoulli random variables, it is

$$\begin{aligned} E(d_t) &\equiv E(\neg A_t \wedge \neg B_t) \\ &\equiv (\neg A_t \times \neg B_t) \times p(\neg A_t \wedge \neg B_t) \\ &\equiv ((+0+1) \times (+0+1)) \times p(\neg A_t \wedge \neg B_t) \\ &\equiv p(\neg A_t \wedge \neg B_t) \\ &\equiv p(d_t) \end{aligned} \tag{27}$$

In general, it is

$$p(a_t) + p(b_t) + p(c_t) + p(d_t) \equiv +1 \tag{28}$$

Table 1 provide us with an overview of the definitions above.

Table 1. The two by two table of Bernoulli random variables

		Conditioned B_t		
		TRUE	FALSE	
Condition A_t	TRUE	$p(a_t)$	$p(b_t)$	$p(A_t)$
	FALSE	$p(c_t)$	$p(d_t)$	$p(\underline{A}_t)$
		$p(B_t)$	$p(\underline{B}_t)$	+1

2.1.6. Binomial random variables

The binomial distribution with parameters n and p has been developed by the Swiss mathematician Jakob Bernoulli (1655-1705) in a proof published in his 1713 book Ars Conjectandi (see Bernoulli, 1713) Part 1. In probability theory and statistics, the probability of getting exactly k successes in n independent Bernoulli trials is given by the probability mass function as

$$p\left(X_{\mathrm{t}}=k\right) \equiv \binom{n}{k} \cdot p^{k} \cdot q^{n-k} \tag{29}$$

is $\binom{n}{k}=\frac{n!}{k!(n-k)!}$ the binomial coefficient while the cumulative distribution function is given as

$$p\left(X_{\mathrm{t}} \leq k\right) \equiv 1-p\left(X_{\mathrm{t}}>k\right) \equiv \sum_{t=0}^{k} \binom{n}{t} \cdot p^{t} \cdot q^{n-t} \tag{30}$$

or as

$$p\left(X_{\mathrm{t}}>k\right) \equiv 1-p\left(X_{\mathrm{t}} \leq k\right) \equiv 1-\sum_{t=0}^{k} \binom{n}{t} \cdot p^{t} \cdot q^{n-t} \tag{31}$$

Furthermore, it is

$$p\left(X_{\mathrm{t}}<k\right) \equiv 1-p\left(X_{\mathrm{t}} \geq k\right) \equiv \sum_{t=0}^{k-1} \binom{n}{t} \cdot p^{t} \cdot q^{n-t} \tag{32}$$

or

$$p\left(X_{\mathrm{t}} \geq k\right) \equiv 1-p\left(X_{\mathrm{t}}<k\right) \equiv 1-\sum_{t=0}^{k-1} \binom{n}{t} \cdot p^{t} \cdot q^{n-t} \tag{33}$$

The binomial distribution is the mathematical foundation of a binomial test. The random variable X_t is counting for different things. The discrete geometric (see Feller, 1950, p. 61) distribution describes under certain circumstances the number of Bernoulli trials needed to get one success. The probability that the first occurrence of success requires k independent trials, each with success probability p, is given by the equation

$$p\left(X_{\mathrm{t}}=k\right) \equiv p \cdot q^{k-1} \tag{34}$$

The negative (see Fisher, 1941, Haldane, 1941) binomial probability is a discrete probability distribution which defines the number of successes (k) in a sequence of independent and identically distributed Bernoulli trials (n) before a specified (non-random) number of failures (denoted r) occurs. The probability mass function of the negative binomial distribution is

$$p\left(X_{\mathrm{t}}=r\right) \equiv \binom{k+r-1}{k-1} p^{k} \cdot q^{r} \tag{35}$$

where k is the number of successes, r is the number of failures, and p is the probability of success.

Definition 2.6 (Expectation value and variance of a binomial random variable).

The variance(see Pearson, 1904a, p. 66) of the binomial distribution with parameters n, the number of independent experiments each asking a yes–no question and p, the probability of a single event, is defined in contrast to Pearson (see Barukčić, Ilija, 2022) as

$$\sigma\left(X_{\mathrm{t}}\right)^{2} \equiv N \times N \times p\left(X_{\mathrm{t}}\right) \times \left(1 - p\left(X_{\mathrm{t}}\right)\right) \tag{36}$$

Definition 2.7 (Two by two table of Binomial random variables).

Let a, b, c, d, A, $\underline{\mathrm{A}}$, B, and $\underline{\mathrm{B}}$ denote expectation values. Under conditions where *the probability of an event, an outcome, a success et cetera is* ***constant*** *from Bernoulli trial to Bernoulli trial t*, it is

$$\begin{aligned} A &= N \times E\left(A_{\mathrm{t}}\right) \\ &\equiv N \times \left(A_{\mathrm{t}} \times p\left(A_{\mathrm{t}}\right)\right) \\ &\equiv N \times \left(p\left(A_{\mathrm{t}}\right) + p\left(B_{\mathrm{t}}\right)\right) \\ &\equiv N \times p\left(A_{\mathrm{t}}\right) \end{aligned} \tag{37}$$

and

$$\begin{aligned} B &= N \times E\left(B_{\mathrm{t}}\right) \\ &\equiv N \times \left(B_{\mathrm{t}} \times p\left(B_{\mathrm{t}}\right)\right) \\ &\equiv N \times \left(p\left(A_{\mathrm{t}}\right) + p\left(c_{\mathrm{t}}\right)\right) \\ &\equiv N \times p\left(B_{\mathrm{t}}\right) \end{aligned} \tag{38}$$

where N might denote the population or even the sample size. Furthermore, it is

$$a \equiv N \times \left(E\left(A_{\mathrm{t}}\right)\right) \equiv N \times \left(p\left(A_{\mathrm{t}}\right)\right) \tag{39}$$

and

$$b \equiv N \times \left(E\left(B_{\mathrm{t}}\right)\right) \equiv N \times \left(p\left(B_{\mathrm{t}}\right)\right) \tag{40}$$

and

$$c \equiv N \times \left(E\left(c_{\mathrm{t}}\right)\right) \equiv N \times \left(p\left(c_{\mathrm{t}}\right)\right) \tag{41}$$

and

$$d \equiv N \times \left(E\left(d_{\mathrm{t}}\right)\right) \equiv N \times \left(p\left(d_{\mathrm{t}}\right)\right) \tag{42}$$

and

$$a + b + c + d \equiv A + \underline{A} \equiv B + \underline{B} \equiv N \tag{43}$$

Table 2 provide us again an overview of a two by two table of Binomial random variables.

Table 2. The two by two table of Binomial random variables

		Conditioned B_t		
		TRUE	FALSE	
Condition	TRUE	a	b	A
A_t	FALSE	c	d	$\underline{A}$
		B	$\underline{B}$	N

2.1.7. Independence

Definition 2.8 (Independence).

In general, an event A_t at the Bernoulli trial t need not but can be independent of the existence or of the occurrence of another event B_t *at the same* Bernoulli trial t. Mathematically, independence (Kolmogoroff, 1933, Moivre, 1718) in terms of probability theory is defined at the same (period of) time t (i.e. Bernoulli trial t) as

$$\begin{aligned} p\left(A_t \wedge B_t\right) &\equiv p\left(A_t\right) \times p\left(B_t\right) \\ &\equiv \frac{\sum_{t=1}^{N}\left(A_t \wedge B_t\right)}{N} \equiv \frac{N \times \left(p\left(a_t\right)\right)}{N} \equiv 1 - p\left(A_t \mid B_t\right) \equiv 1 - p\left(A_t \uparrow B_t\right) \end{aligned} \tag{44}$$

2.1.8. Dependence

Definition 2.9 (Dependence).

The dependence of events (Barukčić, 1989, p. 57-61) is defined as

$$p\left(\underbrace{A_t \wedge B_t \wedge C_t \wedge \ldots}_{n}\right) \equiv \sqrt[n]{\underbrace{p\left(A_t\right) \times p\left(B_t\right) \times p\left(C_t\right) \times \ldots}_{n}} \tag{45}$$

2.1.9. Relative risk (RR)

Relative risk (RR_{nc})

Definition 2.10 (Relative risk (RR_{nc}))**.**

The degree of association between the two binomial variables can be assessed by a number of very different coefficients, the relative (Cornfield, 1951, Sadowsky et al., 1953) risk is one(Barukčić, 2021d) of them. In general, relative risk RR_{nc}, which provides some evidence of a necessary condition, is defined as

$$\begin{aligned} RR(A_t, B_t)_{nc} &\equiv \frac{\frac{p(a_t)}{p(A_t)}}{\frac{p(c_t)}{p(NotA_t)}} \\ &\equiv \frac{p(a_t) \times p(NotA_t)}{p(c_t) \times p(A_t)} \\ &\equiv \frac{N \times p(a_t) \times N \times p(NotA_t)}{N \times p(c_t) \times N \times p(A_t)} \\ &\equiv \frac{a_t \times (NotA_t)}{c_t \times A_t} \\ &\equiv \frac{EER\,(A_t, B_t)}{CER\,(A_t, B_t)} \end{aligned} \tag{46}$$

That what scientist generally understand by relative risk is the ratio of a probability of an event occurring with an exposure versus the probability of an event occurring without an exposure. In other words,

relative risk = (probability(event in exposed group)) / (probability(the same event in not exposed group)).

A $RR(A_t,B_t) = +1$ means that exposure does not affect the outcome or both are independent of each other while $RR(A_t,B_t)$ less than +1 means that the risk of the outcome is decreased by the exposure. In this context, an $RR(A_t,B_t)$ greater than +1 denotes that the risk of the outcome is increased by the exposure. Widely known problems with odds ratio and relative risk are already documented in literature.

Relative risk (RR (sc))

Definition 2.11 (Relative risk (RR (sc)))**.**

The relative risk (sc), which provides some evidence of a sufficient condition, is calculated from the

point of view of an outcome and is defined as

$$\begin{aligned} RR(A_t,B_t)_{sc} &\equiv \frac{\frac{p(a_t)}{p(B_t)}}{\frac{p(b_t)}{p(NotB_t)}} \\ &\equiv \frac{p(a_t)\times p(NotB_t)}{p(b_t)\times p(B_t)} \\ &\equiv \frac{N\times p(a_t)\times N\times p(NotB_t)}{N\times p(b_t)\times N\times p(B_t)} \\ &\equiv \frac{a_t\times (NotB_t)}{b_t\times B_t} \\ &\equiv \frac{OPR\,(A_t,B_t)}{CPR\,(A_t,B_t)} \end{aligned} \tag{47}$$

Relative risk reduction (RRR)

Definition 2.12 (Relative risk reduction (RRR))**.**

$$\begin{aligned} RRR\,(A_t,B_t) &\equiv \frac{CER\,(A_t,B_t)-EER\,(A_t,B_t)}{CER\,(A_t,B_t)} \\ &= 1-RR(A_t,B_t) \end{aligned} \tag{48}$$

Vaccine efficacy (VE)

Definition 2.13 (Vaccine efficacy (VE))**.**

Vaccine efficacy is defined as the percentage reduction of a disease in a vaccinated group of people as compared to an unvaccinated group of people.

$$\begin{aligned} VE\,(A_t,B_t) &\equiv 100\times (1-RR\,(A_t,B_t)) \\ &\equiv 100\times \left(\frac{CER\,(A_t,B_t)-EER\,(A_t,B_t)}{CER\,(A_t,B_t)}\right) \end{aligned} \tag{49}$$

Historically, vaccine efficacy has been designed to evaluate the efficacy of a certain vaccine by Greenwood and Yule in 1915 for the cholera and typhoid vaccines(Greenwood and Yule, 1915) and best measured using double-blind, randomized, clinical controlled trials. However, the calculated vaccine efficacy is depending too much on the study design, can lead to erroneous conclusions and is only of very limited value.

Experimental event rate (EER)

Definition 2.14 (Experimental event rate (EER))**.**

$$EER\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)\equiv\frac{p(a_{\mathrm{t}})}{p(A_{\mathrm{t}})}=\frac{a_{\mathrm{t}}}{a_{\mathrm{t}}+b_{\mathrm{t}}} \tag{50}$$

Definition 2.15 (Control event rate (CER))**.**

$$CER\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)\equiv\frac{p(c_{\mathrm{t}})}{p(\underline{A}_{\mathrm{t}})}=\frac{c_{\mathrm{t}}}{c_{\mathrm{t}}+d_{\mathrm{t}}} \tag{51}$$

Absolute risk reduction (ARR)

Definition 2.16 (Absolute risk reducation (ARR))**.**

$$\begin{aligned} ARR\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)&\equiv\frac{p(c_{\mathrm{t}})}{p(\underline{A}_{\mathrm{t}})}-\frac{p(a_{\mathrm{t}})}{p(A_{\mathrm{t}})}\\ &=\frac{c_{\mathrm{t}}}{c_{\mathrm{t}}+d_{\mathrm{t}}}-\frac{a_{\mathrm{t}}}{a_{\mathrm{t}}+b_{\mathrm{t}}}\\ &=CER\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)-EER\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)\end{aligned} \tag{52}$$

Absolute risk increase (ARI)

Definition 2.17 (Absolute risk increase (ARI))**.**

$$\begin{aligned} ARI\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)&\equiv\frac{p(a_{\mathrm{t}})}{p(A_{\mathrm{t}})}-\frac{p(c_{\mathrm{t}})}{p(\underline{A}_{\mathrm{t}})}\\ &=EER\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)-CER\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)\end{aligned} \tag{53}$$

Number needed to treat (NNT)

Definition 2.18 (Number needed to treat (NNT))**.**

$$NNT\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)\equiv\frac{1}{CER\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)-EER\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)} \tag{54}$$

An ideal number needed to treat(Cook and Sackett, 1995, Laupacis et al., 1988), mathematically the reciprocal of the absolute risk reduction, is NNT = 1. Under these circumstances, everyone improves with a treatment, while no one improves with control. A higher number needed to treat indicates more or less a treatment which is less effective.

Number needed to harm (NNH)

Definition 2.19 (Number needed to harm (NNH))**.**

$$NNH\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)\equiv\frac{1}{EER\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)-CER\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)} \tag{55}$$

The number needed to harm (Massel and Cruickshank, 2002), mathematically the inverse of the absolute risk increase, indicates at the end how many patients need to be exposed to a certain factor, in order to observe a harm in one patient that would not otherwise have been harmed.

Outcome prevalence rate (OPR)

Definition 2.20 (Outcome prevalence rate (OPR))**.**

$$OPR\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)\equiv\frac{p(a_{\mathrm{t}})}{p(B_{\mathrm{t}})}=\frac{a_{\mathrm{t}}}{a_{\mathrm{t}}+c_{\mathrm{t}}} \tag{56}$$

Control prevalence rate (CPR)

Definition 2.21 (Control prevalence rate (CPR))**.**

$$CPR\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)\equiv\frac{p(b_{\mathrm{t}})}{p(\underline{B}_{\mathrm{t}})}=\frac{b_{\mathrm{t}}}{b_{\mathrm{t}}+d_{\mathrm{t}}} \tag{57}$$

Bias and confounding is present to some degree in all research. In order to assess the relationship of exposure with a disease or an outcome, a fictive control group (i.e. of newborn or of young children et cetera) can be of use too. Under certain circumstances, even a CPR = 0 is imaginable.

Absolute prevalence reduction (APR)

Definition 2.22 (Absolute prevalence reduction (APR))**.**

$$APR\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)\equiv CPR\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)-OPR\left(A_{\mathrm{t}},B_{\mathrm{t}}\right) \tag{58}$$

Absolute prevalence increase (API)

Definition 2.23 (Absolute prevalence increase (API))**.**

$$API\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)\equiv OPR\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)-CPR\left(A_{\mathrm{t}},B_{\mathrm{t}}\right) \tag{59}$$

Relative prevalence reduction (RPR)

Definition 2.24 (Relative prevalence reduction (RPR))**.**

$$\begin{aligned} RPR\left(A_{\mathrm{t}},B_{\mathrm{t}}\right) &\equiv \frac{CPR\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)-OPR\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)}{CPR\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)} \\ &= 1-RR(A_{\mathrm{t}},B_{\mathrm{t}})_{\mathrm{sc}} \end{aligned} \tag{60}$$

The index NNS

Definition 2.25 (The index NNS)**.**

$$NNS\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)\equiv\frac{1}{CPR\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)-OPR\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)} \tag{61}$$

Mathematically, the index NNS is the reciprocal of the absolute prevalence reduction.

The index NNI

Definition 2.26 (The index NNI)**.**

$$NNI\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)\equiv\frac{1}{OPR\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)-CPR\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)} \tag{62}$$

Mathematically, the index NNI is the reciprocal of the absolute prevalence increase.

2.1.10. Odds ratio (OR)

Definition 2.27 (Odds ratio (OR))**.**

Odds ratios as an appropriate measure for estimating the relative risk have become widely used in medical reports of case-control studies. The odds ratio(Fisher, 1935, p. 50) is defined(Cox, 1958) as the ratio of the odds of an event occurring in one group with respect to the odds of its occurring in another group. Odds(Yule and Pearson, 1900, p. 273) ratio (OR) is a measure of association which quantifies the relationship between two binomial distributed random variables (exposure vs. outcome) and is related to Yule's (Yule and Pearson, 1900, p. 272) Q(Yule, 1912, p. 585/586). Two events A_t and B_t are regarded as independent if $(A_t, B_t) = 1$. Let

a_t = number of persons exposed to A_t and with disease B_t

b_t = number of persons exposed to A_t but without disease $\underline{B}_t$

c_t = number of persons unexposed $\underline{A}_t$ but with disease B_t

d_t = number of persons unexposed $\underline{A}_t$: and without disease $\underline{B}_t$

a_t+c_t = total number of persons with disease B_t (case-patients)

b_t+d_t = total number of persons without disease $\underline{B}_t$ (controls).

Hereafter, consider the table 3. The odds' ratio (OR) is defined as

Table 3. The two by two table of random variables

		Conditioned/Outcome B_t		
		TRUE	FALSE	
Condition/Exposure	TRUE	a_t	b_t	A_t
A_t	FALSE	c_t	d_t	$\underline{A}_t$
		B_t	$\underline{B}_t$	N_t

$$\begin{aligned} OR(A_t, B_t) &\equiv \left(\frac{a_t}{b_t}\right) / \left(\frac{c_t}{d_t}\right) \\ &\equiv \left(\frac{a_t \times d_t}{b_t \times c_t}\right) \end{aligned} \tag{63}$$

Remark 2.1. *Odds ratios can support logical fallacies and cause difficulties in drawing logically consistent conclusions. The chorus of voices is growing, which demand the immediate ending(Knol, 2012, Sackett et al., 1996) of any use of Odds ratio.*

Under conditions where (b = 0), the measure of association odds ratio will collapse, because we need to divide by zero, as can be seen at eq. 63. However, according to today's rules of mathematics, a

division by zero is neither allowed nor generally accepted as possible. It does no harm to remind ourselves that in the case b = 0 the event A_t is a sufficient condition of B_t. In other words, odds ratio is not able to recognize elementary relationships of objective reality. In fact, it would be a failure not to recognize how dangerous and less valuable odds ratio is.

Under conditions where (c = 0) odds ratio collapses too, because we need again to divide by zero, as can be seen at eq. 63. However, and again, today's rules of mathematics don't allow us a division by zero. In point of fact, in the case c = 0 it is more than necessary to point out that A_t is a necessary condition of B_t. In other words, odds ratio or the cross-product ratio is not able to recognize elementary relationships of nature like necessary conditions. We can and need to overcome all the epistemological obstacles as backed by odds ratio entirety. Sooner rather than later, we should give up this measure of relationship completely.

2.1.11. Study design and bias

Systematic observation and experimentation, inductive and deductive reasoning are essential for any formation and testing of hypotheses and theories about the natural world. In one way or another, logically and mathematically sound scientific methods and concepts are crucial constituents of any scientific progress. When all goes well, different scientists at different times and places using the same scientific methodology should be able to generate the same scientific knowledge. However, more than half (52%) of scientists surveyed believe that studies do not successfully reproduce sufficiently similar or the same results as the original studies (Baker, 2016). In a very large study on publication bias in meta-analyses, Kicinski et al. (Kicinski et al., 2015) found evidence of publication bias even in systematic reviews. Therefore, a careful re-evaluation of the study/experimental design, the statistical methods and other scientific means which underpin scientific inquiry and research goals appears to be necessary once and again. While it is important to recognize the shortcoming of today's science, one issue which has shaped debates over studies published is the question: **has a study really measured what it set out to**? Even if studies carried out can vary greatly in detail, the data from the studies itself provide information about the credibility of the data.

Index of unfairness (IOU)

Definition 2.28 (Index of unfairness).

The index of unfairness (Barukčić, 2019b) (IOU) is defined as

$$p\left(IOU\left(A,B\right)\right) \equiv Absolute\left(\left(\frac{A+B}{N}\right)-1\right) \tag{64}$$

A very good study design should assure as much as possible a p(IOU) = 0. In point of fact, against the background of lacking enough experience with the use of p(IOU), a p(IOU) up to 0.25 could be of use too. An index of unfairness is of use to prove whether sample data are biased and whether sample data can be used for Chi-square based analysis of necessary conditions, of sufficient conditions and of causal relationships.

Index of independence (IOI)

Definition 2.29 (**Index of independence**)**.**

The index of independence(Barukčić, 2019a) (IOI) is defined as

$$p\left(IOI\left(A_{\mathrm{t}},\underline{B}_{\mathrm{t}}\right)\right) \equiv Absolute\left(\left(\frac{A_{\mathrm{t}}+\underline{B}_{\mathrm{t}}}{N}\right)-1\right) \tag{65}$$

or as

$$p\left(IOI\left(\underline{A}_{\mathrm{t}},B_{\mathrm{t}}\right)\right) \equiv Absolute\left(\left(\frac{\underline{A}_{\mathrm{t}}+B_{\mathrm{t}}}{N}\right)-1\right) \tag{66}$$

A very good study design which aims to prove **an exclusion relationship or a causal relationship** should assure as much as possible a p(IOI) = 0. However, once again, against the background of lacking enough experience with the use of p(IOI), sample data with a p(IOI) up to 0.25 are of use too. Today, most double-blind placebo-controlled studies are based on the demand that **p(IOU) = p(IOI)** while the value of p(IOU) of has been widely neglected. Such an approach leads to unnecessary big sample sizes, the increase of cost, the waste of time and, most importantly of all, to epistemological systematically biased sample data and conclusions drawn. A change is necessary.

Index of relationship (IOR)

Definition 2.30 (Index of relationship (IOR))**.**

Due to several reasons, it is not always easy to identify the unique characteristics between two events like A_t and B_t. And more than that, it is difficult to decide what to do, and much more difficult to know in which direction one should think and which decision is right. Sometimes it is helpful to know at least something about the direction of the relationship between two events like A_t and B_t. Under conditions where $p(a_t) = p(A_t \wedge B_t)$, the index of relationship(Barukčić, 2021b), abbreviated as IOR, is defined as

$$\begin{aligned} IOR(A_{\mathrm{t}},B_{\mathrm{t}}) &\equiv \left(\frac{p(A_{\mathrm{t}}\wedge B_{\mathrm{t}})}{p(B_{\mathrm{t}})\times p(A_{\mathrm{t}})}\right)-1 \\ &\equiv \left(\frac{p(a_{\mathrm{t}})}{p(B_{\mathrm{t}})\times p(A_{\mathrm{t}})}\right)-1 \\ &\equiv \left(\left(\frac{N\times N\times p(a_{\mathrm{t}})}{N\times p(B_{\mathrm{t}})\times N\times p(A_{\mathrm{t}})}\right)-1\right) \\ &\equiv \left(\left(\frac{N\times a}{A\times B}\right)-1\right) \end{aligned} \tag{67}$$

where $p(A_t)$ denotes the probability of an event A_t at the Bernoulli trial t and $p(B_t)$ denotes the probability of another event B_t at the same Bernoulli trial t while $p(a_t)$ denotes the joint probability of $p(A_t$ AND $B_t)$ at the same Bernoulli trial t and a, A and B may denote the expectation values.

2.2. Conditions

2.2.1. Exclusion relationship

Definition 2.31 (**Exclusion relationship [*EXCL*]**).

Mathematically, the exclusion (EXCL) relationship, denoted by $p(A_t \mid B_t)$ in terms of statistics and probability theory, is defined(Barukčić, 1989, p. 68-70) as

$$\begin{aligned} p(A_t \mid B_t) &\equiv p(A_t \uparrow B_t) \\ &\equiv p(b_t) + p(c_t) + p(d_t) \\ &\equiv \frac{N \times (p(b_t) + p(c_t) + p(d_t))}{N} \\ &\equiv \frac{\sum_{t=1}^{N} (\underline{A}_t \vee \underline{B}_t)}{N} \equiv \frac{b+c+d}{N} \\ &\equiv \frac{b+\underline{A}}{N} \\ &\equiv \frac{c+\underline{B}}{N} \\ &\equiv +1 \end{aligned} \tag{68}$$

Based on the 1913 Henry Maurice Sheffer (1882-1964) relationship, the Sheffer stroke(Nicod, 1917, Sheffer, 1913) usually denoted by $\uparrow$, it is $p(A_t \wedge B_t) \equiv 1 - p(A_t \mid B_t)$ (see table 4).

Table 4. A_t excludes B_t and vice versa.

		Conditioned (COVID-19) B_t		
		TRUE	FALSE	
Condition (Vaccine)	TRUE	**+0**	$p(b_t)$	$p(A_t)$
A_t	FALSE	$p(c_t)$	$p(d_t)$	$p(\underline{A}_t)$
		$p(B_t)$	$p(\underline{B}_t)$	+1

Example 2.1. *Pfizer Inc. and BioNTech SE announced on Monday, November 09, 2020 - 06:45am results from a Phase 3 COVID-19 vaccine trial with 43.538 participants which provides evidence that their vaccine (BNT162b2) is preventing COVID-19 in participants without evidence of prior SARS-CoV-2 infection. In toto, 170 confirmed cases of COVID-19 were evaluated, with 8 in the vaccine group versus 162 in the placebo group. The exclusion relationship can be calculated as follows.*

$$\begin{aligned} p(Vaccine : BNT162b2 \mid COVID-19(infection)) &\equiv p(b_t) + p(c_t) + p(d_t) \\ &\equiv 1 - p(a_t) \\ &\equiv 1 - \left(\frac{8}{43538}\right) \\ &\equiv +0,99981625 \end{aligned} \tag{69}$$

with a P Value = 0,000184.

Following Kolmogorov's definition of an n-dimensional probability density (see also Kolmogorov, 1950, p. 26) of random variables A_t, B_t et cetera at the point t, we obtain

$$\begin{aligned} p\left(A_t \mid B_t\right) &\equiv p\left(\underline{U}_t \cup \underline{W}_t\right) \\ &\equiv 1 - p\left(A_t \cap B_t\right) \\ &\equiv 1 - \int_{-\infty}^{A_t} \int_{-\infty}^{B_t} f\left(A_t, B_t\right)\, dA_t\, dB_t \\ &\equiv +1 \end{aligned} \tag{70}$$

while $p\left(A_t \mid B_t\right)$ would denote the cumulative distribution function of random variables and $f\left(A_t, B_t\right)$ is the joint density function.

2.2.2. Observational study and exclusion relationship

Under conditions of an observational study, the exclusion relationship follows approximately(see Barukčić, 2021a) as

$$p\left(A_t \mid B_t\right) \equiv p\left(A_t \uparrow B_t\right) \geq 1 - \frac{p\left(a_t\right)}{p\left(B_t\right)} \tag{71}$$

2.2.3. Experimental study and exclusion relationship

Under conditions of an experimental study, the exclusion relationship follows approximately(see Barukčić, 2021a) as

$$p\left(A_t \mid B_t\right) \equiv p\left(A_t \uparrow B_t\right) \geq 1 - \frac{p\left(a_t\right)}{p\left(A_t\right)} \tag{72}$$

2.2.4. The goodness of fit test of an exclusion relationship

Definition 2.32 (The $\tilde{\chi}^2$ goodness of fit test of an exclusion relationship).

Under some well known circumstances, testing hypothesis about an exclusion relationship $p(A_t \mid B_t)$ is possible by the chi-square distribution (also chi-squared or $\tilde{\chi}^2$-distribution) too. The $\tilde{\chi}^2$ goodness of fit test of an exclusion relationship with degree of freedom (d. f.) of d. f. = 1 is calculated as

$$\begin{aligned} {\tilde{\chi}^2}_{\text{Calculated}}\left(\left(A_t \mid B_t\right) \mid A\right) &\equiv \frac{\left(b - (a+b)\right)^2}{A} + \\ &\quad \frac{\left((c+d) - \underline{A}\right)^2}{\underline{A}} \\ &\equiv \frac{a^2}{A} + 0 \\ &\equiv \frac{a^2}{A} \end{aligned} \tag{73}$$

or equally as

$$\begin{aligned}\tilde{\chi}^2{}_{\text{Calculated}}\left((A_t \mid B_t) \mid B\right) &\equiv \frac{\left(c-(a+c)\right)^2}{B}+ \\ &\quad \frac{\left((b+d)-\underline{B}\right)^2}{\underline{B}} \\ &\equiv \frac{a^2}{B}+0 \\ &\equiv \frac{a^2}{B}\end{aligned} \tag{74}$$

and can be compared with a theoretical chi-square value at a certain level of significance α. The $\tilde{\chi}^2$-distribution equals zero when the observed values are equal to the expected/theoretical values of an exclusion relationship/distribution $p(A_t \mid B_t)$, in which case the null hypothesis has to be accepted. Yate's (Yates, 1934) continuity correction was not used under these circumstances.

2.2.5. The left-tailed p Value of an exclusion relationship

Definition 2.33 (The left-tailed p Value of an exclusion relationship).

It is known that as a sample size, N, increases, a sampling distribution of a special test statistic approaches the normal distribution (central limit theorem). Under these circumstances, the left-tailed (lt) p Value (Barukčić, 2019c) of an exclusion relationship can be calculated as follows.

$$\begin{aligned}pValue_{\text{lt}}\left(A_t \mid B_t\right) &\equiv 1-e^{-(1-p(A_t|B_t))} \\ &\equiv 1-e^{-(a/N)}\end{aligned} \tag{75}$$

A low p-value may provide some evidence of statistical significance.

2.2.6. Neither nor conditions

Definition 2.34 (Neither A_t nor B_t conditions [*NOR*]).

Mathematically, a neither A_t nor B_t condition (or rejection according to the French philosopher and logician Jean George Pierre Nicod (1893-1924), i.e. Jean Nicod's statement (Nicod, 1924)) relationship (NOR), denoted by $p(A_t \downarrow B_t)$ in terms of statistics and probability theory, is defined (Barukčić, 1989, p. 68-70) as

$$\begin{aligned}p\left(A_t \downarrow B_t\right) &\equiv p\left(d_t\right) \\ &\equiv \frac{N-\sum_{t=1}^{N}\left(A_t \vee B_t\right)}{N} \equiv \frac{\sum_{t=1}^{N}\left(\underline{A}_t \wedge \underline{B}_t\right)}{N} \equiv \frac{N \times \left(p\left(d_t\right)\right)}{N} \\ &\equiv \frac{d}{N} \\ &\equiv +1\end{aligned} \tag{76}$$

2.2.7. The Chi square goodness of fit test of a neither nor condition relationship

Definition 2.35 (The $\tilde{\chi}^2$ goodness of fit test of a neither A_t nor B_t condition relationship).

A neither A_t nor B_t condition relationship $p(A_t \downarrow B_t)$ can be tested by the chi-square distribution (also chi-squared or $\tilde{\chi}^2$-distribution). The $\tilde{\chi}^2$ goodness of fit test of a neither A_t nor B_t condition relationship with degree of freedom (d. f.) of d. f. = 1 may be calculated as

$$\begin{aligned} \tilde{\chi}^2{}_{\text{Calculated}}\left((A_t \downarrow B_t) \mid A\right) &\equiv \frac{(d-(c+d))^2}{\underline{A}} + \\ &\quad \frac{((a+b)-A)^2}{A} \\ &\equiv \frac{c^2}{\underline{A}} + 0 \end{aligned} \tag{77}$$

or equally as

$$\begin{aligned} \tilde{\chi}^2{}_{\text{Calculated}}\left((A_t \downarrow B_t) \mid B\right) &\equiv \frac{(d-(b+d))^2}{\underline{B}} + \\ &\quad \frac{((a+c)-B)^2}{B} \\ &\equiv \frac{b^2}{\underline{B}} + 0 \end{aligned} \tag{78}$$

Yate's (Yates, 1934) continuity correction has not been used in this context.

2.2.8. The left-tailed p Value of a neither nor B condition relationship

Definition 2.36 (The left-tailed p Value of a neither A_t nor B_t condition relationship).

The left-tailed (lt) p Value (Barukčić, 2019c) of a neither A_t nor B_t condition relationship can be calculated as follows.

$$\begin{aligned} pValue_{\text{lt}}\left(A_t \downarrow B_t\right) &\equiv 1 - e^{-(1-p(A_t \downarrow B_t))} \\ &\equiv 1 - e^{-p(A_t \vee B_t)} \\ &\equiv 1 - e^{-((a+b+c)/N)} \end{aligned} \tag{79}$$

where $\vee$ may denote disjunction or logical inclusive or. In this context, a low p-value indicates again a statistical significance. In general, it is $p\left(A_t \vee B_t\right) \equiv 1 - p\left(A_t \downarrow B_t\right)$ (see table 5).

Table 5. Neither A_t nor B_t relationship.

		Conditioned B_t		
		YES	NO	
Condition A_t	YES	0	0	0
	NO	0	1	1
		0	1	1

2.2.9. Necessary condition

Definition 2.37 (**Necessary condition [*Conditio sine qua non*]**).

Despite the most extended efforts, the current state of research on conditions and conditioned is still incomplete and very contradictory. However, even thousands of years ago and independently of any human mind and consciousness, water has been and is still a necessary condition for (human) life. Without water, there has been and there is no (human) life. It comes therefore as no surprise that one of the first documented attempts to present a rigorous theory of conditions and causation (see also Aristotle et al., 1908, Metaphysica III 2 997a 10 and 13/14) came from the Greek philosopher and scientist Aristotle (384-322 BCE). Thus far, it is amazing that Aristotle himself made already a strict distinction between conditions and causes. Taking Aristotle very seriously, it is necessary to consider that

> "... everything which has a ... ... potency in question ... ... has the potency ... of acting ...
>
> not in all circumstances but on certain conditions ... "
>
> (see also Aristotle et al., 1908, Metaphysica IX 5 1048a 14-19)

Before going into details, Aristotle went on to define the necessary condition as follows.

> "... necessary ... means ...
>
> without ... a condition, a thing cannot live ... "
>
> (see also Aristotle et al., 1908, Metaphysica V 2 1015a 20-22)

In point of fact, Aristotle developed a theory of conditions and causality commonly referred to as the doctrine of four causes. Many aspects and general features of Aristotle's logical concept of causality are meanwhile extensively and critically debated in secondary literature. However, even if the Greek philosophers Heraclitus, Plato, Aristotle et cetera numbers among the greatest philosophers of all time, the philosophy has evolved. Scientific knowledge and objective reality are deeply interrelated and cannot be reduced only to Greek philosophers like Aristotle. As mentioned at the start of the article, the specification of necessary conditions has traditionally been part of the philosopher's investigations of different phenomena. Behind the need of a detailed evidence, it is justified to consider that phi-

losophy or philosophers as such certainly do not possess **a monopoly on the truth** and other areas such as medicine as well as other sciences and technology may transmit truths as well and may be of help to move beyond one's self enclosed unit. Seemingly, **the law's concept of causation** justifies to say few words on this subject, to put some light on some questions. Are there any criteria in law for deciding whether one action or an event A_t has caused another (generally harmful) event B_t? What are these criteria? May causation in legal contexts differ from causation outside the law, for example, in science or in our everyday life and to what extent? Under which circumstances is it justified to tolerate such differences as may be found to exist? To understand just what is the law's concept of causation, it is useful to know how the highest court of states is dealing with causation. In the case *Hayes v. Michigan Central R. Co., 111 U.S. 228*, the U.S. Supreme Court defined 1884 conditio sine qua non as follows: "... **causa sine qua non – a cause which, if it had not existed, the injury would not have taken place**". (Justice Matthews, 1884) The German Bundesgerichtshof für Strafsachen stressed once again the importance of conditio sine qua non relationship in his decision by defining the following: "**Ursache eines strafrechtlich bedeutsamen Erfolges jede Bedingung, die nicht hinweggedacht werden kann, ohne daß der Erfolg entfiele**"(Bundesgerichtshof für Strafsachen, 1951) Another lawyer elaborated on the basic issue of **identity and difference between cause and condition**. Von Bar was writing: "Die erste Voraussetzung, welche erforderlich ist, damit eine Erscheinung als die Ursache einer anderen bezeichnet werden könne, ist, daß jene eine der Bedingungen dieser sein. Würde die zweite Erscheinung auch dann eingetreten sein, wenn die erste nicht vorhanden war, so ist sie in keinem Falle Bedingung und noch weniger Ursache. Wo immer ein Kausalzusammenhang behauptet wird, da muß er wenigstens diese Probe aushalten ... **Jede Ursache ist nothwendig auch eine Bedingung eines Ereignisses; aber nicht jede Bedingung ist Ursache zu nennen**."(Bar, 1871) Von Bar's position translated into English: *The first requirement, which is required, thus that something could be called as the cause of another, is that the one has to be one of the conditions of the other. If the second something had occurred even if the first one did not exist, so it is by no means a condition and still less a cause. Wherever a causal relationship is claimed, the same must at least withstand this test... Every cause is necessarily also a condition of an event too; but not every condition is cause too.* Thus far, let us consider among other the following in order to specify necessary conditions from another, probabilistic point of view. An event (i.e. A_t) which is a necessary condition of another event or outcome (i.e. B_t) must be given, must be present for a conditioned, for an event or for an outcome B_t to occur. A necessary condition (i.e. A_t) is a requirement which must be fulfilled **at every single Bernoulli trial t**, in order for a conditioned or an outcome (i.e. B_t) to occur, but it alone does not determine the occurrence of an event. In other words, if a necessary condition (i.e. A_t) is given, an outcome (i.e. B_t) need not occur. In contrast to a necessary condition, a 'sufficient'condition is the one condition which 'guarantees'that an outcome will take place or must occur for sure. Under which conditions we may infer about the unobserved and whether observations made are able at all to justify predictions about potential observations which have not yet been made or even general claims which my go even beyond the observed (*the 'problem of induction')* is not the issue of the discussion at this point. Besides of the principal necessity of meeting such a challenge, a necessary condition of an event can but need not be at the same Bernoulli trial t a sufficient condition for an event to occur. However, theoretically, it is possible that an event or an outcome is determined by many necessary conditions. Let us focus to some extent on what this means, or in other words how much importance can we attribute to such a special case. *Example*. A human being cannot live without oxygen. A human being

cannot live without water. A human being cannot live without a brain. A human being cannot live without kidneys. A human being cannot live without ... et cetera. Thus far, even if oxygen is given, if water is given, if a brain is given, without functioning kidney's (or something similar) a human being will not survive on the long run. This example is of use to reach the following conclusion. Although it might seem somewhat paradoxical at first sight, **even under circumstances where a condition or an outcome depends on several different necessary conditions it is particularly important that every single of these necessary conditions for itself must be given otherwise the conditioned (i.e. the outcome) will not occur**. Mathematically, the necessary condition (SINE) relationship, denoted by $\mathrm{p}(\mathrm{A_t} \leftarrow \mathrm{B_t})$ in terms of statistics and probability theory, is defined (Barukčić, 1989, p. 15-28) as

$$\begin{aligned} p\left(A_{\mathrm{t}} \leftarrow B_{\mathrm{t}}\right) \equiv p\left(A_{\mathrm{t}} \vee \underline{B}_{\mathrm{t}}\right) &\equiv \frac{\sum_{t=1}^{N}\left(A_{\mathrm{t}} \vee \underline{B}_{\mathrm{t}}\right)}{N} \equiv \frac{\left(A_{\mathrm{t}} \vee \underline{B}_{\mathrm{t}}\right) \times p\left(A_{\mathrm{t}} \vee \underline{B}_{\mathrm{t}}\right)}{\left(A_{\mathrm{t}} \vee \underline{B}_{\mathrm{t}}\right)} \\ &\equiv p\left(a_{\mathrm{t}}\right)+p\left(b_{\mathrm{t}}\right)+p\left(d_{\mathrm{t}}\right) \\ &\equiv \frac{N \times\left(p\left(a_{\mathrm{t}}\right)+p\left(b_{\mathrm{t}}\right)+p\left(d_{\mathrm{t}}\right)\right)}{N} \equiv \frac{E\left(A_{\mathrm{t}} \leftarrow B_{\mathrm{t}}\right)}{N} \\ &\equiv \frac{a+b+d}{N} \equiv \frac{E\left(A_{\mathrm{t}} \vee \underline{B}_{\mathrm{t}}\right)}{N} \\ &\equiv \frac{A+d}{N} \equiv \frac{E\left(A_{\mathrm{t}} \leftarrow B_{\mathrm{t}}\right)}{N} \\ &\equiv \frac{a+\underline{B}}{N} \equiv \frac{E\left(A_{\mathrm{t}} \vee \underline{B}_{\mathrm{t}}\right)}{N} \\ &\equiv +1 \end{aligned} \tag{80}$$

where $E\left(A_{\mathrm{t}} \leftarrow B_{\mathrm{t}}\right) \equiv E\left(A_{\mathrm{t}} \vee \underline{B}_{\mathrm{t}}\right)$ indicates the expectation value of the necessary condition. In general, it is $p\left(A_{\mathrm{t}} \prec B_{\mathrm{t}}\right) \equiv 1-p\left(A_{\mathrm{t}} \leftarrow B_{\mathrm{t}}\right)$ (see Table 6).

Table 6. Necessary condition.

		Conditioned $\mathrm{B_t}$		
		TRUE	FALSE	
Condition	TRUE	$\mathrm{p(a_t)}$	$\mathrm{p(b_t)}$	$\mathrm{p(A_t)}$
$\mathrm{A_t}$	FALSE	**+0**	$\mathrm{p(d_t)}$	$\mathrm{p(\underline{A}_t)}$
		$\mathrm{p(B_t)}$	$\mathrm{p(\underline{B}_t)}$	+1

Remark 2.2. *A necessary condition A_t is characterized itself by the property that another event B_t will not occur if A_t is not given, if A_t did not occur (Barukčić, 1989, 1997, 2005, 2016, 2017a,b, 2020a,b,c,d, Barukčić and Ufuoma, 2020).* ***Example****. Once again, a human being cannot live without water. A human being cannot live without gaseous oxygen, et cetera. Water itself is a necessary condition for human life. However, gaseous oxygen is a necessary condition for human life too. Thus far, even if water is given and even if water is a necessary condition for human life, without gaseous oxygen there will be no human life. In general, if a conditioned or an outcome B_t depends on the necessary condition A_t and equally on numerous other necessary conditions, an event B_t will not occur if A_t itself is not given independently of the occurrence of other necessary conditions.*

Taking into account Kolmogorov's definition of an n-dimensional probability density (see also Kolmogorov, 1950, p. 26) of random variables A_t, B_t et cetera at the (period of) time t, we obtain

$$\begin{aligned} p\left(A_t \leftarrow B_t\right) &\equiv +1 \\ &\equiv +1 - p\left(c_t\right) \\ &\equiv +1 - p\left(\underline{A}_t \cap B_t\right) \\ &\equiv \left(\int_{-\infty}^{A_t} \int_{-\infty}^{B_t} f\left(A_t, B_t\right)\, dA_t\, dB_t \right) + \left(1 - \int_{-\infty}^{B_t} f\left(B_t\right)\, dB_t \right) \end{aligned} \tag{81}$$

while $p\left(A_t \leftarrow B_t\right)$ would denote the cumulative distribution function of random variables of a necessary condition. Another adequate formulation of a necessary condition is possible too.

2.2.10. The Chi-square goodness of fit test of a necessary condition relationship

Definition 2.38 (The $\tilde{\chi}^2$ goodness of fit test of a necessary condition relationship).

Under some well known circumstances, hypothesis about the conditio sine qua non relationship $p(A_t \leftarrow B_t)$ can be tested by the chi-square distribution (also chi-squared or χ^2-distribution), first described by the German statistician Friedrich Robert Helmert (Helmert, 1876) and later rediscovered by Karl Pearson (Pearson, 1900) in the context of a goodness of fit test. The $\tilde{\chi}^2$ goodness of fit test of a conditio sine qua non relationship with degree of freedom (d. f.) of d. f. = 1 is calculated as

$$\begin{aligned} {\tilde{\chi}^2}_{\text{Calculated}}\left(A_t \leftarrow B_t \mid B\right) &\equiv \frac{\left(a - \left(a + c\right)\right)^2}{B} + \\ &\quad \frac{\left(\left(b + d\right) - \underline{B}\right)^2}{\underline{B}} \\ &\equiv \frac{c^2}{B} + 0 \\ &\equiv \frac{c^2}{B} \end{aligned} \tag{82}$$

or equally as

$$\begin{aligned} {\tilde{\chi}^2}_{\text{Calculated}}\left(A_t \leftarrow B_t \mid \underline{A}\right) &\equiv \frac{\left(d - \left(c + d\right)\right)^2}{\underline{A}} + \\ &\quad \frac{\left(\left(a + b\right) - A\right)^2}{A} \\ &\equiv \frac{c^2}{\underline{A}} + 0 \\ &\equiv \frac{c^2}{\underline{A}} \end{aligned} \tag{83}$$

and can be compared with a theoretical chi-square value at a certain level of significance α. It has not yet been finally clarified whether the use of Yate's (Yates, 1934) continuity correction is necessary at all.

2.2.11. The left-tailed p Value of the conditio sine qua non relationship

Definition 2.39 (**The left-tailed p Value of the conditio sine qua non relationship**).

The left-tailed (lt) p Value (Barukčić, 2019c) of the conditio sine qua non relationship can be calculated as follows.

$$\begin{aligned} pValue_{\mathrm{lt}}\left(A_{\mathrm{t}} \leftarrow B_{\mathrm{t}}\right) &\equiv 1 - e^{-\left(1-p\left(A_{\mathrm{t}} \leftarrow B_{\mathrm{t}}\right)\right)} \\ &\equiv 1 - e^{-(c/N)} \end{aligned} \tag{84}$$

2.2.12. Sufficient condition

Definition 2.40 (**Sufficient condition [*Conditio per quam*]**).

Mathematically, the sufficient condition (IMP) relationship, denoted by $\mathrm{p}(\mathrm{A_t} \rightarrow \mathrm{B_t})$ in terms of statistics and probability theory, is defined(Barukčić, 1989, p. 68-70) as

$$\begin{aligned} p\left(A_{\mathrm{t}} \rightarrow B_{\mathrm{t}}\right) \equiv p\left(\underline{A}_{\mathrm{t}} \vee B_{\mathrm{t}}\right) &\equiv \frac{\sum_{t=1}^{N}\left(\underline{A}_{\mathrm{t}} \vee B_{\mathrm{t}}\right)}{N} \equiv \frac{\left(\underline{A}_{\mathrm{t}} \vee B_{\mathrm{t}}\right) \times p\left(\underline{A}_{\mathrm{t}} \vee B_{\mathrm{t}}\right)}{\left(\underline{A}_{\mathrm{t}} \vee B_{\mathrm{t}}\right)} \\ &\equiv p\left(a_{\mathrm{t}}\right) + p\left(c_{\mathrm{t}}\right) + p\left(d_{\mathrm{t}}\right) \\ &\frac{N \times \left(p\left(a_{\mathrm{t}}\right) + p\left(c_{\mathrm{t}}\right) + p\left(d_{\mathrm{t}}\right)\right)}{N} \\ &\equiv \frac{a+c+d}{N} \equiv \frac{E\left(\underline{A}_{\mathrm{t}} \vee B_{\mathrm{t}}\right)}{N} \\ &\equiv \frac{B+d}{N} \equiv \frac{E\left(A_{\mathrm{t}} \rightarrow B_{\mathrm{t}}\right)}{N} \\ &\equiv \frac{a+\underline{A}}{N} \\ &\equiv +1 \end{aligned} \tag{85}$$

It is $p\left(A_{\mathrm{t}} \succ\!\!- B_{\mathrm{t}}\right) \equiv 1 - p\left(A_{\mathrm{t}} \rightarrow B_{\mathrm{t}}\right)$ (see Table 7).

Remark 2.3. *A sufficient condition A_t is characterized by the property that another event B_t will occur if A_t is given, if A_t itself occured (Barukčić, 1989, 1997, 2005, 2016, 2017a,b, 2020a,b,c,d, Barukčić and Ufuoma, 2020). **Example**. The ground, the streets, the trees, human beings and many other objects too will become wet during heavy rain. Especially, **if** it is raining (event A_t), **then** human beings will become wet (event B_t). However, even if this is a common human wisdom, a human being equipped with an appropriate umbrella (denoted by R_t) need not become wet even during heavy rain. An appropriate*

Table 7. Sufficient condition.

		Conditioned B_t		
		TRUE	FALSE	
Condition	TRUE	$p(a_t)$	**+0**	$p(A_t)$
A_t	FALSE	$p(c_t)$	$p(d_t)$	$p(\underline{A}_t)$
		$p(B_t)$	$p(\underline{B}_t)$	+1

umbrella (R_t) is similar to an event with the potential to counteract the occurrence of another event (B_t) and can be understood something as an ***anti-dot*** *of another event. In other words, an appropriate umbrella is an antidote of the effect of rain on human body, an appropriate umbrella has the potential to protect humans from the effect of rain on their body. It is a good rule of thumb that the following relationship*

$$p\left(A_t \to B_t\right) + p\left(R_t \wedge B_t\right) \equiv +1 \tag{86}$$

indicates that R_t is an antidote of A_t. However, taking a shower, swimming in a lake et cetera may make human hair wet too. More than anything else, however, these events does not affect the final outcome, the effect of raining on human body.

2.2.13. The Chi square goodness of fit test of a sufficient condition relationship

Definition 2.41 (The $\tilde{\chi}^2$ goodness of fit test of a sufficient condition relationship).

Under some well known circumstances, testing hypothesis about the conditio per quam relationship $p(A_t \to B_t)$ is possible by the chi-square distribution (also chi-squared or $\tilde{\chi}^2$-distribution) too. The $\tilde{\chi}^2$ goodness of fit test of a conditio per quam relationship with degree of freedom (d. f.) of d. f. = 1 is calculated as

$$\begin{aligned} \tilde{\chi}^2{}_{\text{Calculated}}\left(A_t \to B_t \mid A\right) &\equiv \frac{\left(a-(a+b)\right)^2}{A} + \\ &\quad \frac{\left((c+d)-\underline{A}\right)^2}{\underline{A}} \\ &\equiv \frac{b^2}{A} + 0 \\ &\equiv \frac{b^2}{A} \end{aligned} \tag{87}$$

or equally as

$$\begin{aligned}\tilde{\chi}^2{}_{\text{Calculated}}\left(A_t \rightarrow B_t \mid \underline{B}\right) &\equiv \frac{\left(d-(b+d)\right)^2}{\underline{B}}+ \\ &\quad \frac{\left((a+c)-B\right)^2}{B} \\ &\equiv \frac{b^2}{\underline{B}}+0 \\ &\equiv \frac{b^2}{\underline{B}}\end{aligned} \tag{88}$$

and can be compared with a theoretical chi-square value at a certain level of significance α. The $\tilde{\chi}^2$-distribution equals zero when the observed values are equal to the expected/theoretical values of the conditio per quam relationship/distribution $p(A_t \rightarrow B_t)$, in which case the null hypothesis is accepted. Yate's (Yates, 1934) continuity correction has not been used in this context.

2.2.14. The left-tailed p Value of the conditio per quam relationship

Definition 2.42 (**The left-tailed p Value of the conditio per quam relationship**).

The left-tailed (lt) p Value (Barukčić, 2019c) of the conditio per quam relationship can be calculated as follows.

$$\begin{aligned}pValue_{\text{lt}}\left(A_t \rightarrow B_t\right) &\equiv 1-e^{-\left(1-p\left(A_t \rightarrow B_t\right)\right)} \\ &\equiv 1-e^{-(b/N)}\end{aligned} \tag{89}$$

Again, a low p-value indicates a statistical significance.

2.2.15. Necessary and sufficient conditions

Definition 2.43 (**Necessary and sufficient conditions [*EQV*]**).

The necessary and sufficient condition (EQV) relationship, denoted by $p(A_t \leftrightarrow B_t)$ in terms of statistics and probability theory, is defined(Barukčić, 1989, p. 68-70) as

$$\begin{aligned}p\left(A_t \leftrightarrow B_t\right) &\equiv \frac{\sum_{t=1}^{N}\left(\left(A_t \vee \underline{B}_t\right) \wedge \left(\underline{A}_t \vee B_t\right)\right)}{N} \\ &\equiv p\left(a_t\right)+p\left(d_t\right) \\ &\equiv \frac{N \times \left(p\left(a_t\right)+p\left(d_t\right)\right)}{N} \\ &\equiv \frac{a+d}{N} \\ &\equiv +1\end{aligned} \tag{90}$$

2.2.16. The Chi square goodness of fit test of a necessary and sufficient condition relationship

Definition 2.44 (**The $\tilde{\chi}^2$ goodness of fit test of a necessary and sufficient condition relationship**).

Even the necessary and sufficient condition relationship $p(A_t \leftrightarrow B_t)$ can be tested by the chi-square distribution (also chi-squared or $\tilde{\chi}^2$-distribution) too. The $\tilde{\chi}^2$ goodness of fit test of a necessary and sufficient condition relationship with degree of freedom (d. f.) of d. f. = 1 is calculated as

$$\begin{aligned} \tilde{\chi}^2{}_{\text{Calculated}}\left(A_t \leftrightarrow B_t \mid A\right) &\equiv \frac{\left(a-(a+b)\right)^2}{A}+ \\ &\quad \frac{d-\left((c+d)\right)^2}{\underline{A}} \\ &\equiv \frac{b^2}{A}+\frac{c^2}{\underline{A}} \end{aligned} \tag{91}$$

or equally as

$$\begin{aligned} \tilde{\chi}^2{}_{\text{Calculated}}\left(A_t \leftrightarrow B_t \mid B\right) &\equiv \frac{\left(a-(a+c)\right)^2}{B}+ \\ &\quad \frac{d-\left((b+d)\right)^2}{\underline{B}} \\ &\equiv \frac{c^2}{B}+\frac{b^2}{\underline{B}} \end{aligned} \tag{92}$$

The calculated $\tilde{\chi}^2$ goodness of fit test of a necessary and sufficient condition relationship can be compared with a theoretical chi-square value at a certain level of significance α. Under conditions where the observed values are equal to the expected/theoretical values of a necessary and sufficient condition relationship/distribution $p(A_t \leftrightarrow B_t)$, the $\tilde{\chi}^2$-distribution equals zero. It is to be cleared whether Yate's (Yates, 1934) continuity correction should be used at all.

2.2.17. The left-tailed p Value of a necessary and sufficient condition relationship

Definition 2.45 (**The left-tailed p Value of a necessary and sufficient condition relationship**).

The left-tailed (lt) p Value (Barukčić, 2019c) of a necessary and sufficient condition relationship can be calculated as follows.

$$\begin{aligned} pValue_{\text{lt}}\left(A_t \leftrightarrow B_t\right) &\equiv 1-e^{-(1-p(A_t \leftrightarrow B_t))} \\ &\equiv 1-e^{-((b+c)/N)} \end{aligned} \tag{93}$$

In this context, a low p-value indicates again a statistical significance. Table 8 may provide an overview of the theoretical distribution of a necessary and sufficient condition.

Table 8. Necessary and sufficient condition.

		Conditioned B_t		
		YES	NO	
Condition A_t	YES	1	0	1
	NO	0	1	1
		1	1	2

2.2.18. Either or conditions

Definition 2.46 (Either A_t or B_t conditions [*NEQV*]).

Mathematically, an either A_t or B_t condition relationship (NEQV), denoted by $p(A_t \succ\!\prec B_t)$ in terms of statistics and probability theory, is defined(Barukčić, 1989, p. 68-70) as

$$\begin{aligned} p\left(A_t \succ\!\prec B_t\right) &\equiv \frac{\sum_{t=1}^{N}\left(\left(A_t \wedge \underline{B}_t\right) \vee \left(\underline{A}_t \wedge B_t\right)\right)}{N} \\ &\equiv p\left(b_t\right) + p\left(c_t\right) \\ &\equiv \frac{N \times \left(p\left(b_t\right) + p\left(c_t\right)\right)}{N} \\ &\equiv \frac{b+c}{N} \\ &\equiv +1 \end{aligned} \tag{94}$$

It is $p\left(A_t \succ\!\prec B_t\right) \equiv 1 - p\left(A_t <\!\!> B_t\right)$ (see Table 9).

Table 9. Either A_t or B_t relationship.

		Conditioned B_t		
		YES	NO	
Condition A_t	YES	0	1	1
	NO	1	0	1
		1	1	2

2.2.19. The Chi-square goodness of fit test of an either or condition relationship

Definition 2.47 (The $\tilde{\chi}^2$ goodness of fit test of an either or condition relationship).

An either or condition relationship $p(A_t \succ\!\prec B_t)$ can be tested by the chi-square distribution (also chi-squared or $\tilde{\chi}^2$-distribution) too. The $\tilde{\chi}^2$ goodness of fit test of an either or condition relationship with degree of freedom (d. f.) of d. f. = 1 is calculated as

$$\begin{aligned}\tilde{\chi}^2{}_{\text{Calculated}}\left((A_{\text{t}} \gtrless B_{\text{t}}) \mid A\right) &\equiv \frac{(b-(a+b))^2}{A}+ \\ &\quad \frac{c-((c+d))^2}{\underline{A}} \\ &\equiv \frac{a^2}{A}+\frac{d^2}{\underline{A}}\end{aligned} \tag{95}$$

or equally as

$$\begin{aligned}\tilde{\chi}^2{}_{\text{Calculated}}\left((A_{\text{t}} \gtrless B_{\text{t}}) \mid B\right) &\equiv \frac{(c-(a+c))^2}{B}+ \\ &\quad \frac{b-((b+d))^2}{\underline{B}} \\ &\equiv \frac{a^2}{B}+\frac{d^2}{\underline{B}}\end{aligned} \tag{96}$$

Yate's (Yates, 1934) continuity correction has not been used in this context.

2.2.20. The left-tailed p Value of an either or condition relationship

Definition 2.48 (The left-tailed p Value of an either or condition relationship).

The left-tailed (lt) p Value (Barukčić, 2019c) of an either or condition relationship can be calculated as follows.

$$\begin{aligned}pValue_{\text{lt}}\left(A_{\text{t}} \gtrless B_{\text{t}}\right) &\equiv 1-e^{-(1-p(A_{\text{t}}>-<B_{\text{t}}))} \\ &\equiv 1-e^{-((a+d)/N)}\end{aligned} \tag{97}$$

In this context, a low p-value indicates again a statistical significance.

2.2.21. Causal relationship k

Definition 2.49 (Causal relationship k).

Nonetheless, mathematically, the causal(Barukčić, 2011a,b, 2012) relationship (Barukčić, 1989, 1997, 2005, 2016, 2017b) between a cause U_t (German: Ursache) and an effect W_t (German: Wirkung), denoted by k(U_t, W_t), is defined *at each single Bernoulli trial t* in terms of statistics and probability theory as

$$\begin{aligned} k\left(U_t, W_t\right) &\equiv \frac{\sigma\left(U_t, W_t\right)}{\sigma\left(U_t\right) \times \sigma\left(W_t\right)} \\ &\equiv \frac{p\left(U_t \wedge W_t\right) - p\left(U_t\right) \times p\left(W_t\right)}{\sqrt[2]{\left(p\left(U_t\right) \times \left(1 - p\left(U_t\right)\right)\right) \times \left(p\left(W_t\right) \times \left(1 - p\left(W_t\right)\right)\right)}} \end{aligned} \tag{98}$$

where σ (U_t , W_t) denotes the co-variance between a cause U_t and an effect W_t *at every single Bernoulli trial t*, σ (U_t) denotes the standard deviation of a cause U_t at the same single Bernoulli trial t, σ (W_t) denotes the standard deviation of an effect W_t at same single Bernoulli trial t. Table 10 illustrates the theoretically possible relationships between a cause and an effect.

Table 10. Sample space and the causal relationship k

		Effect B_t		
		TRUE	FALSE	
Cause A_t	TRUE	p(a_t)	p(b_t)	p(U_t)
	FALSE	p(c_t)	p(d_t)	p($\underline{U}_t$)
		p(W_t)	p($\underline{W}_t$)	+1

2.3. Proof methods

Considered from the historical point of view, human reasoning and knowledge appears to be to some extent relative too. Although it seems almost impossible, to proof or to establish the correctness of a statement, a theorem, a theory once and for all, this does not justify any technical or other errors in (human) reasoning which are many times identified the hard way but easy to overlook while in contrast to that **charges and proofs of fallacious reasoning always need time, money, and personal dignity to be accepted by the scientific community**.

> **"Niemals aber kann die Wahrheit einer Theorie erwiesen werden.**
> **Denn niemals weiß man,**
> **daß auch in Zukunft eine Erfahrung bekannt werden wird,**
> **die Ihren Folgerungen widerspricht..."**
> (Einstein, 1919)

Albert Einstein's position translated into English: 'But the truth of a theory can never be proven. For one never knows if future experience will contradict its conclusion; and furthermore there are always other conceptual systems imaginable which might coordinate the very same facts. 'Often, our fear of the unknown appears to overshadow our mind to an objectively unjustified extent. However, logically sound scientific verification and proof techniques are likely to allow us to continue our successful and rapid identification of contradictory scientific findings and are appropriate enough to shed some light even on this unknown. Step by step, by following the time honoured principle of going **from the known (and secured) to the unknown (and unsecured)** we will bring more light into the epistemological darkness which may surround us sometimes. Following Einstein, a theory can very well be found to be incorrect if there is a logical error in its deduction.

> "**Eine Theorie kann also wohl als unrichtig erkannt werden,**
> **wenn in ihren Deduktionen**
> **ein logischer Fehler ist . . .**"
> (Einstein, 1919)

In other words, grain by grain and the hen fills her belly. Scientific proof methods are **a demarcation line between science and non-science** (Popper, Karl Raimund, 2002). In this context, the development of new suitable scientific experimental and non-experimental test methods is of key scientific value. It may be allowed to point out view of these numerous scientific proof (Barukčić, Ilija, 2019) methods.

2.3.1. Proof by counter example

Definition 2.50 (**Proof by counter example**). *Scientific progress can be achieved not only through doing things right, but also by correcting (scientific) mistakes. Both contributions of authors are equivalent to each other and the two sides of the same coin. A* ***proof by counter example*** *is a valid scientific proof technique with the potential to correct horrific and dreadful scientific mistakes, especially in*

philosophy, mathematics and in science as such.

> ***"No amount of experimentation***
> ***can ever prove me right;***
> ***a single experiment***
> ***can prove me wrong."***
> *(Robertson, 1997)*

In particular, the close investigation of counter examples can give us an insight into the many deep and delicate issues surrounding a statement or theorem. A generally valid theorem can be refuted by a single counter example (Bağçe, Samet and Başkent, Can, 2009, Corcoran, 2005, Israël, Hans, 2011, McGee, 1985, Robertson, 1997, Romano and Siegel, 1986, Stoyanov, 2013, Weatherson, 2003) by showing an instance where a given statement, theorem et cetera cannot possibly be correct.

It is worth to emphasise in this context that ***one single counter example*** *refutes a theorem, a theory, a conjecture* ***as effectively as n*** *counter examples.*

2.3.2. Proof by (thought) experiments

Unfortunately, too often, competing scientific positions or even theories of the nature or of our world are excluding each other. A (theoretical) scientific verification becomes pressing, while (thought) experiments are of special importance in this context. In short, **Albert Einstein** wrote in a letter to the student J. S. Switzer on April 23rd, 1953, the following:

> "Development of Western **science** is based on two great achievements: the invention of the formal **logic**al system (in Euclidean geometry) by the Greek philosophers, **and** the discovery of the possibility to find out **causal relationships** by systematic **experiment** (during the Renaissance). "
> (Hu, 2005)

In other words, (thought) experiments are one of the methods to prove theorems and theories.

2.3.3. Modus tollens

From a practical point of view, various proposals (Barukčić and Ufuoma, 2020) have been put forward which criteria of demarcation between science and non-science should be applied, including **modus tollens** as advocated especially by **Karl Popper**. Following Popper,

> **"... it is possible by means of purely deductive inferences**
> **(with the help of the modus tollens of classical logic)**
> **to argue**
> **from the truth of singular statements**

> **to the falsity of universal statements.**"
> (Popper, Karl Raimund, 1935)

2.3.4. Proof by modus inversus

It is noticeable that our today's methods of investigation especially in natural sciences and even the knowledge achieved relies to a very great extent on mathematics and mathematical rules too. Thus far, mathematics as such appears to enjoy a very special esteem within the scientific community and is regarded more or less above all other sciences (Barukčić and Ufuoma, 2020). This view is sometimes further strengthened by the common belief that the laws of mathematics are absolutely certain and indisputable. However, it is noteworthy that objects studied in mathematics are not all the time located in space and time and the methods of investigation of mathematics sometimes differ markedly from the methods of investigation in the natural sciences (Barukčić and Ufuoma, 2020). Therefore, first and after all and in a slightly different way, **today's mathematics itself is more or less a product of human thought and mere human imagination** and belongs as such to a world of human thought and mere human imagination. In point of fact, **human thought and mere human imagination which produces the laws of mathematics is able to produce erroneous or incorrect results too** with the principal consequence that even mathematics or **mathematical theorems, rules or other results valid since thousands of years are in constant danger of being overthrown by newly discovered facts** (Barukčić and Ufuoma, 2020). **Modus inversus** (Barukčić and Ufuoma, 2020, Barukčić, Ilija, 2019, Toohey, 1948) is a suitable proof method to check mathematical position and theorems for logical consistency.

However, **modus inversus** is an additional approach to solve the problem of demarcation between science and non-science (see also: https://doi.org/10.5281/zenodo.4165074). In contrast to **modus ponens**, **modus inversus is designed primarily to preserve at all costs the contradiction**, the falsity, the falseness, the falsehood as such. In contrast to the principle ex contradictione sequitur quodlibet (Carnielli and Marcos, 2001, Priest, 1998, Priest et al., 1989), **from a contradictory premise or a contradictory statement like (+1=+0), does not anything follow but the contradiction itself**. In other words, in the absence of (technical and other) errors, **the contradiction is preserved**. In particular, even if one of the main tasks of modus inversus (Barukčić, Ilija, 2019) is to preserve the contradiction under any circumstances, the main task of modus inversus is to recognize the truth too. The abstract structure of modus inversus is as follows.

Proof by modus inversus. Thus far, let ${}_{R}P_{t}$ denote a premise at a certain point in (space-) time t. Let ${}_{R}C_{t}$ denote the conclusion at the same certain point in (space-) time t.

PREMISES.

(1) If (${}_{R}P_{t}$ is false) then (${}_{R}C_{t}$ is false).

(2) ${}_{R}P_{t}$ is false.

CONCLUSION.

(3) ${}_{R}C_{t}$ is false. □

The following 2x2 table may illustrate modus inversus again. Let ${}_{\mathrm{R}}\mathrm{P}_{\mathrm{t}}$ denote a premise from the standpoint of a stationary observer, a Bernoulli distributed random variable at a certain period of time or Bernoulli trial t (Uspensky, 1937).

Table 11. Modus inversus

		Conclusion ${}_{\mathrm{R}}\mathrm{C}_{\mathrm{t}}$		
		FALSE	TRUE	
Premisse	FALSE	+1	+0	
${}_{\mathrm{R}}\mathrm{P}_{\mathrm{t}}$	TRUE	+1	+1	
				+1

In terms of probability theory, modus inversus can be expressed as follows.

Table 12. Modus inversus II

		Conclusion ${}_{\mathrm{R}}\mathrm{C}_{\mathrm{t}}$		
		FALSE	TRUE	
Premisse	FALSE	$\mathrm{p}(\mathrm{a}_{\mathrm{t}})$	+0	$\mathrm{p}({}_{\mathrm{R}}\mathrm{P}_{\mathrm{t}})$
${}_{\mathrm{R}}\mathrm{P}_{\mathrm{t}}$	TRUE	$\mathrm{p}(\mathrm{c}_{\mathrm{t}})$	$\mathrm{p}(\mathrm{d}_{\mathrm{t}})$	$\mathrm{p}({}_{\mathrm{R}}\underline{\mathrm{P}}_{\mathrm{t}})$
		$\mathrm{p}({}_{\mathrm{R}}\mathrm{C}_{\mathrm{t}})$	$\mathrm{p}({}_{\mathrm{R}}\underline{\mathrm{C}}_{\mathrm{t}})$	+1

The premise ${}_{\mathrm{R}}\mathrm{P}_{\mathrm{t}}$ might take only the values either +0 or +1. Let ${}_{\mathrm{R}}\mathrm{C}_{\mathrm{t}}$ denote a conclusion from the standpoint of a stationary observer R, a Bernoulli distributed random variable at the same period of time or Bernoulli trial t. The conclusion ${}_{\mathrm{R}}\mathrm{C}_{\mathrm{t}}$ itself might take only the values either +0 or +1 too. Under conditions of classical logic, +0 may denote false while +1 may denote true. The modus inversus is defined as if (premise$_{\mathrm{t}}$ is false) then (conclusion$_{\mathrm{t}}$ is false). Formally, modus inversus can be expressed as

$$({}_{\mathrm{R}}P_{\mathrm{t}}) \cup ({}_{\mathrm{R}}\neg C_{\mathrm{t}}) \equiv +1 \tag{99}$$

while the sign $\cup$ denotes inclusive or. It is noticeable and by far not regrettable that according to modus inversus **it is not possible to achieve a true conclusion while starting with a false premise**. The follow-up question should be: what allows the assumption that modus inversus is generally valid or valid at all?

Example: Burning candle experiment

A simple to perform real-world experiment may illustrate the general validity of modus inversus. Let A_{t} denote gaseous oxygen, a Binomial random variable, which can take only two values, either gaseous oxygen is present = +1 or gaseous oxygen is not present = +0. Gaseous oxygen is present means that the amount of gaseous oxygen is enough to assure that a candle can burn. Let B_{t} denote a candle, a Binomial random variable, which can take only two values, either a candle is burning = +1 or a candle is not burning = +0.

In this experiment, an investigator lights the candle wick of some candles (old, young, big, small, red, green, curved, straight et cetera) under different conditions. As next, candle flame reacts with gaseous oxygen such that light and heat which characterizes a candle are produced. The data as obtained by this real-world experiment are illustrated by the following 2x2 table.

Table 13. Example. Modus inversus III

		Candle is burning		
		FALSE	TRUE	
Gaseous	FALSE	+1	+0	
oxygen	TRUE	+1	+1	
				+1

The relationship between gaseous oxygen and the behaviour of a candle produced out of simple wax is studied to demonstrate the relationship of modus inversus to objective reality. In other words, modus inversus is backed by natural processes independent of human mind and consciousness.

For this reason, and especially if different persons with different ideology and believe are aiming to arrive at the same logical conclusions with regard to a difficult and controversy issue of investigation, they will have to agree at least upon some view fundamental laws (axioms) as well as the methods by which other laws can be deduced therefrom. At this point, clarifying some fundamental axioms or starting points of investigations can therefore be essential part of every scientific method and any scientific progress.

2.3.5. Direct proof

The truth or falsehood of a given theorem can be demonstrated too by a straightforward combination of established facts.

2.3.6. Proof by contradiction

Proof by contradiction (Dorolle, 1918, Worrall et al., 1976) is a widely used proof method and goes back at least as far as to ancient times. The truth or the validity of a theorem can be established by **assuming that a statement or a theorem we want to prove is false**. In the following of the proof by showing that such an assumption leads to a contradiction it is justified to conclude that we were wrong to assume the theorem was false. In other words, the theorem must be true.

2.3.7. Proof by other methods

There are of course many other scientific proof methods which can be found in literature.

2.4. Statistical methods

The probability of the necessary (Barukčić, 2021c) condition p(SINE) has been calculated and tested for statistical significance. The probability of the sufficient (Barukčić, 2021c) condition p(IMP) has been calculated, the statistical significance of this relationship has been proofed. The chi-square goodness of fit test with one degree of freedom has been used to test whether the sample data published fit a certain theoretical distribution in the population. The causal relationship k (Barukčić, 2021c) has been calculated to evaluate a possible causal relationship between the events/factors analysed. The hypergeometric(Fisher, 1922, Gonin, 1936, Huygens and van Schooten, 1657, Pearson, 1899) distribution (HGD) has been used to test the one-sided significance of the causal relationship k. The study (design) bias has been controlled by IOI, the index of independence(Barukčić, 2019a) and IOU, the index of unfairness(Barukčić, 2019b). All the data were analysed using MS Excel (Microsoft Corporation, USA). The p values less than 0.05 were considered to indicate a statistically significant difference.

2.5. Axioms

2.5.1. Axiom I. Lex identitatis

In this context, we define axiom I as the expression

$$+1 = +1 \tag{100}$$

2.5.2. Axiom II. Lex contradictionis

In this context, axiom II or **lex contradictionis**, the negative of lex identitatis, or

$$+0 = +1 \tag{101}$$

and equally the most simple form of a contradiction formulated.

2.5.3. Axiom III. Lex negationis

$$\neg(0) \times 0 = 1 \tag{102}$$

where $\neg$ denotes (logical (Boole, 1854) or natural) negation (Ayer, 1952, Förster and Melamed, 2012, Hedwig, 1980, Heinemann, 1943, Horn, 1989, Koch, 1999, Kunen, 1987, Newstadt, 2015, Royce, 1917, Speranza and Horn, 2010, Wedin, 1990). In this context, there is some evidence that $\neg(1) \times 1 = 0$. In other words, it is $(\neg(1) \times 1) \times (\neg(0) \times 0) = 1$

3. Results

3.1. Without gaseous oxygen, no burning candle

Theorem 3.1 (Without gaseous oxygen, no burning candle)**.** *The necessary condition relationship is given and valid independently of any human mind and consciousness, objectively and real. Let A_t denote sufficient amount of gaseous oxygen with two states, either sufficient amount of gaseous oxygen is given ($\equiv +1$ or TRUE) or a sufficient amount of gaseous oxygen is not given (+0 or FALSE). Let B_t denote a candle made out of wax with two states, either a candle is burning ($\equiv +1$ or TRUE) or a candle is not burning (+0 or FALSE). Let $p\left(A_t \leftarrow B_t\right)$ denote the probability by which a necessary condition relationship between sufficient amount of gaseous oxygen and a burning wax candle is given. In general, it is*

$$
\begin{aligned}
p\left(A_t \leftarrow B_t\right) \equiv p\left(A_t \vee \underline{B}_t\right) &\equiv \frac{\sum_{t=1}^{N}\left(A_t \vee \underline{B}_t\right)}{N} \equiv \frac{\left(A_t \vee \underline{B}_t\right) \times p\left(A_t \vee \underline{B}_t\right)}{\left(A_t \vee \underline{B}_t\right)} \\
&\equiv p\left(a_t\right) + p\left(b_t\right) + p\left(d_t\right) \\
&\equiv \frac{N \times \left(p\left(a_t\right) + p\left(b_t\right) + p\left(d_t\right)\right)}{N} \equiv \frac{E\left(A_t \leftarrow B_t\right)}{N} \\
&\equiv \frac{a+b+d}{N} \equiv \frac{E\left(A_t \vee \underline{B}_t\right)}{N} \\
&\equiv \frac{A+d}{N} \equiv \frac{E\left(A_t \leftarrow B_t\right)}{N} \\
&\equiv \frac{a+\underline{B}}{N} \equiv \frac{E\left(A_t \vee \underline{B}_t\right)}{N} \\
&\equiv +1
\end{aligned}
\tag{103}
$$

where $E\left(A_t \leftarrow B_t\right) \equiv E\left(A_t \vee \underline{B}_t\right)$ indicates the expectation value of the necessary condition. Example: Without sufficient amount of gaseous oxygen, no burning candle.

Proof by thought expermiment. Since objective reality posses the power to correct wrong thinking, wrong theories et cetera, a real world experiment has been performed by thought to confront the theorem above with objective reality as such. The following data (see table 14) were obtained. As can be

Table 14. Necessary condition between oxygen and burning candle.

		Burning wax candle B_t		
		TRUE	FALSE	
Gaseous oxygen	TRUE	1	3	4
A_t	FALSE	**0**	5	5
		1	8	9

seen, data show that case c = 0. In other words, an event no sufficient amount of gaseous oxygen but

still burning wax candle has not been observed, while a_t=1, b_t=3, d_t=5. In the end, why is something, the way it is? This relationship of table 14 are illustrated by figure 3.1.

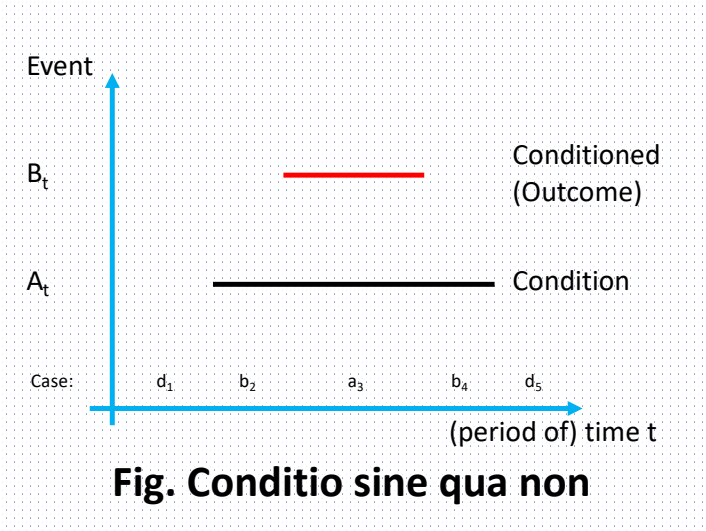

Fig. Conditio sine qua non

Conditio sine qua non.
Case d_1, d_5: no A_t and no B_t
Case b_2, b_4: A_t and no B_t
Case a_3: A_t and B_t
Case c: no A_t and B_t: not observed

The relationship between A_t and B_t is analysed at the same Bernoulli trial / (period of) time t.

Our conclusion is true. **Without** sufficient amount of gaseous oxygen, **no** burning wax candle. □

Remark 3.1. *The sample size of the study above is very small. Thus far, the conclusions drawn could be considered a little uncertain. However, such a basic attitude is not completely justified. Even a study with a smaller sample size (see data of table 14) has the potential to recognize the basic relationship between events. Moreover, from the point of view of sound logical reasoning, it is to be criticized that figure 3.1 illustrates a specific way of analysing the relationship between a sufficient amount of gaseous oxygen (A_t) and a burning candle (B_t) as a sequence of data points collected over an interval of time. Finally, figure 3.1 might be confused with time series analysis and become an unavoidable source of misunderstanding and of frustration even.* ***Example.*** *An illness like gastric cancer existed centuries ago, gastric cancer is existing today too. Therefore, the necessary condition/s of gastric cancer must also have existed centuries ago and is/are existing today too, otherwise gastric cancer would have not existed in the past and would not exist today. However, with the continuing development of human beings and human culture, new objects, products et cetera will become an increasingly important part of human life, while others will increasingly lose significance. At the same time, it is also true that such new objects, products cannot be a necessary condition of human gastric cancer because centuries ago human cancer existed but not these newly objects, products et cetera. In this context, it is necessary to focus at least on one key aspect with respect to a necessary condition: what is time series analysis? As can be seen, after condition A_t at the time b_2 follows the conditioned B_t at the time a_3. Furthermore, after conditioned at the time a_3 follows the condition at the time b_4 et cetera. However, in order to avoid any misunderstanding and in complete contrast to time series, a necessary condition is based on the co-occurrence of events at the same Bernoulli trial / (period of) time t.*

3.2. Observational studies and necessary conditions

The generation of reliable knowledge by a research study is endangered by many factors and circumstances which can be the cause of serious (selection, information, confounding et cetera) bias, study design is one of these factors. Therefore, we must draw the reader's attention to the need to adopt all the measures required to ensure that bias is prevented as much as possible in observational studies (i.e. cross-sectional; case-control and cohort studies) or in experimental studies (randomised control trials, RCTs). One of these measures is the use of mathematical methods, which is completely independent of any study design. Such methods might provide a reliable estimate of the true relationship. A case-control study[1] is a type of observational study commonly used to look at factors or exposures or conditions (an event A_t) responsible for conditioned or outcomes (an event A_t) at a certain Bernoulli trial t. A case-control study is based on a group of cases, which are the individuals who have the outcome or the conditioned B_t of interest. A researcher then tries to construct an appropriate group of individuals, called the controls, who do not have the outcome of interest and compares both groups. However, at least this step can lead to dramatic bias. Mathematically, it is possible to estimate the extent to which an event A_t is a necessary condition of an event B_t (an outcome) independent of a control group.

Theorem 3.2. *In general, the necessary condition relationship follows approximately as*

$$p\left(A_t \leftarrow B_t\right) \geq 1 - \frac{p\left(c_t\right)}{p\left(B_t\right)} \tag{104}$$

Proof by direct proof. The premise

$$+1 \equiv +1 \tag{105}$$

is true. In the following, we rearrange the premise. We obtain

$$p\left(B_\mathrm{t}\right) \equiv p\left(B_\mathrm{t}\right) \tag{106}$$

or

$$p\left(a_\mathrm{t}\right) + p\left(c_\mathrm{t}\right) \equiv p\left(B_\mathrm{t}\right) \tag{107}$$

Rearranging equation 107, it is

$$p\left(a_\mathrm{t}\right) \equiv p\left(B_\mathrm{t}\right) - p\left(c_\mathrm{t}\right) \tag{108}$$

Simplifying equation 108, we obtain

$$\frac{p\left(a_\mathrm{t}\right)}{p\left(B_\mathrm{t}\right)} \equiv \frac{p\left(B_\mathrm{t}\right)}{p\left(B_\mathrm{t}\right)} - \frac{p\left(c_\mathrm{t}\right)}{p\left(B_\mathrm{t}\right)} \tag{109}$$

Equation 109 becomes

$$\frac{p\left(a_\mathrm{t}\right)}{p\left(B_\mathrm{t}\right)} \equiv 1 - \frac{p\left(c_\mathrm{t}\right)}{p\left(B_\mathrm{t}\right)} \tag{110}$$

[1] Steven Tenny et al., Case Control Studies

A basic requirement of a necessary condition relationship is the need that $\frac{p(a_t)}{p(B_t)} \equiv 1$. In general, it is

$$p(A_t \leftarrow B_t) \equiv \frac{p(a_t)}{p(B_t)} \equiv 1 - \frac{p(c_t)}{p(B_t)} \tag{111}$$

However, this relationship is not given under any circumstances. Therefore, the necessary condition relationship can be estimated roughly under conditions of an observational study independently of a control group by the relationship

$$p(A_t \leftarrow B_t) \approx 1 - \frac{p(c_t)}{p(B_t)} \tag{112}$$

□

However, in reality, it can be assumed that the necessary condition relationship will be stronger than the relationship suggested by equation 112. Therefore, equation 112 is of particular value under conditions where a control group is absent or appears to be (completely) unsuitable. In general, it is

$$p(A_t \leftarrow B_t) \geq 1 - \frac{p(c_t)}{p(B_t)} \tag{113}$$

3.3. Experimental studies and necessary conditions

A transparent and rigorous bias[2] assessment is of key importance, especially for high-quality randomized, double-blind placebo-controlled experimental studies, too. In order to prevent false conclusions or bias and to reduce the deviation from the truth in general based on published data, many times the sample size is increased. Nonetheless, withholding a potentially effective treatment from one or more participants in a clinical research study or any unnecessary lengthening of a study, et cetera, faces at least serious ethical problems. Mathematically, it is possible to estimate the extent to which an event A_t is a necessary condition of an event B_t (an outcome) independent of a verum group.

Theorem 3.3. *In general, the necessary condition relationship follows approximately as*

$$p(A_t \leftarrow B_t) \geq 1 - \frac{p(c_t)}{p(\underline{A}_t)} \tag{114}$$

Proof by direct proof. The premise

$$+1 \equiv +1 \tag{115}$$

is true. In the following, we rearrange the premise. We obtain

$$p(\underline{A}_t) \equiv p(\underline{A}_t) \tag{116}$$

or

$$p(c_t) + p(d_t) \equiv p(\underline{A}_t) \tag{117}$$

[2] Hugh Waddington et al., Quasi-experimental study design

Rearranging equation 117, it is

$$p\left(d_{\mathrm{t}}\right) \equiv p\left(\underline{A}_{\mathrm{t}}\right) - p\left(c_{\mathrm{t}}\right) \tag{118}$$

Simplifying equation 118, we obtain

$$\frac{p\left(d_{\mathrm{t}}\right)}{p\left(\underline{A}_{\mathrm{t}}\right)} \equiv \frac{p\left(\underline{A}_{\mathrm{t}}\right)}{p\left(\underline{A}_{\mathrm{t}}\right)} - \frac{p\left(c_{\mathrm{t}}\right)}{p\left(\underline{A}_{\mathrm{t}}\right)} \tag{119}$$

Equation 119 becomes

$$\frac{p\left(d_{\mathrm{t}}\right)}{p\left(\underline{A}_{\mathrm{t}}\right)} \equiv 1 - \frac{p\left(c_{\mathrm{t}}\right)}{p\left(\underline{A}_{\mathrm{t}}\right)} \tag{120}$$

However, another basic requirement of a necessary condition relationship is the need that $\frac{p\left(d_{\mathrm{t}}\right)}{p\left(\underline{A}_{\mathrm{t}}\right)} \equiv 1$. In general, it is

$$p\left(A_{\mathrm{t}} \leftarrow B_{\mathrm{t}}\right) \equiv \frac{p\left(d_{\mathrm{t}}\right)}{p\left(\underline{A}_{\mathrm{t}}\right)} \equiv 1 - \frac{p\left(c_{\mathrm{t}}\right)}{p\left(\underline{A}_{\mathrm{t}}\right)} \tag{121}$$

Regrettably, this reduced relationship of a necessary condition is not given under any circumstances too. In other words, the necessary condition relationship can be estimated roughly under conditions of an experimental study independently of a verum group by the relationship

$$p\left(A_{\mathrm{t}} \leftarrow B_{\mathrm{t}}\right) \approx 1 - \frac{p\left(c_{\mathrm{t}}\right)}{p\left(\underline{A}_{\mathrm{t}}\right)} \tag{122}$$

□

However, in reality, it can be assumed that the necessary condition relationship will be stronger than the relationship suggested by equation 122. Therefore, equation 122 is of particular value under conditions where a verum group is absent or appears to be (completely) inappropriate, et cetera. In general, it is

$$p\left(A_{\mathrm{t}} \leftarrow B_{\mathrm{t}}\right) \geq 1 - \frac{p\left(c_{\mathrm{t}}\right)}{p\left(\underline{A}_{\mathrm{t}}\right)} \tag{123}$$

3.4. Study design and necessary conditions

The study design of an observational or an experimental study should assure that it should be possible to recognize a necessary condition given, it doesn't matter whether data are obtained by an observational or an experimental study. What is a basic requirement of such a study design?

Theorem 3.4. *In general, the necessary condition relationship demands a study design where the index of unfairness (IOU) (Barukčić, 2019b) or p(IOU) is equal to*

$$p\left(IOU\left(A,B\right)\right) \equiv Absolute\left(\left(\frac{A_t + B_t}{N}\right) - 1\right) \equiv 0 \tag{124}$$

Proof by direct proof. The premise

$$+1 \equiv +1 \tag{125}$$

is true. In the following, we rearrange the premise. We obtain

$$p\left(A_{\mathrm{t}} \leftarrow B_{\mathrm{t}}\right) \equiv p\left(A_{\mathrm{t}} \leftarrow B_{\mathrm{t}}\right) \tag{126}$$

Based on equation 111 it is $p\left(A_{\mathrm{t}} \leftarrow B_{\mathrm{t}}\right) \equiv \dfrac{p\left(a_{\mathrm{t}}\right)}{p\left(B_{\mathrm{t}}\right)} \equiv 1 - \dfrac{p\left(c_{\mathrm{t}}\right)}{p\left(B_{\mathrm{t}}\right)}$. Rearranging equation 126, it is

$$1 - \frac{p\left(c_{\mathrm{t}}\right)}{p\left(B_{\mathrm{t}}\right)} \equiv p\left(A_{\mathrm{t}} \leftarrow B_{\mathrm{t}}\right) \tag{127}$$

Based on equation 121 it is $p\left(A_{\mathrm{t}} \leftarrow B_{\mathrm{t}}\right) \equiv \dfrac{p\left(d_{\mathrm{t}}\right)}{p\left(\underline{A}_{\mathrm{t}}\right)} \equiv 1 - \dfrac{p\left(c_{\mathrm{t}}\right)}{p\left(\underline{A}_{\mathrm{t}}\right)}$. Equation 127 simplifies as

$$1 - \frac{p\left(c_{\mathrm{t}}\right)}{p\left(B_{\mathrm{t}}\right)} \equiv 1 - \frac{p\left(c_{\mathrm{t}}\right)}{p\left(\underline{A}_{\mathrm{t}}\right)} \tag{128}$$

Equation 128 becomes

$$-\frac{p\left(c_{\mathrm{t}}\right)}{p\left(B_{\mathrm{t}}\right)} \equiv -\frac{p\left(c_{\mathrm{t}}\right)}{p\left(\underline{A}_{\mathrm{t}}\right)} \tag{129}$$

or

$$\frac{p\left(c_{\mathrm{t}}\right)}{p\left(\underline{A}_{\mathrm{t}}\right)} \equiv \frac{p\left(c_{\mathrm{t}}\right)}{p\left(B_{\mathrm{t}}\right)} \tag{130}$$

Equation 130 can be simplified as

$$p\left(c_{\mathrm{t}}\right) \times p\left(B_{\mathrm{t}}\right) \equiv p\left(c_{\mathrm{t}}\right) \times p\left(\underline{A}_{\mathrm{t}}\right) \tag{131}$$

In the following we ignore $p\left(c_{\mathrm{t}}\right)$ and set $p\left(c_{\mathrm{t}}\right) = +1$. In general, it is

$$p\left(B_{\mathrm{t}}\right) \equiv p\left(\underline{A}_{\mathrm{t}}\right) \tag{132}$$

or

$$p\left(B_{\mathrm{t}}\right) \equiv 1 - p\left(A_{\mathrm{t}}\right) \tag{133}$$

or

$$p\left(A_{\mathrm{t}}\right) + p\left(B_{\mathrm{t}}\right) \equiv 1 \tag{134}$$

Rearranging equation 134, it is

$$N \times p\left(A_{\mathrm{t}}\right) + N \times p\left(B_{\mathrm{t}}\right) \equiv N \tag{135}$$

while N might denote the sample or population size. Furthermore, it follows that

$$A_{\mathrm{t}} + B_{\mathrm{t}} \equiv N \tag{136}$$

Rearranging equation 136, it is

$$\frac{A_{\mathrm{t}} + B_{\mathrm{t}}}{N} \equiv \frac{N}{N} \equiv +1 \tag{137}$$

and the index of unfairness (Barukčić, 2019b) (IOU) follows as

$$IOU\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)\equiv\left(\frac{A_{\mathrm{t}}+B_{\mathrm{t}}}{N}\right)-1\equiv 0 \tag{138}$$

In order to make the obtained results of observational and experimental studies which investigated the necessary condition relationship comparable to each other, the study design should assure as much as possible that

$$p\left(IOU\left(A,B\right)\right)\equiv Absolute\left(\left(\frac{A_{\mathrm{t}}+B_{\mathrm{t}}}{N}\right)-1\right)\equiv 0 \tag{139}$$

□

3.5. Observational studies and exclusion relationship

An exclusion relationship can be investigated by the two major types of observational study designs: the comparative or case-control study, the longitudinal or cohort study or some of their variants. [3] Mathematically, it is possible to estimate the extent to which an event A_t excludes an event B_t (an outcome) independent of a control group.

Theorem 3.5. *In general, an exclusion relationship follows approximately as*

$$p\left(A_t \mid B_t\right)\geq 1-\frac{p\left(a_t\right)}{p\left(B_t\right)} \tag{140}$$

Proof by direct proof. The premise

$$+1\equiv+1 \tag{141}$$

is true. In the following, we rearrange the premise. We obtain

$$p\left(B_{\mathrm{t}}\right)\equiv p\left(B_{\mathrm{t}}\right) \tag{142}$$

or

$$p\left(a_{\mathrm{t}}\right)+p\left(c_{\mathrm{t}}\right)\equiv p\left(B_{\mathrm{t}}\right) \tag{143}$$

Rearranging equation 143, it is

$$p\left(c_{\mathrm{t}}\right)\equiv p\left(B_{\mathrm{t}}\right)-p\left(a_{\mathrm{t}}\right) \tag{144}$$

Simplifying equation 144, we obtain

$$\frac{p\left(c_{\mathrm{t}}\right)}{p\left(B_{\mathrm{t}}\right)}\equiv\frac{p\left(B_{\mathrm{t}}\right)}{p\left(B_{\mathrm{t}}\right)}-\frac{p\left(a_{\mathrm{t}}\right)}{p\left(B_{\mathrm{t}}\right)} \tag{145}$$

Equation 145 becomes

$$\frac{p\left(c_{\mathrm{t}}\right)}{p\left(B_{\mathrm{t}}\right)}\equiv 1-\frac{p\left(a_{\mathrm{t}}\right)}{p\left(B_{\mathrm{t}}\right)} \tag{146}$$

[3] PMID: 18450043

A basic requirement of a exclusion relationship is the need that $\frac{p(c_t)}{p(B_t)} \equiv 1$. In general, it is

$$p(A_t \mid B_t) \equiv \frac{p(c_t)}{p(B_t)} \equiv 1 - \frac{p(a_t)}{p(B_t)} \tag{147}$$

However, even this relationship might not be given under any circumstances. Therefore, the exclusion relationship can be estimated roughly under conditions of an observational study independently of a control group by the relationship

$$p(A_t \mid B_t) \approx 1 - \frac{p(a_t)}{p(B_t)} \tag{148}$$

□

However, in reality, it can be assumed that an exclusion relationship will be stronger than the relationship suggested by equation 148. Therefore, equation 148 is of particular value under conditions where a control group is absent or appears to be (completely) unsuitable. In general, it is

$$p(A_t \mid B_t) \geq 1 - \frac{p(a_t)}{p(B_t)} \tag{149}$$

3.6. Experimental studies and exclusion relationship

An experimental study design necessitates much thought in order to investigate an exclusion relationship. Lack of a good quality experimental study design can induce uncontrolled biases and might doom the experiment to failure. [4] Mathematically, it is possible to estimate the extent to which an event A_t excludes the occurrence of an event B_t (an outcome) and vice versa, independent of a placebo group.

Theorem 3.6. *In general, an exclusion relationship follows approximately as*

$$p(A_t \mid B_t) \geq 1 - \frac{p(a_t)}{p(A_t)} \tag{150}$$

Proof by direct proof. The premise

$$+1 \equiv +1 \tag{151}$$

is true. In the following, we rearrange the premise. We obtain

$$p(A_t) \equiv p(A_t) \tag{152}$$

or

$$p(a_t) + p(b_t) \equiv p(A_t) \tag{153}$$

Rearranging equation 153, it is

$$p(b_t) \equiv p(A_t) - p(a_t) \tag{154}$$

[4] PMID: 7995475

Simplifying equation 154, we obtain

$$\frac{p\left(b_{\mathrm{t}}\right)}{p\left(A_{\mathrm{t}}\right)} \equiv \frac{p\left(A_{\mathrm{t}}\right)}{p\left(A_{\mathrm{t}}\right)} - \frac{p\left(a_{\mathrm{t}}\right)}{p\left(A_{\mathrm{t}}\right)} \tag{155}$$

Equation 155 becomes

$$\frac{p\left(b_{\mathrm{t}}\right)}{p\left(A_{\mathrm{t}}\right)} \equiv 1 - \frac{p\left(a_{\mathrm{t}}\right)}{p\left(A_{\mathrm{t}}\right)} \tag{156}$$

However, another basic requirement of an exclusion relationship is the need that $\frac{p\left(b_{\mathrm{t}}\right)}{p\left(A_{\mathrm{t}}\right)} \equiv 1$. In general, it is

$$p\left(A_{\mathrm{t}} \mid B_{\mathrm{t}}\right) \equiv \frac{p\left(b_{\mathrm{t}}\right)}{p\left(A_{\mathrm{t}}\right)} \equiv 1 - \frac{p\left(a_{\mathrm{t}}\right)}{p\left(A_{\mathrm{t}}\right)} \tag{157}$$

Nonetheless, this reduced relationship of an exclusion relationship is not given under any circumstances too. In other words, the exclusion relationship can be estimated roughly under conditions of an experimental study design independently of a placebo group by the relationship

$$p\left(A_{\mathrm{t}} \mid B_{\mathrm{t}}\right) \approx 1 - \frac{p\left(a_{\mathrm{t}}\right)}{p\left(A_{\mathrm{t}}\right)} \tag{158}$$

□

However, in reality, it can be assumed that an exclusion relationship will be much stronger than the relationship suggested by equation 158. Therefore, equation 158 is of particular value under conditions where a placebo group is absent or appears to be (completely) inappropriate, et cetera. In general, it is

$$p\left(A_{\mathrm{t}} \mid B_{\mathrm{t}}\right) \geq 1 - \frac{p\left(a_{\mathrm{t}}\right)}{p\left(A_{\mathrm{t}}\right)} \tag{159}$$

3.7. The identity of an index of independence

Theorem 3.7. *In general, the necessary condition relationship demands a study design where the index of unfairness (IOU) (Barukčić, 2019b) or p(IOU) is equal to*

$$p\left(IOU\left(A_t, B_t\right)\right) \equiv Absolute\left(\left(\frac{A_t + B_t}{N}\right) - 1\right) \equiv 0 \tag{160}$$

Proof by direct proof. The premise

$$+1 \equiv +1 \tag{161}$$

is true. In the following, we rearrange the premise. We obtain

$$+0 \equiv +0 \tag{162}$$

The index of independence is defined as $p\left(IOI\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)\right)\equiv Absolute\left(\left(\frac{A_{\mathrm{t}}+\underline{B}_{\mathrm{t}}}{N}\right)-1\right)\equiv 0$. Equation 161 becomes

$$\left(\frac{A_{\mathrm{t}}+\underline{B}_{\mathrm{t}}}{N}\right)-1\equiv 0 \tag{163}$$

or

$$\left(\frac{A_{\mathrm{t}}+\underline{B}_{\mathrm{t}}}{N}\right)\equiv +1 \tag{164}$$

or

$$A_{\mathrm{t}}+\underline{B}_{\mathrm{t}}\equiv N \tag{165}$$

or

$$A_{\mathrm{t}}\equiv N-\underline{B}_{\mathrm{t}} \tag{166}$$

One general requirement of a study design in order to ensure the investigation of an exclusion relationship(see Barukčić, 2021a) is the necessity

$$A_{\mathrm{t}}\equiv B_{\mathrm{t}} \tag{167}$$

or

$$a_{\mathrm{t}}+b_{\mathrm{t}}\equiv a_{\mathrm{t}}+c_{\mathrm{t}} \tag{168}$$

or

$$b_{\mathrm{t}}\equiv c_{\mathrm{t}} \tag{169}$$

In general, it is $A_{\mathrm{t}}\equiv N-\underline{A}_{\mathrm{t}}$. Equation 167 becomes

$$N-\underline{A}_{\mathrm{t}}\equiv B_{\mathrm{t}} \tag{170}$$

or

$$N\equiv \underline{A}_{\mathrm{t}}+B_{\mathrm{t}} \tag{171}$$

or

$$\frac{N}{N}\equiv\frac{\underline{A}_{\mathrm{t}}+B_{\mathrm{t}}}{N} \tag{172}$$

Equation 172 simplifies as

$$\frac{\underline{A}_{\mathrm{t}}+B_{\mathrm{t}}}{N}\equiv\frac{N}{N}\equiv +1 \tag{173}$$

or as

$$\frac{\underline{A}_{\mathrm{t}}+B_{\mathrm{t}}}{N}-1\equiv +0 \tag{174}$$

The index of independence(Barukčić, 2019a) (IOI) can be expressed as

$$p\left(IOU\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)\right)\equiv Absolute\left(\left(\frac{\underline{A}_{\mathrm{t}}+B_{\mathrm{t}}}{N}\right)-1\right)\equiv 0 \tag{175}$$

□

3.8. Observational studies and study design

Theorem 3.8 (Observational studies and study design)**.** *Many observational studies are based on the demand that*

$$p\left(IOU\left(A_t,B_t\right)\right)\equiv p\left(IOI\left(A_t,\underline{B_t}\right)\right) \tag{176}$$

Proof by direct proof. **If** the premise

$$\underbrace{+1=+1}_{(Premise)} \tag{177}$$

is true, **then** the following conclusion

$$p\left(IOU\left(A_t,B_t\right)\right)\equiv p\left(IOI\left(A_t,\underline{B_t}\right)\right) \tag{178}$$

is also true, again the absence of any technical errors presupposed. The premise

$$+1\equiv+1 \tag{179}$$

is true. We multiply equation 179 by an expectation value B_t, it is

$$B_t\equiv B_t \tag{180}$$

Many times, the study design of observational studies demands that $B_t\equiv\underline{B_t}$. Equations 180 becomes

$$B_t\equiv\underline{B_t} \tag{181}$$

Adding the expectation value of A_t, it is

$$A_t+B_t\equiv A_t+\underline{B_t} \tag{182}$$

Dividing by the sample/populations size N, it is

$$\frac{A_t+B_t}{N}\equiv\frac{A_t+\underline{B_t}}{N} \tag{183}$$

or

$$\frac{A_t+B_t}{N}-1\equiv\frac{A_t+\underline{B_t}}{N}-1 \tag{184}$$

In general, a study design which demands that $B_t\equiv\underline{B_t}$ is based on the relationship

$$p\left(IOU\left(A_t,B_t\right)\right)\equiv p\left(IOI\left(A_t,\underline{B_t}\right)\right) \tag{185}$$

□

3.9. Experimental studies and study design

Theorem 3.9 (Experimental studies and study design)**.** *Many experimental studies are based on the demand that*

$$p\left(IOU\left(A_t,B_t\right)\right) \equiv p\left(IOI\left(B_t,\underline{A}_t\right)\right) \tag{186}$$

Proof by direct proof. **If** the premise

$$\underbrace{+1=+1}_{(Premise)} \tag{187}$$

is true, **then** the following conclusion

$$p\left(IOU\left(A_t,B_t\right)\right) \equiv p\left(IOI\left(B_t,\underline{A}_t\right)\right) \tag{188}$$

is also true, again the absence of any technical errors presupposed. The premise

$$+1 \equiv +1 \tag{189}$$

is true. We multiply equation 189 by an expectation value A_t, it is

$$A_t \equiv A_t \tag{190}$$

Many times, the study design of observational studies demands that $A_t \equiv \underline{A}_t$. Equations 190 becomes

$$A_t \equiv \underline{A}_t \tag{191}$$

Adding the expectation value of B_t, it is

$$A_t + B_t \equiv B_t + \underline{A}_t \tag{192}$$

Dividing by the sample/populations size N, it is

$$\frac{A_t + B_t}{N} \equiv \frac{B_t + \underline{A}_t}{N} \tag{193}$$

or

$$\frac{A_t + B_t}{N} - 1 \equiv \frac{B_t + \underline{A}_t}{N} - 1 \tag{194}$$

In general, a study design which demands that $A_t \equiv \underline{A}_t$ is based on the relationship

$$p\left(IOU\left(A_t,B_t\right)\right) \equiv p\left(IOI\left(B_t,\underline{A}_t\right)\right) \tag{195}$$

□

3.10. Leflunomide and acute myocardial infarction

Suissa [5] et al. (Suissa et al., 2006) conducted a nested case-control analysis within a cohort of subjects with rheumatoid arthritis (RA), observed between January 1, 1999 and December 31, 2003 to investigate the relationship between leflunomide and the risk of acute myocardial infarction (AMI) while using a database of a NorthAmerican insurance company. Subjects had to be free of the outcome of interest (AMI) and were followed from the date of cohort entry until an outcome of interest occurred. For each AMI case occurred in the cohort, Suissa et al. randomly selected 10 controls. During followup of 5 years, 558 cases of AMI requiring hospitalization occurred. In toto 6/558 AMI cases received leflunomide. The original data and the statistical analysis is presented by table 15.

Table 15. Leflunomide and AMI (Study et al. , 2006).

		AMI		
		YES	NO	
Leflunomide	YES	6	194	200
	NO	552	5386	5938
		558	5580	6138

Statistical analysis.	
Causal relationship k =	-0,0388838898
p Value left tailed (HGD) =	0,0005228
p (EXCL) =	0,9990224829
p (EXCL) approx.=	0,9892473118
$\tilde{\chi}^2$ (EXCL— A_t) =	0,1800
$\tilde{\chi}^2$ (EXCL— B_t) =	0,0645
p Value (EXCL) =	0,0009775171
Relative risk (RR).	
RR (nc) =	0,3227
RR (sc) =	0,3093
Additional measures.	
OR =	0,9700
IOR =	-0,6700
Study design.	
p(IOU)=	0,876507006
p(IOI)=	0,058325187

3.11. Leflunomide and acute myocardial infarction II

The study design of Suissa[6] et al. (Suissa et al., 2006) with p(IOI)=0,058325187 is of good quality, but the same can be improved too. At the end, the matching 1:10 has underestimated the relationship between leflunomide and acute myocardial infarction. The following theorem is based on a study design with p(IOI) = 0. In the control group of Suissa et al. about b=194 subjects out of 5580 subjects

[5] PMID: 16874796
[6] PMID: 16874796

obtained leflunomide without suffering from AMI. However, under conditions of p(IOI) = 0, a study design should assure that c=b=552. This would demand a control group of about (552/194)*5580 = 15877 individuals. The data of more appropriate control group are illustrated by table 16.

Table 16. Leflunomide and AMI (Study Suissa et al.,2006).

		AMI		
		YES	NO	
Leflunomide	YES	6	552	558
	NO	552	15325	15877
		558	15877	16435

Statistical analysis.	
Causal relationship k =	-0,0240145852
p Value left tailed (HGD) =	0,0003912
p (EXCL) =	0,9996349255
p (EXCL) approx.=	0,9892473118
$\tilde{\chi}^2$ (EXCL— A_t) =	0,0645
$\tilde{\chi}^2$ (EXCL— B_t) =	0,0645
p Value (EXCL) =	0,0003650745
Relative risk (RR).	
RR (nc) =	0,3093
RR (sc) =	0,3093
Additional measures.	
OR =	0,9892
IOR =	-0,6833
Study design.	
p(IOU)=	0,932096136
p(IOI)=	0

Leflunomide excludes AMI over about 5 years with a probability better than **p (EXCL) approx. = (1-((6)/558)) = 0,9892473118** or per one year with a probability better than p (EXCL) approx. = (1-((6/5)/558)) = 0,996415770609319. It is important in the first place to put this result in the right light. Biontec's Covid-19 vaccine excluded (see Barukčić, 2021a) the Covid-19 death in individuals in Scotland [7] who were fully vaccinated by Aug 18, 2021 with the probability p = 1 - (47 / 1247026) = 0,9999623103. The result of the relationship between leflunomide and AMI is there for all to see. The result of this statistical analysis is something really impressive. Leflunomide, a medication used in the treatment and management of rheumatoid arthritis, [8] excludes an acute myocardial infarction with a probability of **p = 1 - (6 / 16435) = 0,9996349255** and is not much worse effective than Biontech's Covid-19 vaccine.

[7] PMCID: PMC8553268
[8] PMID: 32491731

3.12. Etoricoxib and coronary artery disease

Li-Chih Wu et al. [9] investigated the effects of the cyclooxygenase-2 (COX II) inhibitor etoricoxib on the risk of coronary artery disease (CAD) by a 10-year population-based case-control study. The data and the statistical analysis are viewed by table 17.

Table 17. Etoricoxib and CAD (Study Wu et al., 2016).

		CAD		
		YES	NO	
Etoricoxib	YES	11	264	275
	NO	335	3502	3837
		346	3766	4112

Statistical analysis.	
Causal relationship k =	-0,0425712814
p Value left tailed (HGD) =	0,0023361
p (EXCL) =	0,9973249027
p (EXCL) approx.=	0,9682080925
$\tilde{\chi}^2$ (EXCL— A_t) =	0,4400
$\tilde{\chi}^2$ (EXCL— B_t) =	0,3497
p Value (EXCL) =	0,0026750973
Relative risk (RR).	
RR (nc) =	0,4581
RR (sc) =	0,4535
'RRR '(%) =	54,1851
Additional measures.	
OR =	0,9600
IOR =	-0,5246
Study design.	
p(IOU)=	0,848978599
p(IOI)=	0,017266537

Following Li-Chih Wu et al. "etoricoxib, but no naproxen and diclofenac were negatively associated with CAD"[10]. The study design with p(IOI)=0,017266537 is acceptable, the exclusion relationship between etoricoxib and coronary artery disease with p (EXCL) = 0,9973249027 is significant (p Value (EXCL) = 0,0026750973). Etoricoxib appears to have protective [11] effects against coronary artery disease. However, the results of the study of Li-Chih Wu et al. contradict the results of the study of Kathrin Thöne et al. [12] and the results of Gwen M C Masclee et al. [13] in this context. Both studies investigated the effect of etoricoxib on acute myocardial infarction.

[9] PMCID: PMC5023908
[10] PMCID: PMC5023908
[11] VIGOR Study Group
[12] PMCID: PMC5567458
[13] PMCID: PMC6211656

3.13. Etoricoxib and coronary artery events

Yao-Min Hung et al. [14] investigated the effect of anti-rheumatic medications for coronary artery disease in a nationwide population-based cohort study from the Taiwan National Health Insurance Research Database. Yao-Min Hung et al. found that "The effect of etoricoxib with reduced CAD risks among RA patients remained constant over the follow up time."The data and the results are presented by table 18.

Table 18. Etoricoxib and CAD events (Study Hung et al. , 2017).

		CAD events		
		YES	NO	
Etoricoxib	YES	12	144	156
	NO	1241	4863	6104
		1253	5007	6260

Statistical analysis.	
Causal relationship k =	-0,0492385193
p Value left tailed (HGD) =	0,0000152
p (EXCL) =	0,9980830671
p (EXCL) approx.=	0,9904229848
$\tilde{\chi}^2$ (EXCL— A_t) =	0,9231
$\tilde{\chi}^2$ (EXCL— B_t) =	0,1149
p Value (EXCL) =	0,0019169329
Relative risk (RR).	
RR (nc) =	0,3784
RR (sc) =	0,3330
'RRR '(%) =	62,1645
Additional measures.	
OR =	0,9231
IOR =	-0,6157
Study design.	
p(IOU)=	0,774920128
p(IOI)=	0,175239617

[14] PMCID: PMC5489160

4. Discussion

The data of Suissa et al. have been presented in this publication more or less only for demonstration purposes. Nonetheless, even if the data as published by Suissa et al. (Suissa et al., 2006) have several possible limitations, it is necessary to note that the same data are of use too. However, even if very convincing, the exclusion relationship between leflunomide and acute myocardial infarction as established by the data of Suissa et al. cannot be considered as certain yet. More studies with harder data will be necessary to ascertain the cardiovascular effects of leflunomide on acute myocardial infarction. However, and until proven otherwise, it can justifiably be accepted that leflunomide excludes acute myocardial infarction (p Value (EXCL) = 0,0003650745) very effectively. Leflunomide is taken orally and becomes metabolized [15] , [16] in the body to its active part known as teriflunomide. As with many other circumstances in life, it is the dosage that makes the poison. An empirical cholestyramine [17] wash-out therapy with four grams of cholestyramine every 6 hours for 14 days (antidote) is recommended for leflunomide toxicity. Hence, it is possible, and it seems only reasonable, to supply those individuals with leflunomide who are particularly exposed to the danger of an acute myocardial infarction or who already suffered from this very dangerous illness. At the same time, the data of the study of Suissa et al. (Suissa et al., 2006) justify very big doubts about today's dominant lipid hypothesis of acute myocardial infarction. In particular with regard to the relationship between etoricoxib and AMI or CAD, the results are very contradictory, and an ultimate knowledge is impossible today. Further research is necessary to investigate the impact of etoricoxib on AMI or CAD. As it has been known for quite a while, there are circumstances where it is impossible to have an event B_t without an event A_t. Such a relationship between an event A_t and an event B_t is described by the notion of necessary condition relationship. While we humans are faced with obvious limitations of human knowledge due to logically inconsistent or at the very least questionable scientific methods like risk ratio, odds ratio et cetera, meanwhile it is mathematically possible and of great practical value to apply the new methods like the necessary condition et cetera as soon as possible to pave the way for the successful solution of various (scientific) problems without any delay.

[15] PMID: 9666414
[16] PMID: 10600330
[17] PMID: 31644034

5. Conclusion

Leflunomide appears to be an antidote against an acute myocardial infarction.

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6. Patient consent for publication

Not required.

Conflict of interest statement

No conflict of interest to declare.

Private note

The definition section of a paper need not and does not necessarily contain new scientific aspects. Above all, it also serves to better understand a scientific publication, to follow every step of the arguments of an author and to explain in greater details the fundamentals on which a publication is based. Therefore, there is no objective need to force authors to reinvent a scientific wheel once and again unless such a need appears obviously factually necessary. The effort to write about a certain subject in an original way in multiple publications does not exclude the necessity simply to cut and paste from an earlier work, and has nothing to do with self-plagiarism. However, such an attitude cannot simply be transferred to the sections' introduction, results, discussion and conclusions et cetera.

References

Aristotle, William David Ross, and John Alexander Smith. *Volume VIII. Metaphysica*. The works of Aristotle. At The Clarendon Press, 1908. URL http://archive.org/details/worksofaristotle12arisuoft.

A. J. Ayer. Negation. *The Journal of Philosophy*, 49(26):797–815, January 1952. doi: 10.2307/2020959. JSTOR.

Monya Baker. 1,500 scientists lift the lid on reproducibility. *Nature*, 533(7604):452–454, 5 2016. ISSN 1476-4687. doi: 10.1038/533452a. PMID: 27225100.

Carl Ludwig von Bar. *Die Lehre vom Kausalzusammenhang im Recht, besonders im Strafrecht*. Verlag von Bernhard Tauchnitz, Leipzig, 1871. URL http://dlib-pr.mpier.mpg.de/m/kleioc/0010/exec/bigpage/%22101657_00000012.gif%22.

Ilija Barukčić. *Die Kausalität*. Wiss.-Verl., Hamburg, 1. aufl. edition, January 1989. ISBN 3-9802216-0-1. ISBN: 978-3-9802216-0-1.

Ilija Barukčić. *Die Kausalität*. Scientia, Wilhelmshaven, 2., völlig überarb. aufl. edition, January 1997. ISBN 3-9802216-4-4. ISBN: 978-3-9802216-4-1.

Ilija Barukčić. *Causality: New statistical methods*. Books on Demand GmbH, Norderstedt, Germany, January 2005. ISBN 978-3-8334-3645-1.

Ilija Barukčić. Anti Heisenberg-Refutation Of Heisenberg's Uncertainty Relation. In *American Institute of Physics - Conference Proceedings*, volume 1327, pages 322–325, Linnaeus University, Växjö, Sweden, June 14 - 17, 2010, January 2011a. doi: 10.1063/1.3567453. AQT. Web of Science. Full text: American Institute of Physics.

Ilija Barukčić. The Equivalence of Time and Gravitational Field. *Physics Procedia*, 22:56–62, January 2011b. ISSN 18753892. doi: 10.1016/j.phpro.2011.11.008. ICPST 2011. Web of Science. Free full text: Elsevier.

Ilija Barukčić. Anti-Bell - Refutation of Bell's theorem: In: Quantum Theory: Reconsideration of Foundations-6 (QTRF6), Växjö, (Sweden), 11-14 June 2012. In *American Institute of Physics - Conference Proceedings*, volume 1508, pages 354–358, Växjo, Sweden, 2012. American Institute of Physics - Conference Proceedings. doi: 10.1063/1.4773147. QTRF 6. Web of Science. Full text: American Institute of Physics.

Ilija Barukčić. The Mathematical Formula of the Causal Relationship k. *International Journal of Applied Physics and Mathematics*, 6(2):45–65, January 2016. doi: 10.17706/ijapm.2016.6.2.45-65. IJAPM. Free full text: IAP.

Ilija Barukčić. *Die Kausalität (1989)*. Books on Demand, Norderstedt, reprint edition, 2017a. ISBN 978-3-7448-1595-6. ISBN-13: 9783744815956.

Ilija Barukčić. *Theoriae causalitatis principia mathematica*. Books on Demand, Norderstedt, 2017b. ISBN 978-3-7448-1593-2. ISBN-13: 9783754331347.

Ilija Barukčić. Index of Independence. *Modern Health Science*, 2(2):1–25, 10 2019a. ISSN 2576-7305. doi: 10.30560/mhs.v2n2p1. URL https://j.ideasspread.org/index.php/mhs/article/view/331. Modern Health Science.

Ilija Barukčić. Index of Unfairness. *Modern Health Science*, 2(1):22, 4 2019b. ISSN 2576-7305, 2576-7291. doi: 10.30560/mhs.v2n1p22. Modern Health Science.

Ilija Barukčić. The P Value of likely extreme events. *International Journal of Current Science Research*, 5(11):1841–1861, 2019c. IJCSR . Free full text: ZENODO.

Ilija Barukčić. Causal relationship k. *International Journal of Mathematics Trends and Technology IJMTT*, 66(10):76–115, 2020a. URL http://www.ijmttjournal.org/archive/ijmtt-v66i10p512. Publisher: Seventh Sense Research Group SSRG.

Ilija Barukčić. Locality and Non locality. *European Journal of Applied Physics*, 2(5):1–13, October 2020b. ISSN 2684-4451. doi: 10.24018/ejphysics.2020.2.5.22. URL https://ej-physics.org/index.php/ejphysics/article/view/22. Free full text: EJAP.

Ilija Barukčić. *N-th index D-dimensional Einstein gravitational field equations. Geometry unchained.*, volume 1. Books on Demand GmbH, Hamburg-Norderstedt, 1 edition, 2020c. ISBN 978-3-7526-4490-6. ISBN-13: 9783752644906 . Free full text (preprint): ZENODO.

Ilija Barukčić. *Zero and infinity. Mathematics without frontiers*. Books on Demand GmbH, Hamburg-Norderstedt, 1 edition, 2020d. ISBN 978-3-7519-1873-2. ISBN-13: 9783751918732.

Ilija Barukčić. Mutually exclusive events. *Causation*, 16(11):5–57, November 2021a. doi: 10.5281/zenodo.5746415. URL https://doi.org/10.5281/zenodo.5746415. Zenodo.

Ilija Barukčić. Index of relationship. *Causation*, 16(8):5–37, April 2021b. doi: 10.5281/zenodo.5163179. URL https://doi.org/10.5281/zenodo.5163179. Zenodo.

Ilija Barukčić. The causal relationship k. *MATEC Web of Conferences*, 336:09032, 2021c. ISSN 2261-236X. doi: 10.1051/matecconf/202133609032. CSCNS2020. Web of Science. Free full text: EDP Sciences.

Ilija Barukčić. The logical content of the risk ratio. *Causation*, 16(4):5–41, February 2021d. doi: 10.5281/zenodo.4679509. Free full text: Zenodo.

Ilija Barukčić and Okoh Ufuoma. *Analysis of Switching Resistive Circuits A Method Based on the Unification of Boolean and Ordinary Algebras*. Books on Demand, Norderstedt, first edition edition, 2020. ISBN 978-3-7519-8474-4. ISBN-13: 9783751984744.

Barukčić, Ilija. The Interior Logic of Inequalities. *International Journal of Mathematics Trends and Technology IJMTT*, 65(7):146–155, 2019. doi: http://www.ijmttjournal.org/Volume-65/Issue-7/IJMTT-V65I7P524.pdf. URL http://www.ijmttjournal.org/archive/ijmtt-v65i7p524.

Barukčić, Ilija. Variance of binomial distribution. *Causation*, 17(1):5–22, 1 2022. URL https://www.causation.eu/index.php/causation/article/view/7.

Bağçe, Samet and Başkent, Can. An Examination of Counterexamples in Proofs and Refutations. *Philosophia Scientae*, 13(2):3–20, October 2009. ISSN 1281-2463, 1775-4283. doi: 10.4000/philosophiascientiae.228. URL http://journals.openedition.org/philosophiascientiae/228.

Jacobi Bernoulli. *Ars conjectandi, Opus posthumus: Accedit Tractatus de seriebus infinitis ; et epistola Gallice scripta De Ludo Pilae Reticularis*. Impensis Thurnisiorum [Tournes], fratrum, Basileae (Basel, Suisse), January 1713. doi: 10.3931/e-rara-9001. Free full text: e-rara, Zurich, CH.

George Boole. *An investigation of the laws of thought, on which are founded mathematical theories of logic and probabilities*. New York, Dover, 1854. Free full text: archive.org, San Francisco, CA 94118, USA.

Bundesanwaltschaft Bundesgerichtshof für Strafsachen. *Entscheidungen des Bundesgerichtshofes*, volume 1 of *Entscheidungen des Bundesgerichtshofes*. Carl Heymanns Verlag, Detmold, 1951. URL https://juris.bundesgerichtshof.de/cgi-bin/rechtsprechung/document.py?Gericht=bgh&Art=en&Datum=2008&Seite=99&nr=43553&pos=2985&anz=3634.

Walter A. Carnielli and João Marcos. Ex contradictione non sequitur quodlibet. *Bulletin of Advanced Reasoning and Knowledge*, 7(1):89–109, 2001. URL https://www.researchgate.net/publication/236647971_Ex_contradictione_non_sequitur_quodlibet.

R. J. Cook and D. L. Sackett. The number needed to treat: a clinically useful measure of treatment effect. *BMJ (Clinical research ed.)*, 310(6977):452–454, 2 1995. ISSN 0959-8138. doi: 10.1136/bmj.310.6977.452. PMID: 7873954. Free full text: PMCID: PMC2548824.

J. Corcoran. Counterexamples and Proexamples. *Bulletin of Symbolic Logic*, 11:460, 2005.

J. Cornfield. A method of estimating comparative rates from clinical data; applications to cancer of the lung, breast, and cervix. *Journal of the National Cancer Institute*, 11(6):1269–1275, 6 1951. ISSN 0027-8874. PMID: 14861651.

D. R. Cox. The regression analysis of binary sequences. *Journal of the Royal Statistical Society. Series B (Methodological)*, 20(2):215–242, 1958. ISSN 0035-9246. JSTOR.

M. Dorolle. La valeur des conclusion par l'absurde. *Révue Philosophique de la France et de l'Étranger*, 86:309–313, 1918. URL https://www.jstor.org/stable/41081615.

Albert Einstein. Induktion and Deduktion in der Physik. *Berliner Tageblatt and Handelszeitung*, page Suppl. 4, December 1919. URL https://einsteinpapers.press.princeton.edu/vol7-trans/124. Berliner Tageblatt and Handelszeitung.

William Feller. *Introduction to Probability Theory and its Applications. Volume I & II.*, volume 1. John Wiley and Sons Inc., 1st edition edition, 1 1950. John Wiley and Sons Inc.

Ronald Aylmer Fisher. On the Interpretation of Chi square from Contingency Tables, and the Calculation of P. *Journal of the Royal Statistical Society*, 85(1):87–94, 1922. ISSN 0952-8385. doi: 10.2307/2340521. JSTOR.

Ronald Aylmer Fisher. The logic of inductive inference. *Journal of the Royal Statistical Society*, 98 (1):39–82, 1935. ISSN 0952-8385. doi: 10.2307/2342435. JSTOR.

Ronald Aylmer Fisher. The negative binomial distribution. *Annals of Eugenics*, 11(1):182–187, 1941. ISSN 2050-1439. doi: 10.1111/j.1469-1809.1941.tb02284.x. Wiley Online Library.

Fisher, Ronald Aylmer. XV.—The Correlation between Relatives on the Supposition of Mendelian Inheritance. *Earth and Environmental Science Transactions of The Royal Society of Edinburgh*, 52(2):399–433, 1919. ISSN 2053-5945. doi: 10.1017/S0080456800012163. Royal Society of Edinburgh.

Eckart Förster and Yitzhak Y Melamed. *"Omnis determinatio est negatio" – Determination, Negation and Self-Negation in Spinoza, Kant, and Hegel. In: Spinoza and German idealism. Eckart Forster & Yitzhak Y. Melamed (eds.).* Cambridge University Press, Cambridge [England]; New York, 2012. ISBN 978-1-283-71468-6. URL https://doi.org/10.1017/CBO9781139135139.

Gauß, Carl Friedrich. *Theoria motus corporum coelestium in sectionibus conicis solem ambientium*. sumtibus Frid. Perthes et I. H. Besser, 1809. hrefhttp://www.e-rara.ch/doi/10.3931/e-rara-522e-rara, Zurich, CH.

H. T. Gonin. XIV. The use of factorial moments in the treatment of the hypergeometric distribution and in tests for regression. *The London, Edinburgh, and Dublin Philosophical Magazine and Journal of Science*, 21(139):215–226, January 1936. ISSN 1941-5982. doi: 10.1080/14786443608561573. Taylor and Francis.

William Sealy Gosset. The probable error of a mean. *Biometrika*, 6(1):1–25, 1908. ISSN 0006-3444. doi: 1. JSTOR.

William Sealy Gosset. The elimination of spurious correlation due to position in time or space. *Biometrika*, 10(1):179–180, 1914. ISSN 0006-3444. doi: 10.2307/2331746. JSTOR.

Major Greenwood and G. Udny Yule. The statistics of anti-typhoid and anti-cholera inoculations, and the interpretation of such statistics in general. *Proceedings of the Royal Society of Medicine*, 8: 113–194, 6 1915. ISSN 0035-9157. doi: 10.1177/003591571500801433. PMID: 19978918. Free full text: PMCID: PMC2004181.

John Burdon Sanderson Haldane. The fitting of binomial distributions. *Annals of Eugenics*, 11(1): 179–181, 1941. ISSN 2050-1439. doi: 10.1111/j.1469-1809.1941.tb02283.x. Wiley Online Library.

Klaus Hedwig. Negatio negationis: Problemgeschichtliche Aspekte einer Denkstruktur. *Archiv für Begriffsgeschichte*, 24(1):7–33, 1980. ISSN 0003-8946. URL www.jstor.org/stable/24359358.

F. H. Heinemann. The Meaning of Negation. *Proceedings of the Aristotelian Society*, 44:127–152, 1943. ISSN 0066-7374. URL www.jstor.org/stable/4544390.

Friedrich Robert Helmert. Ueber die Wahrscheinlichkeit der Potenzsummen der Beobachtungsfehler und über einige damit im Zusammenhange stehende Fragen. *Zeitschrift für Mathematik und Physik*, 21(3):102–219, 1876.

Laurence R. Horn. *A natural history of negation*. University of Chicago Press, Chicago, 1989. ISBN 978-0-226-35337-1. URL https://emilkirkegaard.dk/en/wp-content/uploads/A-natural-history-of-negation-Laurence-R.-Horn.pdf.

Danian Hu. *China and Albert Einstein: the reception of the physicist and his theory in China 1917-1979*. Harvard University Press, Cambridge, MA, 2005. ISBN 978-0-674-01538-8.

Christiaan Huygens and Frans van Schooten. *De ratiociniis in ludo alae: In: Exercitationum mathematicarum liber primus [- quintus]*. ex officina Johannis Elsevirii, Lugdunum Batavorum (Leiden, The Netherlands), January 1657. doi: 10.3931/e-rara-8813. Free full text: e-rara, Zurich, CH.

Israël, Hans. *Hundert Autoren gegen Einstein*. Alo austrian literature online, Graz, 2011. ISBN 978-3-226-00537-0.

Mr. Justice Matthews. Hayes v. Michigan Central R. Co., 111 U.S. 228. *U. S. Supreme Court*, 1884. URL https://supreme.justia.com/cases/federal/us/111/228/.

Michal Kicinski, David A. Springate, and Evangelos Kontopantelis. Publication bias in meta-analyses from the cochrane database of systematic reviews. *Statistics in Medicine*, 34(20):2781–2793, 9 2015. ISSN 1097-0258. doi: 10.1002/sim.6525. PMID: 25988604.

Mirjam J. Knol. Down with odds ratios: risk ratios in cohort studies and randomised clinical trials (article in dutch). *Nederlands Tijdschrift Voor Geneeskunde*, 156(28):A4775, 2012. ISSN 1876-8784. PMID: 22805792.

Anton Friedrich Koch. Die Selbstbeziehung der Negation in Hegels Logik. *Zeitschrift für philosophische Forschung*, 53(1):1–29, 1999. ISSN 0044-3301. URL www.jstor.org/stable/20484868.

A. Kolmogoroff. *Grundbegriffe der Wahrscheinlichkeitsrechnung*. Springer Berlin Heidelberg, Berlin, Heidelberg, January 1933. ISBN 978-3-642-49596-0. doi: 10.1007/978-3-642-49888-6.

Andreĭ Nikolaevich Kolmogorov. *Foundations of the theory of probability*. Chelsea Publishing Company, translated by nathan morrison edition, 1950. ISBN 978-0-486-82159-7. hrefhttps://archive.org/details/foundationsofthe00kolmarchive.org, San Francisco, CA 94118, USA .

Kenneth Kunen. Negation in logic programming. *The Journal of Logic Programming*, 4(4):289–308, December 1987. ISSN 0743-1066. doi: 10.1016/0743-1066(87)90007-0. URL http://www.sciencedirect.com/science/article/pii/0743106687900070.

Pierre Simon de LaPlace. *Théorie analytique des probabilités*. Courcier, 1 1812. e-rara, Zurich, CH.

Andreas Laupacis, David L. Sackett, and Robin S. Roberts. An assessment of clinically useful measures of the consequences of treatment. *New England Journal of Medicine*, 318(26):1728–1733, 1988. doi: 10.1056/NEJM198806303182605. PMID: 3374545. NEJM.

D. Massel and M. K. Cruickshank. The number remaining at risk: an adjunct to the number needed to treat. *The Canadian Journal of Cardiology*, 18(3):254–258, 3 2002. ISSN 0828-282X. PMID: 11907613.

Vann McGee. A Counterexample to Modus Ponens. *The Journal of Philosophy*, 82 (9):462, September 1985. ISSN 0022362X. doi: 10.2307/2026276. URL http://www.pdcnet.org/oom/service?url_ver=Z39.88-2004&rft_val_fmt=&rft.imuse_id=jphil_1985_0082_0009_0462_0471&svc_id=info:www.pdcnet.org/collection.

Abraham de Moivre. *The Doctrine of Chances or a Method of Calculating the Probability of Events in Play*. printed by W. Pearson for the author, London, January 1718. doi: 10.3931/e-rara-10420. Free full text: e-rara, Zurich, CH.

Russell Newstadt. *Omnis Determinatio est Negatio: A Genealogy and Defense of the Hegelian Conception of Negation*. Loyola University Chicago, Chicago (IL), dissertation edition, 2015. Free full text: Loyola University Chicago, USA.

Jerzy Neyman and Egon Sharpe Pearson. IX. On the problem of the most efficient tests of statistical hypotheses. *Philosophical Transactions of the Royal Society of London. Series A, Containing Papers of a Mathematical or Physical Character*, 231(694–706):289–337, 2 1933. ISSN 0264-3952, 2053-9258. doi: 10.1098/rsta.1933.0009. The Royal Society, London, GB.

Jean George Pierre Nicod. A reduction in the number of primitive propositions of logic. *Proceedings of the Cambridge Philosophical Society*, 19:32–41, 1917.

Jean George Pierre Nicod. Les relations des valeurs et les relations de sens en logique formelle. *Revue de métaphysique et de morale*, 31:467–480, 1924.

Karl Pearson. III. Contributions to the Mathematical Theory of Evolution. On the Dissection of Asymmetrical-Frequency Curves. *Philosophical Transactions of the Royal Society of London, Series A*, 185:71–85, 1894. The Royal Society.

Karl Pearson. XV. On certain properties of the hypergeometrical series, and on the fitting of such series to observation polygons in the theory of chance. *The London, Edinburgh, and Dublin Philosophical Magazine and Journal of Science*, 47(285):236–246, January 1899. ISSN 1941-5982. doi: 10.1080/14786449908621253. Taylor and Francis.

Karl Pearson. X. On the criterion that a given system of deviations from the probable in the case of a correlated system of variables is such that it can be reasonably supposed to have arisen from random sampling. *The London, Edinburgh, and Dublin Philosophical Magazine and Journal of Science*, 50(302):157–175, July 1900. ISSN 1941-5982. doi: 10.1080/14786440009463897. Taylor and Francis.

Karl Pearson. III. Mathematical contributions to the theory of evolution. — XII. On a generalised Theory of alternative Inheritance, with special reference to Mendel's laws. *p 66: Standard dev binomial distribution*, 203(359–371):53–86, 1 1904a. doi: 10.1098/rsta.1904.0015. Royal Society.

Karl Pearson. *Mathematical contributions to the theory of evolution. XIII. On the theory of contingency and its relation to association and normal correlation*. Biometric Series I. Dulau and Co., London, January 1904b. Free full text: archive.org, San Francisco, CA 94118, USA.

Popper, Karl Raimund. *The Logic of Scientific Discovery*. Julius Springer, Vienna (Austria), 1935. ISBN 978-0-203-99462-7. URL `http://archive.org/details/PopperLogicScientificDiscovery`. Logik der Forschung first published 1935 by Verlag von Julius Springer, Vienna, Austria. First English edition published 1959 by Hutchinson & Co.

Popper, Karl Raimund. *Conjectures and Refutations: The Growth of Scientific Knowledge*. Routledge, London ; New York, Überarb. a edition, May 2002. ISBN 978-0-415-28594-0.

Graham Priest. What is so Bad about Contradictions? *The Journal of Philosophy*, 95(8):410–426, 1998. ISSN 0022-362X. doi: 10.2307/2564636. URL https://www.jstor.org/stable/2564636.

Graham Priest, Richard Sylvan, Jean Norman, and A. I. Arruda, editors. *Paraconsistent logic: essays on the inconsistent*. Analytica. Philosophia, München ; Hamden [Conn.], 1989. ISBN 978-3-88405-058-3.

Connie Robertson. *The Wordsworth dictionary of quotations*. Wordsworth, Ware, Hertfordshire, 1997. ISBN 978-1-85326-751-2. URL https://archive.org/details/wordsworthdictio00robe.

Joseph P. Romano and A.F. Siegel. *Counterexamples in Probability And Statistics*. Chapman & Hall., New York (USA), 1986. URL https://www.crcpress.com/Counterexamples-in-Probability-And-Statistics/Romano-Siegel/p/book/9780412989018.

Josiah Royce. *Negation*, volume 9 of *Encyclopaedia of Religion and Ethics. J. Hastings (ed.)*. Charles Scribner's Sons, New York (USA), 1917. Free full text: archive.org, San Francisco, CA 94118, USA.

DL Sackett, JJ Deeks, and DG Altman. Sackett dl, deeks jj, altman dg. down with odds ratios! evidence-based med. 1996;1:164–166. *Evidence-Based Med.*, 1:164–166, 1996.

D. A. Sadowsky, A. G. Gilliam, and J. Cornfield. The statistical association between smoking and carcinoma of the lung. *Journal of the National Cancer Institute*, 13(5):1237–1258, 4 1953. ISSN 0027-8874. PMID: 13035448.

Henry Maurice Sheffer. A set of five independent postulates for boolean algebras, with application to logical constants. *Transactions of the American Mathematical Society*, 14(4):481–488, 1913. ISSN 0002-9947, 1088-6850. doi: 10.1090/S0002-9947-1913-1500960-1. Free full text: archive.org, San Francisco, CA 94118, USA.

J. L. Speranza and Laurence R. Horn. A brief history of negation. *Journal of Applied Logic*, 8(3): 277–301, September 2010. ISSN 1570-8683. doi: 10.1016/j.jal.2010.04.001. URL http://www.sciencedirect.com/science/article/pii/S1570868310000236.

Jordan M. Stoyanov. *Counterexamples in Probability*. DOVER PUBN INC, Mineola, New York, third edition edition, 2013. ISBN 978-0-486-49998-7.

S. Suissa, S. Bernatsky, and M. Hudson. Antirheumatic drug use and the risk of acute myocardial infarction. *Arthritis Rheum*, 55(4):531–536, 2006. doi: 10.1002/art.22094. PMID: 16874796.

John Joseph Toohey. *An elementary handbook of logic*. New York, Appleton-Century-Crofts, 1948. URL http://archive.org/details/anelementaryhan00toohgoog.

J. v. Uspensky. *Introduction To Mathematical Probability*. McGraw-Hill Company, New York (USA), 1937. Free full text: archive.org, San Francisco, CA 94118, USA.

Brian Weatherson. What Good are Counterexamples? *Philosophical Studies*, 115(1):1–31, July 2003. ISSN 1573-0883. doi: https://doi.org/10.1023/A:1024961917413.

Michael V. Wedin. Negation and quantification in aristotle. *History and Philosophy of Logic*, 11 (2):131–150, January 1990. ISSN 0144-5340. doi: 10.1080/01445349008837163. URL https://doi.org/10.1080/01445349008837163.

William Allen Whitworth. *Choice and Chance. With 1000 Exercises*. Deighton, Bell & Co., fifth eidtion edition, 1901. archive.org, San Francisco, CA 94118, USA .

John Worrall, Elie Zahar, and Imre Lakatos. *Proofs and Refutations: The Logic of Mathematical Discovery*. Cambridge University Press, Cambridge ; New York, 1976. ISBN 978-0-521-29038-8.

Frank Yates. Contingency Tables Involving Small Numbers and the Chi square Test. *Supplement to the Journal of the Royal Statistical Society*, 1(2):217–235, 1934. ISSN 1466-6162. doi: 10.2307/2983604. JSTOR.

George Udny Yule. On the methods of measuring association between two attributes. *Journal of the Royal Statistical Society*, 75(6):579–652, 1912. ISSN 0952-8385. doi: 10.2307/2340126. JSTOR.

George Udny Yule and Karl Pearson. VII. On the association of attributes in statistics: with illustrations from the material of the childhood society. *Philosophical Transactions of the Royal Society of London. Series A, Containing Papers of a Mathematical or Physical Character*, 194(252–261): 257–319, 1 1900. doi: 10.1098/rsta.1900.0019. The Royal Society, London, GB.

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[i] https://zenodo.org/search?page=1&size=20&q=keywords:%22Baruk%C4%8Di%C4%87,%20Conference%22
[j] https://twitter.com/ilijabarukcic?lang=de
[k] https://twitter.com/Causation_Journ
[l] https://vixra.org/author/ilija_barukcic
[m] https://www.youtube.com/channel/UCwf3w1IngcukIOOjpw8HTwg
[n] https://portal.dnb.de/opac/showNextResultSite?currentResultId=%22Barukcic%22%26any&currentPosition=30