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BCG vaccination excludes Covid 19 death. Part II

Research article

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Abstract

Background:

This study has re-examined the hypothesis whether BCG vaccination (shortly after birth) is responsible for lower COVID-19 mortality rates.

Methods:

New statistical methods were used to re-analyse a part of the data of the study of Michael N Bates et al.

Results:

The study design of the study of Michael N Bates et al. was appropriate enough for our purposes. The data published by Bates et al. provides very convincing support for the following hypothesis.

Conclusion:

BCG vaccine in infancy excludes COVID-19 death ($p(\text{EXCL}) = 0.9997733562$; P Value = 0.0002266438; Sample size $N = 167664$).

Keywords: BCG vaccination; Covod 19; Cause; Effect; Causal relationship k; Causality; Causation

1. Introduction

Long term responses against the SARS-CoV-2 virus or the still ongoing COVID-19 global pandemic, caused by the SARS-CoV-2 virus, might include various measures. Theoretically, even a BCG vaccination could be one of these measures. Michael N Bates et al. ¹ investigated in a case control study with very impressive sample size of 167,664 COVID-19 cases, of whom 5,016 died and 263,039 controls among other whether infant vaccination with the Bacillus Calmette–Guérin (BCG) tuberculosis vaccine, intended primarily to protect against tuberculosis, excludes COVID-19 death. Lastly, Michael N Bates et al. concluded that their “study did not support the hypothesis that BCG in infancy was protective against COVID-19.” Despite all conceivable difficulties in collecting the data in a reasonable manner, the question has to be asked, in the light of contradictory (Barukčić, 2022a) publications, whether such a conclusion is factually justified. We have good reason to believe that such a conclusion is illegitimate.

¹Bates MN, Herron TJ, Lwi SJ, Baldo JV. BCG vaccination at birth and COVID-19: a case-control study among U.S. military Veterans. *Hum Vaccin Immunother.* 2022 Dec 31;18(1):1981084. doi: 10.1080/21645515.2021.1981084. Epub 2021 Oct 13. PMID: 34643480; PMCID: PMC8986214.

2. Material and methods

2.1. Material

Bates et al. investigated anonymized records of U.S. Military Veterans treated by the Department of Veterans Affairs. Controls were Veterans not recorded as having had COVID-19. As a whole, there were 263,039 controls and 167,664 COVID-19 cases. The total number of people who have died while COVID-19 positive has been 5,016 or $(5,016/167,664)*100 = 2.991\%$. Under normal circumstances, 1-2 percent of a population annually will die from heart attacks, cancer, etc. People infected with COVID-19 may also die or be deceased for reasons other than COVID-19 to an extent at least equal to 1,676 subjects. Of the 167,664 COVID-19 positive patients, 4,778 subjects could be identified as having received a BCG vaccination in infancy. However, even the group of BCG vaccinated patients can die from heart attack, stroke and other causes, just like the rest of the general population. For this reason, we expect about 1-2 % deaths in the group of BCG vaccinated patients which are COVID-19 positive, i.e. approx. 477 subjects. However, from another point of view and assuming independence between BCG vaccination and death from COVID-19, we expect $((4778*5016)/167664) = 143$ deaths. In contrast to our justified expectation, Bates et al. reported, that only 38 subjects of this group died. This and other aspects of study of Michael N Bates et al. ² has been re-analysed.

2.2. Methods

Avoiding and treatment of logical fallacies addresses one of the most important aspects of any scientific inquiry. Sometimes logically sound definitions are of great help in order to enable us to properly infer **from something known to the something unknown**. It also goes without any need of further saying that a definition as such should be logically consistent and correct. However, theoretically, circumstances might exist under which it is required to *deal with erroneous definitions* ³ too.

2.2.1. Statistical methods

The probability of the exclusion relationship $p(\text{EXCL})$ has been calculated (Barukčić, 2021a,c) and tested for statistical significance. The chi-square goodness of fit test $\tilde{\chi}^2_{\text{Calculated}}((A_t | B_t) | A)$ and $\tilde{\chi}^2_{\text{Calculated}}((A_t | B_t) | B)$ with one degree of freedom has been used to test whether the sample data published fit the theoretical distribution of an exclusion relationship in the population. Additionally, the P Value has been calculated approximately (see also Barukčić, 2019c). The causal relationship k (Barukčić, 2016b, 2020a, 2021c) has been calculated to evaluate a possible causal relationship between the events. The cumulative, left-tailed hyper-geometric (Fisher, 1922; Gonin, 1936; Huygens and van

²Bates MN, Herron TJ, Lwi SJ, Baldo JV. BCG vaccination at birth and COVID-19: a case-control study among U.S. military Veterans. Hum Vaccin Immunother. 2022 Dec 31;18(1):1981084. doi: 10.1080/21645515.2021.1981084. Epub 2021 Oct 13. PMID: 34643480; PMCID: PMC8986214.

³Strobino, Riccardo, "Ibn Sina's Logic", The Stanford Encyclopedia of Philosophy (Fall 2018 Edition), Edward N. Zalta (ed.), URL = <https://plato.stanford.edu/archives/fall2018/entries/ibn-sina-logic/>.

Schooten, 1657; Pearson, 1899) distribution (HGD) has been used to test the one-sided left-tailed significance of the causal relationship k . As known, a positive causal relationship would contradict an exclusion relationship and vice versa.

Many times, potential publication bias among the studies is assessed by Begg's funnel plot^{4, 5, 6, 7} with something like a treatment effect (horizontal axis) and some measure of weight (inverse variance, standard error, sample size et cetera) on the vertical axis. It is not always an easy task to bring various studies together which differ in different aspects in order to re-analyse the same or for doing a meta-analysis. Due to several reasons, variability in the data of the studies and other difference might be found. These days the heterogeneity among the studies is assessed through a so called I^2 statistics^{8, 9, 10} to. Under usual circumstances, an I^2 value of 25%, 50% and 75% are regarded as low, moderate and high heterogeneity¹¹. In this investigation, we preferred to control the study (design) bias and the heterogeneity among the studies by IOI, the index of independence (Barukčić, 2019a) and by IOU, the index of unfairness (Barukčić, 2019b).

All the data were analysed using MS Excel (Microsoft Corporation, USA). P values less than 0.05 were considered statistically significant.

⁴Light RJ, Pillemer DB. Summing up. The science of reviewing research. Cambridge, MA: Harvard University Press, 1984.

⁵Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ*. 1997 Sep 13;315(7109):629-34. doi: 10.1136/bmj.315.7109.629. PMID: 9310563; PMCID: PMC2127453.

⁶Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. *Biometrics*. 1994 Dec;50(4):1088-101. PMID: 7786990.

⁷Lau J, Ioannidis JP, Terrin N, Schmid CH, Olkin I. The case of the misleading funnel plot. *BMJ*. 2006 Sep 16;333(7568):597-600. doi: 10.1136/bmj.333.7568.597. PMID: 16974018; PMCID: PMC1570006.

⁸Cochran WG. The combination of estimates from different experiments. *Biometrics* 1954; 10(1): 101-29.

⁹Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Stat Med*. 2002 Jun 15;21(11):1539-58. doi: 10.1002/sim.1186. PMID: 12111919.

¹⁰Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ*. 2003 Sep 6;327(7414):557-60. doi: 10.1136/bmj.327.7414.557. PMID: 12958120; PMCID: PMC192859.

¹¹Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ*. 2003 Sep 6;327(7414):557-60. doi: 10.1136/bmj.327.7414.557. PMID: 12958120; PMCID: PMC192859.

3. Results

3.1. BCG vaccination excludes COVID-19 death

The data published by Bates et al. (see table 1) impress with a $p(\text{IOI}) = 0,001419514$ (Barukčić, 2019a) in the positive. The study design of these data can be considered as fair. With some restrictions, we are authorized to assume that these data of the study of Bates et al. are not potentially biased. In other words, the data are of use for our purposes. The causal relationship is negative ($k < 0$). Both, the hyper-geometric distribution (P Value = 0.000000) and the Chi-square distribution as well as the normal distribution (P Value = 0,00022662) support the hypothesis that BCG vaccination excludes COVID-19 death.

3.1.0.1. Fisher's one sided left tailed exact test The hyper-geometric distribution (HGD) describes the probability of x successes in N **draws without replacement** while the same distribution is valid for all sample sizes. In contrast to the hyper-geometric distribution, the binomial distribution describes the probability of x successes in N **draws with replacement**. The one sided left tailed P Value is used when the alternative to independence is that there is a **negative relationship** between the variables investigated. Fisher's exact test (Fisher, 1935b) is a statistical significance test which is based on the hyper-geometric distribution and enable us to calculate the significance of the deviation from a null hypothesis (e.g., P Value) exactly. The left tailed P Value (no replacement, hyper-geometric distribution) (see also Fisher's exact test (see also Barnard, 1945; Boschloo, 1970; Fisher, 1935b)) is calculated as follows:

$$\begin{aligned}
 p(X \leq a) &= \sum_{i=0}^a \frac{\binom{A}{i} \binom{N-A}{B-i}}{\binom{N}{B}} \\
 &= \sum_{i=0}^{38} \frac{\binom{4778}{i} \binom{167663-4778}{5016-i}}{\binom{167663}{5016}} \\
 &= 0,00000000 \\
 &= \text{P Value (one sided left tailed)}
 \end{aligned} \tag{1}$$

Theorem 1 (BCG vaccination and COVID-19 death).

We would like to proof the hypothesis whether BCG vaccination excludes COVID-19 death.

Claim.

Null-hypothesis: BCG vaccination **does exclude** COVID-19 death .

Alternative hypothesis: BCG vaccination **does not exclude** COVID-19 death .

PROOF BY INDUCTION.

Bates et al. provided the following data on the relationship examined.

Table 1. The relationship between BCG vaccination and COVID-19 death (Study of Bates et al. , 2022).

		COVID-19 death		
		YES	NO	
BCG vaccination	YES	38	4740	4778
	NO	4978	157907	162885
		5016	162647	167663

STATISTICAL ANALYSIS.

Causal relationship $k = -0,02208158$

P Value (one sided left tailed) (HGD) = 0,00000000

p (EXCL) = 0,99977335

p (EXCL) approx.= $1-(a/A) > 0,99204688$

p (EXCL) approx.= $1-(a/B) > 0,99242424$

P VALUES.

P Value (one sided left tailed) (HGD) = 0,00000000

$\tilde{\chi}^2$ (EXCL— A_t) = 0,30221850

$\tilde{\chi}^2$ (EXCL— B_t) = 0,28787879

P Value (EXCL) = 0,00022662

PROPORTIONS.

$(a/A) \times 100 = 0,80 \%$

$(b/A) \times 100 = 99,20 \%$

$(c/\text{not } A) \times 100 = 3,06 \%$

$(d/\text{not } A) \times 100 = 96,94 \%$

$(a/B) \times 100 = 0,76 \%$

$(c/B) \times 100 = 99,24 \%$

$(b/\text{not } B) \times 100 = 2,91 \%$

$(d/\text{not } B) \times 100 = 97,09 \%$

$(A/N) \times 100 = 2,85 \%$

$(\text{not } A/N) \times 100 = 97,15 \%$

$(B/N) \times 100 = 2,99 \%$

$(\text{not } B/N) \times 100 = 97,01 \%$

ADDITIONAL STATISTICAL MEASURES.

RELATIVE RISK (RR).

RR (necessary condition) = 0,26023377

RR (sufficient condition) = 0,25995237

Relative risk reduction (RRR) = 73,98 %

OTHER STATISTICAL MEASURES.

Odds ratio (OR) = 0,25430315

Index of relationship (IOR) = -0,73416194

STUDY DESIGN.

$p(\text{IOU}) = 0,94158520$

$p(\text{IOI}) = 0,00141951$

We cannot refute the Null-hypothesis.

4. Discussion

Does it make any sense at all to try to answer the question whether BCG vaccination shortly after birth is responsible for lowering COVID-19 mortality rates more than 20 years later? The time period between BCG vaccination and COVID-19 infection in the study of Michael N Bates et al. was mostly longer than 20 years and cannot be ignored. Are we allowed to assume that the BCG vaccine is still effective even after more than 20 years later? Under these circumstances, is it any wonder that the study of Michael N Bates et al.¹² and of other studies¹³ did not provide any support for the hypothesis before. Nonetheless, is this really the last word in this matter? Absolutely not. It is known that the bacille Calmette-Guérin (BCG) tuberculosis vaccine has various immunity benefits against respiratory^{14, 15, 16, 17} infections. Accordingly, it is not in any way senseless to hypothesize that BCG vaccination might have a protective effect against the SARS-CoV-2 virus and the associated coronavirus disease 2019 (COVID-19) too. Against the assumption of a protective effect of BCG vaccination against COVID-19 infection are contradicting all in all 38 out of 167,664 COVID-19 cases who died while COVID-19 positive although they were vaccinated with BCG. Only, how sure can we be that these 38 patients died exclusively from COVID-19? Couldn't there have been other causes of death? Furthermore, these 38 cases were vaccinated with BCG. In point of fact, is this really the case with absolute certainty and if these 38 deceased patients were indeed vaccinated with BCG, was the vaccination carried out properly and with a BCG vaccine which itself was free of errors? All these possible sources of bias should not lead to the conclusion that we cannot recognise anything in principle. Rather, we should consider that where people are working mistakes have been made and will be made. For these and other reasons, it makes sense to think carefully about the use of an appropriate P Value. In consideration of what we have, our Null-hypothesis of an exclusion relationship between BCG vaccine in infancy and COVID-19 death with $p(\text{EXCL}) = 1 - (38 / 167664) = 0.9997733562$ (P Value = 0.0002266438) cannot be refuted and is in full agreement with already commonly available (Barukčić, 2022a) publications.

¹²Bates MN, Herron TJ, Lwi SJ, Baldo JV. BCG vaccination at birth and COVID-19: a case-control study among U.S. military Veterans. *Hum Vaccin Immunother.* 2022 Dec 31;18(1):1981084. doi: 10.1080/21645515.2021.1981084. Epub 2021 Oct 13. PMID: 34643480; PMCID: PMC8986214.

¹³de Chaisemartin C, de Chaisemartin L. Bacille Calmette-Guérin Vaccination in Infancy Does Not Protect Against Coronavirus Disease 2019 (COVID-19): Evidence From a Natural Experiment in Sweden. *Clin Infect Dis.* 2021 May 18;72(10):e501-e505. doi: 10.1093/cid/ciaa1223. PMID: 32829400; PMCID: PMC7499491.

¹⁴O'Neill LAJ, Netea MG. BCG-induced trained immunity: can it offer protection against COVID-19? *Nat Rev Immunol.* 2020 Jun;20(6):335-337. doi: 10.1038/s41577-020-0337-y. PMID: 32393823; PMCID: PMC7212510.

¹⁵Stensballe LG, Nante E, Jensen IP, Kofoed PE, Poulsen A, Jensen H, Newport M, Marchant A, Aaby P. Acute lower respiratory tract infections and respiratory syncytial virus in infants in Guinea-Bissau: a beneficial effect of BCG vaccination for girls community based case-control study. *Vaccine.* 2005 Jan 26;23(10):1251-7. doi: 10.1016/j.vaccine.2004.09.006. PMID: 15652667.

¹⁶Wardhana, Datau EA, Sultana A, Mandang VV, Jim E. The efficacy of Bacillus Calmette-Guerin vaccinations for the prevention of acute upper respiratory tract infection in the elderly. *Acta Med Indones.* 2011 Jul;43(3):185-90. PMID: 21979284.

¹⁷Nemes E, Geldenhuys H, Rozot V, Rutkowski KT, Ratangee F, Bilek N, Mabwe S, Makhetha L, Erasmus M, Toefy A, Mulenga H, Hanekom WA, Self SG, Bekker LG, Ryall R, Gurunathan S, DiazGranados CA, Andersen P, Kromann I, Evans T, Ellis RD, Landry B, Hokey DA, Hopkins R, Ginsberg AM, Scriba TJ, Hatherill M; C-040-404 Study Team. Prevention of M. tuberculosis Infection with H4:IC31 Vaccine or BCG Revaccination. *N Engl J Med.* 2018 Jul 12;379(2):138-149. doi: 10.1056/NEJMoa1714021. PMID: 29996082; PMCID: PMC5937161.

5. Conclusion

In compliance with the previous research it is justified to deduce the following conclusion.

BCG vaccine excludes COVID-19 death ($p(\text{EXCL}) = 0.9997733562$; P Value = 0.0002266438).

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Erratum

Unfortunately, in the past some misprints appeared especially in the section of definition. Therefore it is necessary reduce such misprints once and again as much as possible and as soon as possible.

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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Supplementary Material

The supplementary material typically includes material that does not really form part of the main article. However, the supplementary material is of use in order to better understand the main article and includes sometimes additional data such as computer code, large tables, additional figures, appendices et cetera as necessary.

6. ad Material and methods

Scientific knowledge and objective reality are more than only interrelated. It cannot be repeated often enough that objective reality or processes of objective reality is the foundation of any scientific knowledge. In point of fact, seen by light, grey is never merely simply grey. In general, human experience teaches us that a high mountain can be conquered by different paths.

6.1. ad Material

In general, it is appropriate to ensure as much as possible a broader consideration of a research question and to take into account the different facets and viewpoints of an issue investigated in order to reach a goal.

6.2. ad Methods

Definitions should help us to provide and assure a systematic approach to a scientific issue. It also goes without the need of further saying that a definition as such need to be logically consistent and correct.

6.2.1. Bernoulli distribution

A single event distribution is more or less a discrete probability distribution of any random variable X which takes a certain (observer independent) single value X_t at a **Bernoulli trial** (Uspensky, 1937, p. 45) (period of time) t with the probability $p(X_t)$. The same random variable X takes a certain single anti value \underline{X}_t at a Bernoulli trial (period of time) t with the probability $1-p(X_t)$. There are conditions in nature where a random variable X can take only the values either $+0$ or $+1$ (see Birnbaum, 1961). Under these conditions, the random variable X takes the value 1 with probability $p(X_t = +1)$ and the value 0 with probability $q(X_t = +0) = 1 - p(X_t = +1)$ while the single event distribution passes over into the **Bernoulli distribution**, named after Swiss mathematician Jacob Bernoulli (Bernoulli, 1713). Less formally, many times, the Bernoulli distribution is represented by a (possibly not biased) coin toss where 1 and 0 would represent ‘heads’ and ‘tails’ (or vice versa), respectively. However, the

relationship between random variables (Gosset, 1914) can be investigated by many (Gosset, 1908) methods, including the tools of probability theory, too.

Definition 6.1 (Two by two table of single event random variables).

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

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

$$p(A_t) \equiv p(a_t) + p(b_t) \quad (2)$$

The expectation value $E(A_t)$ follows as

$$\begin{aligned} E(A_t) &\equiv A_t \times p(A_t) \\ &\equiv A_t \times (p(a_t) + p(b_t)) \\ &\equiv (A_t \times p(a_t)) + (A_t \times p(b_t)) \\ &\equiv E(a_t) + E(b_t) \end{aligned} \quad (3)$$

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

$$\begin{aligned} E(A_t) &\equiv A_t \times p(A_t) \\ &\equiv (+0 + 1) \times p(A_t) \\ &\equiv p(A_t) \\ &\equiv p(a_t) + p(b_t) \end{aligned} \quad (4)$$

Furthermore, it is

$$p(\underline{A}_t) \equiv p(c_t) + p(d_t) \equiv (1 - p(A_t)) \quad (5)$$

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

$$\begin{aligned} E(\underline{A}_t) &\equiv A_t \times (1 - p(A_t)) \\ &\equiv A_t \times (p(c_t) + p(d_t)) \\ &\equiv (A_t \times p(c_t)) + (A_t \times p(d_t)) \\ &\equiv E(c_t) + E(d_t) \end{aligned} \quad (6)$$

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

$$\begin{aligned} E(\underline{A}_t) &\equiv A_t \times (1 - p(A_t)) \\ &\equiv (+0 + 1) \times (1 - p(A_t)) \\ &\equiv (1 - p(A_t)) \\ &\equiv p(c_t) + p(d_t) \end{aligned} \quad (7)$$

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

$$p(B_t) \equiv p(a_t) + p(c_t) \quad (8)$$

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

$$\begin{aligned} E(B_t) &\equiv B_t \times p(B_t) \\ &\equiv B_t \times (p(a_t) + p(c_t)) \\ &\equiv (B_t \times p(a_t)) + (B_t \times p(c_t)) \\ &\equiv E(a_t) + E(c_t) \end{aligned} \quad (9)$$

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

$$\begin{aligned} E(B_t) &\equiv B_t \times p(B_t) \\ &\equiv (+0 + 1) \times p(B_t) \\ &\equiv p(B_t) \\ &\equiv p(a_t) + p(c_t) \end{aligned} \quad (10)$$

Furthermore, it is

$$p(\underline{B}_t) \equiv p(b_t) + p(d_t) \equiv (1 - p(B_t)) \quad (11)$$

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

$$\begin{aligned} E(\underline{B}_t) &\equiv B_t \times (1 - p(B_t)) \\ &\equiv B_t \times (p(b_t) + p(d_t)) \\ &\equiv (B_t \times p(b_t)) + (B_t \times p(d_t)) \\ &\equiv E(b_t) + E(d_t) \end{aligned} \quad (12)$$

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

$$\begin{aligned} E(\underline{B}_t) &\equiv B_t \times (1 - p(B_t)) \\ &\equiv (+0 + 1) \times (1 - p(B_t)) \\ &\equiv (1 - p(B_t)) \\ &\equiv p(b_t) + p(d_t) \end{aligned} \quad (13)$$

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

$$\begin{aligned} E(a_t) &\equiv E(A_t \wedge B_t) \\ &\equiv (A_t \times B_t) \times p(A_t \wedge B_t) \\ &\equiv (A_t \times B_t) \times p(a_t) \end{aligned} \quad (14)$$

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

$$\begin{aligned}
 E(a_t) &\equiv E(A_t \wedge B_t) \\
 &\equiv (A_t \times B_t) \times p(A_t \wedge B_t) \\
 &\equiv ((+0+1) \times (+0+1)) \times p(A_t \wedge B_t) \\
 &\equiv p(A_t \wedge B_t) \\
 &\equiv p(a_t)
 \end{aligned} \tag{15}$$

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

$$\begin{aligned}
 E(b_t) &\equiv E(A_t \wedge \neg B_t) \\
 &\equiv (A_t \times \neg B_t) \times p(A_t \wedge \neg B_t) \\
 &\equiv (A_t \times \neg B_t) \times p(b_t)
 \end{aligned} \tag{16}$$

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

$$\begin{aligned}
 E(b_t) &\equiv E(A_t \wedge \neg B_t) \\
 &\equiv (A_t \times \neg B_t) \times p(A_t \wedge \neg B_t) \\
 &\equiv ((+0+1) \times (+0+1)) \times p(A_t \wedge \neg B_t) \\
 &\equiv p(A_t \wedge \neg B_t) \\
 &\equiv p(b_t)
 \end{aligned} \tag{17}$$

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

$$\begin{aligned}
 E(c_t) &\equiv E(\neg A_t \wedge B_t) \\
 &\equiv (\neg A_t \wedge B_t) \times p(\neg A_t \wedge B_t) \\
 &\equiv (\neg A_t \wedge B_t) \times p(c_t)
 \end{aligned} \tag{18}$$

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

$$\begin{aligned}
 E(c_t) &\equiv E(\neg A_t \wedge B_t) \\
 &\equiv (\neg A_t \times B_t) \times p(\neg A_t \wedge B_t) \\
 &\equiv ((+0+1) \times (+0+1)) \times p(\neg A_t \wedge B_t) \\
 &\equiv p(\neg A_t \wedge B_t) \\
 &\equiv p(c_t)
 \end{aligned} \tag{19}$$

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

$$\begin{aligned}
 E(d_t) &\equiv E(\neg A_t \times \neg B_t) \\
 &\equiv (\neg A_t \times \neg B_t) \times p(\neg A_t \wedge \neg B_t) \\
 &\equiv (\neg A_t \times \neg B_t) \times p(d_t)
 \end{aligned} \tag{20}$$

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

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

In general, it is

$$p(a_t) + p(b_t) + p(c_t) + p(d_t) \equiv +1 \tag{22}$$

Table 2 provide us with an overview of the definitions above.

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

		Conditioned B _t		
		TRUE	FALSE	
Condition A _t	TRUE	p(a _t)	p(b _t)	p(A _t)
	FALSE	p(c _t)	p(d _t)	p(<u>A</u> _t)
		p(B _t)	p(<u>B</u> _t)	+1

In our understanding, it is

$$p(B_t) + p(\Lambda_t) \equiv p(a_t) + p(c_t) + p(\Lambda_t) \equiv p(a_t) + p(b_t) \equiv p(A_t) \tag{23}$$

or

$$p(c_t) + p(\Lambda_t) \equiv p(b_t) \tag{24}$$

Under conditions of Einstein's general theory of relativity, Λ denotes the Einstein cosmological (Einstein, 1917) 'constant'.

6.2.2. Binomial random variables

The binomial (see Pearson, 1895, p. 351) distribution (see Cramér, 1937) 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

$$p(X_t = k) \equiv \binom{n}{k} \cdot p^k \cdot q^{n-k} \tag{25}$$

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

$$p(X_t \leq k) \equiv 1 - p(X_t > k) \equiv \sum_{t=0}^k \binom{n}{t} \cdot p^t \cdot q^{n-t} \tag{26}$$

or as

$$p(X_t > k) \equiv 1 - p(X_t \leq k) \equiv 1 - \sum_{t=0}^k \binom{n}{t} \cdot p^t \cdot q^{n-t} \quad (27)$$

Furthermore, it is

$$p(X_t < k) \equiv 1 - p(X_t \geq k) \equiv \sum_{t=0}^{k-1} \binom{n}{t} \cdot p^t \cdot q^{n-t} \quad (28)$$

or

$$p(X_t \geq k) \equiv 1 - p(X_t < k) \equiv 1 - \sum_{t=0}^{k-1} \binom{n}{t} \cdot p^t \cdot q^{n-t} \quad (29)$$

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

$$p(X_t = k) \equiv p \cdot q^{k-1} \quad (30)$$

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

$$p(X_t = r) \equiv \binom{k+r-1}{k-1} p^k \cdot q^r \quad (31)$$

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

Definition 6.2 (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, 2022d](#)) as

$$\sigma(X_t)^2 \equiv N \times N \times p(X_t) \times (1 - p(X_t)) \quad (32)$$

Definition 6.3 (Two by two table of Binomial random variables).

Let $a, b, c, d, A, \underline{A}, B$, and \underline{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

$$\begin{aligned} A &= N \times E(A_t) \\ &\equiv N \times (A_t \times p(A_t)) \\ &\equiv N \times (p(A_t) + p(B_t)) \\ &\equiv N \times p(A_t) \end{aligned} \quad (33)$$

and

$$\begin{aligned}
 B &= N \times E(B_t) \\
 &\equiv N \times (B_t \times p(B_t)) \\
 &\equiv N \times (p(A_t) + p(c_t)) \\
 &\equiv N \times p(B_t)
 \end{aligned} \tag{34}$$

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

$$a \equiv N \times (E(A_t)) \equiv N \times (p(A_t)) \tag{35}$$

and

$$b \equiv N \times (E(B_t)) \equiv N \times (p(B_t)) \tag{36}$$

and

$$c \equiv N \times (E(c_t)) \equiv N \times (p(c_t)) \tag{37}$$

and

$$d \equiv N \times (E(d_t)) \equiv N \times (p(d_t)) \tag{38}$$

and

$$a + b + c + d \equiv A + \underline{A} \equiv B + \underline{B} \equiv N \tag{39}$$

Table 3 provide us again an overview of a two by two contingency (see also [Pearson, 1904b](#), p. 33) table of Binomial random variables.

Table 3. The two by two table of Binomial random variables

		Conditioned B_t		
		TRUE	FALSE	
Condition A_t	TRUE	a	b	A
	FALSE	c	d	<u>A</u>
		B	<u>B</u>	N

“Such a table is termed a contingency table, and the ultimate scientific statement of description of the relation between two things can always be thrown back upon such a contingency table ... Once the reader realizes the nature of such a table, he will have grasped the essence of the conception of association between cause and effect, and the nature of its ideal limit in causation. ”

(see also [Pearson, 1911](#), p. 159)

6.3. Hyper-geometric distribution

In general, the probability distribution of a hyper-geometric random variable X is called a hyper-geometric distribution. In contrast to the binomial distribution, the hyper-geometric distribution is characterised by the lack of replacements. With this in mind, the probability mass function of the hyper-geometric distribution (see [Fisher, 1922](#); [Gonin, 1936](#); [Huygens and van Schooten, 1657](#); [Pearson, 1899](#)), denoted as $p(X = a)$, is defined as

$$p(X = a) = \frac{\binom{A}{a} \binom{N-A}{B-a}}{\binom{N}{B}} \quad (40)$$

6.3.1. Fisher's exact test

Fisher's exact test is a statistical significance test which is often used in the analysis of contingency tables while applying the hyper-geometric distribution ¹⁸. This statistical methodology opens up the possibility to calculate the significance of the deviation from a null hypothesis (e.g., P Value) exactly. Strangely enough, it is common practice to use Fisher's exact test ([Fisher, 1935b](#)) for a sample which is very small. However, it is necessary to point out that Fisher's exact test is valid for all sample sizes without any restriction. Fisher's Exact Test is using the following null and alternative hypotheses:

H_0 : (null hypothesis)

The two random variables are independent.

H_1 : (alternative hypothesis)

The two random variables are not independent.

A cumulative hyper-geometric probability denotes whether a hyper-geometric random variable is greater than or equal to some specified lower limit and less than or equal to some specified upper limit. The P Value of an one-sided right tailed Fisher's exact test is calculated as

$$p(X \geq a) = 1 - \sum_{i=0}^{a-1} \frac{\binom{A}{i} \binom{N-A}{B-i}}{\binom{N}{B}} \quad (41)$$

The P Value of an one-sided left tailed Fisher's exact test is calculated as

$$p(X \leq a) = \sum_{i=0}^a \frac{\binom{A}{i} \binom{N-A}{B-i}}{\binom{N}{B}} \quad (42)$$

¹⁸Kim HY. Statistical notes for clinical researchers: Chi-squared test and Fisher's exact test. *Restor Dent Endod.* 2017 May;42(2):152-155. doi: 10.5395/rde.2017.42.2.152. Epub 2017 Mar 30. PMID: 28503482; PMCID: PMC5426219.

6.3.2. Bonferroni correction

Sometimes, the more inferences are made on a certain data body (i. e. subgroup analyses), the more likely erroneous inferences might realise. In other words, several independent or dependent statistical tests performed simultaneously on the same data body can induce the so called multiple testing problem. Various statistical techniques have been developed to address this problem. The Bonferroni multiple-comparison correction (see [Bonferroni, 1936](#); [Dunn, 1961](#)) is one of the solutions proposed to compensate for the number of inferences being made.

Example

An investigation is testing $m = 20$ hypotheses with a desired $\alpha = 0.05$. Under these circumstances, the Bonferroni correction proposes to test each individual hypothesis at a single α_i

$$\alpha_i = \frac{\alpha}{m} = \frac{0,05}{20} = 0,0025 \quad (43)$$

level where m is the total number hypotheses tested and α is the significance level. By requiring a stricter significance threshold, **an inflation of false positive rates** can be prevented. In the context of further scientific development, there have been several trials to improve the Bonferroni method. One of these attempts is the so called Rom's Method published 1990 by Rom (see [Rom, 1990](#)) himself.

6.3.3. Sensitivity and specificity

Definition 6.4 (Sensitivity and specificity).

A (medical) test should measure what is supposed to measure. However, the extent to which a test measures what it is supposed to measure varies and is seldom equal to 100 %. In other words, it is necessary to check once and again the accuracy or the validity of a test, we have to fight it out in detail. In clinical practice, the concept of sensitivity and specificity is commonly used to quantify the diagnostic ability of a (medical) test. Sensitivity and specificity were introduced by the American ¹⁹, ²⁰, ²¹, ²² biostatistician Jacob Yerushalmy (see also Yerushalmy, 1947) in the year 1947. The interior logic of sensitivity and specificity is best illustrated using a conventional two- by-two (2 x 2) table (see table 4).

Table 4. Sensitivity and specificity

		Disease B_t		
		present	absent	
Test	positive	a (true positive)	b (false positive)	A
A_t	negative	c (false negative)	d (true negative)	\underline{A}
		B	\underline{B}	N

The ability of a positive test (A_t) to correctly classify an individual as diseased (B_t) is defined as the proportion of true positives that are correctly identified by the test (a) divided by the individuals being truly diseased (B_t). In general, sensitivity follows as

$$\text{Sensitivity}(A | B) \equiv p(a | B) \equiv \frac{a}{B} \quad (44)$$

The specificity of a test is the ability of a negative test (\underline{A}_t) to correctly classify an individual as not diseased (\underline{B}_t) and is defined as the proportion of true negative that are correctly identified by the test (d) divided by the individuals being truly not diseased (\underline{B}_t). In general, specificity is given by the equation

$$\text{Specificity}(\underline{A}, \underline{B}) \equiv p(d | \underline{B}) \equiv \frac{d}{\underline{B}} \quad (45)$$

The positive predictive value (PPV) is defined as

$$PPV(A, B) \equiv \frac{a}{a + b} \quad (46)$$

¹⁹Yerushalmy Jacob. Statistical problems in assessing methods of medical diagnosis, with special reference to X-ray techniques. Public Health Rep. 1947 Oct 3;62(40):1432-49. PMID: 20340527.

²⁰Galen RS, Gambino SR. Beyond normality-the predictive value and efficiency of medical diagnosis. New York: NY:Wiley; 1975.

²¹Altman DG, Bland JM. Diagnostic tests. 1: Sensitivity and specificity. BMJ. 1994 Jun 11;308(6943):1552. doi: 10.1136/bmj.308.6943.1552. PMID: 8019315; PMCID: PMC2540489.

²²Parikh R, Mathai A, Parikh S, Chandra Sekhar G, Thomas R. Understanding and using sensitivity, specificity and predictive values. Indian J Ophthalmol. 2008 Jan-Feb;56(1):45-50. doi: 10.4103/0301-4738.37595. PMID: 18158403; PMCID: PMC2636062.

The negative predictive value (NPV) is defined as

$$NPV(A, B) \equiv \frac{d}{c + d} \quad (47)$$

Example.

The importance of sensitivity and specificity in any research should certainly not be underestimated. However, it is essential not to lose sight of the major advantages and limitations²³ of these measures. In the following, in order to avoid misconceptions about sensitivity, specificity et cetera, let us consider a test with a sensitivity of 95 % and a specificity of 95 %. A two-by-two table is used as an illustration (see table 5).

Table 5. Sensitivity and specificity

		Disease B _t		
		present	absent	
Test	positive	95	5	100
A _t	negative	5	95	100
		100	100	200

Sensitivity is calculated as

$$Sensitivity(A | B) \equiv p(a | B) \equiv 100 \times \frac{a}{B} \equiv \frac{95}{100} \equiv 95\% \quad (48)$$

There are at least two kinds of medical tests, diagnostic tests and screening tests. Depending on the type of medical test, there are other logical implications. A screening test should correctly identify all people who suffer from a certain disease or all people with a certain outcome. Therefore, the sensitivity of a screening test should be at best 100 %. Under these conditions, we obtain **without** positive test **no** disease/outcome present. However, confusion should be avoided with regard to the adequacy and usefulness of the sensitivity of a screening test. The sensitivity of a test does not take into account events which are false positive (b) or which are true negative (d), the meaning of these events is ignored completely by sensitivity. Therefore, sensitivity is blind on one eye since its inception and underestimates the extent to which a screening test is able to identify the likely presence of a condition of interest. We calculated a 95 % sensitivity while the true possibility of the test to detect a disease is (see table 5)

$$SINE(A, B) \equiv 100 \times \frac{a + b + d}{N} \equiv \frac{95 + 5 + 95}{200} \equiv 97.5\% \quad (49)$$

In a way similar to sensitivity, specificity is not much better. Diagnostic tests are able to identify people who do not have a certain condition. Specificity is calculated as

$$Specificity(\underline{A} | \underline{B}) \equiv p(d | \underline{B}) \equiv 100 \times \frac{d}{\underline{B}} \equiv \frac{95}{100} \equiv 95\% \quad (50)$$

²³Trevethan R. Sensitivity, Specificity, and Predictive Values: Foundations, Plabilities, and Pitfalls in Research and Practice. *Front Public Health*. 2017 Nov 20;5:307. doi: 10.3389/fpubh.2017.00307. PMID: 29209603; PMCID: PMC5701930.

However, specificity does not take into account any individuals who suffer from a disease, who do have the condition and is well-known for being imperfect because of this fact too. Specificity underestimates the possibility of a diagnostic test to detect a disease. Above, the specificity has been calculated as being 95 %. In point of fact, the ability of the test to detect a disease or the relationship **if** test positive **then** disease present is much better and has to be calculated as (see table 5)

$$IMP(A,B) \equiv \frac{a+c+d}{N} \equiv \frac{95+5+95}{200} \equiv 97.5\% \quad (51)$$

As can be seen, the test detected the disease in 97.5 % while specificity allows only 95 %. How valuable is such a measure epistemologically? Measures like sensitivity and specificity are blurring of the issue, do risk leading us astray and disorient us systematically again and again. These measures should be abandoned.

6.3.4. Odds ratio (OR)

Definition 6.5 (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, 1935a, 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 6. The odds' ratio (OR) is defined as

Table 6. The two by two table of random variables

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

$$\begin{aligned}
 OR(A_t, B_t) &\equiv \left(\frac{a_t}{b_t} \right) / \left(\frac{c_t}{d_t} \right) \\
 &\equiv \left(\frac{a_t \times d_t}{b_t \times c_t} \right)
 \end{aligned}
 \tag{52}$$

Remark 6.1. 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. 52. 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. 52. 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.

6.3.5. Yule's coefficient of association (Q)

At the end, odds ratio (Cox, 1958; Fisher, 1935a, p. 50) is nothing more but Yule's coefficient of association (Yule and Pearson, 1900) Q re-written in a non-normalized form. It is

$$\begin{aligned}
 Q(A_t, B_t) &\equiv \frac{(OR(A_t, B_t)) - 1}{(OR(A_t, B_t)) + 1} \\
 &\equiv \frac{\left(\frac{a_t \times d_t}{b_t \times c_t}\right) - 1}{\left(\frac{a_t \times d_t}{b_t \times c_t}\right) + 1} \\
 &\equiv \frac{\left(\frac{a_t \times d_t}{b_t \times c_t}\right) - \frac{b_t \times c_t}{b_t \times c_t}}{\left(\frac{a_t \times d_t}{b_t \times c_t}\right) + \frac{b_t \times c_t}{b_t \times c_t}} \\
 &\equiv \frac{(a_t \times d_t) - (b_t \times c_t)}{(a_t \times d_t) + (b_t \times c_t)} \\
 &\equiv \frac{(a_t \times d_t) - (b_t \times c_t)}{(a_t \times d_t) + (b_t \times c_t)}
 \end{aligned} \tag{53}$$

6.3.6. Relative risk (RR)

6.3.6.1. Relative risk (RR_{nc})

Definition 6.6 (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

$$\begin{aligned}
 RR(A_t, B_t)_{nc} &\equiv \frac{\frac{p(a_t)}{p(A_t)}}{\frac{p(c_t)}{p(NotA_t)}} \\
 &\equiv \frac{p(a_t) \times p(NotA_t)}{p(c_t) \times p(A_t)} \\
 &\equiv \frac{N \times p(a_t) \times N \times p(NotA_t)}{N \times p(c_t) \times N \times p(A_t)} \\
 &\equiv \frac{a_t \times (NotA_t)}{c_t \times A_t} \\
 &\equiv \frac{EER(A_t, B_t)}{CER(A_t, B_t)}
 \end{aligned} \tag{54}$$

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.

6.3.6.2. Relative risk (RR (sc))

Definition 6.7 (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

$$\begin{aligned}
 RR(A_t, B_t)_{sc} &\equiv \frac{\frac{p(a_t)}{p(B_t)}}{\frac{p(b_t)}{p(Not B_t)}} \\
 &\equiv \frac{p(a_t) \times p(Not B_t)}{p(b_t) \times p(B_t)} \\
 &\equiv \frac{N \times p(a_t) \times N \times p(Not B_t)}{N \times p(b_t) \times N \times p(B_t)} \\
 &\equiv \frac{a_t \times (Not B_t)}{b_t \times B_t} \\
 &\equiv \frac{OPR(A_t, B_t)}{CPR(A_t, B_t)}
 \end{aligned} \tag{55}$$

6.3.6.3. Relative risk reduction (RRR)

Definition 6.8 (Relative risk reduction (RRR)).

In general, an intervention which leads to relative risk (RR) greater than 1, might increase the risk of a bad outcome to; if the RR is less than 1, then the risk of a bad outcome is usually decreased. Relative risk reduction (RRR) is an indicator of the amount to which a an intervention (i.e. treatment) reduced the risk of bad outcomes relative to a control group which was not exposed to an intervention (i.e. no treatment or placebo).

$$\begin{aligned}
 RRR(A_t, B_t) &\equiv \frac{CER(A_t, B_t) - EER(A_t, B_t)}{CER(A_t, B_t)} \\
 &= 1 - RR_{nc}(A_t, B_t)
 \end{aligned} \tag{56}$$

6.3.6.4. Vaccine efficacy (VE)

Definition 6.9 (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.

$$\begin{aligned} VE(A_t, B_t) &\equiv 100 \times (1 - RR(A_t, B_t)) \\ &\equiv 100 \times \left(\frac{CER(A_t, B_t) - EER(A_t, B_t)}{CER(A_t, B_t)} \right) \end{aligned} \quad (57)$$

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.

6.3.6.5. Experimental event rate (EER)

Definition 6.10 (Experimental event rate (EER)).

$$EER(A_t, B_t) \equiv \frac{p(a_t)}{p(A_t)} = \frac{a_t}{a_t + b_t} \quad (58)$$

Definition 6.11 (Control event rate (CER)).

$$CER(A_t, B_t) \equiv \frac{p(c_t)}{p(\underline{A}_t)} = \frac{c_t}{c_t + d_t} \quad (59)$$

6.3.6.6. Absolute risk reduction (ARR)

Definition 6.12 (Absolute risk reduction (ARR)).

$$\begin{aligned} ARR(A_t, B_t) &\equiv \frac{p(c_t)}{p(\underline{A}_t)} - \frac{p(a_t)}{p(A_t)} \\ &= \frac{c_t}{c_t + d_t} - \frac{a_t}{a_t + b_t} \\ &= CER(A_t, B_t) - EER(A_t, B_t) \end{aligned} \quad (60)$$

6.3.6.7. Absolute risk increase (ARI)

Definition 6.13 (Absolute risk increase (ARI)).

$$\begin{aligned} ARI(A_t, B_t) &\equiv \frac{p(a_t)}{p(A_t)} - \frac{p(c_t)}{p(\underline{A}_t)} \\ &= EER(A_t, B_t) - CER(A_t, B_t) \end{aligned} \quad (61)$$

6.3.6.8. Number needed to treat (NNT)

Definition 6.14 (Number needed to treat (NNT)).

$$NNT(A_t, B_t) \equiv \frac{1}{CER(A_t, B_t) - EER(A_t, B_t)} \quad (62)$$

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.

6.3.6.9. Number needed to harm (NNH)

Definition 6.15 (Number needed to harm (NNH)).

$$NNH(A_t, B_t) \equiv \frac{1}{EER(A_t, B_t) - CER(A_t, B_t)} \quad (63)$$

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.

6.3.6.10. Outcome prevalence rate (OPR)

Definition 6.16 (Outcome prevalence rate (OPR)).

$$OPR(A_t, B_t) \equiv \frac{p(a_t)}{p(B_t)} = \frac{a_t}{a_t + c_t} \quad (64)$$

6.3.6.11. Control prevalence rate (CPR)

Definition 6.17 (Control prevalence rate (CPR)).

$$CPR(A_t, B_t) \equiv \frac{p(b_t)}{p(\underline{B}_t)} = \frac{b_t}{b_t + d_t} \quad (65)$$

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.

6.3.6.12. Absolute prevalence reduction (APR)

Definition 6.18 (Absolute prevalence reduction (APR)).

$$APR(A_t, B_t) \equiv CPR(A_t, B_t) - OPR(A_t, B_t) \quad (66)$$

6.3.6.13. Absolute prevalence increase (API)

Definition 6.19 (Absolute prevalence increase (API)).

$$API(A_t, B_t) \equiv OPR(A_t, B_t) - CPR(A_t, B_t) \quad (67)$$

6.3.6.14. Relative prevalence reduction (RPR)

Definition 6.20 (Relative prevalence reduction (RPR)).

$$\begin{aligned} RPR(A_t, B_t) &\equiv \frac{CPR(A_t, B_t) - OPR(A_t, B_t)}{CPR(A_t, B_t)} \\ &= 1 - RR(A_t, B_t)_{sc} \end{aligned} \quad (68)$$

6.3.6.15. The index NNS

Definition 6.21 (The index NNS).

$$NNS(A_t, B_t) \equiv \frac{1}{CPR(A_t, B_t) - OPR(A_t, B_t)} \quad (69)$$

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

6.3.6.16. The index NNI

Definition 6.22 (The index NNI).

$$NNI(A_t, B_t) \equiv \frac{1}{OPR(A_t, B_t) - CPR(A_t, B_t)} \quad (70)$$

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

6.3.7. Index of relationship (IOR)

Definition 6.23 (Index of relationship (IOR)).

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

$$\begin{aligned} IOR(A_t, B_t) &\equiv \left(\frac{p(A_t \wedge B_t)}{p(B_t) \times p(A_t)} \right) - 1 \\ &\equiv \left(\frac{p(a_t)}{p(B_t) \times p(A_t)} \right) - 1 \\ &\equiv \left(\left(\frac{N \times N \times p(a_t)}{N \times p(B_t) \times N \times p(A_t)} \right) - 1 \right) \\ &\equiv \left(\left(\frac{N \times a}{A \times B} \right) - 1 \right) \end{aligned} \quad (71)$$

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 $p(A_t \text{ AND } B_t)$ at the same Bernoulli trial t and a , A and B may denote the expectation values.

Definition 6.24 (Multi dimensional index of relationship (NIOR)).

The multi dimensional index of relationship (NIOR) is defined as

$$\begin{aligned} NIOR(A_t, B_t) &\equiv \left(\frac{N^k \times p(1A_t \wedge 2A_t \cdots kA_t)}{N \times (p(1A_t)) N \times (p(2A_t)) \cdots N \times (p(kA_t))} \right) - 1 \\ &\equiv \left(\frac{N^{k-1} \times E(1A_t \wedge 2A_t \cdots kA_t)}{E(1A_t) \times E(2A_t) \cdots E(kA_t)} \right) - 1 \end{aligned} \quad (72)$$

where N is the sample size and $p(1A_t \wedge 2A_t \cdots kA_t)$ is the joint distribution function.

However, there might exist circumstances where a multi dimensional index of relationship might take the form of the following equation.

$$\begin{aligned} NIOR(A_t, B_t) &\equiv \left(\frac{1N \times 2N \times \cdots kN \times p(1A_t \wedge 2A_t \cdots kA_t)}{(1N \times p(1A_t)) \times (2N \times p(2A_t)) \cdots (kN \times p(kA_t))} \right) - 1 \\ &\equiv \left(\frac{1N \times 2N \times \cdots kN \times p(1A_t \wedge 2A_t \cdots kA_t)}{E(1A_t) \times E(2A_t) \cdots E(kA_t)} \right) - 1 \end{aligned} \quad (73)$$

6.3.8. Independence

Definition 6.25 (Independence).

The philosophical, mathematical (Kolmogoroff, Andreï Nikolaevich, 1933) and physical (Einstein, 1948) et cetera concept of independence is of fundamental (Kolmogoroff, Andreï Nikolaevich, 1933) importance in (natural) sciences as such. Therefore, it is appropriate to investigate the concept of independence as completely as possible. In fact, de Moivre sums it up in his book *The Doctrine of Chances* (see also Moivre, 1718). “Two Events are **independent**, when they have no connexion one with the other, and that the happening of one neither forwards nor obstructs the happening of the other. Two events are **dependent**, when they are so connected together as that the Probability of either’s happening is alter’d by the happening of the other.” (see also Moivre, 1756, p. 6) We should consider Kolmogorov’s position on independence before the mind’s eye too. “The concept of mutual independence of two or more experiments holds, in a certain sense, a central position in the theory of probability.” (see also Kolmogorov, Andreï Nikolaevich, 1950, p. 8) Furthermore, it is insightful to recall even 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 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 . De Moivre brings it to the point. “From what has been said, it follows, that if a Fraction expresses the Probability of an Event, and another Fraction the Probability of another Event, and those two Events are independent ; the Probability that both those Events will Happen, will be the Product of those two Fractions.” (see also Moivre, 1718, p. 4). Mathematically, in terms of probability theory, independence (Kolmogoroff, Andreï Nikolaevich, 1933) of events at the same (period of) time (i.e. Bernoulli trial) t is defined as

$$\begin{aligned} p(A_t \wedge B_t) &\equiv p(A_t) \times p(B_t) \equiv p(a_t) \\ &\equiv \frac{\sum_{t=1}^N (A_t \wedge B_t)}{N} \equiv \frac{N \times (p(a_t))}{N} \equiv 1 - p(A_t | B_t) \equiv 1 - p(A_t \uparrow B_t) \end{aligned} \quad (74)$$

while $p(A_t \cap B_t)$ is the joint probability of the events A_t and B_t at a same Bernoulli trial t , $p(A_t)$ is the probability of an event A_t at a same Bernoulli trial t , and $p(B_t)$ is the probability of an event B_t at a same Bernoulli trial t . With respect to a two-by-two table, **under conditions of independence**, it is

$$p(b_t) \equiv p(A_t) \times p(\underline{B}_t) \quad (75)$$

or

$$p(c_t) \equiv p(\underline{A}_t) \times p(B_t) \quad (76)$$

and

$$p(d_t) \equiv p(\underline{A}_t) \times p(\underline{B}_t) \quad (77)$$

Example. 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). Thus far, as a result of the thoughts before, 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)? Meanwhile, this question is more or less already answered 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. It is remarkable that **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.

6.3.9. Dependence

Definition 6.26 (Dependence).

Whilst it may be true that the occurrence of an event A_t does not affect the occurrence of an other event B_t the contrary is of no minor importance. Under these other conditions, events, trials and random variables et cetera are dependent on each other too. The dependence of events (Barukčić, 1989, p. 57-61) is defined as

$$p\left(\underbrace{A_t \wedge B_t \wedge C_t \wedge \dots}_{n \text{ random variables}}\right) \equiv \sqrt[n]{\underbrace{p(A_t) \times p(B_t) \times p(C_t) \times \dots}_{n \text{ random variables}}} \quad (78)$$

6.4. Conditions

Is there a difference and what is the difference between a cause and a condition? Even if a condition and a cause are deeply related, there are circumstances where a sharp distinction between a cause and a condition is necessary. However, exactly this has been denied by John Stuart Mill (1806-1873) and his regularity view of causality (see [Mill, 1843b](#)) and several (see [Hansemann, David Paul von, 1912](#); [Verworn, 1912](#)) other (see [Ducasse, 1926](#), p. 58) authors (see [Mackie, 1965, 1974](#)) too. What might seem to be a theoretical difficulty for numerous, renowned authors (see [Bar, Carl Ludwig von, 1871](#)) is none for Mill. Mill simply reduced a cause to a condition and claimed that “... the real cause of the phenomenon is the assemblage of all its conditions.” (see [Mill, 1843a](#), p. 403) There are, however, many difficulties in this account. Reduction of a cause to a simple condition is logically inconsistent and theoretically not understandable neither from a fundamental theoretical point of view nor in other aspects like our everyday life.

Theorem 2 (The difference between a cause and a necessary condition). *A cause and a necessary condition are not identical.*

Proof by counter-example. Whatever the attitude of the individual to the necessary condition and to the cause might be, we all cannot avoid essential and generally known facts. In point of fact, it is and it can be considered a well known and certain human knowledge that without gaseous oxygen, water and other factors, there would be no human life; hence gaseous oxygen, water and other factors are necessary conditions for the existence of human beings. Nevertheless, necessary conditions such as gaseous oxygen, water and other necessary conditions cannot be considered as the cause of human life. In other words, a cause and a necessary condition are different. □

However, this difference, which is obvious, is also a relative difference too and not an absolute difference. We know that **without** a cause **no** effect. Thus far, even if a cause is not identical with a necessary condition, at the same time, a cause is a necessary condition too.

Theorem 3 (The difference between a cause and a sufficient condition). *A cause and a sufficient condition are not identical.*

Proof by counter-example. Is it possible to generalize the finding before? One may like it or not, gaseous oxygen, water and other factors are necessary conditions for the existence of human beings. However, this what we have take to be ordinarily knowledge has further consequences. A consequence of this nature given relationship is that it is true that **if** living people can be identified, **then** gaseous oxygen is be present too. However, this does not mean that living people are also the cause of the gaseous oxygen. We must therefore accept in principle that a cause and a sufficient condition differ, both are not identical. □

Even if this conclusion is correct, it is also correct too that the relationship **if** cause **then** effect is also valid and need to be valid too, if the causal relationship is a deterministic one. While it is possible and necessary to distinguish these different notions like other fundamental scientific concepts, the difficulties in providing complete precision in answering the question of necessary and sufficient conditions lead us straightforward to the relationship between a cause and its own effect. By time in Bio-sciences, **conditions** have more or less been suppressed by **risk factors**, a pre-stage of conditions.

6.4.1. Exclusion relationship

Definition 6.27 (Exclusion relationship [EXCL]).

Mathematically, the exclusion(see also Barukčić, 2021a) relationship ²⁴ (EXCL), denoted by $p(A_t | B_t)$ in terms of statistics and probability theory, is defined(see also Barukčić, 1989, p. 68-70) as

$$\begin{aligned}
 p(A_t | B_t) &\equiv p(A_t \uparrow B_t) \\
 &\equiv p(b_t) + p(c_t) + p(d_t) \\
 &\equiv \frac{N \times (p(b_t) + p(c_t) + p(d_t))}{N} \\
 &\equiv \frac{\sum_{t=1}^N (\underline{A_t} \vee \underline{B_t})}{N} \equiv \frac{b + c + d}{N} \\
 &\equiv \frac{b + \underline{A}}{N} \\
 &\equiv \frac{c + \underline{B}}{N} \\
 &\equiv +1
 \end{aligned} \tag{79}$$

Based on the 1913 Henry Maurice Sheffer (1882-1964) relationship, the Sheffer stroke(Nicod, 1917; Sheffer, 1913) usually denoted by \uparrow , it is $p(A_t \wedge B_t) \equiv 1 - p(A_t | B_t)$ (see table 7).

Table 7. A_t excludes B_t and vice versa.

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

Example 6.1. Pfizer Inc. and BioNTech SE ²⁵ reported results from a Phase 3 COVID-19 vaccine trial. “A total of ... 43,448 received injections: 21,720 with BNT162b2 and 21,728 with placebo. There were 8 cases of Covid-19 ... among participants assigned to receive BNT162b2 and 162 cases among those assigned to placebo; ” (see Polack et al., 2020). The following table (see table 8) provides us with a suitable overview.

²⁴Barukčić, Ilija. (2021). Mutually exclusive events. Causation, 16(11), 5–57. <https://doi.org/10.5281/zenodo.5746415>

²⁵Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, Perez JL, Pérez Marc G, Moreira ED, Zerbini C, Bailey R, Swanson KA, Roychoudhury S, Koury K, Li P, Kalina WV, Cooper D, Frenck RW Jr, Hammitt LL, Türeci Ö, Nell H, Schaefer A, Ünal S, Tresnan DB, Mather S, Dormitzer PR, Şahin U, Jansen KU, Gruber WC; C4591001 Clinical Trial Group. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. N Engl J Med. 2020 Dec 31;383(27):2603-2615. doi: 10.1056/NEJMoa2034577. Epub 2020 Dec 10. PMID: 33301246; PMCID: PMC7745181.

Table 8. BNT162b and COVID-19 (Study Polack et al., 2020).

		COVID-19		
		YES	NO	
BNT162b	YES	8	21712	21720
	NO	162	21566	21728
		170	43278	43448
STATISTICAL ANALYSIS.				
Causal relationship k =		-0,0567641832		
p (EXCL) =		0,9998158718		
p (EXCL) approx.=		0,9529411765		
$\tilde{\chi}^2$ (EXCL— A _t) =		0,0029		
$\tilde{\chi}^2$ (EXCL— B _t) =		0,3765		
p Value (EXCL) =		0,0001841112		
RELATIVE RISK (RR).				
RR (nc) =		0,0494		
RR (sc) =		0,0938		
Vaccine efficacy (%) =		95,0599		
ADDITIONAL MEASURES.				
OR =		0,4965		
IOR =		-0,9059		
STUDY DESIGN.				
p(IOU)=		0,496179341		
p(IOI)=		0,495995213		

The exclusion relationship is calculated in detail as follows.

$$\begin{aligned}
 p(\text{Vaccine : BNT162b2} \mid \text{COVID} - 19(\text{infection})) &\equiv p(b_t) + p(c_t) + p(d_t) \\
 &\equiv 1 - p(a_t) \\
 &\equiv 1 - \left(\frac{8}{43538} \right) \\
 &\equiv +0,99981625
 \end{aligned} \tag{80}$$

with a P Value = 0,000184.

6.4.1.1. Fisher's exact test Fisher's exact test is a statistical significance test which enable us to calculate the significance of the deviation from a null hypothesis (e.g., P-value) exactly. It is common practice to use Fisher's exact test (Fisher, 1935b) often when the sample is very small but Fisher's exact test is valid for all sample sizes.

$$\begin{aligned}
p(X \leq a) &= \sum_{i=0}^a \frac{\binom{A}{i} \binom{N-A}{B-i}}{\binom{N}{B}} \\
&= \sum_{i=0}^8 \frac{\binom{21720}{i} \binom{43448-21720}{170-i}}{\binom{43448}{170}} \\
&= \frac{6.7686358877995}{100\,000\,000\,000\,000\,000\,000} \\
&= 6.7686358877995e-20 \\
&= \text{P Value (one sided left tailed)}
\end{aligned} \tag{81}$$

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

$$\begin{aligned}
p(A_t | B_t) &\equiv p(\underline{A}_t \cup \underline{B}_t) \\
&\equiv 1 - p(A_t \cap B_t) \\
&\equiv 1 - \int_{-\infty}^{A_t} \int_{-\infty}^{B_t} f(A_t, B_t) dA_t dB_t \\
&\equiv +1
\end{aligned} \tag{82}$$

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

6.4.2. Observational study and exclusion relationship

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

$$p(A_t | B_t) \equiv p(A_t \uparrow B_t) \geq 1 - \frac{p(a_t)}{p(B_t)} \tag{83}$$

6.4.3. Experimental study and exclusion relationship

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

$$p(A_t | B_t) \equiv p(A_t \uparrow B_t) \geq 1 - \frac{p(a_t)}{p(A_t)} \tag{84}$$

6.4.4. The goodness of fit test of an exclusion relationship

Definition 6.28 (The $\tilde{\chi}^2$ goodness of fit test of an exclusion relationship).

Under some well known circumstances, testing hypothesis about an exclusion relationship $p(A_t | B_t)$ 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

$$\begin{aligned}\tilde{\chi}^2_{\text{Calculated}}((A_t | B_t) | A) &\equiv \frac{(b - (a + b))^2}{A} + \frac{((c + d) - \underline{A})^2}{\underline{A}} \\ &\equiv \frac{a^2}{A} + 0 \\ &\equiv \frac{a^2}{A}\end{aligned}\tag{85}$$

or equally as

$$\begin{aligned}\tilde{\chi}^2_{\text{Calculated}}((A_t | B_t) | B) &\equiv \frac{(c - (a + c))^2}{B} + \frac{((b + d) - \underline{B})^2}{\underline{B}} \\ &\equiv \frac{a^2}{B} + 0 \\ &\equiv \frac{a^2}{B}\end{aligned}\tag{86}$$

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

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

Definition 6.29 (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

(It) p Value ([Barukčić, 2019c](#)) of an exclusion relationship can be calculated as follows.

$$\begin{aligned} pValue_{lt}(A_t | B_t) &\equiv 1 - e^{-(1-p(A_t|B_t))} \\ &\equiv 1 - e^{-(a/N)} \end{aligned} \quad (87)$$

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

6.4.6. Neither nor conditions

Definition 6.30 (Neither A_t nor B_t conditions [NOR]).

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

$$\begin{aligned}
 p(A_t \downarrow B_t) &\equiv p(d_t) \\
 &\equiv \frac{N - \sum_{t=1}^N (A_t \vee B_t)}{N} \equiv \frac{\sum_{t=1}^N (\underline{A}_t \wedge \underline{B}_t)}{N} \equiv \frac{N \times (p(d_t))}{N} \\
 &\equiv \frac{d}{N} \\
 &\equiv +1
 \end{aligned} \tag{88}$$

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

Definition 6.31 (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

$$\begin{aligned}
 \tilde{\chi}^2_{\text{Calculated}}((A_t \downarrow B_t) | A) &\equiv \frac{(d - (c + d))^2}{\underline{A}} + \\
 &\quad \frac{((a + b) - A)^2}{A} \\
 &\equiv \frac{c^2}{\underline{A}} + 0
 \end{aligned} \tag{89}$$

or equally as

$$\begin{aligned}
 \tilde{\chi}^2_{\text{Calculated}}((A_t \downarrow B_t) | B) &\equiv \frac{(d - (b + d))^2}{\underline{B}} + \\
 &\quad \frac{((a + c) - B)^2}{B} \\
 &\equiv \frac{b^2}{\underline{B}} + 0
 \end{aligned} \tag{90}$$

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

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

Definition 6.32 (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.

$$\begin{aligned} pValue_{lt}(A_t \downarrow B_t) &\equiv 1 - e^{-(1-p(A_t \downarrow B_t))} \\ &\equiv 1 - e^{-p(A_t \vee B_t)} \\ &\equiv 1 - e^{-((a+b+c)/N)} \end{aligned} \quad (91)$$

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 $p(A_t \vee B_t) \equiv 1 - p(A_t \downarrow B_t)$ (see table 9).

Table 9. 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

6.4.9. Necessary condition

Definition 6.33 (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 (see Barukčić, 2022c) condition for (human) life. **Without** water, there has been and there is **no** (human) life²⁶. 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, of 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, of 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, of 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. Among many other issues, the specification of necessary conditions has traditionally been part of the philosopher's investigations of different phenomena. However, 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

²⁶Barukčić, Ilija. (2022). *Conditio sine qua non* (Version 1). Zenodo. <https://doi.org/10.5281/zenodo.5854744>

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 re-consider 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 entfiel**" (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, Carl Ludwig von, 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 need to 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 such an event. In other words, if a necessary condition (i.e. A_t) is given, an outcome (i.e. B_t) need not to occur. In contrast to a necessary condition, a 'sufficient' condition is the one condition which 'guarantees' that an outcome will take place or will 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 may 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 a brain is given ... et cetera, without water 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

$$\begin{aligned}
 p(A_t \leftarrow B_t) &\equiv p(A_t \vee \underline{B}_t) \equiv \frac{\sum_{t=1}^N (A_t \vee \underline{B}_t)}{N} \equiv \frac{(A_t \vee \underline{B}_t) \times p(A_t \vee \underline{B}_t)}{(A_t \vee \underline{B}_t)} \\
 &\equiv p(a_t) + p(b_t) + p(d_t) \\
 &\equiv \frac{N \times (p(a_t) + p(b_t) + p(d_t))}{N} \equiv \frac{E(A_t \leftarrow B_t)}{N} \\
 &\equiv \frac{a + b + d}{N} \equiv \frac{E(A_t \vee \underline{B}_t)}{N} \\
 &\equiv \frac{A + d}{N} \equiv \frac{E(A_t \leftarrow B_t)}{N} \\
 &\equiv \frac{a + \underline{B}}{N} \equiv \frac{E(A_t \vee \underline{B}_t)}{N} \\
 &\equiv +1
 \end{aligned} \tag{92}$$

where $E(A_t \leftarrow B_t) \equiv E(A_t \vee \underline{B}_t)$ indicates the expectation value of the necessary condition. In general, it is $p(A_t \leftarrow B_t) \equiv 1 - p(A_t \leftarrow B_t)$ (see Table 10).

Table 10. 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

A necessary condition A_t is characterised itself by the property that another event B_t will not occur if A_t is not given, if A_t did not occur (Barukčić, 1989, 1997, 2005, 2016b, 2017b,c, 2020a,b,c,d; Barukčić and Ufuoma, 2020). Taking into account Kolmogorov's definition of an n-dimensional probability density (see also Kolmogorov, Andrei Nikolaevich, 1950, p. 26) of random variables A_t , B_t et cetera at the (period of) time t , we obtain

$$\begin{aligned}
 p(A_t \leftarrow B_t) &\equiv +1 \\
 &\equiv +1 - p(c_t) \\
 &\equiv +1 - p(\underline{A}_t \cap B_t) \\
 &\equiv \left(\int_{-\infty}^{A_t} \int_{-\infty}^{B_t} f(A_t, B_t) dA_t dB_t \right) + \left(1 - \int_{-\infty}^{B_t} f(B_t) dB_t \right)
 \end{aligned} \tag{93}$$

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

are met, then necessary conditions and sufficient conditions are one way or another converses of each other, too. It is

$$p(A_t \leftarrow B_t) \equiv \underbrace{(A_t \vee B_t)}_{\text{(Necessary condition)}} \equiv \underbrace{(B_t \vee A_t)}_{\text{(Sufficient condition)}} \equiv p(B_t \rightarrow A_t) \quad (94)$$

These relationships are illustrated by the following tables.

Table 11. Without A_t no B_t

		B_t		
		TRUE	FALSE	
A_t	TRUE	a_t	b_t	A_t
	FALSE	$c_t = 0$	d_t	$\underline{A_t}$
		B_t	$\underline{B_t}$	+1

Table 12. If B_t then A_t

		A_t		
		TRUE	FALSE	
B_t	TRUE	a_t	$c_t = 0$	B_t
	FALSE	b_t	d_t	$\underline{B_t}$
		A_t	$\underline{A_t}$	+1

There are circumstances under which

$$p(A_t \leftarrow B_t) \equiv \underbrace{(A_t \vee B_t)}_{\text{(Necessary condition)}} \equiv \underbrace{(\underline{A_t} \vee B_t)}_{\text{(Sufficient condition)}} \equiv p(A_t \rightarrow B_t) \quad (95)$$

However, equation 94 does not imply the relationship of equation 95 under any circumstances.

Example I.

A wax candle is characterised by various properties, but is also subject to certain conditions. **Without** sufficient amounts of gaseous oxygen **no** burning wax candle, gaseous oxygen is a necessary condition of a burning candle. However, the converse relationship **if** burning wax candle, **then** sufficient amounts of gaseous oxygen are given is at the same (period of) time t / Bernoulli trial t true. The following tables are illustrating these relationships.

Table 13. Without gaseous oxygen no burning candle

		Burning candle		
		TRUE	FALSE	
Gaseous oxygen	TRUE	a_t	b_t	A_t
	FALSE	$c_t = 0$	d_t	$\underline{A_t}$
		B_t	$\underline{B_t}$	+1

Table 14. If burning candle then gaseous oxygen

		Gaseous oxygen		
		TRUE	FALSE	
Burning candle	TRUE	a_t	$c_t = 0$	B_t
	FALSE	b_t	d_t	$\underline{B_t}$
		A_t	$\underline{A_t}$	+1

Example II.

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.

Example III.

Another different aspect of a necessary condition relationship is appropriate to be focused upon here. As a direct consequence of a necessary condition **without** sufficient amounts of gaseous oxygen **no** burning wax candle is a special case of an exclusion relationship. The absence of sufficient amounts of gaseous oxygen A_t excludes (see Barukčić, 2021a) a burning wax candle B_t . Thus far, if we want to stop the burning of a wax candle, we would have to significantly reduce the amounts of gaseous oxygen A_t . Under these conditions, a wax candle will stop burning. The following tables (table 15 and table 16) may illustrate this aspect of a necessary condition in more detail.

Table 15. Without gaseous oxygen no burning candle

		Burning candle		
		TRUE	FALSE	
Gaseous oxygen	TRUE	a_t	b_t	A_t
	FALSE	$c_t = 0$	d_t	\underline{A}_t
		B_t	\underline{B}_t	+1

Table 16. Absent gaseous oxygen excludes burning wax candle

		Burning candle		
		TRUE	FALSE	
Gaseous oxygen	FALSE	$c_t = 0$	d_t	B_t
	TRUE	a_t	b_t	\underline{B}_t
		A_t	\underline{A}_t	+1

The necessary condition relationship follows approximately (see Barukčić, 2022c) as

$$p(A_t \leftarrow B_t) \geq 1 - \frac{p(c_t)}{p(B_t)} \quad (96)$$

and as

$$p(A_t \leftarrow B_t) \geq 1 - \frac{p(c_t)}{p(\underline{A}_t)} \quad (97)$$

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

Definition 6.34 (The $\tilde{\chi}^2$ goodness of fit test of a necessary condition relationship).

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

$$\begin{aligned}
\tilde{\chi}^2_{\text{Calculated}}(A_t \leftarrow B_t \mid B) &\equiv \frac{(a - (a + c))^2}{B} + \frac{((b + d) - \underline{B})^2}{\underline{B}} \\
&\equiv \frac{c^2}{B} + 0 \\
&\equiv \frac{c^2}{B}
\end{aligned} \tag{98}$$

or equally as

$$\begin{aligned}
\tilde{\chi}^2_{\text{Calculated}}(A_t \leftarrow B_t \mid \underline{A}) &\equiv \frac{(d - (c + d))^2}{\underline{A}} + \frac{((a + b) - A)^2}{A} \\
&\equiv \frac{c^2}{\underline{A}} + 0 \\
&\equiv \frac{c^2}{\underline{A}}
\end{aligned} \tag{99}$$

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

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

Definition 6.35 (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.

$$\begin{aligned}
pValue_{lt}(A_t \leftarrow B_t) &\equiv 1 - e^{-(1 - p(A_t \leftarrow B_t))} \\
&\equiv 1 - e^{-(c/N)}
\end{aligned} \tag{100}$$

6.4.12. Sufficient condition

Definition 6.36 (Sufficient condition [*Conditio per quam*]).

Mathematically, the sufficient (Barukčić, 2021c, p. 68-70) condition (see Barukčić, 2022b) (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

$$\begin{aligned}
 p(A_t \rightarrow B_t) &\equiv p(\underline{A}_t \vee B_t) \equiv \frac{\sum_{t=1}^N (\underline{A}_t \vee B_t)}{N} \equiv \frac{(\underline{A}_t \vee B_t) \times p(\underline{A}_t \vee B_t)}{(\underline{A}_t \vee B_t)} \\
 &\equiv p(a_t) + p(c_t) + p(d_t) \\
 &\equiv \frac{N \times (p(a_t) + p(c_t) + p(d_t))}{N} \\
 &\equiv \frac{a + c + d}{N} \equiv \frac{E(\underline{A}_t \vee B_t)}{N} \\
 &\equiv \frac{B + d}{N} \equiv \frac{E(A_t \rightarrow B_t)}{N} \\
 &\equiv \frac{a + A}{N} \\
 &\equiv +1
 \end{aligned} \tag{101}$$

In general, it is $p(A_t \succ B_t) \equiv 1 - p(A_t \rightarrow B_t)$ (see Table 17).

6.4.12.1. Mackie's INUS Condition John Leslie Mackie (1917-1981) critically examined the theories of causation of various (see Ducasse, 1926) philosophers such as Hume (Book I, Part III, of the Treatise) (see Mackie, 1974, pp. 3-28), Kant (as well as Kantian approaches offered by Strawson and Bennett), Mill and other. Mackie rightly claims that Hume's regularity theory of causation offer only an incomplete picture of the nature of causation. Mackie writes: "It seems appropriate to begin by examining and criticizing it, so that we can take over from it whatever seems to be defensible but develop an improved account by correcting its errors and deficiencies." (see Mackie, 1974, p. 3). Nonetheless, in his trial to develop an improved account of Hume's theory of causation, Mackie's own account of the nature of causation follows Hume's principles of causation very closely (see Mackie, 1974, pp. 3-28). Mackie himself proposed already in 1965 that "the so-called cause is ... an *insufficient* but *necessary* part of a condition which is itself *unnecessary* but *sufficient* for the result ... let us call such a condition ... an INUS condition." (see Mackie, 1965, p. 245). However Mackie's account needs modification, and can be modified and when it is modified we can explain much more satisfactorily what Mackie ordinarily take to be a cause. Mackie is of the opinion that "... cause is ... part of a condition ..." (see Mackie, 1965, p. 245) and that "... a condition ... is ... *unnecessary* but *sufficient* for the result [i. e. effect, author]." (see Mackie, 1965, p. 245). To put it very simply one could say that Mackie reduces a cause to a sufficient condition, "... cause is ... a condition which is itself ... *sufficient* ..." (see Mackie, 1965, p. 245). Indeed, there are circumstances, where several

different events ²⁷ might be necessary or sufficient et cetera at the same time in order to determine **a compound/complex sufficient condition relationship**. Thus far, it seems appropriate to take over from Mackie's INUS condition whatever seems to be acceptable but to develop an improved account by correcting its deficiencies and errors in order to do justice to the complexity of affairs. Equation 102 illustrates one real-world example of a compound/complex sufficient condition relationship in more detail.

$$\begin{aligned}
 p(((X_t \wedge X_t \wedge X_t \wedge \dots) \wedge A_t) \rightarrow B_t) &\equiv p\left(\frac{((X_t \wedge X_t \wedge X_t \wedge \dots) \wedge A_t) \vee B_t}{N}\right) \\
 &\equiv \frac{\sum_{t=1}^N \left(\frac{((X_t \wedge X_t \wedge X_t \wedge \dots) \wedge A_t) \vee B_t}{N}\right)}{N} \\
 &\equiv +1
 \end{aligned} \quad (102)$$

Again, 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

$$\begin{aligned}
 p(A_t \rightarrow B_t) &\equiv +1 \\
 &\equiv +1 - p(B_t) \\
 &\equiv +1 - p(A_t \cap \underline{B}_t) \\
 &\equiv \left(\int_{-\infty}^{A_t} \int_{-\infty}^{B_t} f(A_t, B_t) dA_t dB_t \right) + \left(1 - \int_{-\infty}^{A_t} f(A_t) dA_t \right)
 \end{aligned} \quad (103)$$

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

Table 17. Sufficient condition.

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

Remark 6.2. 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 occurred (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

²⁷Barukčić, Ilija. (2022). *Conditio per quam*. Causation, 17(3), 5–86. <https://doi.org/10.5281/zenodo.6369831>

(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

$$p(A_t \rightarrow B_t) + p(R_t \wedge B_t) \equiv +1 \quad (104)$$

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.

The approximate (see Barukčić, 2022b) value of the material implication is given as

$$p(A_t \rightarrow B_t) \geq 1 - \frac{p(b_t)}{p(A_t)} \quad (105)$$

and alternatively as

$$p(A_t \rightarrow B_t) \geq 1 - \frac{p(b_t)}{p(\underline{B}_t)} \quad (106)$$

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

Definition 6.37 (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 $p(A_t \rightarrow B_t)$ 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

$$\begin{aligned} \tilde{\chi}^2_{\text{Calculated}}(A_t \rightarrow B_t | A) &\equiv \frac{(a - (a+b))^2}{A} + \frac{((c+d) - \underline{A})^2}{\underline{A}} \\ &\equiv \frac{b^2}{A} + 0 \\ &\equiv \frac{b^2}{A} \end{aligned} \quad (107)$$

or equally as

$$\begin{aligned}
 \tilde{\chi}^2_{\text{Calculated}}(A_t \rightarrow B_t \mid \underline{B}) &\equiv \frac{(d - (b + d))^2}{\underline{B}} + \frac{((a + c) - B)^2}{B} \\
 &\equiv \frac{b^2}{\underline{B}} + 0 \\
 &\equiv \frac{b^2}{\underline{B}}
 \end{aligned} \tag{108}$$

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

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

Definition 6.38 (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.

$$\begin{aligned}
 pValue_{lt}(A_t \rightarrow B_t) &\equiv 1 - e^{-(1-p(A_t \rightarrow B_t))} \\
 &\equiv 1 - e^{-(b/N)}
 \end{aligned} \tag{109}$$

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

6.4.15. Necessary and sufficient conditions

Definition 6.39 (Necessary and sufficient conditions [EQV]).

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

$$\begin{aligned}
 p(A_t \leftrightarrow B_t) &\equiv \frac{\sum_{t=1}^N ((A_t \vee \underline{B}_t) \wedge (\underline{A}_t \vee B_t))}{N} \\
 &\equiv p(a_t) + p(d_t) \\
 &\equiv \frac{N \times (p(a_t) + p(d_t))}{N} \\
 &\equiv \frac{a + d}{N} \\
 &\equiv +1
 \end{aligned} \tag{110}$$

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

Definition 6.40 (The $\tilde{\chi}^2$ goodness of fit test of a necessary and sufficient condition relationship).

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

$$\begin{aligned}
 \tilde{\chi}^2_{\text{Calculated}}(A_t \leftrightarrow B_t \mid A) &\equiv \frac{(a - (a+b))^2}{A} + \frac{d - ((c+d))^2}{\underline{A}} \\
 &\equiv \frac{b^2}{A} + \frac{c^2}{\underline{A}}
 \end{aligned} \tag{111}$$

or equally as

$$\begin{aligned}
 \tilde{\chi}^2_{\text{Calculated}}(A_t \leftrightarrow B_t \mid B) &\equiv \frac{(a - (a+c))^2}{B} + \frac{d - ((b+d))^2}{\underline{B}} \\
 &\equiv \frac{c^2}{B} + \frac{b^2}{\underline{B}}
 \end{aligned} \tag{112}$$

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

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

Definition 6.41 (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.

$$\begin{aligned} pValue_{lt}(A_t \leftrightarrow B_t) &\equiv 1 - e^{-(1-p(A_t \leftrightarrow B_t))} \\ &\equiv 1 - e^{-((b+c)/N)} \end{aligned} \quad (113)$$

In this context, a low p-value indicates again a statistical significance. Table 18 may provide an overview of the theoretical distribution of a necessary and sufficient condition.

Table 18. Necessary and sufficient condition.

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

6.4.18. Either or conditions

Definition 6.42 (Either A_t or B_t conditions [NEQV]).

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

$$\begin{aligned}
 p(A_t \succless B_t) &\equiv \frac{\sum_{t=1}^N ((A_t \wedge \underline{B}_t) \vee (\underline{A}_t \wedge B_t))}{N} \\
 &\equiv p(b_t) + p(c_t) \\
 &\equiv \frac{N \times (p(b_t) + p(c_t))}{N} \\
 &\equiv \frac{b + c}{N} \\
 &\equiv +1
 \end{aligned} \tag{114}$$

It is $p(A_t \succless B_t) \equiv 1 - p(A_t \lessgtr B_t)$ (see Table 19).

Table 19. 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

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

Definition 6.43 (The $\tilde{\chi}^2$ goodness of fit test of an either or condition relationship).

An either or condition relationship $p(A_t \succless B_t)$ 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

$$\begin{aligned}
 \tilde{\chi}^2_{\text{Calculated}}((A_t \succless B_t) | A) &\equiv \frac{(b - (a + b))^2}{A} + \\
 &\quad \frac{c - ((c + d))^2}{\underline{A}} \\
 &\equiv \frac{a^2}{A} + \frac{d^2}{\underline{A}}
 \end{aligned} \tag{115}$$

or equally as

$$\begin{aligned}\tilde{\chi}^2_{\text{Calculated}}((A_t \succ \prec B_t) \mid B) &\equiv \frac{(c - (a + c))^2}{B} + \frac{b - ((b + d))^2}{B} \\ &\equiv \frac{a^2}{B} + \frac{d^2}{B}\end{aligned}\quad (116)$$

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

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

Definition 6.44 (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.

$$\begin{aligned}pValue_{lt}(A_t \succ \prec B_t) &\equiv 1 - e^{-(1 - p(A_t \succ \prec B_t))} \\ &\equiv 1 - e^{-((a+d)/N)}\end{aligned}\quad (117)$$

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

6.5. Causation

6.5.1. Causation in general

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"** (see Pearl, 2000, p. 340).

At the beginning of the 20th 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 were not only a number of differences between Einstein and Heisenberg, these two physicists did not really love 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 mechanics**, 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 epidemiological 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 than 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 by various modern authors ([Barukčić, 1989, 1997, 2005, 2016b, 2017a,c](#); [Bohr, 1937](#); [Chisholm, 1946](#); [Dempster, 1990](#); [Espejo, 2007](#); [Goodman, 1947](#); [Granger, 1969](#); [Hessen, Johannes, 1928](#); [Hesslow, 1976, 1981](#); [Korch, Helmut, 1965](#); [Lewis, David Kellogg, 1973, 1974](#); [Pearl, 2000](#); [Schlick, Friedrich Albert Moritz, 1931](#); [Spohn, 1983](#); [Suppes, 1970](#); [Todd, 1968](#); [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?

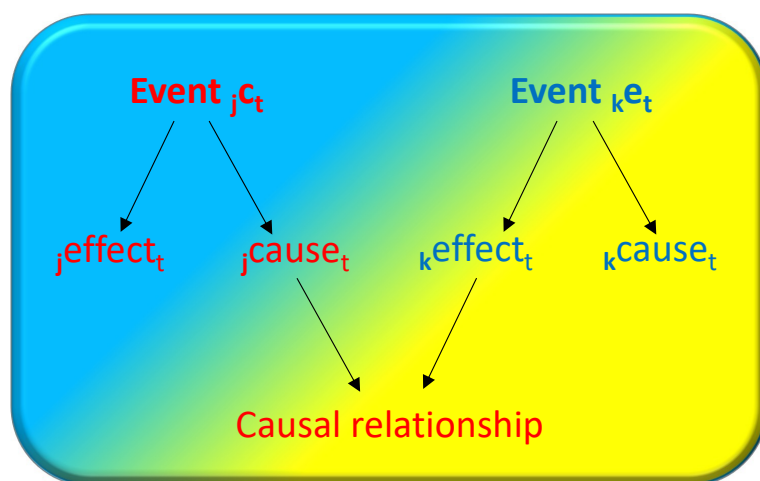
6.5.2. Cause and effect

Besides all, there are several further aspects of causation for which our attention so far has not been adequately fixed in this context. In the causal relationship, cause and effect are united, a cause is an effect and an effect is a cause.

“Thus, in the causal relation, cause and effect are inseparable; a cause which had no effect would not be a cause, just as an effect which had no cause would no longer be an effect. ”

(see Hegel, Georg Wilhelm Friedrich, 1991, p. 151)

The unity of cause and effect is a unity of two which are not the same. Cause and effect as inseparable in the causal relation are at the same time mutually related as sheer others; each of both as united in its own self to the other of itself is able to pass over into its own other and vice versa. Yet, to approach from a different point of view, a cause and an effect are separated in the same relation too, a cause is not an effect and an effect is not a cause, both are different in the same relation.



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“Therefore, though the **cause** has an **effect** and is at the same time itself **effect**, and the **effect** not only has a **cause** but is also itself **cause**, yet the **effect** which the **cause** has, and the **effect** which it is, are different, as are also the **cause** which the **effect** has, and the **cause** which it is.” (see Hegel, Georg Wilhelm Friedrich, 1991, p. 565/566)

6.5.2.1. What is a cause, what is an effect? An important fact to which we must pay attention here is that in a causal relation, under certain circumstances, an individual cause and an individual effect are related to each other in their own particular way. An effect which vanishes in its own cause in the same respect equally becomes again in it and vice versa. A cause which is merely extinguished in its own effect becomes again in the same. In fact, each of these determinations presupposes in its own other its own self and constitutes the intimate tie between an individual cause and its own individual

effect. Thus far, 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 20 may illustrate this relationship. A matter of great theoretical importance is the fundamental

Table 20. 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

relationship between a cause and a condition. Are both, cause and condition, at the end identical? As of now, following Mill (see [Mill, 1843a](#), p. 403), Verworn (see [Verworn, 1912](#)), Mackie and others, we can give a clear ‘Yes’ in reply to this question: “... cause is ... a condition which is itself ... *sufficient* ... ” (see [Mackie, 1965](#), p. 245). However, this issue is not as simple as it sounds, according to Mackie. Thus far, it is essential to eliminate some errors. Indeed, there are circumstances where a cause and a condition are identical, a cause and a condition are equivalent. However, as outlined in this publication, both, a cause and a condition, are different too and a cause and a condition are not identical either.

“Jede Ursache ist nothwendig auch eine Bedingung eines Ereignisses;
aber nicht jede Bedingung ist Ursache zu nennen. ”

(see [Bar, Carl Ludwig von, 1871](#), p. 4)

The crux of the matter is that not every condition is a cause too, in German: “... nicht jede Bedingung ist Ursache ... ”(see [Bar, Carl Ludwig von, 1871](#), p. 4). However, and in contrast to a condition, every cause as such is indeed a condition too, in German: “Jede Ursache ist ... auch eine Bedingung ... ”(see [Bar, Carl Ludwig von, 1871](#), p. 4). In general, a cause U_t is a necessary condition of an effect W_t . In other words, **without** a cause U_t **no** effect W_t . One consequence of the necessary condition relationship between cause and effect is that “... an effect which had no cause would no longer be an effect. ” (see [Hegel, Georg Wilhelm Friedrich, 1991](#), p. 151). However, a cause U_t being a necessary condition of an effect W_t is equivalent to an effect W_t being a sufficient condition of the same cause U_t and vice versa too. In our everyday words,

without

U_t

no

W_t

is equivalent with

if

W_t

then

U_t

and vice versa. 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

$$(U_t \vee \underline{W}_t) \equiv (\underline{W}_t \vee U_t) \equiv ((U_t \vee \underline{W}_t) \wedge (\underline{W}_t \vee U_t)) \equiv +1 \quad (118)$$

		Effect W_t		
		TRUE	FALSE	
Cause	TRUE	a_t	b_t	U_t
U_t	FALSE	$c_t = 0$	d_t	\underline{U}_t
		W_t	\underline{W}_t	+1

Table 21. Without U_t no W_t

		Cause U_t		
		TRUE	FALSE	
Effect	TRUE	a_t	$c_t = 0$	W_t
W_t	FALSE	b_t	d_t	\underline{W}_t
		U_t	\underline{U}_t	+1

Table 22. If W_t then U_t

The other side of the causal relation at the same (period of) time / Bernoulli trial t is the fact that a cause U_t is equally a sufficient condition of an effect W_t too or shortly **if** cause U_t **then** effect W_t . One straightforward consequence of this fundamental relationship between a cause and an effect is that "... a cause which had no effect would not be a cause ... " (see [Hegel, Georg Wilhelm Friedrich, 1991](#), p. 151). But even this is not without difficulties, because a cause U_t being a sufficient condition of an effect W_t is equivalent to effect W_t being a necessary condition of the same cause U_t . In different words,

if

U_t

then

W_t

is equivalent with

without

W_t

no

U_t .

		Effect W_t		
		TRUE	FALSE	
Cause	TRUE	a_t	$b_t = 0$	U_t
U_t	FALSE	c_t	d_t	\underline{U}_t
		W_t	\underline{W}_t	+1

Table 23. If U_t then W_t

		Cause U_t		
		TRUE	FALSE	
Effect	TRUE	a_t	c_t	W_t
W_t	FALSE	$b_t = 0$	d_t	\underline{W}_t
		U_t	\underline{U}_t	+1

Table 24. Without W_t no U_t

To bring it to the point, necessary and sufficient conditions are at the end converses (see [Gomes, Gilberto, 2009](#)) of each other and far more than this. In fact, there is a kind of reciprocity or mirroring between cause and effect. 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

$$(\underline{U}_t \vee W_t) \equiv (W_t \vee \underline{U}_t) \equiv ((\underline{U}_t \vee W_t) \wedge (W_t \vee \underline{U}_t)) \equiv +1 \quad (119)$$

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. And we should use this relationships to make our point. In general, **without** gaseous oxygen (U_t), there is **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 everyday knowledge is known and secured since centuries and might be illustrated as follows.

		Wax candle B_t		
		burning	not burning	
Gaseous	present	a_t	b_t	A_t
oxygen _t	not present	$c_t = 0$	d_t	\underline{A}_t
		B_t	\underline{B}_t	+1

Table 25. Without A_t no B_t

		Gaseous oxygen A_t		
		present	not present	
Wax candle	burning	a_t	$c_t = 0$	B_t
	not burning	b_t	d_t	\underline{B}_t
		A_t	\underline{A}_t	+1

Table 26. If B_t then A_t

Nonetheless, and independently of this secured everyday knowledge, **a burning wax candle is a sufficient condition of gaseous oxygen but not the cause of gaseous oxygen.**

Given all the circumstances, it is at least this simple **counter-example** which provides us with a convincing evidence that **a sufficient condition alone is not enough to describe a cause completely.** In general, a cause as such cannot be reduced to a simple sufficient condition.

In contrast to this obvious fact, other authors prefer another approach to the definition of a cause. “So that, more explicitly, if a given particular event is regarded as having been sufficient to the occurrence of another, it is said to have been its cause; if regarded as having been necessary to the occurrence of another, it is said to have been a condition of it; ...” (see [Ducasse, 1926](#), p. 58). 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. Under certain conditions, the causal relationship between U_t and W_t , when correctly defined and recognised, is closely allied with the requirement that a certain study or that at least other, different studies provided 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

$$(U_t \vee \underline{W}_t) \wedge (\underline{U}_t \vee W_t) \equiv +1 \quad (120)$$

However, I think it necessary to make a clear distinction between a necessary and sufficient condition and the converse relationship (Eq. 118) above.

$$((U_t \vee \underline{W}_t) \wedge (\underline{W}_t \vee U_t)) \neq (U_t \vee \underline{W}_t) \wedge (\underline{U}_t \vee W_t) \quad (121)$$

6.5.2.2. The direction of causation In general, a cause is related to its own effect in its own way and vice versa (see Mackie, 1966, p. 160) too. The effect (see Black, 1956) of this cause is itself related to its own cause in some way in which the cause is not related to its own effect (see Dummett and Flew, 1954). This can be considered as one of the reasons why the relation between cause and effect is taken to be asymmetrical.

6.5.2.3. The priority of cause to effect Contemporary discussions of causation are greatly influenced by the causal relation that ‘an effect W_t is causally dependent upon a cause U_t ’. However, under certain conditions (mono-causality), to say that ‘an effect W_t is causally dependent upon a cause U_t ’ is to say that ‘if a cause U_t had not occurred, then an effect W_t would not have occurred too.’ (see Lewis, David Kellogg, 1973, 1974). However, what came first, the hen or the egg, the cause or the effect?

6.5.3. Definition causal relationship k

Definition 6.45 (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 theory²⁸, ²⁹, ³⁰ as

$$\begin{aligned} k(U_t, W_t) &\equiv \frac{\sigma(U_t, W_t)}{\sigma(U_t) \times \sigma(W_t)} \\ &\equiv \frac{p(U_t \wedge W_t) - p(U_t) \times p(W_t)}{\sqrt{(p(U_t) \times (1 - p(U_t))) \times (p(W_t) \times (1 - p(W_t)))}} \end{aligned} \quad (122)$$

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 27 illustrates the theoretically possible relationships between a cause and an effect.

Table 27. Sample space and the causal relationship k

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

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 Bravais ('Analyse mathématique sur les probabilités 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

²⁸Ilija Barukčić, "The Mathematical Formula of the Causal Relationship k," International Journal of Applied Physics and Mathematics vol. 6, no. 2, pp. 45-65, 2016. <https://doi.org/10.17706/ijapm.2016.6.2.45-65>

²⁹Barukčić, Ilija. (2015). The Mathematical Formula Of The Causal Relationship k. <https://doi.org/10.5281/zenodo.3944666>

³⁰Ilija Barukčić. The causal relationship k. MATEC Web Conf., 336 (2021) 09032 DOI: <https://doi.org/10.1051/mateconf/202133609032>

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.

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I was born October, 1st 1961 in Novo Selo, Bosnia and Herzegovina, former Yugoslavia. I am of Croatian origin. From 1982-1989 C.E., I studied human medicine at the University of Hamburg, Germany. Meanwhile, I am working as a specialist of internal medicine. My basic field of research since my high school days at the Wirtschaftsgymnasium Bruchsal, Baden Württemberg, Germany is the mathematization of the relationship between a cause and an effect valid without any restriction under any circumstances including the conditions of classical logic, probability theory, quantum mechanics, special and general theory of relativity, human medicine et cetera. I endeavour to investigate positions of quantum mechanics, relativity theory, mathematics et cetera, only insofar as these positions put into question or endanger **the general validity of the principle of causality**.



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ⁱ<https://zenodo.org/search?page=1&size=20&q=keywords:%22Baruk%C4%8Di%C4%87,%20Conference%22>

^j<https://twitter.com/ilijabarukcic?lang=de>

^khttps://twitter.com/Causation_Journ

^lhttps://vixra.org/author/ilija_barukcic

^m<https://www.youtube.com/channel/UCwf3w1IngcukIO0jpw8HTwg>

ⁿ<https://portal.dnb.de/opac/showNextResultSite?currentResultId=%22Barukcic%22%26any¤tPosition=30>