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The logical content of the risk ratio

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ABSTRACT

Many different measures of association are used by medical literature, the relative risk is one of these measures. However, to judge whether results of studies are reliable, it is essential to use among other, measures of association which are logically consistent. In this paper, we will present how to deal with one of the most commonly used measures of association, the relative risk. As an example, data of view Covid-19 vaccine studies 2020/2021 are used. The conclusion is inescapable: the relative risk is logically inconsistent and should not be used any longer.

Keywords: Statistical methods, logical consistency — — measures of relationships — relative risk

1. INTRODUCTION

The relation between data actually obtained (the sample) and hypotheses is studied by a mathematical and conceptual discipline called statistics. In particular, the data of a sample can be biased which can be a source of incorrect conclusions with serious consequences.
In general, in almost all scientific research, empirical data or facts are investigated by specific statistical methods in order to evaluate some hypotheses of a particular kind. However, the statistical methods, in turn, need to be at least logically consistent. Central to the correctness of statistical methods is this problem of logical consistency, which concerns the justification of any statistical method. In point of fact, even if statistics provide us with various methods and means to evaluate hypotheses it is insightful to consider that statistics may harbour a large variety of errors and logical fallacies too even if sometimes hidden behind highly abstract mathematical stuff. One of such commonly used statistical methods is the risk ratio or relative risk (RR) which is designed to detect or to measure the relation between an exposure to an event A_t and an outcome of an event B_t.
Despite the frequent use of RR, founded doubts regarding the correctness and logical consistency of RR are not automatically excluded. In any case, the issue is not how often RR is used, but whether RR is logically correct or not logically correct.

2. MATERIAL AND METHODS

From the beginning of statistics onward the same is interrelated with probability theory. However, what kinds of 'things'are probabilistic statements, or more generally under which circumstances are probabilistic statements true or false and to what extent?

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2.1. *Material*

The subject of study in statistics is among other the relation between data and hypotheses. Summing up, it remains problematic to study anything without some definitions.

2.1.1. *Definitions*

Definition 2.1 (Independence)**.**

The independence(Barukčić 2021) [1] of two events A_t and B_t regarded from the standpoint of a certain observer was defined by de Moivre on page 7 as "... therefore, those two Events being independent, the Probability of their both happening will be 1/13 * 1/13 = 1/169 "[2] and Kolmogoroff [3] and other, as

$$p(B_t) \times p(A_t) = p(a_t) \tag{1}$$

where $p(A_t)$ denotes the probability of an event A_t at the Bernoulli trial t and $p(B_t)$ denotes the probability of another event B_t at the same Bernoulli trial t while $p(a_t)$ denotes the joint probability of $p(A_t$ AND $B_t)$ at the same Bernoulli trial t.

Definition 2.2 (Dependence)**.**

The Dependence(Barukčić 2021) [4] of two events A_t and B_t regarded from the standpoint of a certain observer is defined as

$$p(a_t) = (p(B_t) \times p(A_t))^{1/2} \tag{2}$$

where $p(A_t)$ denotes the probability of an event A_t at the Bernoulli trial t and $p(B_t)$ denotes the probability of another event B_t at the same Bernoulli trial t while $p(a_t)$ denotes the joint probability of $p(A_t$ AND $B_t)$ at the same Bernoulli trial t while the dependence of n events[5] follows as

$$p(a_{1,t}, a_{2,t}, ..., a_{n,t}) = (p(A_{1,t}) \times p(A_{2,t}) \times ... \times p(A_{n,t}))^{1/n} \tag{3}$$

Definition 2.3 (Contingency table)**.**

The relationship between two Binomial or Bernoulli(Barukčić 2021) [6] distributed random variables A_t and B_t at a certain Bernoulli trial (or period of time) t can be illustrated by a 2 by 2 table. Furthermore, a 2 by 2 contingency table is able to provide a basic picture of the interrelation between two binomial distributed random variables and is of use to analyse the relationships between them in detail. Karl Pearson was the first to use the term contingency table in his paper "On the Theory of Contingency and Its Relation to Association and Normal Correlation"[7].

Relative risk		Outcome		Total
		YES	NO	
Exposed	YES	$p(a_t)$	$p(b_t)$	$p(A_t)$
	NO	$p(c_t)$	$p(d_t)$	$p(\underline{A}_t)$
	Total	$p(B_t)$	$p(\underline{B}_t)$	+1

[1] https://www.matec-conferences.org/articles/matecconf/abs/2021/05/matecconf_cscns20_09032/matecconf_cscns20_09032.html

[2] https://doi.org/10.3931/e-rara-10420

[3] https://doi.org/10.1007/978-3-642-49888-6

[4] https://www.matec-conferences.org/articles/matecconf/abs/2021/05/matecconf_cscns20_09032/matecconf_cscns20_09032.html

[5] Ilija Barukčić, Die Kausalität, Hamburg: Wissenschaftsverlag, 1989, pp. 57-59.

[6] https://www.matec-conferences.org/articles/matecconf/abs/2021/05/matecconf_cscns20_09032/matecconf_cscns20_09032.html

[7] https://archive.org/details/cu31924003064833/page/n2/mode/2up

where $p(a_t)$ denotes the joint probability of A_t and B_t, $p(b_t)$ denotes the joint probability of A_t and Not B_t, $p(c_t)$ denotes the joint probability of not A_t and B_t and $p(d_t)$ denotes the joint probability of not A_t and Not B_t.

Definition 2.4 (Basic relationships between probabilities of a 2 by 2 table)**.**

In general, it is

$$p(A_t) = p(a_t) + p(b_t) \tag{4}$$

and

$$p(NotA_t) = 1 - p(A_t) = p(c_t) + p(d_t) \tag{5}$$

and

$$p(B_t) = p(a_t) + p(c_t) \tag{6}$$

and

$$p(NotB_t) = 1 - p(B_t) = p(b_t) + p(d_t) \tag{7}$$

where $p(a_t)$ denotes the joint probability of A_t and B_t. In general, it is

$$p(a_t) + p(b_t) + p(c_t) + p(d_t) = +1 \tag{8}$$

Definition 2.5 (Experimental[8] event rate (EER))**.**

$$EER(A_t, B_t) \equiv \frac{p(a_t)}{p(A_t)} = \frac{a_t}{a_t + b_t} \tag{9}$$

Definition 2.6 (Control[9] event rate (CER))**.**

$$CER(A_t, B_t) \equiv \frac{p(c_t)}{p(\underline{A}_t)} = \frac{c_t}{c_t + d_t} \tag{10}$$

Definition 2.7 (Absolute[10] risk reducation (ARR))**.**

$$\begin{aligned} ARR(A_t, B_t) &\equiv \frac{p(c_t)}{p(\underline{A}_t)} - \frac{p(a_t)}{p(A_t)} \\ &= \frac{c_t}{c_t + d_t} - \frac{a_t}{a_t + b_t} \\ &= CER(A_t, B_t) - EER(A_t, B_t) \end{aligned} \tag{11}$$

Definition 2.8 (Number needed to treat[11] (NNT))**.**

$$NNT(A_t, B_t) \equiv \frac{1}{CER(A_t, B_t) - EER(A_t, B_t)} \tag{12}$$

Definition 2.9 (Number needed to harm[12] (NNH))**.**

$$NNH(A_t, B_t) \equiv \frac{1}{EER(A_t, B_t) - CER(A_t, B_t)} \tag{13}$$

Definition 2.10 (Relative [13] risk (RR))**.**

[8] https://grunigen.lib.uci.edu/sites/all/docs/gml/RRR_ARR_NNT.pdf
[9] https://grunigen.lib.uci.edu/sites/all/docs/gml/RRR_ARR_NNT.pdf
[10] https://grunigen.lib.uci.edu/sites/all/docs/gml/RRR_ARR_NNT.pdf
[11] https://pubmed.ncbi.nlm.nih.gov/7873954/
[12] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3083982/
[13] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2545775/

The degree of association between the two binomial variables can be assessed by a number of very different coefficients, the relative risk [14] is one of them. In this context, see also Sir Ronald Aylmer Fisher's (1890 - 1962) contribution in his publication "The Logic of Inductive Inference"[15] (see also Fisher 1935, p. 50). In general, relative risk is defined as

$$RR(A_t, B_t) = \frac{\frac{p(a_t)}{p(A_t)}}{\frac{p(c_t)}{p(NotA_t)}} = \frac{p(a_t) \times p(NotA_t)}{p(c_t) \times p(A_t)} = \frac{EER\,(A_t, B_t)}{CER\,(A_t, B_t)} \tag{14}$$

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 [16] [17] and relative risk [18] are already documented [19] [20] in literature.

Example.

According to the Centers for Disease Control and Prevention (CDC)[21], an outbreak of varicella (chickenpox) in Oregon (USA) in 2002 was diagnosed in 18 of 152 (12%) vaccinated students[22] compared with 3 of 7 (43%) unvaccinated students.

Table 1. Outbreak of varicella (chickenpox) in Oregon in 2002

		Varicella B_t		
		TRUE	FALSE	
Vaccinated	TRUE	$a_t = 18$	$b_t = 134$	$A_t = 152$
A_t	FALSE	$c_t = 3$	$d_t = 4$	$\underline{A}_t = 7$
		$B_t = 21$	$\underline{B}_t = 138$	$N_t = 159$

The risk ratio RR is calculated as follows.

$$\begin{aligned} RR\,(A_t, B_t) &\equiv \frac{\frac{p(a_t)}{p(A_t)}}{\frac{p(c_t)}{p(NotA_t)}} = \frac{p(a_t) \times p(NotA_t)}{p(A_t) \times p(c_t)} \\ &\equiv \left(\frac{a_t \times \underline{A}_t}{c_t \times A_t}\right) \\ &\equiv \left(\frac{18 \times 7}{3 \times 152}\right) \\ &\equiv \frac{0.118}{0.42} \\ &\equiv 0.28 \end{aligned} \tag{15}$$

The risk ratio is RR = 0.28 and less than 1.0 which indicates a decreased risk or protective effect for the children which where vaccinated (exposed to vaccine). However, the risk ratio of 0.28 is completely misleading in this context as can be seen by table 2 .

[14] https://www.ncbi.nlm.nih.gov/books/NBK430824/

[15] https://www.jstor.org/stable/pdf/2342435.pdf?seq=1

[16] https://www.ncbi.nlm.nih.gov/pubmed/9832001

[17] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6178613/

[18] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC522855/

[19] https://www.crcpress.com/Principles-of-Biostatistics-Second-Edition/Pagano-Gauvreau/p/book/9781138593145

[20] https://www.biometricsociety.org/wp-content/uploads/2018/07/IBS-IBC2012-Final-Programme.compressed.pdf

[21] https://www.cdc.gov/csels/dsepd/ss1978/lesson3/section5.html

[22] https://pubmed.ncbi.nlm.nih.gov/14993534/

Table 2. Vaccinated and Varicella.

		Varicella		
		YES	NO	
Vaccinated	YES	18	134	152
	NO	3	4	7
		21	138	159

Causal relationship k =	-0,1879
p Value left tailed (HGD) =	0,0493
p (SINE) =	0,9811
$\tilde{\chi}^2$ (SINE — B_t) =	0,4286
$\tilde{\chi}^2$ (SINE — $\underline{A}_t$) =	1,2857
p Value (SINE) =	0,0187
p(IOI)=	0,8239
p(IOU)=	0,0881

Taking the data as published by CDC for granted, we need to conclude the following: **without** vaccination **no** outbreak of varicella (chickenpox) in Oregon (USA) in 2002 (p(SINE) = 0,9811; p Value (SINE) = 0,0187; p(IOU)= 0,0881).

However, such a conclusion(Barukčić 2021) [23] is neither completely justified nor free or errors. A negative causal relationship k (k = -0,1879), even if p(IOU) = 0,0881 is very impressive, does not support the hypothesis of necessary condition. In other words, the data as presented by CDC are self-contradictory[24] and cannot be used for such a conclusion. In contrast to this, the close connection between vaccination and outbreak of varicella (chickenpox) in Oregon in 2002 is rather masked than discovered by the risk ratio. Even though it is considered highly desirable, the conclusion that the vaccination protected against an outbreak of varicella (chickenpox) in Oregon (USA) in 2002 is not justified for sure due to the data published[25] by CDC. Reason: the study design with p(IOI)=0,8239 has been extremely biased.

Definition 2.11 (Relative risk reduction (RRR))**.**

$$\begin{aligned} RRR\left(A_t, B_t\right) &\equiv \frac{CER\left(A_t, B_t\right) - EER\left(A_t, B_t\right)}{CER\left(A_t, B_t\right)} \\ &= 1 - RR(A_t, B_t) \end{aligned} \tag{16}$$

Definition 2.12 (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.

$$\begin{aligned} VE\left(A_t, B_t\right) &\equiv 100 \times \left(1 - RR\left(A_t, B_t\right)\right) \\ &\equiv 100 \times \left(\frac{CER\left(A_t, B_t\right) - EER\left(A_t, B_t\right)}{CER\left(A_t, B_t\right)}\right) \end{aligned} \tag{17}$$

Historically, vaccine efficacy has been designed to evaluate the efficacy a certain vaccine by Greenwood and Yule[26] 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 to much on the study design, can lead to erroneous conclusions and is only of very limited value.

[23] https://www.matec-conferences.org/articles/matecconf/abs/2021/05/matecconf_cscns20_09032/matecconf_cscns20_09032.html

[24] https://pubmed.ncbi.nlm.nih.gov/14993534/

[25] https://pubmed.ncbi.nlm.nih.gov/14993534/

[26] https://journals.sagepub.com/doi/10.1177/003591571500801433

Definition 2.13 (Odds ratio[27,28])**.**

Odds(see also Yule and Pearson 1900, p. 273) ratio (OR) is a measure of association[29] which quantifies the relationship[30] between two binomial distributed random variables (exposure vs. outcome) and is related to Yule's (see also Yule and Pearson 1900, p. 272) Q(see also Yule 1912, p. 585/586). Hereafter, consider the table 3.

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

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

where
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).
The odds ratio (OR) is defined as

$$\begin{aligned} OR\left(A_t, B_t,\right) &\equiv \left(\frac{a_t}{b_t}\right) \times \left(\frac{c_t}{d_t}\right) \\ &\equiv \left(\frac{a_t \times d_t}{b_t \times c_t}\right) \end{aligned} \tag{18}$$

Remark. 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. 18. 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 recognise elementary relationships of objective reality. In fact, it would be a failure not to recognise how dangerous and less valuable odds ratio is.

Remark. Under conditions where (c = 0) odds ratio collapses too, because we need again to divide by zero as can be seen at eq. 18. 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 recognise 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.

Let us recall againg that it is

$$p\left(a_t\right) + p\left(b_t\right) + p\left(c_t\right) + p\left(d_t\right) \equiv +1 \tag{19}$$

Definition 2.14 (Exclusion relationship)**.**

The exclusion(Barukčić 2021) [31] relationship (A_t excludes B_t and vice versa) is defined as

$$p(A_t \mid B_t) = p(b_t) + p(c_t) + p(d_t) = +1 \tag{20}$$

Definition 2.15 (Conditio sine[32] qua non relationship)**.**

The conditio sine qua non relationship (A_t is a necessary condtion of B_t) is defined as

$$p(A_t \longleftarrow B_t) = p(a_t) + p(b_t) + p(d_t) = +1 \tag{21}$$

[27] https://bestpractice.bmj.com/info/toolkit/learn-ebm/how-to-calculate-risk/
[28] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2938757/
[29] https://www.cdc.gov/csels/dsepd/ss1978/lesson3/section5.html
[30] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2545775/
[31] https://www.matec-conferences.org/articles/matecconf/abs/2021/05/matecconf_cscns20_09032/matecconf_cscns20_09032.html
[32] https://www.matec-conferences.org/articles/matecconf/abs/2021/05/matecconf_cscns20_09032/matecconf_cscns20_09032.html

Remark. Since thousands of years, human mankind is familiar with the concept of necessary conditions. For example, we all know that air or gaseous oxygen as such is a necessary condition for (human) life. In other words, without gaseous[33] oxygen, there is no (human) life. However, the first documented mathematiziation of the concept of a necessary condition (**conditio sine qua non**) has been published by Barukčić 1989 [34]. Conditions may be necessary without being sufficient and vice versa. Sufficient conditions need not to be necessary. However, there may exist conditions which are both, necessary and sufficient. Nonetheless, any form of a mechanical understanding of a necessary condition may not stand the test of reality forever.

Human experience knows about the relationship between water and human life. It is part of the established knowledge of all of us that **without** water **no** human life. In other words, water itself is a necessary condition of human life. However, there may be some circumstances under which something can turn into its own other and vice versa. In other words, a person who drinks over 1000 litres of water at once (i. e. sea water) will die. Under these certain circumstances, water which is a necessary condition of human life in general turns into the other of itself, into a sufficient condition of human death. It is of great importance to be exact and precise in describing the circumstances, the minima and the maxima, the terms, the definitions, the inclusion and exclusion criteria et cetera of an investigation. In this sense, it is more than appropriate to pay the necessary tribute to Giordano Bruno (1548-1600) who wrote: : "So ist denn von zwei Entgegengesetzten das eine zugleich das Prinzip des anderen $\cdots$ Wer also die tiefsten Geheimnisse der Natur ergründen will, beobachte und betrachte die Minima und die Maxima des Entgegengesetzten und Widerstreitenden."(see also Bruno 1583, p. 148/149). Translated into English: 'So it is from two opposites at the same time the one the principle of the other $\cdots$ So **if you want to discover the deepest secrets of nature, observe and consider the minima and maxima of the opposite and conflicting**.'

Definition 2.16 (Conditio per[35] quam relationship)**.**

The conditio per quam(Barukčić 2021) [36] relationship (if A_t then B_t relationship) is defined [37] [38] [39] [40] [41] [42] [43] [44] as

$$p(A_t \longrightarrow B_t) = p(a_t) + p(c_t) + p(d_t) = +1 \tag{22}$$

Conditio per quam		Street is wet		
		YES	NO	
It is raining	YES	+1	+0	A_t
	NO	+1	+1	$\underline{A}_t$
		B_t	$\underline{B}_t$	

[33] https://www.matec-conferences.org/articles/matecconf/abs/2021/05/matecconf_cscns20_09032/matecconf_cscns20_09032.html
[34] Ilija Barukčić, Die Kausalität, Hamburg: Wissenschaftsverlag, 1989
[35] https://www.matec-conferences.org/articles/matecconf/abs/2021/05/matecconf_cscns20_09032/matecconf_cscns20_09032.html
[36] https://www.matec-conferences.org/articles/matecconf/abs/2021/05/matecconf_cscns20_09032/matecconf_cscns20_09032.html
[37] https://aip.scitation.org/doi/abs/10.1063/1.3567453
[38] https://aip.scitation.org/doi/abs/10.1063/1.4773147
[39] https://www.scirp.org/journal/paperinformation.aspx?paperid=69478
[40] https://www.scirp.org/journal/paperinformation.aspx?paperid=67272
[41] http://www.ijapm.org/show-64-515-1.html
[42] https://www.sciencedirect.com/science/article/pii/S1875389211006626
[43] https://view.publitas.com/amph/rjr_2018_4_art-02/page/1
[44] http://jddtonline.info/index.php/jddt/article/view/3385

Remark. Chile's **Atacama desert** is a desert plateau covering about 1,000-km (600-mi) strip of land on the Pacific coast. In contrast to the equator where it rains very often, the Atacama desert is widely considered as world's driest nonpolar desert with an average rainfall of as little as 0.04 inches per year. However, a **conditio per quam** relationship between raining and a street which is wet can be investigated even under these circumstances.

Under conditions of the Atacama desert a thought experiment is performed and the following data were achieved. It rained seldom at this occasion thus that the experimenter put 999 times some water on the street by himself where he performed measurements in order to study what happens if it is not raining.

Conditio per quam (Atacama desert)		**The street is wet**		
		YES	NO	
It is raining	YES	1000	**0**	1000
	NO	999	1	1000
		1999	1	2000

Figure 1. Counterexample. Risk ratio.

The relative risk follows as

$$RR(A_t, B_t) = \frac{p(a_t) \times p(NotA_t)}{p(A_t) \times p(c_t)} = \frac{1000 \times 1000}{999 \times 1000} = 1.0010 \tag{23}$$

The relative risk has been calculated as RR = 1.0010 while the 95% CI is 0.9990 to 1.0030 and the P value is P = 0.3173. In other words, according to the relative risk, raining is not a risk factor of a wet street or raining and a wet street are independent of each other. For the better understanding, let us repeat this fact again. According to the risk ratio (RR), raining at a certain (period of) time t and a street which is wet at the same (period of) time t are independent of each other. Such a risk ratio based erroneous conclusion is far away from any possible reality and everyday human experience. Therefore, what is becoming more and more visible is how risk ratio is forcing us in an intolerable manner to see reality through foggy statistical glasses. The counterexample (see fig. 1) has provided evidence of the logical inconsistency of the risk ratio. The risk ratio collapsed by the counterexample (see fig. 1) at last like a rotten piece of wood. Formally, even if relative risk is able to recognise a **conditio per quam relationship** in reality the same does not. Above any suspicion, depending upon **study design and other factors**, the relative risk present us a false and completely misleading picture of objective reality. Without any doubt, it is really no longer necessary to hold onto relative risk at all.

2.1.2. *Axioms*

Axiom 1. Lex identitatis [45] [46] [47].

$$+1 = +1 \tag{24}$$

Axiom 2. Lex contradictionis[48] [49] [50].

$$+0 = +1 \tag{25}$$

2.2. *Methods*

2.2.1. *Proof methods*

Proof methods like a direct proof [51], proof by contradiction[52], modus ponens[53], modus inversus[54] [55] and other methods are of use to detect inconsistencies and inadequacies in scientific theories.

[45] https://www.scirp.org/journal/paperinformation.aspx?paperid=69478
[46] https://www.ncbi.nlm.nih.gov/nlmcatalog/101656626
[47] https://doi.org/10.22270/jddt.v9i2.2389
[48] https://www.ncbi.nlm.nih.gov/nlmcatalog/101656626
[49] https://doi.org/10.22270/jddt.v9i2.2389
[50] https://doi.org/10.22270/jddt.v10i1-s.3856
[51] http://www.ijmttjournal.org/Volume-65/Issue-7/IJMTT-V65I7P524.pdf
[52] https://aip.scitation.org/doi/abs/10.1063/1.3567453
[53] http://www.ijmttjournal.org/Volume-65/Issue-7/IJMTT-V65I7P524.pdf
[54] http://www.ijmttjournal.org/Volume-65/Issue-7/IJMTT-V65I7P524.pdf
[55] https://vixra.org/pdf/1911.0410v1.pdf

3. RESULTS

3.1. *Independence of A_t and B_t*

Theorem 1 (**INDEPENDENCE OF A_T AND B_T**).

CLAIM.
In general, under circumstances of independence(Barukčić 2021) [56] of of A_t and B_t, it is

$$p(B_t) = \frac{p(a_t)}{p(A_t)} \tag{26}$$

PROOF BY MODUS PONENS.
The premise of modus ponens [57] in the case of independence according to de Moivre [58] and Kolmogoroff [59] and other, is that

$$p(B_t) \times p(A_t) = p(a_t) \tag{27}$$

Dividing by p(A_t), we obtain

$$\frac{p(B_t) \times p(A_t)}{p(A_t)} = \frac{p(a_t)}{p(A_t)} \tag{28}$$

At the end, the conclusion

$$p(B_t) = \frac{p(a_t)}{p(A_t)} \tag{29}$$

is true.
QUOD ERAT DEMONSTRANDUM.

3.2. *Independence of Not A_t and B_t*

Theorem 2 (**INDEPENDENCE OF NOT A_T AND B_T**).

CLAIM.

In general, under circumstances of independence(Barukčić 2021) [60] of of A_t and B_t, it is

$$p(B_t) = \frac{p(c_t)}{p(NotA_t)} \tag{30}$$

PROOF BY MODUS PONENS.
The premise of modus ponens in the case of independence according to de Moivre [61] and Kolmogoroff [62] and other, is that

$$p(B_t) \times p(NotA_t) = p(c_t) \tag{31}$$

Dividing by p(Not A_t), we obtain

$$\frac{p(B_t) \times p(NotA_t)}{p(NotA_t)} = \frac{p(c_t)}{p(NotA_t)} \tag{32}$$

At the end, the conclusion

$$p(B_t) = \frac{p(c_t)}{p(NotA_t)} \tag{33}$$

is true.
QUOD ERAT DEMONSTRANDUM.

[56] https://www.matec-conferences.org/articles/matecconf/abs/2021/05/matecconf_cscns20_09032/matecconf_cscns20_09032.html
[57] http://www.ijmttjournal.org/archive/ijmtt-v65i7p524
[58] https://doi.org/10.3931/e-rara-10420
[59] https://doi.org/10.1007/978-3-642-49888-6
[60] https://www.matec-conferences.org/articles/matecconf/abs/2021/05/matecconf_cscns20_09032/matecconf_cscns20_09032.html
[61] https://doi.org/10.3931/e-rara-10420
[62] https://doi.org/10.1007/978-3-642-49888-6

3.3. *Necessary condition and risk ratio.*

Theorem 3 (**Necessary condition and risk ratio**).

Claim.
In general, under some circumstances the risk ratio, denoted as RR_{nc} (A_t, B_t), defined as

$$RR_{nc}(A_t, B_t) = \frac{a \times \underline{A}}{c \times A} \tag{34}$$

provides only a very approximate and equally a very imprecise picture of a necessary condition.

Proof By Modus Ponens.
The premise of modus ponens [63] is that

$$+1 = +1 \tag{35}$$

If this premise is true, then the conclusion is also true, the absence of any technical and other errors of human reasoning assumed. The premise is true. Multiplying the premise (i. e. eq. 35) by $(p(A_t) \times p(B_t))$ it is

$$p(A_t) \times p(B_t) = p(A_t) \times p(B_t) \tag{36}$$

Under conditions of probability theory and in the case of independence of both events A_t and B_t at a certain (period of) time / Bernoulli (see also Uspensky 1937) trial t it is according to de Moivre [64] and Kolmogoroff [65] and other

$$p(a_t) = p(A_t \wedge B_t) = p(A_t) \times p(B_t) \tag{37}$$

According to eq. 6 it is $p(B_t) = (p(a_t) + p(c_t))$ Eq. 37 changes too

$$p(a_t) = p(A_t) \times (p(a_t) + p(c_t)) \tag{38}$$

or too

$$p(a_t) = (p(a_t) \times p(A_t)) + (p(c_t) \times p(A_t)) \tag{39}$$

Rearranging eq. 39 it is

$$p(a_t) - (p(a_t) \times p(A_t)) = (p(c_t) \times p(A_t)) \tag{40}$$

or

$$p(a_t) \times (1 - p(A_t)) = (p(c_t) \times p(A_t)) \tag{41}$$

Based on eq. 5 it is $p(\underline{A}_t) \equiv (1 - p(A_t))$. **Under conditions of independence eq. 41 changes further**. In general, is is necessary to accept that

$$p(a_t) \times p(\underline{A}_t) = p(c_t) \times p(A_t) \tag{42}$$

Under conditions of independence eq. 42 implies too that

$$\frac{p(a_t)}{p(A_t)} = \frac{X \times p(a_t)}{X \times p(A_t)} = \frac{p(c_t)}{p(\underline{A}_t)} \tag{43}$$

Eq. 43 can be tested by a kind of a Chi-square goodness of fit test as $\tilde{\chi}^2{}_{\text{Calculated}} = N \times \sum_{t=1}^{t=N} \left(\frac{\left(\frac{p(a_t)}{p(A_t)} - \frac{p(c_t)}{p(\underline{A}_t)} \right)^2}{\frac{p(c_t)}{p(\underline{A}_t)}} \right)$, a sum of differences between the observed and the expected. From 43 follows too that

[63] http://www.ijmttjournal.org/archive/ijmtt-v65i7p524
[64] https://doi.org/10.3931/e-rara-10420
[65] https://doi.org/10.1007/978-3-642-49888-6

$$p(a_t) = p(c_t) \times \frac{p(A_t)}{p(\underline{A}_t)} \tag{44}$$

or that

$$p(c_t) = p(a_t) \times \frac{p(\underline{A}_t)}{p(A_t)} \tag{45}$$

Multiplying eq. 45 by N, the sample size or the size of the whole population, it is

$$N \times p(c_t) = N \times p(a_t) \times \frac{N \times p(\underline{A}_t)}{N \times p(A_t)} \tag{46}$$

or

$$c = a \times \frac{\underline{A}}{A} \tag{47}$$

where a, c, A and $\underline{A}$ may denote the expectation values. Under conditions where A is the sample of the verum group, $\underline{A}$ is the sample of the placebo group and a is the number of cases in the verum group where the event B_t has been observed, c can be calculated very precisely. However, eq. 42 derived as $p(a_t) \times p(\underline{A}_t) = p(c_t) \times p(A_t)$ can be rearranged further as

$$\frac{p(a_t) \times p(\underline{A}_t)}{p(c_t) \times p(A_t)} = +1 \tag{48}$$

which is the definition of the risk ratio RR_{nc} (A_t, B_t) as

$$RR_{nc}(A_t, B_t) = \frac{p(a_t) \times p(\underline{A}_t)}{p(c_t) \times p(A_t)} = +1 \tag{49}$$

Under conditions where each trial is independent of another trial and where the probability of an event is constant from trial to trial it is equally

$$RR_{nc}(A_t, B_t) = \frac{p(a_t) \times p(\underline{A}_t)}{p(c_t) \times p(A_t)} = \frac{N^2 \times p(a_t) \times p(\underline{A}_t)}{N^2 \times p(c_t) \times p(A_t)} = \frac{a \times \underline{A}}{c \times A} = +1 \tag{50}$$

where a, c, A (i. e. verum) and $\underline{A}$ (i. e. placebo) may denote the expectation values and our conclusion is true.

QUOD ERAT DEMONSTRANDUM.

A $RR_{nc}(A_t, B_t) = \frac{p(a_t) \times p(\underline{A}_t)}{p(c_t) \times p(A_t)} = \frac{N^2 \times p(a_t) \times p(\underline{A}_t)}{N^2 \times p(c_t) \times p(A_t)} = \frac{a \times \underline{A}}{c \times A} > +1$ may provide some, even if very slight evidence, that A_t is a necessary condition of B_t. However, it makes much more sense to use the original(see also Barukčić 2021) necessary[66] condition formula.

[66] https://www.matec-conferences.org/articles/matecconf/abs/2021/05/matecconf_cscns20_09032/matecconf_cscns20_09032.html

3.4. *Case $p(c_t) = 0$: The relative risk RR is not defined*

Theorem 4 (Case $p(C_T) = 0$: The relative risk RR is not defined).

Claim.
In general, under circumstances $p(c_t) = 0$, the relative risk RR is not defined due to

$$RR(A_t, B_t) = \frac{p(a_t) \times p(d_t)}{0} \tag{51}$$

Proof.
The premise of modus ponens is that the relative risk RR is true. Thus far, again it is

$$RR(A_t, B_t) = \frac{p(a_t) \times p(notA_t)}{p(A_t) \times p(c_t)} \tag{52}$$

which is equivalent with

$$RR(A_t, B_t) = \frac{p(a_t) \times (p(c_t) + p(d_t))}{(p(a_t) + p(b_t)) \times p(c_t)} \tag{53}$$

Under conditions where $p(c_t) = 0$, the equation before changes to

$$RR(A_t, B_t) = \frac{p(a_t) \times (0 + p(d_t))}{(p(a_t) + p(b_t)) \times 0} \tag{54}$$

or to

$$RR(A_t, B_t) = \frac{p(a_t) \times (0 + p(d_t))}{(p(a_t) + p(b_t)) \times 0} \tag{55}$$

or to

$$RR(A_t, B_t) = \frac{p(a_t) \times p(d_t)}{0} \tag{56}$$

However, today, the division by zero is not accepted. Therefore, the conclusion that

$$RR(A_t, B_t) = \frac{p(a_t) \times p(d_t)}{0} \tag{57}$$

the relative risk RR is not defined under circumstances where $p(c_t) = 0$ is true.
Quod erat demonstrandum.

Remark. Theoretically, a conditio sine qua non relationship is determined by the fact that $p(c_t) = 0$. However, under these circumstances the relative risk RR collapses into logical absurdity and cannot detect a necessary condition, a **conditio sine qua non** at all. The following figure may illustrate the relationship again.

Conditio sine qau non		Human being alive		
		YES	NO	
Oxygen	YES	$p(a_t)$	$p(b_t)$	$p(A_t)$
	NO	0	$p(d_t)$	$p(\underline{A}_t)$
		$p(B_t)$	$p(\underline{B}_t)$	+1

A **necessary and sufficient condition** is determined by the fact that $\mathbf{p(c_t) = 0}$ **AND** $\mathbf{p(b_t) = 0}$. However, even under these circumstances, the relative risk breaks together too, because

$$RR(A_t, B_t) = \frac{p(a_t) \times (0 + p(d_t))}{(p(a_t) + 0) \times 0} \tag{58}$$

Marcello Pagano and Kimberlee Gauvreau (Pagano 2018) proposed an illogical trick to circumvent the fundamental problems with the risk ratio and the odds ratio. Pagano and Gauvreau proposed to add 0.5 to the cells a, b, c, d. To avoid any confusion on this issue, such an approach is misleading and the principle problems with the risk ratio and the odds ratio become even more blurred.

3.5. *Sufficient condition and risk ratio*

Theorem 5 (**Sufficient condition and risk ratio**).

Claim.
In general, under some circumstances the risk ratio, denoted as RR_{sc} (A_t, B_t), defined as

$$RR_{sc}(A_t, B_t) = \frac{a \times \underline{B}}{b \times B} = +1 \tag{59}$$

provides only a very approximate and equally a very imprecise picture of a sufficient condition.

Proof By Modus Ponens.
The premise of modus ponens [67] is that

$$+1 = +1 \tag{60}$$

If this premise is true, then the conclusion is also true, the absence of any technical and other errors of human reasoning assumed. The premise is true. Multiplying the premise (i. e. eq. 60) by $(p(A_t) \times p(B_t))$ it is

$$p(A_t) \times p(B_t) = p(A_t) \times p(B_t) \tag{61}$$

Under conditions of probability theory and in the case of independence of both events A_t and B_t at a certain (period of) time / Bernoulli (see also Uspensky 1937) trial t it is according to de Moivre [68] and Kolmogoroff [69] and other

$$p(a_t) = p(A_t \wedge B_t) = p(A_t) \times p(B_t) \tag{62}$$

According to eq. 4 it is $p(A_t) = (p(a_t) + p(b_t))$. Eq. 62 changes too

$$p(a_t) = (p(a_t) + p(b_t)) \times p(B_t) \tag{63}$$

or too

$$p(a_t) = (p(a_t) \times p(B_t)) + (p(b_t) \times p(B_t)) \tag{64}$$

Rearranging eq. 64 it is

$$p(a_t) - (p(a_t) \times p(B_t)) = p(b_t) \times p(B_t) \tag{65}$$

or

$$p(a_t) \times (1 - p(B_t)) = p(b_t) \times p(B_t) \tag{66}$$

Based on eq. 7 it is $p(\underline{B}_t) \equiv (1 - p(B_t))$. **Under conditions of independence eq. 66 changes further**. In general, is is necessary to accept that

$$p(a_t) \times p(\underline{B}_t) = p(b_t) \times p(B_t) \tag{67}$$

Under conditions of independence eq. 67 implies too that

$$\frac{p(a_t)}{p(B_t)} = \frac{X \times p(a_t)}{X \times p(B_t)} = \frac{p(b_t)}{p(\underline{B}_t)} \tag{68}$$

Eq. 68 can be tested by a kind of a Chi-square goodness of fit test as $\tilde{\chi}^2{}_{\text{Calculated}} = N \times \sum_{t=1}^{t=N} \left(\frac{\left(\frac{p(a_t)}{p(B_t)} - \frac{p(b_t)}{p(\underline{B}_t)} \right)^2}{\frac{p(b_t)}{p(\underline{B}_t)}} \right)$, a sum of differences between the observed and the expected. From 68 follows too that

[67] http://www.ijmttjournal.org/archive/ijmtt-v65i7p524
[68] https://doi.org/10.3931/e-rara-10420
[69] https://doi.org/10.1007/978-3-642-49888-6

$$p(a_t) = p(b_t) \times \frac{p(B_t)}{p(\underline{B}_t)} \tag{69}$$

or that

$$p(b_t) = p(a_t) \times \frac{p(\underline{B}_t)}{p(B_t)} \tag{70}$$

However, eq. 67 derived as $p(a_t) \times p(\underline{B}_t) = p(b_t) \times p(B_t)$ can be rearranged further as

$$\frac{p(a_t) \times p(\underline{B}_t)}{p(b_t) \times p(B_t)} = +1 \tag{71}$$

which is a very approximate and equally a very imprecise picture of a sufficient condition provided to us by the risk ratio RR_{sc} (A_t, B_t) as

$$RR_{sc}(A_t, B_t) = \frac{p(a_t) \times p(\underline{B}_t)}{p(b_t) \times p(B_t)} = +1 \tag{72}$$

Under conditions where each trial is independent of another trial and where the probability of an event is constant from trial to trial it is equally

$$RR_{sc}(A_t, B_t) = \frac{p(a_t) \times p(\underline{B}_t)}{p(b_t) \times p(B_t)} = \frac{N^2 \times p(a_t) \times p(\underline{B}_t)}{N^2 \times p(b_t) \times p(B_t)} = \frac{a \times \underline{B}}{b \times B} = +1 \tag{73}$$

where a, b, B (i. e. cases) and $\underline{B}$ (i. e. controls) may denote the expectation values and our conclusion is true.

QUOD ERAT DEMONSTRANDUM.

A $RR_{sc}(A_t, B_t) = \frac{p(a_t) \times p(\underline{B}_t)}{p(b_t) \times p(B_t)} = \frac{N^2 \times p(a_t) \times p(\underline{B}_t)}{N^2 \times p(b_t) \times p(B_t)} = \frac{a \times \underline{B}}{b \times B} > +1$ may provide some, even if very slight evidence, that A_t is a sufficient condition of B_t. However, it makes much more sense to use the original(see also Barukčić 2021) sufficient[70] condition formula.

[70] https://www.matec-conferences.org/articles/matecconf/abs/2021/05/matecconf_cscns20_09032/matecconf_cscns20_09032.html

3.6. *Case $p(b_t) = 0$: The relative risk RR is defined*

Theorem 6 (Case $p(B_T) = 0$: The relative risk RR is defined).

Claim.
In general, under circumstances $p(b_t) = 0$, the relative risk RR is determined as

$$RR(A_t, B_t) = \frac{p(notA_t)}{p(c_t)} \tag{74}$$

Proof By Modus Ponens.
The premise of modus ponens is that the relative risk RR is true. Thus far, it is

$$RR(A_t, B_t) = \frac{p(a_t) \times p(notA_t)}{p(A_t) \times p(c_t)} \tag{75}$$

which is equivalent with

$$RR(A_t, B_t) = \frac{p(a_t) \times p(notA_t)}{(p(a_t) + p(b_t)) \times p(c_t)} \tag{76}$$

Under conditions where $p(b_t) = 0$, the equation before changes to

$$RR(A_t, B_t) = \frac{p(a_t) \times p(notA_t)}{(p(a_t) + 0) \times p(c_t)} \tag{77}$$

or to

$$RR(A_t, B_t) = \frac{p(a_t) \times p(notA_t)}{p(a_t) \times p(c_t)} \tag{78}$$

Under circumstances where $p(b_t) = 0$ the conclusion

$$RR(A_t, B_t) = \frac{p(notA_t)}{p(c_t)} \tag{79}$$

is true.
Quod erat demonstrandum.

Remark. Theoretically, the relative risk RR has the potential to detect a sufficient condition (**conditio per quam**) relationship, but only if **RR > +1**. However, a significant and positive relative risk does not provide evidence of a conditio per quam relationship. Furthermore and depending especially upon study design, an existing conditio per quam relationship need not to be detected by the relative risk as proofed before. The following figure may illustrate the relationship again.

Conditio per quam		Street is wet		
		YES	NO	
It is raining	YES	+1	+0	A_t
	NO	+1	+1	$\underline{A}_t$
		B_t	$\underline{B}_t$	

3.7. *Case $p(a_t) = 0$: The relative risk RR is defined*

Theorem 7 (Case $p(A_T) = 0$: The relative risk RR is defined).

Claim.
In general, under circumstances $p(a_t) = 0$, the relative risk RR is determined as

$$RR(A_t, B_t) = \frac{\frac{p(a_t)}{p(A_t)}}{\frac{p(c_t)}{p(notA_t)}} = \frac{p(a_t) \times p(notA_t)}{p(A_t) \times p(c_t)} = 0. \tag{80}$$

Proof By Modus Ponens.
The premise of modus ponens is that the relative risk RR is true. Thus far, it is

$$RR(A_t, B_t) = \frac{p(a_t) \times p(notA_t)}{p(A_t) \times p(c_t)} \tag{81}$$

Under conditions where $p(a_t) = 0$, it is

$$RR(A_t, B_t) = \frac{0 \times p(notA_t)}{p(A_t) \times p(c_t)} \tag{82}$$

Under these circumstances the conclusion

$$RR(A_t, B_t) = 0 \tag{83}$$

is true.
Quod erat demonstrandum.

Remark. An $RR_{nc}(A_t, B_t) = RR_{sc}(A_t, B_t) = +0$ may provide some evidence that A_t excludes B_t and vice versa. However, it makes much more sense to use the original(see also Barukčić 2021) exclusion[71] relationship formula. In other words, the relative risk has the potential to **detect an exclusion relationship**, but only if RR = 0. The following figure may illustrate the basic relationships again.

Relative risk		Outcome		Total
		YES	NO	
Exposed	YES	$p(a_t)$	$p(b_t)$	$p(A_t)$
	NO	$p(c_t)$	$p(d_t)$	$p(\underline{A}_t)$
	Total	$p(B_t)$	$p(\underline{B}_t)$	+1

[71] https://www.matec-conferences.org/articles/matecconf/abs/2021/05/matecconf_cscns20_09032/matecconf_cscns20_09032.html

3.8. *Examples: Covid 19 vaccine studies 2020/2021*

Since its emergence in December 2019, first reported in Wuhan, China, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has caused millions of infections and deaths worldwide. Developing effective vaccines at an unprecedented speed to halt the Covid-19 pandemic [72] is of great importance.

3.8.1. *Sputnik V (Russia)*

Study 3.8.1.1 (Covid-19 vector Vaccine Sputnik V (Russia))**.**

The Russian, heterologous recombinant adenovirus (rAd)-based vaccine, Gam-Covid-Vac (Sputnik V), showed good humoral and cellular immune responses and has been tested in a phase 3 trial [73] (see table 4).

Table 4. Sputnik V ®and Covid-19 infection.

		Covid-19 infection		
		YES	NO	
Sputnik V®	YES	16	14964	14980
	NO	62	4824	4886
		78	19788	19866

Causal relationship k =	-0,0800
p Value left tailed (HGD) =	0,0000000
p (EXCL) =	0,99919460
$\tilde{\chi}^2$ (EXCL— A_t) =	0,0171
$\tilde{\chi}^2$ (EXCL— B_t) =	3,2821
p Value (EXCL) =	0,00080507
p(IOI)=	0,7501
Vaccine efficacy (%) =	91,5828

The original data as presented by Logunov et al. (Logunov et al. 2021) suggest a vaccine efficacy of about 91,5828 % (see table 4). However, even the original data of Logunov et al. (Logunov et al. 2021) allow the conclusion that "Sputnik V ®"vaccination excludes a Covid-19 infection with the probability of p = 0,99919460 (see table 4). In other words, in about **8 out of 10.000 cases**, the "Sputnik V "®vaccine would not prevent from a Covid-19 infection. However, the study design of the study of Logunov et al. (Logunov et al. 2021) with p(IOI) = 0,7501 has been extremely unfair. A fair study design (b = c = 14964) assumed (see table 5) without changing vaccine efficacy, we should obtain data similar to the following, fictive data.

Table 5. Sputnik V ®(fair study) and Covid 19 infection.

		Covid 19 infection		
		YES	NO	
Sputnik V ®(fair study)	YES	16	14964	14980
	NO	14964	1164295	1179259
		14980	1179259	1194239

Causal relationship k =	-0,0116
p Value left tailed (HGD) =	0,0000000
p (EXCL) =	0,99998660
$\tilde{\chi}^2$ (EXCL— A_t) =	0,0171
$\tilde{\chi}^2$ (EXCL— B_t) =	0,0171
p Value (EXCL) =	0,00001340
p(IOI)=	0,0000
Vaccine efficacy (%) =	91,5828

[72] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7785400/

[73] https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00234-8/fulltext

Under conditions of a fair study design “Sputnik V ®”is of much better help. Under these conditions, only in about **1 out of 100.000 cases** a “Sputnik V ®”vaccine would not protect against a Covid-19 infection. The calculated vaccine efficacy (VE) with 91,5828 % (see table 4) underestimates the efficiency of the “Sputnik V®”vaccine dramatically.

3.8.2. *Comirnaty ®(Germany)*

Study 3.8.2.1 (Covid-19 mRNA Vaccine Comirnaty ®(Germany))**.**

The rapidity with which vaccines against Covid-19 have been developed is unimaginable [74]. Pfizer ®and BioNTech ®(Polack et al. 2020)[75] Manufacturing GmbH (R) presented the following data (see table 6).

Table 6. Comirnaty®mRNA Vaccine and Covid 19 infection.

		Covid 19 infection		
		YES	NO	
Comirnaty®mRNA Vaccine	YES	8	18190	18198
	NO	162	18163	18325
		170	36353	36523

Causal relationship k =	-0,0617
p Value left tailed (HGD) =	0,0000000
p (EXCL) =	0,99978096
$\tilde{\chi}^2$ (EXCL— A_t) =	0,0035
$\tilde{\chi}^2$ (EXCL— B_t) =	0,3765
p Value (EXCL) =	0,00021902
p(IOI)=	0,4936
Vaccine efficacy (%) =	95,0273

However, even the study design of the study of Pfizer ®and BioNTech®Manufacturing GmbH has been biased (p(IOI)=0,4936). Thus far and despite of these difficulties, the data presented by Pfizer ®and BioNTech®Manufacturing GmbH do support the conclusion that the vaccine Comirnaty®excludes Covid -19 infection in 99978 out of 100000 cases. The calculated vaccine efficacy is 95,0273% and underestimates the efficacy of Comirnaty®. The data published by Pfizer ®and BioNTech®Manufacturing GmbH suggest too that in about **2 out of 10.000 cases** Comirnaty®will not protect against a Covid-19 infection.

Under conditions of a fair study design (b = c = 18190), data similar to the following fictive data (see table 7) would have to be documented.

[74] https://www.ema.europa.eu/en/documents/product-information/comirnaty-epar-product-information_en.pdf

[75] https://www.nejm.org/doi/full/10.1056/NEJMoa2034577?query=featured_home

Table 7. Comirnaty mRNA Vaccine (fair study) and Covid 19 infection.

		Covid 19 infection		
		YES	NO	
Comirnaty®mRNA Vaccine (fair study)	YES	8	18190	18198
	NO	18190	2039413	2057603
		18198	2057603	2075801

Causal relationship k =	-0,0084
p Value left tailed (HGD) =	0,0000000
p (EXCL) =	0,99999615
$\tilde{\chi}^2$ (EXCL— A_t) =	0,0035
$\tilde{\chi}^2$ (EXCL— B_t) =	0,0035
p Value (EXCL) =	0,00000385
p(IOI)=	0,0000
Vaccine efficacy (%) =	95,0273

The calculated vaccine efficacy of 95,0273% has not changed. However, Comirnaty®would not protect against a Covid -19 infection in about **4 out of 1.000.000 cases**. In other words, the inappropriate study design has lead to biased data. Comirnaty®is of better help than suggested by the original data published.

Study 3.8.2.2 (Maccabi Healthcare Services Covid-19 mRNA Vaccine Comirnaty ®re-evaluation study data)**.**

Maccabi Healthcare Services, an Israeli healthcare provider, vaccinated more than half a million people with both doses of the Pfizer®Covid-19 mRNA Vaccine Comirnaty ®. In the following, only 544 people have been subsequently diagnosed with the coronavirus, no people died [76] , [77]. The data presented by Maccabi Healthcare Services are illustrated by table 8.

Table 8. Comirnaty ®mRNA Vaccine and Covid 19 infection.

		Covid 19 infection		
		YES	NO	
Comirnaty ®mRNA Vaccine	YES	544	522456	523000
	NO	18425	609575	628000
		18969	1132031	1151000

Causal relationship k =	-0,1107
p Value left tailed (HGD) =	0,0000000
p (EXCL) =	0,99952737
$\tilde{\chi}^2$ (EXCL— A_t) =	0,5658
$\tilde{\chi}^2$ (EXCL— B_t) =	15,6010
p Value (EXCL) =	0,00047252
p(IOI)=	0,4379
Vaccine efficacy (%) =	96,4547

It is necessary to point out once again that the study design of Maccabi Healthcare Services has been unfair (p(IOI) = 0,4379) too. Based on the data of Maccabi Healthcare Services, the Comirnaty ®mRNA vaccine would not[78] protect against a Covid 19 virus infection in about **5 out of 10.000 cases**.

Study 3.8.2.3 (Covid-19 mRNA Vaccine Comirnaty ®(Germany) and adolescents 12 to 15 years of age)**.**

Pfizer ®Inc. (NYSE: PFE) and BioNTech ®SE (Nasdaq: BNTX) announced on Wednesday, March 31, 2021 - 06:45am [79] that their Covid 19 vaccine BNT162b2 demonstrated an 100 % efficacy and robust antibody responses

[76] https://www.timesofisrael.com/hmo-sees-only-544-Covid-infections-among-523000-fully-vaccinated-israelis/

[77] https://www.zeit.de/wissen/gesundheit/2021-02/biontech-impfstoff-wirksamkeit-studie-israel-corona-impfung-virusvarianten

[78] https://www.reuters.com/article/health-coronavirus-pfizer/pfizer-biontech-covid-19-shot-91-effective-in-updated-data-protective-against-south-african-variant-i

[79] https://www.pfizer.com/news/press-release/press-release-detail/pfizer-biontech-announce-positive-topline-results-pivotal

in a Phase 3 trial in adolescents 12 to 15 years of age. “The trial enrolled 2,260 adolescents 12 to 15 years of age in the United States. In the trial, 18 cases of COVID-19 were observed in the placebo group (n=1,129) versus none in the vaccinated group (n=1,131). ”[80] The data of this trial are viewed by the following 2x2 table 9.

Table 9. Comirnaty mRNA Vaccine and Covid 19 infection age: 12-15 years .

		Covid 19 infection age: 12-15 years		
		YES	NO	
Comirnaty mRNA Vaccine	YES	0	1131	1131
	NO	18	1111	1129
		18	2242	2260

Causal relationship k =	-0,0897
p Value left tailed (HGD) =	0,0000035
p (EXCL) =	1,00000000
$\tilde{\chi}^2$ (EXCL— A_t) =	0,0000
$\tilde{\chi}^2$ (EXCL— B_t) =	0,0000
p Value (EXCL) =	0,00000000
p(IOI)=	0,4925
p(IOU)=	0,4916
Vaccine efficacy (%) =	100,0000

The study design of the trial mentioned has been unfair (p(IOI)=0,4925). Despite this obvious disadvantage, the data obtained by the study support the hypothesis that a vaccination with the Comirnaty®mRNA vaccine excludes(Barukčić 2021) [81] a Covid-19 infection/disease (p (EXCL) = 1,00000000, p Value (EXCL) =0,00000000).

3.8.3. *Moderna ®(USA) Covid-19 vaccine (mRNA-1273)*

Study 3.8.3.1 (Covid-19 vaccine (mRNA-1273) ®(USA))**.**

A lipid nanoparticle-encapsulated mRNA-1273-based vaccine(Baden et al. 2020) to prevent coronavirus disease 2019 (Covid-19) and to protect persons from SARS-CoV-2, the virus that causes Covid-19, has been developed by the company Moderna®. The data[82] [83] published are viewed by table 10.

Table 10. Covid-19 vaccine (mRNA-1273) ®and Covid 19 infection.

		Covid 19 infection		
		YES	NO	
Covid-19 vaccine (mRNA-1273) ®	YES	11	14123	14134
	NO	185	13888	14073
		196	28011	28207

Causal relationship k =	-0,0744
p Value left tailed (HGD) =	0,0000000
p (EXCL) =	0,99961003
$\tilde{\chi}^2$ (EXCL— A_t) =	0,0086
$\tilde{\chi}^2$ (EXCL— B_t) =	0,6173
p Value (EXCL) =	0,00038990
p(IOI)=	0,4941
Vaccine efficacy (%) =	94,0797

[80] https://www.pfizer.com/news/press-release/press-release-detail/pfizer-biontech-announce-positive-topline-results-pivotal

[81] https://www.matec-conferences.org/articles/matecconf/abs/2021/05/matecconf_cscns20_09032/matecconf_cscns20_09032.html

[82] https://www.nejm.org/doi/10.1056/NEJMoa2035389

[83] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7787219/

The vaccine efficacy(Baden et al. 2020) has been calculated about 94,0797%. In other words, Moderna's Covid-19 vaccine (mRNA-1273) ®does not protect from Covid-19 infection in about **4 out of 10.000 cases**. Again, the study design has been unfair (p(IOI) = 0,4941) too. A fair study design assumed (b = c = 14123), we would obtain data similar to the following data (see table 11). In other words, Covid-19 vaccine (mRNA-1273) ®would not protect from a Covid -19 infection only in about **1 out of 100.000 cases**. It is quite clear that Moderna's Covid-19 vaccine (mRNA-1273) ®is much better than what a vaccine efficacy of 94,0797% lead us to believe.

Table 11. Covid-19 vaccine (mRNA-1273) ®(fair study) and Covid 19 infection .

		Covid 19 infection		
		YES	NO	
Covid-19 vaccine (mRNA-1273) ®(fair study)	YES	11	14123	14134
	NO	14123	1060217	1074340
		14134	1074340	1088474

Causal relationship k =	-0,0124
p Value left tailed (HGD) =	0,0000000
p (EXCL) =	0,99998989
$\tilde{\chi}^2$ (EXCL— A_t) =	0,0086
$\tilde{\chi}^2$ (EXCL— B_t) =	0,0086
p Value (EXCL) =	0,00001011
p(IOI)=	0,0000
Vaccine efficacy (%) =	94,0797

3.8.4. *AstraZeneca®(GB, Sweden) Covid-19 vaccine*

AstraZeneca®(GB, Sweden) Covid-19 vaccine original data —

Study 3.8.4.1 (Covid-19 vector vaccine AstraZeneca®(GB, Sweden))**.**

AstraZeneca®developed a monovalent vaccine composed of a single recombinant, replication-deficient chimpanzee adenovirus (ChAdOx1) vector encoding the SARS-CoV-2 Spike glycoprotein to prevent coronavirus disease[84]. The data presented by AstraZeneca®are illustrated by table 12.

Table 12. Covid-19 vaccine AstraZeneca ®and Covid 19 infection.

		Covid 19 infection		
		YES	NO	
Covid-19 vaccine AstraZeneca ®	YES	64	5194	5258
	NO	154	5056	5210
		218	10250	10468

Causal relationship k =	-0,0609
p Value left tailed (HGD) =	0,0000000
p (EXCL) =	0,99388613
$\tilde{\chi}^2$ (EXCL— A_t) =	0,7790
$\tilde{\chi}^2$ (EXCL— B_t) =	18,7890
p Value (EXCL) =	0,00609522
p(IOI)=	0,4815
Vaccine efficacy (%) =	58,8209

In other words, in about **6 out of 1.000 cases** the vector based vaccine of AstraZeneca ®would not be able to protect people from a Covid-19 infection. In spite of that obvious disadvantage, the calculated vaccine efficacy

[84] https://www.ema.europa.eu/en/documents/product-information/Covid-19-vaccine-astrazeneca-product-information-approved-chmp-29-january-2021-pending-en.pdf

of about 58,8209% is gross underestimating the potential of the vaccine of AstraZeneca ®and make us belief that AstraZeneca ®vaccine is worthless. Quite the contrary, AstraZeneca ®vaccine is able to avoid personal disaster for about **994 out of 1.000 cases**, which can not be said often enough. Whereas it is necessary to consider that the study design of the study of AstraZeneca ®has been unfair (p(IOI) = 0,4815). A fair (b = c = 5194) study design assumed, we would have to obtain data similar to the following (fictive) data (see table 13).

Table 13. Covid-19 vaccine AstraZeneca ®(fair study) and Covid 19 infection.

		Covid 19 infection		
		YES	NO	
Covid-19 vaccine AstraZeneca ®(fair study)	YES	64	5194	5258
	NO	5194	170525	175719
		5258	175719	180977

Causal relationship k =	-0,0174
p Value left tailed (HGD) =	0,0000000
p (EXCL) =	0,99964636
$\tilde{\chi}^2$ (EXCL— A_t) =	0,7790
$\tilde{\chi}^2$ (EXCL— B_t) =	0,7790
p Value (EXCL) =	0,00035357
p(IOI)=	0,0000
Vaccine efficacy (%) =	58,8210

It is extremely important to realise that only in about **4 out of 10.000 cases** the vector based vaccine of AstraZeneca ®would not be able to protect against a Covid-19 infection.

Covid-19 vector Vaccine AstraZeneca®Cases > 14 days after second dose (GB, Sweden) —

Study 3.8.4.2 (Covid-19 vector Vaccine AstraZeneca®Cases > 14 days after second dose (GB, Sweden))**.**

A regimen of a low primary dose and a standard booster dose may have an impact on the efficacy of a vaccine. Three single-blind randomised controlled trials provided additional data [85] ,[86] on vaccine efficacy of AstraZeneca®vaccine under these conditions. Detailed information can be found at the table 14.

Table 14. Covid-19 vaccine AstraZeneca ®(unfair study) and Covid 19 infection.

		Covid 19 infection		
		YES	NO	
Covid-19 vaccine AstraZeneca ®(unfair study)	YES	10	1386	1396
	NO	51	1351	1402
		61	2737	2798

Causal relationship k =	-0,1000
p Value left tailed (HGD) =	0,0000000
p (EXCL) =	0,99642602
$\tilde{\chi}^2$ (EXCL— A_t) =	0,0716
$\tilde{\chi}^2$ (EXCL— B_t) =	1,6393
p Value (EXCL) =	0,00356760
p(IOI)=	0,4771
Vaccine efficacy (%) =	80,3079

[85] https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3777268

[86] https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00432-3/fulltext

In other words, in about **4 out of 1.000 cases** the vector based vaccine of AstraZeneca ®would not be able to prevent a primary symptomatic Covid-19 infection after more than 14 days after second dose. However, there were no hospital admissions for Covid-19 in the AstraZeneca ®vaccine group after the initial 21-day exclusion period.

Covid-19 vector vaccine AstraZeneca®(GB, Sweden) and death —

Study 3.8.4.3 (Covid-19 vector vaccine AstraZeneca®(GB, Sweden) and death)**.**

The authors[87] ,[88] reported about "...seven deaths considered unrelated to vaccination (two in the ChAdOx1 nCov-19 group and five in the control group) "with "12282 participants in the ChAdOx1nCoV-19 group and ...11962 participants in the control group ..."[89] ,[90]. The data are viewed by the table 15.

Table 15. Covid-19 vaccine AstraZeneca ®(unfair study) and Death.

		Death		
		YES	NO	
Covid-19 vaccine AstraZeneca ®(unfair study)	YES	2	12280	12282
	NO	5	11957	11962
		7	24237	24244

Causal relationship k =	-0,0075
p Value left tailed (HGD) =	0,2158443
p (EXCL) =	0,99991751
$\tilde{\chi}^2$ (EXCL— A_t) =	0,0003
$\tilde{\chi}^2$ (EXCL— B_t) =	0,5714
p Value (EXCL) =	0,00008249
p(IOI)=	0,5063
Vaccine efficacy (%) =	61,0422

In other words, the vector based vaccine of AstraZeneca ®protects against the death with the probability of **p (EXCL) = 0,99991751**.

Covid-19 vector vaccine AstraZeneca®(GB, Sweden) and cerebral venous thrombosis —

Study 3.8.4.4 (Covid-19 vector vaccine AstraZeneca®(GB, Sweden) and cerebral venous thrombosis)**.**

The value[91] of the incidence[92] of cerebral[93] venous thrombosis (CVT) in a population depends on neuroimaging techniques too and is very controversial. Currently, in the medical literature the value of the incidence[94] of CVT ranges from 1.32 per 100,000 people per year(Coutinho et al. 2012) (Netherlands[95], 2012) over 1.57 cases per 100,000 people per year(Devasagayam et al. 2016) (City of Adelaide[96], Australia, 2016) to 1.75 cases per 100,000 people(Kristoffersen et al. 2020) per year (Norway[97], 2020). In other words, we just don't know absolutely for sure the exact incidence of cerebral venous thrombosis, neither in a sample nor in a population. Under these conditions, it appears to be almost completely impossible to draw correct conclusions about a possible relationship between the vaccination with AstraZeneca's Covid-19 vaccine and the cerebral venous thrombosis as such. Definitely, even if this issue is associated with many inadequacies and is overshadowed with a lot of uncertainties, especially if incorrect statistical methods are used to evaluate this relationship, we are not completely and helplessly at the mercy of this unknown and very abstract threat.

Firstly.

First of all, the hypothesis **if** vaccination with AstraZeneca's Covid-19 vaccine **then** CVT cannot be accepted. In other words, a vaccination with AstraZeneca's Covid-19 vaccine is not a sufficient condition of a CVT.

[87] https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3777268
[88] https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00432-3/fulltext
[89] https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3777268
[90] https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00432-3/fulltext
[91] https://pubmed.ncbi.nlm.nih.gov/24129682/
[92] https://pubmed.ncbi.nlm.nih.gov/29627811/
[93] https://pubmed.ncbi.nlm.nih.gov/30132621/
[94] https://pubmed.ncbi.nlm.nih.gov/28820187/
[95] https://pubmed.ncbi.nlm.nih.gov/22996960/
[96] https://pubmed.ncbi.nlm.nih.gov/27435401/
[97] https://pubmed.ncbi.nlm.nih.gov/32883194/

Reasons.

In Germany, at the end of the year 2020 there were about 83 157 201 [98] inhabitant's.

The German state authority 'Paul-Ehrlich-Institut'announced publicly on March, 29 2021 the following:

"Laut Impfquotenmonitoring des RKI wurden bis einschließlich 29.03.2021 (Montag) 2.697.479 Erstdosen plus 767 Zweitdosen von Vaxzevria verimpft:

Bis zum 29.03.2021 (Montagmittags) wurden dem Paul-Ehrlich-Institut 31 Fälle einer Sinusvenenthrombose nach Impfung mit dem COVID-19 Impfstoff von AstraZeneca (Vaxzevria) im Rahmen der Spontanerfassung gemeldet.

In 19 Fällen wurde zusätzlich eine Thrombozytopenie gemeldet.

In neun Fällen war der Ausgang tödlich.

Mit Ausnahme von zwei Fällen betrafen alle Meldungen Frauen im Alter von 20 bis 63 Jahren. Die beiden Männer waren 36 und 57 Jahre alt."[99]

The present public proclamation of the German state authority 'Paul-Ehrlich-Institut'translated into English:

"According to the RKI's vaccination rate monitoring system, **2,697,479** first doses plus 767 second doses of Vaxzevria were vaccinated up to and including March 29, 2021 (Monday):

By March 29, 2021 (Monday noon), **31 cases of cerebral venous thrombosis** after vaccination with the COVID-19 vaccine from AstraZeneca (Vaxzevria) were reported to the Paul Ehrlich Institute as part of the spontaneous recording.

Thrombocytopenia was also reported in 19 cases.

The outcome was fatal in nine cases.

With the exception of two cases, all reports concerned women aged 20 to 63 years. The two men were 36 and 57 years old. "

It is important to point out that not all cases of cerebral venous thrombosis which occur in Germany are reported to the German state authority 'Paul-Ehrlich-Institut but only those which may be somehow related to the vaccination.

Based on these data, the incidence of cerebral venous thrombosis in the population of vaccinated with the COVID-19 vaccine from AstraZeneca (Vaxzevria) per 100.000 vaccinated follows as

$$Incidence(CVT;verum) = \frac{a}{A} \times 100.000 = \frac{31}{2697479} \times 100.000 = 1,149645355 \tag{84}$$

The COVID-19 vaccine from AstraZeneca (Vaxzevria) had 2697479 times the chance to be the cause of cerebral venous thrombosis. Nothing and nobody did forbid the COVID-19 vaccine from AstraZeneca (Vaxzevria) 2697479 times to cause cerebral venous thrombosis. However, this vaccine did not had the capacity to act so. Only 31 cases of cerebral venous thrombosis out of 2697479 cases vaccinated where observed. The question is justified are these 31 cases pure coincidence or is there a cause effect relationship given? Under conditions where X times more people are vaccinated with the COVID-19 vaccine from AstraZeneca (Vaxzevria) the incidence calculated will more or less not change. We obtain

$$Incidence(CVT;verum) = \frac{X \times a}{X \times A} \times 100.000 = \frac{X \times 31}{X \times 2697479} \times 100.000 = 1,149645355 \tag{85}$$

For preliminary purposes **we assume** that the event vaccination with the COVID-19 vaccine from AstraZeneca (Vaxzevria) and the event cerebral venous thrombosis are **independent** of each other.

Under these conditions, according to equation 47 the number of cases of cerebral venous thrombosis in the German population of not vaccinated by the COVID-19 vaccine from AstraZeneca (Vaxzevria) can be calculated (see also table 16) very precisely as

$$c = a \times \frac{\underline{A}}{A} = 31 \times \frac{80458600}{2697479} = 925 \tag{86}$$

where a, c, A and $\underline{A}$ may denote the expectation values. Under conditions of independence, the number of cases of cerebral venous thrombosis within the German population follows as

[98] https://www.destatis.de/DE/Themen/Gesellschaft-Umwelt/Bevoelkerung/Bevoelkerungsstand/Tabellen/zensus-geschlecht-staatsangehoerigkeit-2020.html;jsessionid=ABE2D76733C15949BEDC0794D3E7765E.internet721

[99] https://www.pei.de/DE/service/presse/aktuelles/aktuelles-inhalt.html;jsessionid=7C63F1E4F9A2A12E296611B36952A6F0.intranet241

$$B = a + c = 31 + 925 = 956 \tag{87}$$

as is illustrated by table 16 too.

Based on these calculations, the incidence of cerebral venous thrombosis in the German population per 100.000 inhabitants follows as

$$Incidence = \frac{B}{N} \times 100.000 = \frac{956}{83156079} \times 100.000 = 1,149645355 \tag{88}$$

In other words, we expect an incidence of cerebral venous thrombosis in the German population per 100.000 people of about 1,149645355, a value which is going against the current trend. In the medical literature the value of the incidence[100] of CVT ranges from 1.32 per 100,000 people per year(Coutinho et al. 2012) (Netherlands[101], 2012) over 1.57 cases per 100,000 people per year(Devasagayam et al. 2016) (City of Adelaide[102], Australia, 2016) to 1.75 cases per 100,000 people(Kristoffersen et al. 2020) per year (Norway[103], 2020). Completely surprising and contrary to any expectation, there is clear evidence that the number of cases of cerebral venous thrombosis in the verum group (people vaccinated with the COVID-19 vaccine from AstraZeneca (Vaxzevria)) is significantly lower than in the group of non-vaccinated (placebo group) which may seem somewhat strange. These data are viewed by table 16.

Table 16. Covid-19 vaccine AstraZeneca ®and cerebral venous thrombosis.

		cerebral venous thrombosis		
		YES	NO	
Covid-19 vaccine AstraZeneca ®	YES	31	2697448	2697479
	NO	925	80457675	80458600
		956	83155123	83156079

Causal relationship k =	-0,0000002291
p (EXCL) =	0,9999996272
$\tilde{\chi}^2$ (EXCL— A_t) =	0,0004
$\tilde{\chi}^2$ (EXCL— B_t) =	1,0052
p Value (EXCL) =	0,0000003728
p(IOI)=	0,0324
p(IOU)=	0,9675

An attentive reader might critically note that the incidence is not calculated in a correct way. Only about three months of a year are considered for the calculations above. Therefore, the incidence calculated is erroneous. In point of fact, the same reader may claim that the true incidence is

$$Incidence = 4 \times \frac{B}{N} \times 100.000 = 4 \times \frac{956}{83156079} \times 100.000 = 4 \times 1,149645355 = 4,598581422 \tag{89}$$

which would provide clear evidence against the COVID-19 vaccine from AstraZeneca (Vaxzevria). However, such a reasoning is obviously deeply flawed.

Reasons.

It is to be emphasised that the whole Germany population has been observed for about 3 months. In particular, it is of course possible to observe the whole German population four times more or four times longer. In this case, the incidence will not change. We obtain approximately

$$Incidence = \frac{4}{4} \times \frac{B}{N} \times 100.000 = \frac{4}{4} \times \frac{956}{83156079} \times 100.000 = 1,149645355 \tag{90}$$

[100] https://pubmed.ncbi.nlm.nih.gov/28820187/

[101] https://pubmed.ncbi.nlm.nih.gov/22996960/

[102] https://pubmed.ncbi.nlm.nih.gov/27435401/

[103] https://pubmed.ncbi.nlm.nih.gov/32883194/

otherwise other statistical methods (i. e. the hyper-geometric distribution et cetera) need to be used to perform the calculations desired. Based on these assumptions before and the calculations as presented by table 16, it is not absurd to conclude, that the Covid-19 vaccine of AstraZeneca ®protects against cerebral venous thrombosis (causal relationship negative, exclusion relationship highly significant, p(IOI) very appropriate). In point of fact, in these issues, much depends on the quality of the data and the logical consistency of the statistical methods used. However that may be, it is unfounded to assume that a vaccination with Covid-19 vaccine of AstraZeneca ®is a sufficient condition of cerebral venous thrombosis because 2697448 out of 2697479 persons which where vaccinated by the Covid-19 vaccine of AstraZeneca ®suffered not from cerebral venous thrombosis.

For a causal relationship between a Covid-19 vaccine of AstraZeneca ®and cerebral venous thrombosis both is needed, a necessary condition and a sufficient condition. Since a sufficient condition relationship between AstraZeneca ®Covid-19 vaccine and cerebral venous thrombosis is not given in general and for sure, it is extremely difficult to consider a cause effect relationship between AstraZeneca ®Covid-19 vaccine and cerebral venous thrombosis as proven. However, may be AstraZeneca ®Covid-19 vaccine is a necessary condition of cerebral venous thrombosis. The data for a period of 3 month of a year may be presented again by table 17.

Table 17. Covid-19 vaccine AstraZeneca ®and cerebral venous thrombosis.

		cerebral venous thrombosis		
		YES	NO	
Covid-19 vaccine AstraZeneca ®	YES	31	2697448	2697479
	NO	925	80457675	80458600
		956	83155123	83156079

Causal relationship k =	-0,0000002291
p (EXCL) =	0,9999996272
$\tilde{\chi}^2$ (EXCL— A_t) =	0,0004
$\tilde{\chi}^2$ (EXCL— B_t) =	1,0052
p Value (EXCL) =	0,0000003728
p(IOI)=	0,0324
p(IOU)=	0,9675

We reasonably assume that about 925 cases of cerebral venous thrombosis (see table 17) occurred in the population of 80458077 non-vaccinated with the Covid-19 vaccine of AstraZeneca ®without being reported to the authority 'Paul-Ehrlich-Institut'. Basically, one case as such is enough to refute the assumption/hypothesis of a necessary condition relationship between the Covid-19 vaccine of AstraZeneca ®and cerebral venous thrombosis. It is also to be referred to the fact that history itself has already provided evidence that a Covid-19 vaccine AstraZeneca ®is not a necessary condition of cerebral venous thrombosis independently of the data as illustrated by table 17.

Before the existence of the Covid-19 vaccine of AstraZeneca ®people already suffered from cerebral venous thrombosis.

As an example, we may point to the known relationship:

without gaseous oxygen **no** human life.

If this relationship is generally valid, we are not allowed to find one single human being which is still alive even if there is no gaseous oxygen. In other words, one single case is enough to refute a relationship of a necessary condition.

However, we reasonably expect that about 925 cases of cerebral venous thrombosis will occur in the population of non-vaccinated by the Covid-19 vaccine of AstraZeneca ®. This is not possible if Covid-19 vaccine of AstraZeneca ®were a necessary condition of cerebral venous thrombosis.

The hypothesis: **without** Covid-19 vaccine of AstraZeneca ®**no** cerebral venous thrombosis is refuted by data and by history.

According to the European Medicines Agency (EMA):

"The number of thromboembolic events in vaccinated people is no higher than the number seen in the general population. As of 10 March 2021, 30 cases1 of thromboembolic events had been reported among close to 5 million people vaccinated with COVID-19 Vaccine AstraZeneca in the European Economic Area.

EMA will further communicate as the assessment progresses."[104]

Besides of the public statement of EMA several member states of the European Economic Area paused its vaccination campaign against COVID-19 using the ChAdOx1 nCoV-19 (AZD1222) vaccine Vaxzevria (previously COVID-19 Vaccine AstraZeneca) from Oxford–AstraZeneca.

Meanwhile, besides of this article there is enough other[105] public evidence available to the contrary. As an example:

"In a population of 5 million people (ie, size matching the approximate number of people having received the Oxford–AstraZeneca COVID-19 vaccine in Europe by March 10, 20214), this incidence would correspond to approximately 169 expected cases of venous thromboembolism per week, or 736 expected cases per month (if based on the incidence rate among the 18–99-year-old Danes). Similarly, if estimated based on the incidence rate among 18–64-year-old Danes, one would expect 91 cases of venous thromboembolism per week, or 398 cases per month ... However, although affected by several limitations, these data suggest that **the reported number of thromboembolic events among Europeans who have received the Oxford–AstraZeneca COVID-19 vaccine (at least those reported as deriving from the venous system) does not seem to be increased relative to the expected number** estimated from incidence rates from the entire Danish population before the introduction of the vaccination programme. "[106]

I do believe, as has been demonstrated beyond any reasonable doubt, that any systematic, continued and amateurish use of inappropriate and dangerous statistical methods by authorities and by other forced upon people like a blind, unconscious force present in all of nature has the potential to impose a kind of mental terror on human beings and human culture. I am deeply convinced that such a practice by authorities and by other takes us back far beyond the long and dark era of Middle Ages we hoped was behind us and is opening the floodgates to epistemological despotism while equally so inhuman that the same cannot be tolerated for a second any longer.

Example I: Abraham Lincoln

Abraham Lincoln, the 16th president of the United States, has been assassinated in 1865. John Doe, an US citizen, has been born 2020. An action or feature of John Doe is suspected by the authorities to be the cause of Abraham Lincoln's death. Consequently, John Doe is accused in the year 2021 by the authorities of being the murder of Abraham Lincoln. How much sense does such an approach of the authorities make with respect of the killing of Abraham Lincoln.

None.

Reasons.

One necessary condition of the assassination of Abraham Lincoln by John Doe (2020) in 1865 is at least the existence of John Doe in the year of killing (1865) of Abraham Lincoln. However, this has not been the case. Therefore, neither the existence of John Doe (2020) nor any action of John Doe (2020) can be accepted as a necessary condition of the killing of Abraham Lincoln in the year 1865.

In other words, if an outcome or an event B (killing of Abraham Lincoln in 1865) can occur without a condition A (any action of John Doe in the year 2021) then this is equally the proof that A, any action of John Doe in 2021, cannot be treated as a necessary condition of B, the killing of Abraham Lincoln in 1865. Reason: event B obviously occurred at the time t without an event A at the time t.

A prerequisite of a certain **event A** to be a **necessary condition of another event B** is that event A need to be given at the time t of the occurrence of event B. Otherwise, **the condition A cannot be treated as a necessary condition of the conditioned B**.

In general, prior to the existence of AstraZeneca's Covid-19 vaccine there were cerebral venous thrombosis. This historical fact already provides evidence that AstraZeneca's Covid-19 vaccine is not a necessary condition of cerebral venous thrombosis and is therefore not causally linked with cerebral venous thrombosis.

Example II: Automobiles

Carl Friedrich Benz (1844 – 1929), a German engine designer and automotive engineer, applied on January 29, 1886 for a patent for a vehicle powered by a gas engine[107]. The patent – number 37435 – received for the motorcar in 1886 may be regarded as the birth certificate of the automobile.

Theoretically it is possible that view people believe that the existence of automobiles is a necessary condition of human death.

Can we dismiss such a fear easily as unfounded?

To some extent, yes.

[104] https://www.ema.europa.eu/en/news/covid-19-vaccine-astrazeneca-prac-investigating-cases-thromboembolic-events-vaccines-benefits

[105] http://www.adrreports.eu/en/index.html

[106] https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00762-5/fulltext

[107] https://www.daimler.com/company/tradition/company-history/1885-1886.html

Before the existence of automobiles people already died. This provides evidence against the hypothesis **without** automobiles **no** human death.

However, in our days automobiles do exist and people die sometimes as a consequence of an impact of automobiles. Therefore, what kind of relationship does exist between automobiles and human death in our days?

Even in our days, people die without any contact or impact by automobiles. In other words, even in our days, an automobile as such is not a necessary condition of human death.

However, this does not exclude that automobiles are a sufficient condition of human death. Contrary to expectation, the hypothesis **if** automobiles **then** human death cannot be accepted too. Evidence against such a hypothesis is provided by the fact that even today, people are living even if automobiles do exist.

However, under certain circumstances, a small sample size of people die because of the impact of automobiles. Therefore, the hypothesis **if** automobile/s and other conditions **then** death of humans can be proven as correct. In other words, it is necessary to be very precise on issues like these. A study design with appropriate definitions, inclusion and exclusion criteria which investigates such a relationship must ensure that a cause effect can be detected.

For every single person who has lost his life in the crash of a car, the car as such was both a necessary and a sufficient condition of person's death. Because, without the existence and the impact of the car, the person in question would not have died. At the same time, because the car acted on this person in the appropriate way, the person died.

In this context, the hypothesis **if** vaccination with the COVID-19 vaccine from AstraZeneca (Vaxzevria) **and** other conditions **then** cerebral venous thrombosis can be tested. However, it is necessary to describe **other conditions** precisely (clear definitions, inclusion and exclusion criteria et cetera) in order to evaluate this relationship for sure. As discussed above, there is good reason to believe that the COVID-19 vaccine from AstraZeneca (Vaxzevria) may actually protect against cerebral venous thrombosis. It should therefore be very difficult to prove the contrary in this regard.

Thrombocytopenia and cerebral venous thrombosis —

Study 3.8.4.5 (Thrombocytopenia and cerebral venous thrombosis)**.**

Again, the German state authority 'Paul-Ehrlich-Institut'announced publicly on March, 29 2021 the following:

"Bis zum 29.03.2021 (Montagmittags) wurden dem Paul-Ehrlich-Institut 31 Fälle einer Sinusvenenthrombose nach Impfung mit dem COVID-19 Impfstoff von AstraZeneca (Vaxzevria) im Rahmen der Spontanerfassung gemeldet.

In 19 Fällen wurde zusätzlich eine Thrombozytopenie gemeldet.

In neun Fällen war der Ausgang tödlich.

Mit Ausnahme von zwei Fällen betrafen alle Meldungen Frauen im Alter von 20 bis 63 Jahren. Die beiden Männer waren 36 und 57 Jahre alt."[108]

The present public proclamation of the German state authority 'Paul-Ehrlich-Institut'translated into English:

"By March 29, 2021 (Monday noon), 31 cases of cerebral venous thrombosis after vaccination with the COVID-19 vaccine from AstraZeneca (Vaxzevria) were reported to the Paul Ehrlich Institute as part of the spontaneous recording.

Thrombocytopenia was also reported in 19 cases.

The outcome was fatal in nine cases.

With the exception of two cases, all reports concerned women aged 20 to 63 years. The two men were 36 and 57 years old. "

Which conclusions can be drawn from all of this data (see table 18).

[108] https://www.pei.de/DE/service/presse/aktuelles/aktuelles-inhalt.html;jsessionid=7C63F1E4F9A2A12E296611B36952A6F0.intranet241

Table 18. Thrombocytopenia and cerebral venous thrombosis.

		cerebral venous thrombosis		
		YES	NO	
Thrombocytopenia	YES	19	1	20
	NO	12	19	31
		31	20	51

Causal relationship k =	0,5629
p Value right tailed (HGD) =	0,0000
p (SINE) =	0,7647
$\tilde{\chi}^2$ (SINE — B_t) =	4,6452
$\tilde{\chi}^2$ (SINE — $\underline{A}_t$) =	4,6452
p (IMP) =	0,9804
$\tilde{\chi}^2$ (IMP — A_t) =	0,0500
$\tilde{\chi}^2$ (IMP — $\underline{B}_t$) =	0,0500
p (SINE∩IMP) =	0,7451
$\tilde{\chi}^2$ (SINE∩IMP)$_1$ =	4,6952
$\tilde{\chi}^2$ (SINE∩IMP)$_2$ =	4,6952
p(IOI)=	0,2157
p(IOU)=	0,0000

The state authority 'Paul-Ehrlich-Institut'has not presented a control group. However, a control group is not required to work out a possible connection between thrombocytopenia and cerebral venous thrombosis. Provided that the study design is fair, the data of the control group can be estimated roughly. It is assumed that in the population no more than about 1/20 or 5% of the population suffer from a thrombocytopenia while at the same time this part of the population do not suffer from cerebral venous thrombosis. These fictive data are coloured red inside the table 18 above. In other words, the assumption of a possible causal[109] relationship between thrombocytopenia and cerebral venous thrombosis is not completely absurd. There is some, even if slight evidence, that thrombocytopenia is causally related to cerebral venous thrombosis. Some authors are writing: "Dieser Pathomechanismus schließt zwar nicht aus, dass den Sinus-/Hirnvenenthrombosen nach Impfung mit dem AstraZeneca COVID-19 Vakzin auch andere Ursachen zugrunde liege"[110] Translated into English: This pathomechanism does not rule out that the sinus / cerebral vein thrombosis after vaccination with the AstraZeneca COVID-19 vaccine also has other causes.

As proofed before, there is no reliable evidence that a vaccination with COVID-19 vaccine from AstraZeneca leads to thrombocytopenia nor is a cause or the cause of thrombocytopenia. In the population it often happens that people suffer from thrombocytopenia but do not suffer from cerebral venous thrombosis at the same time. In other words, thrombocytopenia cannot be treated as a sufficient condition of cerebral venous thrombosis.

Therefore, which came first, the hen or the egg.

The data of table 18 can be view from a different point of view as illustrated by table 19.

[109] https://www.uni-greifswald.de/universitaet/information/aktuelles/detail/n/therapie-fuer-seltene-hirnvenenthrombosen-gefunden/

[110] https://gth-online.org/wp-content/uploads/2021/03/GTH_Stellungnahme_AstraZeneca_3_22_2021.pdf

Table 19. cerebral venous thrombosis and Thrombocytopenia .

		Thrombocytopenia		
		YES	NO	
cerebral venous thrombosis	YES	19	12	31
	NO	1	19	20
		20	31	51

$\tilde{\chi}^2$ (SINE — B_t) = 0,0500
$\tilde{\chi}^2$ (IMP — A_t) = 4,6452
$\tilde{\chi}^2$ (IMP — $\underline{B_t}$) = 4,6452

It appears to be possible to accept the hypothesis (based on fictive data): **without** cerebral venous thrombosis **no** thrombocytopenia at a certain level of significance but not vice versa.

The hypothesis: **if** thrombocytopenia **then** cerebral venous thrombosis is refuted every day once again otherwise every single individual who suffers from thrombocytopenia who have to suffer from cerebral venous thrombosis too. This is for sure not the case and can be testified by every single general practitioner all around the world. As a consequence of this, thrombocytopenia cannot be a necessary and sufficient condition of the event cerebral venous thrombosis. One consequence of this is that thrombocytopenia cannot be regarded as a cause or as the cause of cerebral venous thrombosis. The evidence on this point is overwhelming. However and even if based on preliminary and fictive data, it is necessary to consider the possibility that cerebral venous thrombosis itself can lead to thrombocytopenia as demonstrated by table 19. At this point, more precision is required. Assumed that AstraZeneca COVID-19 vaccine is a sufficient condition of thrombocytopenia than every single individual who has been vaccinated by AstraZeneca's COVID-19 vaccine would have to suffer from thrombocytopenia. This is obviously not the case. Therefore, those who are of the opinion that AstraZeneca COVID-19 vaccine is responsible for cerebral venous thrombosis should consider the possibility of so-called **post-mortem analyzes** by PCR, ISH et cetera.

Cum hoc ergo propter hoc —**Cum hoc ergo propter hoc**

Correct human thinking and reasoning is threatened by many different logical (informal) fallacies and other factors too. Decisions of individuals as well as state authorities which are based on logical fallacies may result in a timely manner in disastrous and catastrophic consequences. In our everyday struggle for survival, it is important to be very careful and not to fall into the clutches of a logical fallacy. One of the many identified and existing logical fallacies is the generally known logical false cause fallacy or the **cum hoc ergo propter hoc**[111] logical fallacy which demands something like the following: "with this, therefore because of this". In German, "mit diesem, folglich wegen diesem"

Cum hoc ergo propter hoc - Example

If a roster crows, then the sun rises. Once and again, both events obviously occur together. Therefore, both events are causally related or the rooster crowing is the cause of the sun rise.

Such an incorrect form of reasoning is defined as fallacious already centuries ago. Nonetheless, those who have doubts about this relationship may behead a crowing rooster and see if this has any effect on the sunrise.

However, it is as it has been. A frequent coincidence of events alone is not enough to establish a cause effect relationship between events. In general, events which occur together at a certain (period of) time / Bernoulli trial t need not because of this co-occurrence be caused by each other.

These arguments reinforce our view that a coincidence between a Covid-19 vaccine of AstraZeneca ®and cerebral venous thrombosis does not provide any evidence of a cause effect relationship between both events. Much more is necessary to establish a reliable cause effect relationship between these two events. As demonstrated before, clear evidence to the contrary has been provided on this point.

3.8.5. *Johnson & Johnson®(USA) Covid-19 vaccine*

Study 3.8.5.1 (Recombinant vector based Covid-19 vaccine of Johnson & Johnson®(USA))**.**

[111] https://thebestschools.org/magazine/15-logical-fallacies-know/

The U.S. Food and Drug Administration[112] ,[113] issued on February 27, 2021 an emergency use authorization (EUA) for the Janssen Covid-19 Vaccine to be distributed in the U.S for use in individuals 18 years of age and older. The decision is based on the data as viewed by the table 20.

Table 20. Covid-19 vaccine of Johnson & Johnson ®and Covid-19 infection.

		Covid-19 infection		
		YES	NO	
Covid-19 vaccine of Johnson & Johnson ®	YES	116	19514	19630
	NO	348	19343	19691
		464	38857	39321

Causal relationship k =	-0,0545
p Value left tailed (HGD) =	0,0000000
p (EXCL) =	0,99704992
p Value (EXCL) =	0,00294573
p(IOI)=	0,4874
Vaccine efficacy (%) =	66,5631

In other words, in about **3 out of 1.000 cases** the vector based vaccine of Johnson & Johnson ®would not be able to prevent a Covid-19 infection while the study design has been very unfair (p(IOI)= 0,4874). The vaccine efficacy of VE = 66,5631 (%) is comparable to the vaccine efficacy of AstraZeneca ®but still underestimating the potential of the vaccine of Johnson & Johnson ®. SARS-CoV-2 is the virus which causes Covid-19. The Janssen vaccine is a recombinant vector vaccine which used a modified adenovirus in the vaccine, so that the same can no longer replicate in humans and cause illness. Following Johnson & Johnson[114] a single-shot Janssen Covid-19 vaccine, called Ad.26.COV2.S or JNJ-78436725, developed by Janssen®Pharmaceuticals appears to be safe[115] and effective as demonstrated by a randomized, double-blind, placebo-controlled phase 3 Study (ENSEMBLE[116] Trial). The vaccine Johnson & Johnson can be stored in a refrigerator for months and requires only a single injection. The onset of protection has been observed as early as day 14 with no cases in vaccinated participants reported after day 49. A complete protection against Covid-related hospitalization and death 28 days post-vaccination has been found. The interim data of Johnson & Johnson®are viewed by table 21.

Table 21. Covid-19 vaccine of Johnson & Johnson ®and death.

		Death		
		YES	NO	
Covid-19 vaccine of Johnson & Johnson ®	YES	3	19627	19630
	NO	16	19675	19691
		19	39302	39321

p (EXCL) =	0,99992370
p Value (EXCL) =	0,00007629

In toto, 99.992 out of 100.000 persons are protected by this vaccine against the death. A fair (b = c = 19514) study design assured, we would obtain data similar to the following (table 22).

[112] https://www.fda.gov/news-events/press-announcements/fda-issues-emergency-use-authorization-third-Covid-19-vaccine

[113] https://www.jnj.com/johnson-johnson-announces-single-shot-janssen-Covid-19-vaccine-candidate-met-primary-endpoints-in-interim-analysis-of-its-phase-3-

[114] https://www.jnj.com/johnson-johnson-announces-single-shot-janssen-Covid-19-vaccine-candidate-met-primary-endpoints-in-interim-analysis-of-its-phase-3-

[115] https://www.nih.gov/news-events/news-releases/janssen-investigational-Covid-19-vaccine-interim-analysis-phase-3-clinical-data-released

[116] https://www.clinicaltrials.gov/ct2/show/NCT04505722?term=NCT04505722&draw=2&rank=1

Table 22. Covid-19 vaccine of Johnson & Johnson ®and Covid-19 infection.

		Covid-19 infection		
		YES	NO	
Covid-19 vaccine of Johnson & Johnson ®	YES	116	19514	19630
	NO	19514	1084653	1104167
		19630	1104167	1123797

Causal relationship k =	-0,0118
p Value left tailed (HGD) =	0,0000000
p (EXCL) =	0,99989678
p Value (EXCL) =	0,00010322
p(IOI)=	0,0000
p(IOU)=	0,9651
Vaccine efficacy (%) =	66,5631

The Covid-19 vaccine of Johnson & Johnson ®would not protect from a Covid-19 infection in about **1 out of 10.000 cases**.

3.9. *Ranking of Covid-19 vaccines*

The ranking of view Covid-19 vaccines based on an unfair study design according to the original data published can be viewed by table 23.

Table 23. Ranking of vaccines under conditions of unfair study design.

Ranking	Vaccine:	No help for	out of
1	Covid-19 mRNA Vaccine Comirnaty (unfair study design)	2.19	10.000 persons
2	Covid-19 vaccine (mRNA-1273) (unfair study design)	3.90	10.000 persons
3	Covid-19 vector Vaccine Sputnik V (unfair study design)	8.05	10.000 persons
4	Covid-19 vector Vaccine Johnson & Johnson (unfair study design)	29.46	10.000 persons
5	Covid-19 vaccine AstraZeneca (unfair study design)	60.95	10.000 persons

However, the study design of all studies analysed has been unfair with the consequence that the data of the studies presented are more or less biased. Under conditions of a fair study design, the ranking would not change. However, the efficacy of the vaccines are much better then the original data do suggest.

Table 24. Ranking of vaccines under conditions of a fair study design.

Ranking	Vaccine:	No help for	out of
1	Covid-19 mRNA Vaccine Comirnaty (fair study design)	4	1.000.000 persons
2	Covid-19 vaccine (mRNA-1273) (fair study design)	10	1.000.000 persons
3	Covid-19 vector Vaccine Sputnik V (fair study design)	13	1.000.000 persons
4	Covid-19 vector Vaccine Johnson & Johnson (fair study design)	103	1.000.000 persons
5	Covid-19 vaccine AstraZeneca (fair study design)	353	1.000.000 persons

It is of vital importance that the Russian vector vaccine Sputnik V is as good as the Moderna mRNA vaccine. However, the storage of the Russian vector vaccine Sputnik V is not as complicated as the storage of a mRNA vaccine. The Covid-19 vaccine of Johnson & Johnson is little better than the vaccine of AstraZeneca. The Covid-19 vaccine AstraZeneca is not as good as the other the Covid-19 vaccine. However, AstraZeneca's Covid-19 vaccine is much better than the original data do suggest.

4. DISCUSSION

The relative risk is a measure of association used in the statistical analysis of the data of different studies. Unfortunately, this publication has recognised the fundamental problems as associated with the relative risk. The relative risk depends to much on study design and can lead to contradictory and highly misleading results. The relative risk cannot recognise the conditio sine qua non relationship (theorem 4) and fails in principle on the conditio per quam relationship. The relative risk [117] is logically inconsistent, unreliable and highly dangerous, and will not be helpful either for decision makers, who will be unable to rely on the results achieved by the relative risk and to translate the same into effective interventions or action, or scientists, who will be unable to relate the relationship between two events to a causal mechanism.

In particular, inappropriate or logically inconsistent or erroneous statistical methods like the risk ratio (RR) or the vaccine efficacy (VE) and other methods too may lead to false or misleading statements and conclusions tending to discredit valuable vaccines like AstraZeneca's Covid-19 vaccine and other too. Such a factually unfounded attitude may prevent people from being vaccinated while to many of them may unnecessarily die from the Covid-19 infection. In last consequence, highly questionable statistical methods are potential mass murderers of people. In general, vaccinations can help to prevent the development of a dangerous and long lasting vicious circles consisting of pandemics, poverty, civil unrest and civil wars from the beginning.

[117] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5841621/

5. CONCLUSION

There are many studies in clinical research published which rely on the relative risk. In this publication, we have re-investigated the interior logic of the relative risk. The risk ration provide us with a very vague and inadequate picture of objective reality. Under certain circumstances, the relative risk is logically inconsistent and under these circumstances at the end completely useless. In last consequence, we cannot rely on the relative risk to a necessary extent. The hope is that this publication may be of help for clinicians and others when reading medical literature.

6. IMPORTANT NOTE

The reader who is reading this article is invited to be aware that in our times it was not possible to publish the content of this article by a Web of Science, EBSCO, Scopus, PubMed/Medline et cetera and similar indexed journal. So one should be extremely cautious and very careful before taking the theorems derived in this publication formally as new or established scientifically validated knowledge.

7. PATIENT CONSENT OF PUBLICATION

Not required.

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