CAUSATION
International Journal of Science

CAUSATION, 17(1): 23–102

DOI:10.5281/zenodo.5854744
Received: June 1, 2020 (viXra)
Accepted: January 15, 2022
Published: January 16, 2022
urn:nbn:de:101:1-20220116140750765542l1

# 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 a necessary condition relationships (within a dataset).

**Keywords: Necessary condition; Conditio sine qua non; Cause; Effect; Causation**

## 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, Andreĭ Nikolaevich, 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, Andreĭ Nikolaevich, 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

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

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

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

where $\Psi\left(X\right)$ is the wave-function of X, $\Psi^*\left(X\right)$ is the complex conjugate wave-function of X.

### 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, Andreĭ Nikolaevich, 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):*

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

while $E(\underline{X}) \equiv X - E(X)$. Based on equation 6, it is

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

or

$$\frac{E(X)^2}{E(X^2)} + \frac{\sigma(X)^2}{E(X^2)} \equiv p(X) + \frac{\sigma(X)^2}{E(X^2)} \equiv +1 \tag{8}$$

In other words, the variance of a random variable is a determining part of the probability of a random variable. The wave function follows in general as

$$\Psi(X) \equiv \frac{1}{\Psi^*(X)} - \frac{\sigma(X)^2}{(\Psi^*(X) \times E(X^2))} \equiv \frac{\left(E\left(X^2\right) - \sigma(X)^2\right)}{(\Psi^*(X) \times E(X^2))} \tag{9}$$

**Definition 2.5** (**The First Moment Expectation of a Random Variable of $\underline{X}$ (anti X)**). *Thus far, let $E(\underline{X}) \equiv X - E(X)$ denote a (discrete) random variable with the probability $p(\underline{X}) \equiv 1 - p(X)$. The first moment expectation value (see Huygens and van Schooten, 1657, Kolmogorov, Andreĭ Nikolaevich, 1950, LaPlace, 1812, Whitworth, 1901) of anti X, denoted as E($\underline{X}$), is a number defined as follows:*

$$E(\underline{X}) \equiv X \times (1 - p(X)) \equiv X \times p(\underline{X}) \tag{10}$$

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

$$\begin{aligned} E(\underline{X})^2 &\equiv p(\underline{X}) \times X \times p(\underline{X}) \times X \\ &\equiv p(\underline{X}) \times p(\underline{X}) \times X \times X \\ &\equiv (p(\underline{X}) \times X)^2 \\ &\equiv E(\underline{X}) \times E(\underline{X}) \end{aligned} \tag{11}$$

**Definition 2.6** (**The Second Moment Expectation of a Random Variable of $\underline{X}$ (anti X)**). *The second(see Kolmogorov, Andreĭ Nikolaevich, 1950, p. 42 ) moment expectation value (or more or less arithmetic mean) of a (large) number of independent realizations of a random variable anti X follows as:*

$$\begin{aligned} E(\underline{X}^2) &\equiv p(\underline{X}) \times X^2 \\ &\equiv (p(\underline{X}) \times X) \times X \\ &\equiv E(\underline{X}) \times X \\ &\equiv X \times E(\underline{X}) \end{aligned} \tag{12}$$

**Definition 2.7** (**The n-th Moment Expectation of a Random Variable of $\underline{X}$ (anti X)**). *The n-th(see Barukčić, 2020a, 2021c) moment expectation value of a (large) number of independent realizations of a random variable anti X follows as:*

$$\begin{aligned} E(\underline{X}^n) &\equiv p(\underline{X}) \times X^n \\ &\equiv (p(\underline{X}) \times X) \times X^{n\text{-}1} \\ &\equiv E(\underline{X}) \times X^{n\text{-}1} \end{aligned} \tag{13}$$

### 2.1.5. 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

$$p\left(X_{\mathrm{t}}=k\right)\equiv\binom{n}{k}\cdot p^{k}\cdot q^{n-k} \tag{14}$$

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

$$p\left(X_{\mathrm{t}}\leq k\right)\equiv 1-p\left(X_{\mathrm{t}}>k\right)\equiv\sum_{t=0}^{k}\binom{n}{t}\cdot p^{t}\cdot q^{n-t} \tag{15}$$

or as

$$p\left(X_{\mathrm{t}}>k\right)\equiv 1-p\left(X_{\mathrm{t}}\leq k\right)\equiv 1-\sum_{t=0}^{k}\binom{n}{t}\cdot p^{t}\cdot q^{n-t} \tag{16}$$

Furthermore, it is

$$p\left(X_{\mathrm{t}}<k\right)\equiv 1-p\left(X_{\mathrm{t}}\geq k\right)\equiv\sum_{t=0}^{k-1}\binom{n}{t}\cdot p^{t}\cdot q^{n-t} \tag{17}$$

or

$$p\left(X_{\mathrm{t}}\geq k\right)\equiv 1-p\left(X_{\mathrm{t}}<k\right)\equiv 1-\sum_{t=0}^{k-1}\binom{n}{t}\cdot p^{t}\cdot q^{n-t} \tag{18}$$

The binomial distribution is the mathematical foundation of a binomial test. The random variable $X_{\mathrm{t}}$ 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

$$p\left(X_{\mathrm{t}}=k\right)\equiv p\cdot q^{k-1} \tag{19}$$

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

$$p\left(X_{\mathrm{t}}=r\right)\equiv\binom{k+r-1}{k-1}p^{k}\cdot q^{r} \tag{20}$$

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

**Definition 2.8 (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

$$\sigma\left(X_{\mathrm{t}}\right)^{2} \equiv N \times N \times p\left(X_{\mathrm{t}}\right) \times \left(1 - p\left(X_{\mathrm{t}}\right)\right) \tag{21}$$

**Definition 2.9 (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

$$\begin{aligned} A &= N \times E\left(A_{\mathrm{t}}\right) \\ &\equiv N \times \left(A_{\mathrm{t}} \times p\left(A_{\mathrm{t}}\right)\right) \\ &\equiv N \times \left(p\left(A_{\mathrm{t}}\right) + p\left(B_{\mathrm{t}}\right)\right) \\ &\equiv N \times p\left(A_{\mathrm{t}}\right) \end{aligned} \tag{22}$$

and

$$\begin{aligned} B &= N \times E\left(B_{\mathrm{t}}\right) \\ &\equiv N \times \left(B_{\mathrm{t}} \times p\left(B_{\mathrm{t}}\right)\right) \\ &\equiv N \times \left(p\left(A_{\mathrm{t}}\right) + p\left(c_{\mathrm{t}}\right)\right) \\ &\equiv N \times p\left(B_{\mathrm{t}}\right) \end{aligned} \tag{23}$$

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

$$a \equiv N \times \left(E\left(A_{\mathrm{t}}\right)\right) \equiv N \times \left(p\left(A_{\mathrm{t}}\right)\right) \tag{24}$$

and

$$b \equiv N \times \left(E\left(B_{\mathrm{t}}\right)\right) \equiv N \times \left(p\left(B_{\mathrm{t}}\right)\right) \tag{25}$$

and

$$c \equiv N \times \left(E\left(c_{\mathrm{t}}\right)\right) \equiv N \times \left(p\left(c_{\mathrm{t}}\right)\right) \tag{26}$$

and

$$d \equiv N \times \left(E\left(d_{\mathrm{t}}\right)\right) \equiv N \times \left(p\left(d_{\mathrm{t}}\right)\right) \tag{27}$$

and

$$a + b + c + d \equiv A + \underline{A} \equiv B + \underline{B} \equiv N \tag{28}$$

Table 1 provide us again an overview of a two by two table of Binomial random variables.

**Table 1.** 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 |

2.1.6. Independence

**Definition 2.10 (Independence).**

The philosophical, mathematical(Kolmogoroff, Andreĭ Nikolaevich, 1933) and physical(Einstein, 1948) concept of independence is of fundamental(Kolmogoroff, Andreĭ Nikolaevich, 1933) importance in (natural) sciences as such. In fact, it is insightful to recall again before the mind's eye Einstein's theoretical approach to the concept of independence. "*Ohne die Annahme einer ... Unabhängigkeit der ... Dinge voneinander ... wäre physikalisches Denken ... nicht möglich.*"(Einstein, 1948). In a narrower sense, the conditio sine qua non relationship concerns itself at the end only with the case whether the presence of an event $A_t$ (condition) enables or guarantees the presence of another event $B_t$ (conditioned). As a result of these thoughts, another question worth asking concerns the relationship between the independence of an event $A_t$ (a condition) and another event $B_t$ (conditioned) and the necessary condition relationship. To be confronted with the danger of bias and equally with the burden of inappropriate conclusions drawn, another fundamental question at this stage is whether is it possible that an event $A_t$ (a condition) is a necessary condition of event $B_t$ (conditioned) even under circumstances where the event $A_t$ (a condition) (a necessary condition) is independent of an event $B_t$ (conditioned)? This question is already answered more or less to the negative (Barukčić, 2018b). An event $A_t$ which is a necessary condition of another event $B_t$ is equally an event without which another event ($B_t$) could not be, could not occur, and implies as such already a kind of dependence. However, it is not mandatory that such a kind of dependence is a causal one. Thus far, **data which provide evidence of a significant conditio sine qua non relationship between two events like $A_t$ and $B_t$ and equally support the hypothesis that $A_t$ and $B_t$ are independent of each other are more or less self-contradictory and of very restricted or of none value for further analysis**. In fact, if the opposite view would be taken as plausible, contradictions are more or less inescapable. 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(Moivre, 1718), independence (Kolmogoroff, Andreĭ Nikolaevich, 1933) in terms of probability theory is defined at the same (period of) time (i.e. Bernoulli trial) t as

$$\begin{aligned} p(A_t \wedge B_t) &\equiv p(A_t) \times p(B_t) \equiv p(a_t) \\ &\equiv \frac{\sum_{t=1}^{N} (A_t \wedge B_t)}{N} \equiv \frac{N \times (p(a_t))}{N} \equiv 1 - p(A_t \mid B_t) \equiv 1 - p(A_t \uparrow B_t) \end{aligned} \tag{29}$$

while $p\left(A_t \cap B_t\right)$ is the joint probability of the events $A_t$ and $B_t$ at a same Bernoulli trial t, $p\left(A_t\right)$ is the probability of an event $A_t$ at a same Bernoulli trial t, and $p\left(B_t\right)$ is the probability of an event $B_t$ at a same Bernoulli trial t.

### 2.1.7. Dependence

**Definition 2.11 (Dependence).**

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

$$p\left(\underbrace{A_t \wedge B_t \wedge C_t \wedge \ldots}_{n \text{ random variables}}\right) \equiv \sqrt[n]{\underbrace{p\left(A_t\right) \times p\left(B_t\right) \times p\left(C_t\right) \times \ldots}_{n \text{ random variables}}} \tag{30}$$

2.1.8. Relative risk (RR)

**Relative risk ($RR_{nc}$)**

**Definition 2.12** (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

$$\begin{aligned} RR(A_t, B_t)_{nc} &\equiv \frac{\frac{p(a_t)}{p(A_t)}}{\frac{p(c_t)}{p(NotA_t)}} \\ &\equiv \frac{p(a_t) \times p(NotA_t)}{p(c_t) \times p(A_t)} \\ &\equiv \frac{N \times p(a_t) \times N \times p(NotA_t)}{N \times p(c_t) \times N \times p(A_t)} \\ &\equiv \frac{a_t \times (NotA_t)}{c_t \times A_t} \\ &\equiv \frac{EER\,(A_t, B_t)}{CER\,(A_t, B_t)} \end{aligned} \tag{31}$$

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 2.13** (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

$$\begin{aligned} RR(A_t,B_t)_{sc} &\equiv \frac{\frac{p(a_t)}{p(B_t)}}{\frac{p(b_t)}{p(NotB_t)}} \\ &\equiv \frac{p(a_t)\times p(NotB_t)}{p(b_t)\times p(B_t)} \\ &\equiv \frac{N\times p(a_t)\times N\times p(NotB_t)}{N\times p(b_t)\times N\times p(B_t)} \\ &\equiv \frac{a_t\times (NotB_t)}{b_t\times B_t} \\ &\equiv \frac{OPR\,(A_t,B_t)}{CPR\,(A_t,B_t)} \end{aligned} \tag{32}$$

**Relative risk reduction (RRR)**

**Definition 2.14** (Relative risk reduction (RRR))**.**

$$\begin{aligned} RRR\,(A_t,B_t) &\equiv \frac{CER\,(A_t,B_t)-EER\,(A_t,B_t)}{CER\,(A_t,B_t)} \\ &= 1-RR(A_t,B_t) \end{aligned} \tag{33}$$

**Vaccine efficacy (VE)**

**Definition 2.15** (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.

$$\begin{aligned} VE\,(A_t,B_t) &\equiv 100\times(1-RR\,(A_t,B_t)) \\ &\equiv 100\times\left(\frac{CER\,(A_t,B_t)-EER\,(A_t,B_t)}{CER\,(A_t,B_t)}\right) \end{aligned} \tag{34}$$

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 2.16** (Experimental event rate (EER))**.**

$$EER\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)\equiv\frac{p(a_{\mathrm{t}})}{p(A_{\mathrm{t}})}=\frac{a_{\mathrm{t}}}{a_{\mathrm{t}}+b_{\mathrm{t}}} \tag{35}$$

**Definition 2.17** (Control event rate (CER))**.**

$$CER\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)\equiv\frac{p(c_{\mathrm{t}})}{p(\underline{A}_{\mathrm{t}})}=\frac{c_{\mathrm{t}}}{c_{\mathrm{t}}+d_{\mathrm{t}}} \tag{36}$$

**Absolute risk reduction (ARR)**

**Definition 2.18** (Absolute risk reducation (ARR))**.**

$$\begin{aligned} ARR\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)&\equiv\frac{p(c_{\mathrm{t}})}{p(\underline{A}_{\mathrm{t}})}-\frac{p(a_{\mathrm{t}})}{p(A_{\mathrm{t}})}\\ &=\frac{c_{\mathrm{t}}}{c_{\mathrm{t}}+d_{\mathrm{t}}}-\frac{a_{\mathrm{t}}}{a_{\mathrm{t}}+b_{\mathrm{t}}}\\ &=CER\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)-EER\left(A_{\mathrm{t}},B_{\mathrm{t}}\right) \end{aligned} \tag{37}$$

**Absolute risk increase (ARI)**

**Definition 2.19** (Absolute risk increase (ARI))**.**

$$\begin{aligned} ARI\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)&\equiv\frac{p(a_{\mathrm{t}})}{p(A_{\mathrm{t}})}-\frac{p(c_{\mathrm{t}})}{p(\underline{A}_{\mathrm{t}})}\\ &=EER\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)-CER\left(A_{\mathrm{t}},B_{\mathrm{t}}\right) \end{aligned} \tag{38}$$

### Number needed to treat (NNT)

**Definition 2.20** (Number needed to treat (NNT))**.**

$$NNT\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)\equiv\frac{1}{CER\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)-EER\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)} \tag{39}$$

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 2.21** (Number needed to harm (NNH))**.**

$$NNH\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)\equiv\frac{1}{EER\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)-CER\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)} \tag{40}$$

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 2.22** (Outcome prevalence rate (OPR))**.**

$$OPR\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)\equiv\frac{p(a_{\mathrm{t}})}{p(B_{\mathrm{t}})}=\frac{a_{\mathrm{t}}}{a_{\mathrm{t}}+c_{\mathrm{t}}} \tag{41}$$

### Control prevalence rate (CPR)

**Definition 2.23** (Control prevalence rate (CPR))**.**

$$CPR\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)\equiv\frac{p(b_{\mathrm{t}})}{p(\underline{B}_{\mathrm{t}})}=\frac{b_{\mathrm{t}}}{b_{\mathrm{t}}+d_{\mathrm{t}}} \tag{42}$$

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 2.24** (Absolute prevalence reduction (APR))**.**

$$APR\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)\equiv CPR\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)-OPR\left(A_{\mathrm{t}},B_{\mathrm{t}}\right) \tag{43}$$

**Absolute prevalence increase (API)**

**Definition 2.25** (Absolute prevalence increase (API))**.**

$$API\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)\equiv OPR\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)-CPR\left(A_{\mathrm{t}},B_{\mathrm{t}}\right) \tag{44}$$

**Relative prevalence reduction (RPR)**

**Definition 2.26** (Relative prevalence reduction (RPR))**.**

$$\begin{aligned} RPR\left(A_{\mathrm{t}},B_{\mathrm{t}}\right) &\equiv \frac{CPR\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)-OPR\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)}{CPR\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)} \\ &= 1-RR(A_{\mathrm{t}},B_{\mathrm{t}})_{\mathrm{sc}} \end{aligned} \tag{45}$$

**The index NNS**

**Definition 2.27** (The index NNS)**.**

$$NNS\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)\equiv\frac{1}{CPR\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)-OPR\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)} \tag{46}$$

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

**The index NNI**

**Definition 2.28** (The index NNI)**.**

$$NNI\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)\equiv\frac{1}{OPR\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)-CPR\left(A_{\mathrm{t}},B_{\mathrm{t}}\right)} \tag{47}$$

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

### 2.1.9. Odds ratio (OR)

**Definition 2.29** (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 2. The odds' ratio (OR) is defined as

**Table 2.** 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 | $c_t$ | $d_t$ | $\underline{A}_t$ |
| | | $B_t$ | $\underline{B}_t$ | $N_t$ |

$$\begin{aligned} OR(A_t, B_t) &\equiv \left(\frac{a_t}{b_t}\right) / \left(\frac{c_t}{d_t}\right) \\ &\equiv \left(\frac{a_t \times d_t}{b_t \times c_t}\right) \end{aligned} \tag{48}$$

**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, DL and Deeks, JJ and Altman, DG, 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. 48. 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. 48. 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.*

### 2.1.10. 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 2.30** (**Index of unfairness**)**.**

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

$$p\left(IOU\left(A,B\right)\right) \equiv Absolute\left(\left(\frac{A+B}{N}\right)-1\right) \tag{49}$$

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 2.31** (**Index of independence**)**.**

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

$$p\left(IOI\left(A_{\mathrm{t}},\underline{B}_{\mathrm{t}}\right)\right) \equiv Absolute\left(\left(\frac{A_{\mathrm{t}}+\underline{B}_{\mathrm{t}}}{N}\right)-1\right) \tag{50}$$

or as

$$p\left(IOI\left(\underline{A}_{\mathrm{t}},B_{\mathrm{t}}\right)\right) \equiv Absolute\left(\left(\frac{\underline{A}_{\mathrm{t}}+B_{\mathrm{t}}}{N}\right)-1\right) \tag{51}$$

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 2.32** (Index of relationship (IOR))**.**

Due to several reasons, it is not always easy to identify the unique characteristics between two events like $A_{\mathrm{t}}$ and $B_{\mathrm{t}}$. 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 $A_{\mathrm{t}}$ and $B_{\mathrm{t}}$. Under conditions where $p(a_{\mathrm{t}}) = p(A_{\mathrm{t}} \wedge B_{\mathrm{t}})$, the index of relationship(Barukčić, 2021b), abbreviated as IOR, is defined as

$$\begin{aligned} IOR(A_{\mathrm{t}},B_{\mathrm{t}}) &\equiv \left(\frac{p(A_{\mathrm{t}} \wedge B_{\mathrm{t}})}{p(B_{\mathrm{t}}) \times p(A_{\mathrm{t}})}\right)-1 \\ &\equiv \left(\frac{p(a_{\mathrm{t}})}{p(B_{\mathrm{t}}) \times p(A_{\mathrm{t}})}\right)-1 \\ &\equiv \left(\left(\frac{N \times N \times p(a_{\mathrm{t}})}{N \times p(B_{\mathrm{t}}) \times N \times p(A_{\mathrm{t}})}\right)-1\right) \\ &\equiv \left(\left(\frac{N \times a}{A \times B}\right)-1\right) \end{aligned} \tag{52}$$

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.

**Definition 2.33** (The $\tilde{\chi}^2$ goodness of fit test of the Index of relationship (IOR))**.**

The $\tilde{\chi}^2$ goodness of fit test of the Index of relationship (IOR) is defined as follows:

$$\tilde{\chi}^2{}_{\text{Calculated}}\left(IOR\left(A_t, B_t\right)\right) \equiv \frac{\left(\left(N \times a\right) - \left(A_t \times B_t\right)\right)^2}{A_t \times B_t} + 0 \tag{53}$$

*2.2. Conditions*

2.2.1. Exclusion relationship

**Definition 2.34** (**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

$$\begin{aligned} p(A_t \mid B_t) &\equiv p(A_t \uparrow B_t) \\ &\equiv p(b_t) + p(c_t) + p(d_t) \\ &\equiv \frac{N \times (p(b_t) + p(c_t) + p(d_t))}{N} \\ &\equiv \frac{\sum_{t=1}^{N} (\underline{A}_t \vee \underline{B}_t)}{N} \equiv \frac{b+c+d}{N} \\ &\equiv \frac{b+\underline{A}}{N} \\ &\equiv \frac{c+\underline{B}}{N} \\ &\equiv +1 \end{aligned} \tag{54}$$

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 3).

**Table 3.** $A_t$ 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.*

$$\begin{aligned} p(Vaccine : BNT162b2 \mid COVID-19(infection)) &\equiv p(b_t) + p(c_t) + p(d_t) \\ &\equiv 1 - p(a_t) \\ &\equiv 1 - \left(\frac{8}{43538}\right) \\ &\equiv +0,99981625 \end{aligned} \tag{55}$$

*with a P Value = 0,000184.*

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

$$\begin{aligned} p\left(A_t \mid B_t\right) &\equiv p\left(\underline{U}_t \cup \underline{W}_t\right) \\ &\equiv 1 - p\left(A_t \cap B_t\right) \\ &\equiv 1 - \int_{-\infty}^{A_t} \int_{-\infty}^{B_t} f\left(A_t, B_t\right)\, dA_t\, dB_t \\ &\equiv +1 \end{aligned} \tag{56}$$

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

$$p\left(A_t \mid B_t\right) \equiv p\left(A_t \uparrow B_t\right) \geq 1 - \frac{p\left(a_t\right)}{p\left(B_t\right)} \tag{57}$$

### 2.2.3. Experimental study and exclusion relationship

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

$$p\left(A_t \mid B_t\right) \equiv p\left(A_t \uparrow B_t\right) \geq 1 - \frac{p\left(a_t\right)}{p\left(A_t\right)} \tag{58}$$

### 2.2.4. The goodness of fit test of an exclusion relationship

**Definition 2.35 (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

$$\begin{aligned}\tilde{\chi}^2{}_{\text{Calculated}}\left((A_{\text{t}} \mid B_{\text{t}}) \mid A\right) &\equiv \frac{(b-(a+b))^2}{A}+ \\ &\quad \frac{((c+d)-\underline{A})^2}{\underline{A}} \\ &\equiv \frac{a^2}{A}+0 \\ &\equiv \frac{a^2}{A}\end{aligned} \tag{59}$$

or equally as

$$\begin{aligned}\tilde{\chi}^2{}_{\text{Calculated}}\left((A_{\text{t}} \mid B_{\text{t}}) \mid B\right) &\equiv \frac{(c-(a+c))^2}{B}+ \\ &\quad \frac{((b+d)-\underline{B})^2}{\underline{B}} \\ &\equiv \frac{a^2}{B}+0 \\ &\equiv \frac{a^2}{B}\end{aligned} \tag{60}$$

and can be compared with a theoretical chi-square value at a certain level of significance $\alpha$. The $\tilde{\chi}^2$-distribution equals zero when the observed values are equal to the expected/theoretical values of an exclusion relationship/distribution $\text{p}(\text{A}_{\text{t}} \mid \text{B}_{\text{t}})$, 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 2.36 (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.

$$\begin{aligned}pValue_{\text{lt}}\left(A_{\text{t}} \mid B_{\text{t}}\right) &\equiv 1-e^{-(1-p(A_{\text{t}}|B_{\text{t}}))} \\ &\equiv 1-e^{-(a/N)}\end{aligned} \tag{61}$$

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

### 2.2.6. Neither nor conditions

**Definition 2.37 (Neither $\text{A}_{\text{t}}$ nor $\text{B}_{\text{t}}$ 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

$$\begin{aligned} p\left(A_t \downarrow B_t\right) &\equiv p\left(d_t\right) \\ &\equiv \frac{N - \sum_{t=1}^{N} \left(A_t \vee B_t\right)}{N} \equiv \frac{\sum_{t=1}^{N} \left(\underline{A}_t \wedge \underline{B}_t\right)}{N} \equiv \frac{N \times \left(p\left(d_t\right)\right)}{N} \\ &\equiv \frac{d}{N} \\ &\equiv +1 \end{aligned} \tag{62}$$

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

**Definition 2.38 (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

$$\begin{aligned} {\tilde{\chi}^2}_{\text{Calculated}}\left(\left(A_t \downarrow B_t\right) \mid A\right) &\equiv \frac{\left(d - \left(c + d\right)\right)^2}{\underline{A}} + \\ &\quad \frac{\left(\left(a + b\right) - A\right)^2}{A} \\ &\equiv \frac{c^2}{\underline{A}} + 0 \end{aligned} \tag{63}$$

or equally as

$$\begin{aligned} {\tilde{\chi}^2}_{\text{Calculated}}\left(\left(A_t \downarrow B_t\right) \mid B\right) &\equiv \frac{\left(d - \left(b + d\right)\right)^2}{\underline{B}} + \\ &\quad \frac{\left(\left(a + c\right) - B\right)^2}{B} \\ &\equiv \frac{b^2}{\underline{B}} + 0 \end{aligned} \tag{64}$$

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 2.39 (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.

$$\begin{aligned} pValue_{\text{lt}}\left(A_t \downarrow B_t\right) &\equiv 1 - e^{-(1-p(A_t \downarrow B_t))} \\ &\equiv 1 - e^{-p(A_t \vee B_t)} \\ &\equiv 1 - e^{-((a+b+c)/N)} \end{aligned} \tag{65}$$

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 4).

**Table 4.** 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 2.40** (**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, The Greek philsopher from Stageira 384 - 322 B. C. E, 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, The Greek philsopher from Stageira 384 - 322 B. C. E, 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, The Greek philsopher from Stageira 384 - 322 B. C. E, 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 philosophy 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, Mr., 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 $p(A_t \leftarrow B_t)$ in terms of statistics and probability theory, is defined (Barukčić, 1989, p. 15-28) as

$$\begin{aligned} p\left(A_t \leftarrow B_t\right) \equiv p\left(A_t \vee \underline{B}_t\right) &\equiv \frac{\sum_{t=1}^{N}\left(A_t \vee \underline{B}_t\right)}{N} \equiv \frac{\left(A_t \vee \underline{B}_t\right) \times p\left(A_t \vee \underline{B}_t\right)}{\left(A_t \vee \underline{B}_t\right)} \\ &\equiv p\left(a_t\right) + p\left(b_t\right) + p\left(d_t\right) \\ &\equiv \frac{N \times \left(p\left(a_t\right) + p\left(b_t\right) + p\left(d_t\right)\right)}{N} \equiv \frac{E\left(A_t \leftarrow B_t\right)}{N} \\ &\equiv \frac{a+b+d}{N} \equiv \frac{E\left(A_t \vee \underline{B}_t\right)}{N} \\ &\equiv \frac{A+d}{N} \equiv \frac{E\left(A_t \leftarrow B_t\right)}{N} \\ &\equiv \frac{a+\underline{B}}{N} \equiv \frac{E\left(A_t \vee \underline{B}_t\right)}{N} \\ &\equiv +1 \end{aligned} \tag{66}$$

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. In general, it is $p\left(A_t \prec B_t\right) \equiv 1 - p\left(A_t \leftarrow B_t\right)$ (see Table 5).

**Remark 2.2.** *A necessary condition $A_t$ is characterized itself by the property that another event $B_t$*

**Table 5.** Necessary condition.

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

*will not occur if $A_t$ is not given, if $A_t$ did not occur (Barukčić, 1989, 1997, 2005, 2016b, 2017b,c, 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, Andreĭ Nikolaevich, 1950, p. 26) of random variables $A_t$, $B_t$ et cetera at the (period of) time t, we obtain

$$\begin{aligned} p\left(A_t \leftarrow B_t\right) &\equiv +1 \\ &\equiv +1 - p\left(c_t\right) \\ &\equiv +1 - p\left(\underline{A}_t \cap B_t\right) \\ &\equiv \left( \int_{-\infty}^{A_t} \int_{-\infty}^{B_t} f\left(A_t, B_t\right)\, dA_t\, dB_t \right) + \left( 1 - \int_{-\infty}^{B_t} f\left(B_t\right)\, dB_t \right) \end{aligned} \tag{67}$$

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 2.41 (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 $\chi^2$-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

$$\begin{aligned}\tilde{\chi}^2{}_{\text{Calculated}}\left(A_{\text{t}} \leftarrow B_{\text{t}} \mid B\right) &\equiv \frac{\left(a-(a+c)\right)^2}{B}+ \\ &\quad \frac{\left((b+d)-\underline{B}\right)^2}{\underline{B}} \\ &\equiv \frac{c^2}{B}+0 \\ &\equiv \frac{c^2}{B}\end{aligned} \tag{68}$$

or equally as

$$\begin{aligned}\tilde{\chi}^2{}_{\text{Calculated}}\left(A_{\text{t}} \leftarrow B_{\text{t}} \mid \underline{A}\right) &\equiv \frac{\left(d-(c+d)\right)^2}{\underline{A}}+ \\ &\quad \frac{\left((a+b)-A\right)^2}{A} \\ &\equiv \frac{c^2}{\underline{A}}+0 \\ &\equiv \frac{c^2}{\underline{A}}\end{aligned} \tag{69}$$

and can be compared with a theoretical chi-square value at a certain level of significance $\alpha$. 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 2.42 (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.

$$\begin{aligned}pValue_{\text{lt}}\left(A_{\text{t}} \leftarrow B_{\text{t}}\right) &\equiv 1-e^{-\left(1-p\left(A_{\text{t}} \leftarrow B_{\text{t}}\right)\right)} \\ &\equiv 1-e^{-(c/N)}\end{aligned} \tag{70}$$

### 2.2.12. Sufficient condition

**Definition 2.43 (Sufficient condition [*Conditio per quam*]).**

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

$$\begin{aligned} p\left(A_t \rightarrow B_t\right) \equiv p\left(\underline{A}_t \vee B_t\right) &\equiv \frac{\sum_{t=1}^{N}\left(\underline{A}_t \vee B_t\right)}{N} \equiv \frac{\left(\underline{A}_t \vee B_t\right) \times p\left(\underline{A}_t \vee B_t\right)}{\left(\underline{A}_t \vee B_t\right)} \\ &\equiv p\left(a_t\right)+p\left(c_t\right)+p\left(d_t\right) \\ &\frac{N \times \left(p\left(a_t\right)+p\left(c_t\right)+p\left(d_t\right)\right)}{N} \\ &\equiv \frac{a+c+d}{N} \equiv \frac{E\left(\underline{A}_t \vee B_t\right)}{N} \\ &\equiv \frac{B+d}{N} \equiv \frac{E\left(A_t \rightarrow B_t\right)}{N} \\ &\equiv \frac{a+\underline{A}}{N} \\ &\equiv +1 \end{aligned} \tag{71}$$

It is $p\left(A_t \succ\!\!- B_t\right) \equiv 1 - p\left(A_t \rightarrow B_t\right)$ (see Table 6).

**Table 6.** 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 |

**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, 2016b, 2017b,c, 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 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*

$$p\left(A_t \rightarrow B_t\right) + p\left(R_t \wedge B_t\right) \equiv +1 \tag{72}$$

*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 2.44** (**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

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

or equally as

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

and can be compared with a theoretical chi-square value at a certain level of significance $\alpha$. 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 $p(A_t \to B_t)$, 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 2.45** (**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.

$$\begin{aligned} pValue_{\mathrm{lt}}\left(A_{\mathrm{t}} \rightarrow B_{\mathrm{t}}\right) &\equiv 1-e^{-(1-p(A_{\mathrm{t}} \rightarrow B_{\mathrm{t}}))} \\ &\equiv 1-e^{-(b/N)} \end{aligned} \tag{75}$$

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

### 2.2.15. Necessary and sufficient conditions

**Definition 2.46** (**Necessary and sufficient conditions [*EQV*]**).

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

$$\begin{aligned} p\left(A_{\mathrm{t}} \leftrightarrow B_{\mathrm{t}}\right) &\equiv \frac{\sum_{t=1}^{N}\left(\left(A_{\mathrm{t}} \vee \underline{B}_{\mathrm{t}}\right) \wedge \left(\underline{A}_{\mathrm{t}} \vee B_{\mathrm{t}}\right)\right)}{N} \\ &\equiv p\left(a_{\mathrm{t}}\right)+p\left(d_{\mathrm{t}}\right) \\ &\equiv \frac{N \times \left(p\left(a_{\mathrm{t}}\right)+p\left(d_{\mathrm{t}}\right)\right)}{N} \\ &\equiv \frac{a+d}{N} \\ &\equiv +1 \end{aligned} \tag{76}$$

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

**Definition 2.47** (**The $\tilde{\chi}^2$ goodness of fit test of a necessary and sufficient condition relationship**).

Even the necessary and sufficient condition relationship $\mathrm{p}(\mathrm{A_t} \leftrightarrow \mathrm{B_t})$ 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

$$\begin{aligned} {\tilde{\chi}^2}_{\mathrm{Calculated}}\left(A_{\mathrm{t}} \leftrightarrow B_{\mathrm{t}} \mid A\right) &\equiv \frac{\left(a-(a+b)\right)^2}{A}+ \\ &\quad \frac{d-\left((c+d)\right)^2}{\underline{A}} \\ &\equiv \frac{b^2}{A}+\frac{c^2}{\underline{A}} \end{aligned} \tag{77}$$

or equally as

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

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 $\alpha$. Under conditions where the observed values are equal to the expected/theoretical values of a necessary and sufficient condition relationship/distribution $\text{p}(\text{A}_\text{t} \leftrightarrow \text{B}_\text{t})$, 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 2.48 (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.

$$\begin{aligned}pValue_{\text{lt}}\left(A_{\text{t}} \leftrightarrow B_{\text{t}}\right) &\equiv 1-e^{-(1-p(A_{\text{t}} \leftrightarrow B_{\text{t}}))} \\ &\equiv 1-e^{-((b+c)/N)}\end{aligned} \tag{79}$$

In this context, a low p-value indicates again a statistical significance. Table 7 may provide an overview of the theoretical distribution of a necessary and sufficient condition.

**Table 7.** Necessary and sufficient condition.

| | | Conditioned $\text{B}_\text{t}$ | | |
|---|---|---|---|---|
| | | YES | NO | |
| Condition $\text{A}_\text{t}$ | YES | 1 | 0 | 1 |
| | NO | 0 | 1 | 1 |
| | | 1 | 1 | 2 |

### 2.2.18. Either or conditions

**Definition 2.49 (Either $\text{A}_\text{t}$ or $\text{B}_\text{t}$ 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

$$\begin{aligned} p\left(A_t \succ\!\prec B_t\right) &\equiv \frac{\sum_{t=1}^{N}\left(\left(A_t \wedge \underline{B}_t\right) \vee \left(\underline{A}_t \wedge B_t\right)\right)}{N} \\ &\equiv p\left(b_t\right) + p\left(c_t\right) \\ &\equiv \frac{N \times \left(p\left(b_t\right) + p\left(c_t\right)\right)}{N} \\ &\equiv \frac{b+c}{N} \\ &\equiv +1 \end{aligned} \tag{80}$$

It is $p\left(A_t \succ\!\prec B_t\right) \equiv 1 - p\left(A_t <\!\!\succ B_t\right)$ (see Table 8).

**Table 8.** 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 2.50 (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

$$\begin{aligned} \tilde{\chi}^2{}_{\text{Calculated}}\left(\left(A_t \succ\!\prec B_t\right) \mid A\right) &\equiv \frac{\left(b-\left(a+b\right)\right)^2}{A} + \\ &\quad \frac{c-\left(\left(c+d\right)\right)^2}{\underline{A}} \\ &\equiv \frac{a^2}{A} + \frac{d^2}{\underline{A}} \end{aligned} \tag{81}$$

or equally as

$$\begin{aligned}\tilde{\chi}^2{}_{\text{Calculated}}\left((A_{\text{t}} \succ\!\prec B_{\text{t}}) \mid B\right) &\equiv \frac{(c-(a+c))^2}{B}+ \\ &\quad \frac{b-((b+d))^2}{\underline{B}} \\ &\equiv \frac{a^2}{B}+\frac{d^2}{\underline{B}}\end{aligned} \tag{82}$$

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 2.51 (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.

$$\begin{aligned}pValue_{\text{lt}}\left(A_{\text{t}} \succ\!\prec B_{\text{t}}\right) &\equiv 1-e^{-(1-p(A_{\text{t}}>-<B_{\text{t}}))} \\ &\equiv 1-e^{-((a+d)/N)}\end{aligned} \tag{83}$$

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

2.2.21. Causal relationship k

The history of the denialism of causality in Philosophy, Mathematics, Statistics, Physics et cetera is very long. We only recall David Hume's (1711-1776) account of causation and his inappropriate reduction of the cause-effect relationship to a simple habitual connection in human thinking or Immanuel Kant's (1724-1804) initiated trial to consider causality as nothing more but a '*a priori*'given category (Langsam, 1994) in human reasoning and other similar attempts too. It is worth noting in this context that especially Karl Pearson (1857 - 1936) himself has been engaged in a long lasting and never-ending crusade against causation too. "**Pearson categorically denies the need for an independent concept of causal relation beyond correlation ... he *exterminated* causation from statistics before it had a chance to take root** "(Pearl, 2000) At the beginning of the 20$^{th}$ century notable proponents of **conditionalism** like the German anatomist and pathologist David Paul von Hansemann (Hansemann, David Paul von, 1912) (1858 - 1920) and the biologist and physiologist Max Richard Constantin Verworn(Verworn, 1912) (1863 - 1921) started a new attack(Kröber, 1961) on the principle of causality. In his essay "Kausale und konditionale Weltanschauung"Verworn(Verworn, 1912) presented "an exposition of 'conditionism'as contrasted with 'causalism,'(Unknown, 1913) while ignoring cause and effect relationships completely. "**Das Ding ist also identisch mit der Gesamtheit seiner Bedingungen**."(Verworn, 1912) However, Verworn's goal to exterminate causality completely out of science was hindered by the further development of research. The history of futile attempts to refute **the principle of causality** culminated in a publication by the German born physicist Werner Karl Heisenberg (1901 - 1976). Heisenberg put forward an illogical, inconsistent and confusing uncertainty principle which opened the door to wishful thinking and logical fallacies in physics and in science as such. Heisenberg's unjustified reasoning ended in an act of a manifestly unfounded conclusion: "**Weil alle Experimente den Gesetzen der Quantenmechanik und damit der Gleichung (1) unterworfen sind, so wird durch die Quantenmechanik die Ungültigkeit des Kausalgesetzes definitiv festgestellt**."(Heisenberg, Werner Karl, 1927) while 'Gleichung (1)'denotes Heisenberg's uncertainty principle. Einstein's himself, a major contributor to quantum theory and in the same respect a major critic of quantum theory, disliked Heisenberg's uncertainty principle fundamentally while Einstein's opponents used Heisenberg's Uncertainty Principle against Einstein. After the End of the German Nazi initiated Second World War with unimaginable brutality and high human losses and a death toll due to an industrially organised mass killing of people by the German Nazis which did not exist in this way before, Werner Heisenberg visited Einstein in Princeton (New Jersey, USA) in October 1954 (Neffe, 2006). Einstein agreed to meet Heisenberg only for a very short period of time but their encounter lasted longer. However, there where not only a number of differences between Einstein and Heisenberg, these two physicists did not really loved each other. "Einstein remarked that the inventor of the uncertainty principle was a 'big Nazi'... "(Neffe, 2006) Albert Einstein (1879 - 1955) took again the opportunity to refuse to endorse **Heisenberg's uncertainty principle** as a fundamental law of nature and rightly too. Meanwhile, Heisenberg's uncertainty principle is refuted (see Barukčić, 2011a, 2014, 2016a) for several times but still not exterminated completely out of physics and out of science as such. In contrast to such extreme anti-causal positions as advocated by Heisenberg and the **Copenhagen interpretation of quantum mechancis**, the search for a (mathematical) solution of *the issue of causal inferences* is as old as human mankind itself ("*i. e. Aristotle's Doctrine of the Four Causes*") (Hennig, 2009) even if there is still little to go on. It is appropriate to specify especially

the position of D'Holbach(Holbach, Paul Henri Thiry Baron de, 1770). D'Holbach (1723-1789) himself linked cause and effect or causality as such to changes. "**Une *cause*, est un être qui e met un autre en mouvement, ou qui produit quelque changement en lui. *L'effet* est le changement qu'un corps produit dans un autre ...**"(Holbach, Paul Henri Thiry Baron de, 1770) D'Holbach infers in the following: "**De l'action et de la réaction continuelle de tous les êtres que la nature renferme, il résulte une suite de causes et d'effets ..**"(Holbach, Paul Henri Thiry Baron de, 1770) With more or less meaningless or none progress on the matter in hand even in the best possible conditions, it is not surprising that authors are suggesting more and more different approaches and models for causal inference. Indeed, the hope is justified that logically consistent *statistical methods of causal inference* can help scientist to achieve so much with so little. One of the methods of causal inference in Bio-sciences are based on the known *Henle(Henle, 1840) (1809–1885) - Koch(Koch, 1878) (1843–1910) postulates* (Carter, 1985) which are applied especially for the identification of a causative agent of an (infectious) disease. However, the pathogenesis of most chronic diseases is more or less very complex and potentially involves the interaction of several factors. In practice, from the 'pure culture' requirement of the Henle-Koch postulates insurmountable difficulties may emerge. In light of subsequent developments (PCR methodology, immune antibodies et cetera) it is appropriate to review the full validity of the Henle-Koch postulates in our days. In 1965, Sir Austin Bradford Hill (Hill, 1965) published nine criteria (the '*Bradford Hill Criteria* ') in order to determine whether observed epidemiologic associations are causal. Somewhat worrying, is at least the fact that, Hill's "... fourth characteristic is *the temporal relationship of the association* " and so-to-speak just a reformulation of the '*post hoc ergo propter hoc'(Barukčić, 1989, Woods and Walton, 1977)* logical fallacy through the back-door and much more then this. It is questionable whether association as such can be treated as being identical with causation. Unfortunately, due to several reasons, it seems therefore rather problematic to rely on Bradford Hill Criteria carelessly. Meanwhile, several other and competing mathematical or statistical approaches for causal inference have been discussed (Barukčić, 1989, 1997, 2005, 2016b, 2017a,c, Bohr, 1937, Dempster, 1990, Espejo, 2007, Hessen, Johannes, 1928, Hesslow, 1976, 1981, Korch, Helmut, 1965, Pearl, 2000, Schlick, Friedrich Albert Moritz, 1931, Suppes, 1970, Zesar, 2013) or even established (Barukčić, 1989, 1997, 2005, 2016b, 2017a,c). Nevertheless, the question is still not answered, is it at all possible to establish a cause effect relationship between two factors while applying only certain statistical (Sober, 2001) methods?

**Definition 2.52** (**Causal relationship k**).

Nonetheless, mathematically, the causal(Barukčić, 2011a,b, 2012) relationship (Barukčić, 1989, 1997, 2005, 2016b, 2017a,c, 2021c) 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(Thompson, 2006) Bernoulli trial t* in terms of statistics and probability theory as

$$\begin{aligned} k(U_t,W_t) &\equiv \frac{\sigma(U_t,W_t)}{\sigma(U_t)\times\sigma(W_t)} \\ &\equiv \frac{p(U_t\wedge W_t)-p(U_t)\times p(W_t)}{\sqrt[2]{(p(U_t)\times(1-p(U_t)))\times(p(W_t)\times(1-p(W_t)))}} \end{aligned} \tag{84}$$

where $\sigma$ ($U_t$ , $W_t$) denotes the co-variance between a cause $U_t$ and an effect $W_t$ *at every single*

*Bernoulli trial t*, $\sigma$ ($U_t$) denotes the standard deviation of a cause $U_t$ at the same single Bernoulli trial t, $\sigma$ ($W_t$) denotes the standard deviation of an effect $W_t$ at same single Bernoulli trial t. Table 9 illustrates the theoretically possible relationships between a cause and an effect.

**Table 9.** Sample space and the causal relationship k

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

However, even if one thinks to recognise the trace of Bravais (Bravais, 1846) (1811-1863) - Pearson's (1857-1936) "*product-moment coefficient of correlation*"(Galton, 1877, Pearson, 1896) inside the causal relationship k (Barukčić, 1989, 1997, 2005, 2016b, 2017a,c) both are completely different. According to Pearson: "*The fundamental theorems of correlation were for the first time and almost exhaustively discussed by B r a v a i s ('Analyse mathematique sur les probabilities des erreurs de situation d'un point.' Memoires par divers Savans, T. IX., Paris, 1846, pp. 255-332) nearly half a century ago.*"(Pearson, 1896) Neither does it make much sense to elaborate once again on the issue causation(Blalock, 1972) and correlation, since both are not identical (Sober, 2001) nor does it make sense to insist on the fact that "*Pearson's philosophy discouraged him from looking too far behind phenomena.*"(Haldane, 1957) Whereas it is essential to consider that the causal relationship k, in contrast to Pearson's product-moment coefficient of correlation(Pearson, 1896) or to Pearson's phi coefficient(Pearson, 1904b), is defined at every single Bernoulli trial t. This might be a very *small* difference. However, even a small difference might determine a difference. However, in this context and in any case, this small difference *makes*(Barukčić, 2018a) the difference.

### 2.2.22. Cause and effect

**Definition 2.53 (Cause and effect).**

**What is the cause, what is the effect?** Under conditions of a **positive** causal relationship k, an event $U_t$ which is for sure a cause of another event $W_t$ is at the same time t a necessary and sufficient condition of an event $W_t$. Table 10 may illustrate this relationship.

As can be seen, there is a kind of strange mirroring between $U_t$ and $W_t$ at the same Bernoulli trial t. Lastly, both are converses of each other too. In other words, $U_t$'s being a necessary condition of $W_t$'s is equivalent to $W_t$'s being a sufficient condition of $U_t$'s (and vice versa). In general, it is

$$(U_t \vee \underline{W}_t) \equiv (\underline{W}_t \vee U_t) \equiv ((U_t \vee \underline{W}_t) \wedge (\underline{W}_t \vee U_t)) \equiv +1 \tag{85}$$

In our everyday words,

**Table 10.** What is the cause, what is the effect?

| | | Effect $W_t$ | | |
|---|---|---|---|---|
| | | TRUE | FALSE | |
| Cause | TRUE | **+1** | **+0** | $p(U_t)$ |
| $U_t$ | FALSE | **+0** | **+1** | $p(\underline{U}_t)$ |
| | | $p(W_t)$ | $p(\underline{W}_t)$ | +1 |

**without**

$U_t$

**no**

$W_t$

is equivalent with

**if**

$W_t$

**then**

$U_t$

and vice versa.

Necessary and sufficient conditions are relationships used to describe the relationship between two events at the same Bernoulli trial t. In more detail, if $U_t$ then $W_t$ is equivalent with $W_t$ is necessary for $U_t$, because the truth of $U_t$ guarantees the truth of $W_t$. In general, it is

$$(\underline{U}_t \vee W_t) \equiv (W_t \vee \underline{U}_t) \equiv ((\underline{U}_t \vee W_t) \wedge (W_t \vee \underline{U}_t)) \equiv +1 \tag{86}$$

In other words, it is impossible to have $U_t$ without $W_t$ (Bloch, 2011). Similarly, $U_t$ is sufficient for $W_t$, because $U_t$ being true always implies that $W_t$ is true, but $U_t$ not being true does not always imply that $W_t$ is not true.

For instance, **without** gaseous oxygen ($U_t$), there would be **no** burning wax candle ($W_t$); hence the relationship **if** burning wax candle ($W_t$) **then** gaseous oxygen ($U_t$) is equally true and given.

This simple example may illustrate the reason why a sufficient condition alone is not enough to describe a cause completely. The relationship **if** burning wax candle ($W_t$) **then** gaseous oxygen ($U_t$) is given. Independently of this fact, a burning wax candle is not the cause of gaseous oxygen. Therefore, in order to be a cause of oxygen, additional evidence is necessary that a burning wax candle is a

necessary condition of gaseous oxygen too. However, even if the relationship **without** gaseous oxygen **no** burning wax candle is given, this relationship is not given vice versa. The relationship **without** burning wax candle **no** gaseous oxygen is not given. Like other fundamental concepts, the concepts of cause and effect can be associated with difficulties too. In order to recognise a causal relationship between $U_t$ and $W_t$, it is necessary that the same study or that at least different studies provide evidence of a necessary condition between $U_t$ and $W_t$ and of a sufficient condition between $U_t$ and $W_t$ and if possible of **a necessary and sufficient condition** between $U_t$ and $W_t$ too.

Mathematically, a necessary and sufficient condition between $U_t$ and $W_t$ is defined as

$$(U_t \vee \underline{W}_t) \wedge (\underline{U}_t \vee W_t) \equiv +1 \tag{87}$$

However, I think it necessary to make a clear distinction between a necessary and sufficient condition and the converse relationship (Eq. 85) above.

$$((U_t \vee \underline{W}_t) \wedge (\underline{W}_t \vee U_t)) \neq (U_t \vee \underline{W}_t) \wedge (\underline{U}_t \vee W_t) \tag{88}$$

*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 2.54** (**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 ${}_{\mathrm{R}}\mathrm{P}_{\mathrm{t}}$ denote a premise at a certain point in (space-) time t. Let ${}_{\mathrm{R}}\mathrm{C}_{\mathrm{t}}$ denote the conclusion at the same certain point in (space-) time t.

**PREMISES.**

**(1)** If (${}_{\mathrm{R}}\mathrm{P}_{\mathrm{t}}$ is false) then (${}_{\mathrm{R}}\mathrm{C}_{\mathrm{t}}$ is false).

**(2)** ${}_{\mathrm{R}}\mathrm{P}_{\mathrm{t}}$ is false.

**CONCLUSION.**

**(3)** ${}_{\mathrm{R}}\mathrm{C}_{\mathrm{t}}$ 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 | $p(a_t)$ | +0 | $p({}_{\mathrm{R}}\mathrm{P}_{\mathrm{t}})$ |
| ${}_{\mathrm{R}}\mathrm{P}_{\mathrm{t}}$ | TRUE | $p(c_t)$ | $p(d_t)$ | $p({}_{\mathrm{R}}\underline{\mathrm{P}}_{\mathrm{t}})$ |
| | | $p({}_{\mathrm{R}}\mathrm{C}_{\mathrm{t}})$ | $p({}_{\mathrm{R}}\underline{\mathrm{C}}_{\mathrm{t}})$ | +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 ($\mathrm{premise}_{\mathrm{t}}$ is false) then ($\mathrm{conclusion}_{\mathrm{t}}$ is false). Formally, modus inversus can be expressed as

$$({}_{\mathrm{R}}P_{\mathrm{t}}) \cup ({}_{\mathrm{R}}\neg C_{\mathrm{t}}) \equiv +1 \tag{89}$$

while the sign ∪ 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 hyper-geometric(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

$$+1 = +1 \tag{90}$$

### 2.5.2. Axiom II. Lex contradictionis

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

$$+0 = +1 \tag{91}$$

and equally the most simple form of a contradiction formulated.

### 2.5.3. Axiom III. Lex negationis

$$\neg\,(0) \times 0 = 1 \tag{92}$$

where $\neg$ denotes (logical (Boole, 1854) or natural) negation (Ayer, 1952, Förster and Melamed, 2012, Hedwig, 1980, Heinemann, Fritz H., 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 $p(A_t \leftarrow B_t)$ 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*

$$\begin{aligned} p(A_t \leftarrow B_t) \equiv p(A_t \vee \underline{B}_t) &\equiv \frac{\sum_{t=1}^{N} (A_t \vee \underline{B}_t)}{N} \equiv \frac{(A_t \vee \underline{B}_t) \times p(A_t \vee \underline{B}_t)}{(A_t \vee \underline{B}_t)} \\ &\equiv p(a_t) + p(b_t) + p(d_t) \\ &\equiv \frac{N \times (p(a_t) + p(b_t) + p(d_t))}{N} \equiv \frac{E(A_t \leftarrow B_t)}{N} \\ &\equiv \frac{a+b+d}{N} \equiv \frac{E(A_t \vee \underline{B}_t)}{N} \\ &\equiv \frac{A+d}{N} \equiv \frac{E(A_t \leftarrow B_t)}{N} \\ &\equiv \frac{a+\underline{B}}{N} \equiv \frac{E(A_t \vee \underline{B}_t)}{N} \\ &\equiv +1 \end{aligned} \tag{93}$$

*where $E(A_t \leftarrow B_t) \equiv E(A_t \vee \underline{B}_t)$ 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 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 last consequence, our conclusion is true. **Without** sufficient amount of gaseous oxygen, **no** burning wax candle. □

In the end, why is something, the way it is? This relationship of table 14 are illustrated by figure 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

**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 |

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 (conditio sine qua non) 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.

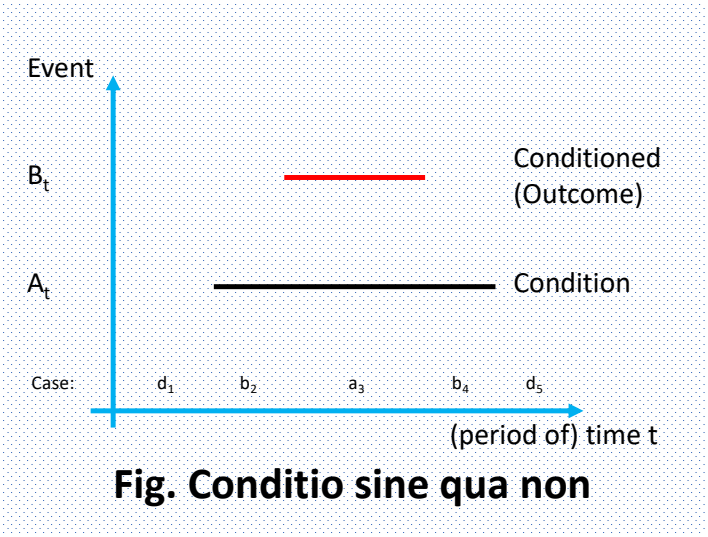


**Fig. Conditio sine qua non**

**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.

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 $A_{t=2}$ at the time $t_2$ follows the conditioned $B_{t=3}$ at the time $t_3$. Furthermore, after conditioned $B_{t=3}$ at the time $t_3$ follows the condition $A_{t=4}$ at the time $t_4$ et cetera. Figure

(time series vs. conditions) might illustrate the issue discussed.

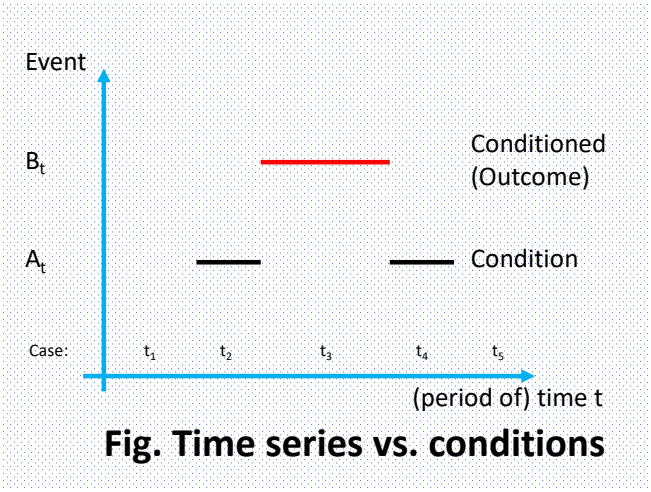


**Fig. Time series vs. conditions**

**Time series vs. conditio sine qua non.**
The relationship between $A_t$ and $B_t$
analysed under condition of
time series does not guarantee at all
to recognize a necessary conditions.
Reason.
At the time $t_3$ the conditioned $B_{t=3}$
is given even if a condition $A_{t=3}$
does not exist at all.
This contradicts the concept of
a necessary condition.

For these reasons, 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.

[1] Tenny S, Kerndt CC, Hoffman MR. Case Control Studies. 2021 Jul 9. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan–. PMID: 28846237.

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

$$p\left(A_t \leftarrow B_t\right) \geq 1 - \frac{p\left(c_t\right)}{p\left(B_t\right)} \tag{94}$$

*Proof by direct proof.* The premise

$$+1 \equiv +1 \tag{95}$$

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

$$p\left(B_{\mathrm{t}}\right) \equiv p\left(B_{\mathrm{t}}\right) \tag{96}$$

or

$$p\left(a_{\mathrm{t}}\right) + p\left(c_{\mathrm{t}}\right) \equiv p\left(B_{\mathrm{t}}\right) \tag{97}$$

Rearranging equation 97, it is

$$p\left(a_{\mathrm{t}}\right) \equiv p\left(B_{\mathrm{t}}\right) - p\left(c_{\mathrm{t}}\right) \tag{98}$$

Simplifying equation 98, we obtain

$$\frac{p\left(a_{\mathrm{t}}\right)}{p\left(B_{\mathrm{t}}\right)} \equiv \frac{p\left(B_{\mathrm{t}}\right)}{p\left(B_{\mathrm{t}}\right)} - \frac{p\left(c_{\mathrm{t}}\right)}{p\left(B_{\mathrm{t}}\right)} \tag{99}$$

Equation 99 becomes

$$\frac{p\left(a_{\mathrm{t}}\right)}{p\left(B_{\mathrm{t}}\right)} \equiv 1 - \frac{p\left(c_{\mathrm{t}}\right)}{p\left(B_{\mathrm{t}}\right)} \tag{100}$$

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

$$p\left(A_{\mathrm{t}} \leftarrow B_{\mathrm{t}}\right) \equiv \frac{p\left(a_{\mathrm{t}}\right)}{p\left(B_{\mathrm{t}}\right)} \equiv 1 - \frac{p\left(c_{\mathrm{t}}\right)}{p\left(B_{\mathrm{t}}\right)} \tag{101}$$

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

$$p\left(A_{\mathrm{t}} \leftarrow B_{\mathrm{t}}\right) \approx 1 - \frac{p\left(c_{\mathrm{t}}\right)}{p\left(B_{\mathrm{t}}\right)} \tag{102}$$

□

However, in reality, it can be assumed that the necessary condition relationship will be stronger than the relationship suggested by equation 102. Therefore, equation 102 is of particular value under conditions where a control group is absent or appears to be (completely) unsuitable. In general, it is

$$p\left(A_{\mathrm{t}} \leftarrow B_{\mathrm{t}}\right) \geq 1 - \frac{p\left(c_{\mathrm{t}}\right)}{p\left(B_{\mathrm{t}}\right)} \tag{103}$$

### 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*

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

*Proof by direct proof.* The premise

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

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

$$p\left(\underline{A}_{\mathrm{t}}\right) \equiv p\left(\underline{A}_{\mathrm{t}}\right) \tag{106}$$

or

$$p\left(c_{\mathrm{t}}\right) + p\left(d_{\mathrm{t}}\right) \equiv p\left(\underline{A}_{\mathrm{t}}\right) \tag{107}$$

Rearranging equation 107, it is

$$p\left(d_{\mathrm{t}}\right) \equiv p\left(\underline{A}_{\mathrm{t}}\right) - p\left(c_{\mathrm{t}}\right) \tag{108}$$

Simplifying equation 108, we obtain

$$\frac{p\left(d_{\mathrm{t}}\right)}{p\left(\underline{A}_{\mathrm{t}}\right)} \equiv \frac{p\left(\underline{A}_{\mathrm{t}}\right)}{p\left(\underline{A}_{\mathrm{t}}\right)} - \frac{p\left(c_{\mathrm{t}}\right)}{p\left(\underline{A}_{\mathrm{t}}\right)} \tag{109}$$

Equation 109 becomes

$$\frac{p\left(d_{\mathrm{t}}\right)}{p\left(\underline{A}_{\mathrm{t}}\right)} \equiv 1 - \frac{p\left(c_{\mathrm{t}}\right)}{p\left(\underline{A}_{\mathrm{t}}\right)} \tag{110}$$

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

$$p\left(A_{\mathrm{t}} \leftarrow B_{\mathrm{t}}\right) \equiv \frac{p\left(d_{\mathrm{t}}\right)}{p\left(\underline{A}_{\mathrm{t}}\right)} \equiv 1 - \frac{p\left(c_{\mathrm{t}}\right)}{p\left(\underline{A}_{\mathrm{t}}\right)} \tag{111}$$

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

$$p\left(A_{\mathrm{t}} \leftarrow B_{\mathrm{t}}\right) \approx 1 - \frac{p\left(c_{\mathrm{t}}\right)}{p\left(\underline{A}_{\mathrm{t}}\right)} \tag{112}$$

[2] Waddington H, Aloe AM, Becker BJ, Djimeu EW, Hombrados JG, Tugwell P, Wells G, Reeves B. Quasi-experimental study designs series-paper 6: risk of bias assessment. J Clin Epidemiol. 2017 Sep;89:43-52. *doi* : 10.1016/*j.jclinepi*.2017.02.015. Epub 2017 Mar 27. PMID: 28351693.

□

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 verum group is absent or appears to be (completely) inappropriate, et cetera. In general, it is

$$p\left(A_{\mathrm{t}} \leftarrow B_{\mathrm{t}}\right) \geq 1-\frac{p\left(c_{\mathrm{t}}\right)}{p\left(\underline{A}_{\mathrm{t}}\right)} \tag{113}$$

### *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*

$$p\left(IOU\left(A,B\right)\right) \equiv Absolute\left(\left(\frac{A_t+B_t}{N}\right)-1\right) \equiv 0 \tag{114}$$

*Proof by direct proof.* The premise

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

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

$$p\left(A_{\mathrm{t}} \leftarrow B_{\mathrm{t}}\right) \equiv p\left(A_{\mathrm{t}} \leftarrow B_{\mathrm{t}}\right) \tag{116}$$

Based on equation 101 it is $p\left(A_{\mathrm{t}} \leftarrow B_{\mathrm{t}}\right) \equiv \frac{p\left(a_{\mathrm{t}}\right)}{p\left(B_{\mathrm{t}}\right)} \equiv 1-\frac{p\left(c_{\mathrm{t}}\right)}{p\left(B_{\mathrm{t}}\right)}$. Rearranging equation 116, it is

$$1-\frac{p\left(c_{\mathrm{t}}\right)}{p\left(B_{\mathrm{t}}\right)} \equiv p\left(A_{\mathrm{t}} \leftarrow B_{\mathrm{t}}\right) \tag{117}$$

Based on equation 111 it is $p\left(A_{\mathrm{t}} \leftarrow B_{\mathrm{t}}\right) \equiv \frac{p\left(d_{\mathrm{t}}\right)}{p\left(\underline{A}_{\mathrm{t}}\right)} \equiv 1-\frac{p\left(c_{\mathrm{t}}\right)}{p\left(\underline{A}_{\mathrm{t}}\right)}$. Equation 117 simplifies as

$$1-\frac{p\left(c_{\mathrm{t}}\right)}{p\left(B_{\mathrm{t}}\right)} \equiv 1-\frac{p\left(c_{\mathrm{t}}\right)}{p\left(\underline{A}_{\mathrm{t}}\right)} \tag{118}$$

Equation 118 becomes

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

or

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

Equation 120 can be simplified as

$$p(c_t) \times p(B_t) \equiv p(c_t) \times p(\underline{A}_t) \tag{121}$$

In the following we ignore $p(c_t)$ and set $p(c_t) = +1$. In general, it is

$$p(B_t) \equiv p(\underline{A}_t) \tag{122}$$

or

$$p(B_t) \equiv 1 - p(A_t) \tag{123}$$

or

$$p(A_t) + p(B_t) \equiv 1 \tag{124}$$

Rearranging equation 124, it is

$$N \times p(A_t) + N \times p(B_t) \equiv N \tag{125}$$

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

$$A_t + B_t \equiv N \tag{126}$$

Rearranging equation 126, it is

$$\frac{A_t + B_t}{N} \equiv \frac{N}{N} \equiv +1 \tag{127}$$

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

$$IOU(A_t, B_t) \equiv \left(\frac{A_t + B_t}{N}\right) - 1 \equiv 0 \tag{128}$$

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

$$p(IOU(A,B)) \equiv Absolute\left(\left(\frac{A_t + B_t}{N}\right) - 1\right) \equiv 0 \tag{129}$$

□

### *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.

[3] Hoffmann RG, Lim HJ. Observational study design. Methods Mol Biol. 2007;404:19-31. *doi* : 10.1007/978 – 1 – 59745 – 530 – 5$_2$. PMID: 18450043.

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

$$p\left(A_t \mid B_t\right) \geq 1 - \frac{p\left(a_t\right)}{p\left(B_t\right)} \tag{130}$$

*Proof by direct proof.* The premise

$$+1 \equiv +1 \tag{131}$$

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

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

or

$$p\left(a_\mathrm{t}\right) + p\left(c_\mathrm{t}\right) \equiv p\left(B_\mathrm{t}\right) \tag{133}$$

Rearranging equation 133, it is

$$p\left(c_\mathrm{t}\right) \equiv p\left(B_\mathrm{t}\right) - p\left(a_\mathrm{t}\right) \tag{134}$$

Simplifying equation 134, we obtain

$$\frac{p\left(c_\mathrm{t}\right)}{p\left(B_\mathrm{t}\right)} \equiv \frac{p\left(B_\mathrm{t}\right)}{p\left(B_\mathrm{t}\right)} - \frac{p\left(a_\mathrm{t}\right)}{p\left(B_\mathrm{t}\right)} \tag{135}$$

Equation 135 becomes

$$\frac{p\left(c_\mathrm{t}\right)}{p\left(B_\mathrm{t}\right)} \equiv 1 - \frac{p\left(a_\mathrm{t}\right)}{p\left(B_\mathrm{t}\right)} \tag{136}$$

A basic requirement of a exclusion relationship is the need that $\frac{p\left(c_\mathrm{t}\right)}{p\left(B_\mathrm{t}\right)} \equiv 1$. In general, it is

$$p\left(A_\mathrm{t} \mid B_\mathrm{t}\right) \equiv \frac{p\left(c_\mathrm{t}\right)}{p\left(B_\mathrm{t}\right)} \equiv 1 - \frac{p\left(a_\mathrm{t}\right)}{p\left(B_\mathrm{t}\right)} \tag{137}$$

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

$$p\left(A_\mathrm{t} \mid B_\mathrm{t}\right) \approx 1 - \frac{p\left(a_\mathrm{t}\right)}{p\left(B_\mathrm{t}\right)} \tag{138}$$

□

However, in reality, it can be assumed that an exclusion relationship will be stronger than the relationship suggested by equation 138. Therefore, equation 138 is of particular value under conditions where a control group is absent or appears to be (completely) unsuitable. In general, it is

$$p\left(A_\mathrm{t} \mid B_\mathrm{t}\right) \geq 1 - \frac{p\left(a_\mathrm{t}\right)}{p\left(B_\mathrm{t}\right)} \tag{139}$$

### 3.6. Experimental studies and exclusion relationship

An experimental [4] , [5] , [6] 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. [7] 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*

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

*Proof by direct proof.* The premise

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

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

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

or

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

Rearranging equation 143, it is

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

Simplifying equation 144, we obtain

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

Equation 145 becomes

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

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

$$p\left(A_{\mathrm{t}} \mid B_{\mathrm{t}}\right) \equiv \frac{p\left(b_{\mathrm{t}}\right)}{p\left(A_{\mathrm{t}}\right)} \equiv 1 - \frac{p\left(a_{\mathrm{t}}\right)}{p\left(A_{\mathrm{t}}\right)} \tag{147}$$

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

$$p\left(A_{\mathrm{t}} \mid B_{\mathrm{t}}\right) \approx 1 - \frac{p\left(a_{\mathrm{t}}\right)}{p\left(A_{\mathrm{t}}\right)} \tag{148}$$

[4] Peirce, Charles Sanders (1887). "Illustrations of the Logic of Science". Open Court (10 June 2014). ISBN 0812698495.

[5] Peirce, Charles Sanders (1883). "A Theory of Probable Inference". In C. S. Peirce (Ed.), Studies in logic by members of the Johns Hopkins University (p. 126–181). Little, Brown and Co (1883)

[6] Fisher, Ronald A. (1971) [1935]. The Design of Experiments (9th ed.). Macmillan. ISBN 0-02-844690-9.

[7] Moorhead JE, Rao PV, Anusavice KJ. Guidelines for experimental studies. Dent Mater. 1994 Jan;10(1):45-51. *doi* : 10.1016/0109 – 5641(94)90021 – 3. PMID: 7995475.

□

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

$$p\left(A_{\mathrm{t}} \mid B_{\mathrm{t}}\right) \geq 1-\frac{p\left(a_{\mathrm{t}}\right)}{p\left(A_{\mathrm{t}}\right)} \tag{149}$$

*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*

$$p\left(IOU\left(A_t, B_t\right)\right) \equiv Absolute\left(\left(\frac{\underline{A_t}+B_t}{N}\right)-1\right) \equiv 0 \tag{150}$$

*Proof by direct proof.* The premise

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

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

$$+0 \equiv +0 \tag{152}$$

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 151 becomes

$$\left(\frac{A_{\mathrm{t}}+\underline{B_{\mathrm{t}}}}{N}\right)-1 \equiv 0 \tag{153}$$

or

$$\left(\frac{A_{\mathrm{t}}+\underline{B_{\mathrm{t}}}}{N}\right) \equiv +1 \tag{154}$$

or

$$A_{\mathrm{t}}+\underline{B_{\mathrm{t}}} \equiv N \tag{155}$$

or

$$A_{\mathrm{t}} \equiv N-\underline{B_{\mathrm{t}}} \tag{156}$$

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

$$A_{\mathrm{t}} \equiv B_{\mathrm{t}} \tag{157}$$

or

$$a_{\mathrm{t}}+b_{\mathrm{t}} \equiv a_{\mathrm{t}}+c_{\mathrm{t}} \tag{158}$$

or

$$b_t \equiv c_t \tag{159}$$

In general, it is $A_t \equiv N - \underline{A}_t$. Equation 157 becomes

$$N - \underline{A}_t \equiv B_t \tag{160}$$

or

$$N \equiv \underline{A}_t + B_t \tag{161}$$

or

$$\frac{N}{N} \equiv \frac{\underline{A}_t + B_t}{N} \tag{162}$$

Equation 162 simplifies as

$$\frac{\underline{A}_t + B_t}{N} \equiv \frac{N}{N} \equiv +1 \tag{163}$$

or as

$$\frac{\underline{A}_t + B_t}{N} - 1 \equiv +0 \tag{164}$$

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

$$p\left(IOU\left(A_t, B_t\right)\right) \equiv Absolute\left(\left(\frac{\underline{A}_t + B_t}{N}\right) - 1\right) \equiv 0 \tag{165}$$

□

*3.8. Observational studies and study design*

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

$$p\left(IOU\left(A_t, B_t\right)\right) \equiv p\left(IOI\left(A_t, \underline{B}_t\right)\right) \tag{166}$$

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

$$\underbrace{+1 = +1}_{(Premise)} \tag{167}$$

is true, **then** the following conclusion

$$p\left(IOU\left(A_t, B_t\right)\right) \equiv p\left(IOI\left(A_t, \underline{B}_t\right)\right) \tag{168}$$

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

$$+1 \equiv +1 \tag{169}$$

is true. We multiply equation 169 by an expectation value $B_t$, it is

$$B_t \equiv B_t \tag{170}$$

Many times, the study design of observational studies demands that $B_t \equiv \underline{B}_t$. Equations 170 becomes

$$B_t \equiv \underline{B}_t \tag{171}$$

Adding the expectation value of $A_t$, it is

$$A_t + B_t \equiv A_t + \underline{B}_t \tag{172}$$

Dividing by the sample/populations size N, it is

$$\frac{A_t + B_t}{N} \equiv \frac{A_t + \underline{B}_t}{N} \tag{173}$$

or

$$\frac{A_t + B_t}{N} - 1 \equiv \frac{A_t + \underline{B}_t}{N} - 1 \tag{174}$$

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

$$p\left(IOU\left(A_t, B_t\right)\right) \equiv p\left(IOI\left(A_t, \underline{B}_t\right)\right) \tag{175}$$

□

### *3.9. Experimental studies and study design*

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

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

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

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

is true, **then** the following conclusion

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

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 $A_t$, it is

$$A_t \equiv A_t \tag{180}$$

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

$$A_t \equiv \underline{A}_t \tag{181}$$

Adding the expectation value of $B_t$, it is

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

Dividing by the sample/populations size N, it is

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

or

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

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

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

□

### *3.10. Leflunomide and acute myocardial infarction*

Suissa [8] 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 Suissa 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 |

[8] Suissa S, Bernatsky S, Hudson M. Antirheumatic drug use and the risk of acute myocardial infarction. Arthritis Rheum. 2006 Aug 15;55(4):531-6. *doi* : 10.1002/*art*.22094. PMID: 16874796.

### *3.11. Leflunomide and acute myocardial infarction II*

The study design of Suissa[9] 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 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

[9] Suissa S, Bernatsky S, Hudson M. Antirheumatic drug use and the risk of acute myocardial infarction. Arthritis Rheum. 2006 Aug 15;55(4):531-6. *doi* : 10.1002/*art*.22094. PMID: 16874796.

in Scotland [10] 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, [11] 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.

### *3.12. Etoricoxib and coronary artery disease*

Li-Chih Wu et al. [12] 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.

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[12] Wu LC, Leong PY, Yeo KJ, Li TY, Wang YH, Chiou JY, Wei JC. Celecoxib and sulfasalazine had negative association with coronary artery diseases in patients with ankylosing spondylitis: A nation-wide, population-based case-control study. Medicine (Baltimore). 2016 Sep;95(36):e4792. doi: 10.1097/MD.0000000000004792. PMID: 27603385; PMCID: PMC5023908.

**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"[13]. 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 [14] 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. [15] and the results of Gwen M C Masclee et al. [16] in this context. Both studies

[13]Wu LC, Leong PY, Yeo KJ, Li TY, Wang YH, Chiou JY, Wei JC. Celecoxib and sulfasalazine had negative association with coronary artery diseases in patients with ankylosing spondylitis: A nation-wide, population-based case-control study. Medicine (Baltimore). 2016 Sep;95(36):e4792. doi: 10.1097/MD.0000000000004792. PMID: 27603385; PMCID: PMC5023908.

[14]Bombardier C, Laine L, Reicin A, Shapiro D, Burgos-Vargas R, Davis B, Day R, Ferraz MB, Hawkey CJ, Hochberg MC, Kvien TK, Schnitzer TJ; VIGOR Study Group. Comparison of upper gastrointestinal toxicity of rofecoxib and naproxen in patients with rheumatoid arthritis. VIGOR Study Group. N Engl J Med. 2000 Nov 23;343(21):1520-8, 2 p following 1528. *doi* : 10.1056/*NEJM*200011233432103. PMID: 11087881.

[15]Thöne K, Kollhorst B, Schink T. Non-Steroidal Anti-Inflammatory Drug Use and the Risk of Acute Myocardial Infarction in the General German Population: A Nested Case-Control Study. Drugs Real World Outcomes. 2017 Sep;4(3):127-137. *doi* : 10.1007/*s*40801 – 017 – 0113 – *x*. PMID: 28676983; PMCID: PMC5567458.

[16]Masclee GMC, Straatman H, Arfè A, Castellsague J, Garbe E, Herings R, Kollhorst B, Lucchi S, Perez-Gutthann S, Romio S, Schade R, Schink T, Schuemie MJ, Scotti L, Varas-Lorenzo C, Valkhoff VE, Villa M, Sturkenboom MCJM. Risk of acute myocardial in-

investigated the effect of etoricoxib on acute myocardial infarction.

### *3.13. Etoricoxib and coronary artery events*

Yao-Min Hung et al. [17] 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 |

farction during use of individual NSAIDs: A nested case-control study from the SOS project. PLoS One. 2018 Nov 1;13(11):e0204746. *doi* : 10.1371/*journal.pone*.0204746. PMID: 30383755; PMCID: PMC6211656.

[17] Hung YM, Lin L, Chen CM, Chiou JY, Wang YH, Wang PY, Wei JC. The effect of anti-rheumatic medications for coronary artery diseases risk in patients with rheumatoid arthritis might be changed over time: A nationwide population-based cohort study. PLoS One. 2017 Jun 28;12(6):e0179081. *doi* : 10.1371/*journal.pone*.0179081. PMID: 28658301; 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 [18] , [19] 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 [20] 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.

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## 5. Conclusion

Leflunomide appears to be effective against an acute myocardial infarction. It is possible to detect a necessary condition relationships (within a dataset).

**Acknowledgments**

No funding or any financial support by a third party was received.

## 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.

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