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Full Review

Relative risk versus absolute risk: one cannot be interpreted without the other

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ABSTRACT

For the presentation of risk, both relative and absolute measures can be used. The relative risk is most often used, especially in studies showing the effects of a treatment. Relative risks have the appealing feature of summarizing two numbers (the risk in one group and the risk in the other) into one. However, this feature also represents their major weakness, that the underlying absolute risks are concealed and readers tend to overestimate the effect when it is presented in relative terms. In many situations, the absolute risk gives a better representation of the actual situation and also from the patient's point of view absolute risks often give more relevant information. In this article, we explain the concepts of both relative and absolute risk measures. Using examples from nephrology literature we illustrate that unless ratio measures are reported with the underlying absolute risks, readers cannot judge the clinical relevance of the effect. We therefore recommend to report both the relative risk and the absolute risk with their 95% confidence intervals, as together they provide a complete picture of the effect and its implications.

Keywords: absolute risk difference, epidemiology, number needed to treat, relative risk, risk reduction

INTRODUCTION

Every day one reads statements in the media like 'one alcoholic drink per day increases the risk of breast cancer by 5%' or 'diabetes mellitus doubles the risk of heart disease'. These kinds of statements mostly refer to relative risks and tell us how much more, or less, likely the outcome is in one group compared with another. However, relative risks do not tell us anything about the likelihood that the outcome would occur in each of these groups and how much higher or lower this risk is. To make sense out of a relative risk one needs to know the absolute risk that is simply the likelihood that an outcome will occur.

So, risk can be presented both in relative and in absolute terms using either the relative risk or the absolute risk. Understanding what these risk measures represent is essential for the accurate interpretation of study results. In this article, we therefore explain the concept of risk. We then discuss the differences between relative and the absolute risk measures and how both concepts can be applied and interpreted. Finally, we discuss the advantages and disadvantages of both approaches based on examples from the nephrology literature and give recommendations for the reporting of risk measures in research papers.

EPIDEMIOLOGICAL STUDIES

Before we start explaining the difference between absolute and relative risk, it is important to understand that in most epidemiological studies one aims to compare the occurrence of a disease or other health outcome between two groups: a group that is exposed to a certain treatment or risk factor—the exposed group—and a group that is not exposed to this treatment or risk factor, which is called the unexposed or control group. In both of these groups the outcome of interest is measured. Based on the outcomes measured one can calculate for each of the two groups, the risk or the incidence rate of the outcome.

WHAT IS RISK?

In a group that is free of the outcome of interest at the start of observation, risk, in the strict sense of the term, is the ratio of the number of subjects developing the outcome of interest over a specific time period to the total number of subjects followed over that same period of time (Box 1) [1, 2]. Risk is expressed as a percentage or proportion and can only be correctly interpreted if the time period to which the risk applies is defined [2]. The risk of death may be the simplest example showing why this is necessary. Everyone can be sure that their risk of death in the next 200 years is 100%, while the risk of death in the next week will be very small for most people.

A drawback of calculating a risk using the simple formula (Box 1) is that all subjects need to have a complete follow-up because the risk formula provides strongly biased results when there are subjects lost to follow-up. However, the longer subjects are followed over time, the higher the chance that they will be lost to follow-up.

Also the occurrence of so-called competing events will lead to biased results because subjects are then no longer at risk of developing the outcome of interest [3]. For example, if one aims to study the risk of dying from cancer and a subject dies from a myocardial infarction, he or she is no longer at risk of dying from cancer. The risk of dying from other causes can then be considered as 'competing' with the risk of the event of interest.

Because competing events and loss to follow-up often play a significant role, in practice often more advanced statistical methods need to be applied, such as the Kaplan–Meier method, which is a method for survival analysis. Alternatively, the incidence rate may be used instead of risk. The incidence rate is the ratio of the number of subjects developing the outcome of interest to the time at risk of that outcome (Box 1) [2]. The advantage of the incidence rate is that the time a subject is 'at risk' of developing the outcome, the so-called person time, is taken into account. As a result, the incidence rate reflects the speed at which outcomes occur.

Another measure that is very similar to the incidence rate and that is specifically used in survival analysis is the hazard rate. In the context of survival analysis, the hazard rate reflects the number of deaths (or other events) in relation to the time at risk of death (or another event) [4]. This means that the hazard rate can be thought of as the incidence rate of death or this other event. The slight difference between these two concepts is that the incidence rate provides an overall rate estimated for the entire period of observation, which thus assumes that the rate is constant over the period, while the hazard function in survival analysis may be estimated without this time-constant assumption. If the incidence rate is approximately constant over the entire period, it provides a good estimate of the hazard function [5].

In this article, we will, for the sake of clarity, discuss 'risk' in the broadest sense of the word and this may include either the actual risk in the strict sense of the word, the incidence rate or the hazard rate.

Box 1: Overview of absolute and relative measures of risk

	Outcome of interest Yes	Outcome of interest No	Total	Person time
Exposed to risk factor	a	b	$a + b$	$T1$
Unexposed to risk factor	c	d	$c + d$	$T0$
Total	$a + c$	$b + d$	$a + b + c + d$	

a = number of incident cases in 1 year in the exposed group.
$a + b$ = total number of subjects at risk of the outcome of interest at inclusion in the exposed group.
c = number of incident cases in 1 year in the unexposed group.
d = total number of subjects at risk of the outcome of interest at inclusion in the unexposed group.
$T1$ = person time of subjects in the exposed group.
$T0$ = person time of subjects in the unexposed group.

Risk (assuming there is no loss to follow-up and no competing event during the first year):
Risk at 1 year after inclusion in exposed group ($R1$) = $a/a + b$
Risk at 1 year after inclusion in unexposed group ($R0$) = $c/c + d$

Incidence rate:
Incidence rate in exposed group ($I1$) = $a/T1$
Incidence rate in unexposed group ($I0$) = $c/T0$

Relative measure of the effect:
Risk ratio = relative risk (RR) = $R1/R0$
Incidence rate ratio = $I1/I0$

Absolute measure of the effect:
Risk difference = $R1 - R0$
Number needed to treat = 1/risk difference

RELATIVE MEASURES OF RISK

Based on the risks or incidence rates in the exposed and unexposed groups, one can calculate so-called measures of effect. The relative risk is such an effect measure that is commonly calculated in different types of study designs including randomized controlled trials (RCTs) and cohort studies, and reflects the strength of an association between an exposure and an outcome [6]. As was explained before, in these studies one generally aims to compare the occurrence of a disease or other health outcome between the exposed and unexposed group. The relative risk is the ratio of the risk in the exposed group to the risk in the unexposed group, as is summarized in Box 1.

Depending on the study design and statistical method applied, the relative risk can be presented using different measures of effect, such as the incidence rate ratio and hazard ratio. Relative measures of effect range from 0 to infinity and are free of unit. Their interpretation is similar and straightforward; a relative risk of 1.0 indicates that the risk is the same in the exposed and unexposed groups. A relative risk greater than 1.0 indicates that there is an increased risk in the exposed group compared with the unexposed group, whereas a relative risk less than 1.0 indicates a reduction in the risk in the exposed group compared with the unexposed group. For example, a relative risk of 1.5 means that the risk of the outcome of interest is 50% higher in the exposed group than in the unexposed group, while a relative risk of 3.0 means that the risk in the exposed group is three times as high as in the unexposed group. Conversely, a

relative risk of 0.8 means that the risk in the exposed group is 20% lower than in the unexposed group.

Nevertheless, the sole reporting of relative risks has a major drawback, because it may obscure the magnitude of the effect of an intervention. When relative risks are used for the presentation of effects of a treatment, this can make the treatment seem better than it actually is. For example, investigators may claim that a certain treatment reduces mortality by 50% when the intervention reduces death rates from 0.002% to 0.001%, an improvement the clinical relevance of which may be questioned.

Relative risks can become extremely large when the chance of an event in the unexposed group is low. For instance, last year Vogelzang *et al.* published a study in which they aimed to quantify the mortality risk attributed to infections and malignancies in dialysis patients and kidney transplant recipients when compared with the general population [7]. For infection-related mortality the investigators found an overall mortality rate ratio (adjusted for age and sex) that was 82-fold higher in dialysis patients than in the general population. This relative risk of 82 was already impressive, but for some specific patient groups the relative risk was even higher. For example, for women aged 20–29 years, the mortality rate ratio was as high as 565, meaning that women in that age category who were treated with dialysis had a 565 times higher risk of dying from infections than women of the same age in the general population. This tremendously large relative risk was simply caused by the extremely low occurrence of death from infections of 0.01 per 1000 patient years in the unexposed group represented by the general population.

So, when the outcome is rare in the general population, a large relative risk may not be so important for public health, although it can be important to an individual in a high risk category. Conversely, when the outcome of interest is common—also in the control group—even a moderately increased relative risk might indicate clinically important differences in public health terms.

ABSOLUTE MEASURES OF RISK

Risk can also be expressed in absolute terms by means of the absolute risk difference (synonym: attributable risk). This absolute measure of effect represents the difference between the risks in two groups; usually between an exposed and an unexposed group (Box 1). Since we define risk in the broadest sense of the word, in this article a risk difference can reflect either the difference between two risks (expressed as percentage), or between two incidence rates or hazard rates (expressed as number of events per time unit).

Absolute risk differences can be very small and even an extremely effective treatment or other important exposure may not lead to a substantial absolute risk difference. Nevertheless, the information that risk differences provide give, in some situations, better insight into what is really going on when compared with relative risks. For example, in 2013 newspapers reported a '70% increase in cancer risk' among females exposed as infants to the Fukushima Daiichi nuclear disaster in Japan in 2011. This relative risk was drawn from statistics showing that about 1.25 out of every 100 girls (1.25%) in the area developed thyroid cancer due to the radiation exposure, instead of the natural rate of about 0.75%.

Indeed, this is an increase of almost 70%. However, experts from the World Health Organization correctly emphasized that due to the low baseline rates of thyroid cancer, even a large relative increase represents a small absolute increase in risks of 0.50% [8].

In Figures 1 and 2, it is illustrated how two completely different scenarios with different background risks can lead to the same relative risk. We present a hypothetical study including 120 subjects: 60 in the group exposed to an environmental factor and 60 in the unexposed group. At the end of the follow-up period of 2 years the occurrence of the outcome of interest is measured in both groups. In Figure 1, we see the situation in which the outcome of interest is rare. There were three cases in the exposed group and two in the unexposed group, resulting in risks of 5% and 3% in 2 years, respectively. These risks resulted in a relative risk of 1.67, meaning that the risk of the disease was 67% higher in the exposed group. However, the underlying risks were low and also the absolute risk difference was small (2%). In Figure 2, a similar study is presented that found exactly the same relative risk of 1.67. The underlying risks were, however, much higher and also the absolute risk difference was substantially larger: 24%. These figures clearly show why reporting only the relative risk gives incomplete information.

Finally, the following example once more illustrates how the presentation of absolute risks gives insight into the actual size of a risk. Muzaale *et al.* aimed to assess whether kidney donors

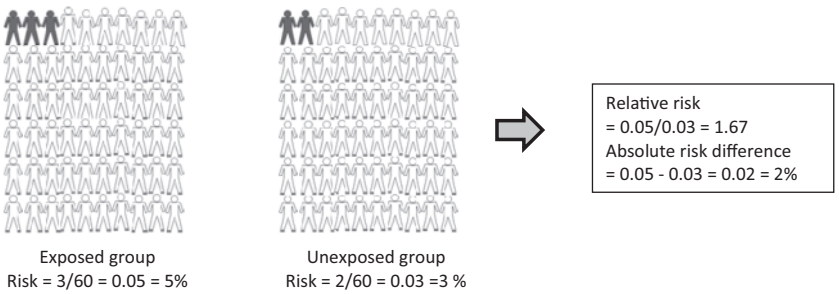

FIGURE 1: Hypothetical example of a study including 120 subjects: 60 in the group exposed to an environmental factor and 60 in the unexposed group. After 2 years of follow-up it was measured whether subjects had the outcome of interest (black) or did not have the outcome of interest (white).

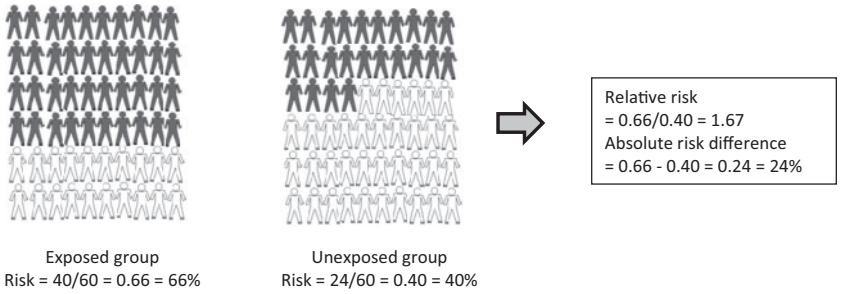

FIGURE 2: Hypothetical example of a study including 120 subjects: 60 in the group exposed to an environmental factor and 60 in the unexposed group. After 2 years of follow-up it was measured whether subjects had the outcome of interest (black) or did not have the outcome of interest (white).

have a higher risk of developing end-stage renal disease (ESRD) than subjects from the general population [9]. For that purpose they compared the risk of developing ESRD in donors with a cohort of non-donors who were at an equally low risk of renal disease and free of contraindications for living donation. They found that the risk of ESRD was indeed higher in donors than in the matched non-donors. However, the absolute risk increase was only small. The difference in the incidence between the living donors (i.e. those exposed to donor nephrectomy) and the non-donor control group was reported as the absolute risk difference. They found that the absolute risk of ESRD was highest in the black race group, with an incidence of 74.7 per 10 000 among black donors and of 23.9 per 10 000 among black non-donors, resulting in an absolute risk increase in this race group of 50.8 per 10 000.

Not only in the reporting of studies are absolute risk measures important. Also from the patient's point of view, an absolute risk measure provides the most information because it expresses what they can expect from certain treatment options. To predict the risk of an outcome for individual patients and thus to identify patients at high risk, prediction models can be used. The risk predictions or risk scores resulting from these models reflect individual absolute risk estimates and can be applied for different purposes, as is described in the paper by van Diepen *et al.* in this issue of *Nephrology Dialysis Transplantation* [10].

NUMBER NEEDED TO TREAT

The absolute risk difference can be used to calculate the number needed to treat (NNT), which is a relevant measure in the evaluation of the effectiveness of a healthcare intervention, typically a treatment with medication [6]. The NNT is the inverse of the absolute risk difference and can thus simply be calculated by dividing 1 by the absolute risk difference (Box 1). It is mostly used to evaluate (the prevention of) adverse outcomes. In an attempt to prevent adverse outcomes, the NNT is the average number of patients who need to be treated to prevent one additional adverse outcome. The ideal NNT would be 1, meaning that all patients who are receiving the studied treatment show an improvement, while none of the patients receiving the control treatment shows an improvement. The higher the NNT, the less effective the treatment. Usually a NNT between 20 and 50 is considered as a good score. For example, suppose one aims to study a new drug and the study results show that the risk of the disease was 0.14 (14%) in the group exposed to the new drug and 0.18 (18%) in the control group unexposed to the drug. The absolute risk reduction would then be $0.18 - 0.14 = 0.04$, yielding a NNT of $1/0.04 = 25$. This means that 25 patients need to be treated with the new drug to prevent one new case of the disease, which can be considered as a good result that supports the use of the new drug.

REPORTING OF RISK MEASURES

In many reports about the benefits of treatments results are presented as relative risk reductions rather than absolute risk reductions. Both doctors and lay people tend to overestimate the effect when it is presented in terms of relative risk. Already in 1994, Bucher *et al.* showed that physicians' views of the effectiveness of lipid-lowering drugs and the decision to prescribe such drugs is affected by the predominant use of the reduction of relative risk in trial reports and advertisements [11]. For clinical interpretation, however, it is useful to report both the relative risk and the risks per group with the absolute risk difference. In addition, it is important to report their 95% confidence interval to give information about the precision of the result and the statistical significance. A relative risk is considered statistically significant when the value of 1.0 is not in the 95% confidence interval, whereas absolute risk differences are considered statistically significant when the value of 0.0 is not in the 95% confidence interval.

In 2011, Hochman and McCormick published a systematic review on endpoint selection and relative versus absolute risk reporting in published medication trials [12]. For this purpose they analysed all randomized medication trials published in the six highest impact general medicine journals between June 2008 and September 2010 and determined the percentage of papers reporting results in the abstract only in relative terms. Of the 316 identified trials, 157 reported positive and statistically significant findings. Nevertheless, 69 (44%) of these positive trials reported only relative and no absolute measures of risk in their abstract. Similar findings were reported by Schwartz *et al.*, who performed a survey of abstracts of 222 articles published in leading medical journals [13]. They found that this problem was

Box 2: Recommendations on the reporting of relative and absolute risk measures in the CONSORT and STROBE statements

CONSORT (version 2010):
Item 17b: 'For binary outcomes, presentation of both absolute and relative effect sizes is recommended'
[14, 15]

STROBE (2007):
Item 16c: 'If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period'
[16, 17]

even larger in observational studies than in RCTs; in 62% of abstracts of randomized trials both relative and absolute risk measures were given, while this was only the case in 21% of abstracts of cohort studies. This difference is hardly surprising because in cohort studies usually the effect of multiple exposures is studied, while only one exposure is studied in most RCTs. Especially when all effects should be described within a limited number of words, such as in an abstract, it may be more difficult to add absolute effect measures.

In 1996, the first version of the Consolidated Standards of Reporting Trials (CONSORT) statement was published to improve the quality of the reporting of the results of RCTs. A second update of the guideline—published in 2010—recommends that both the relative effect and the absolute effect should be reported with their confidence intervals, as neither the relative nor the absolute measure alone gives a complete picture of the effect and its implications (Box 2) [14]. In addition, the study group recommends that 'for binary outcomes, the denominators or event rates should be reported so that readers can understand how risk ratios and risk differences are calculated' [15]. So, results should not be presented solely as summary measures, such as relative risks.

The 'STrengthening the Reporting of OBservational studies in Epidemiology' (STROBE) statement for the reporting of results from observational studies such as cohort studies and case-control studies was published in 2007 [16, 17]. This guideline recommends 'to consider translating estimates of relative risk into absolute risk if this is possible' (Box 2). Although these two widely accepted and applied statements for the reporting of studies give clear recommendations about the reporting of relative and absolute measures of risk, it seems that not all their recommendations are very well adopted in practice. This was confirmed by a recent study by Rao *et al.* showing continuing deficiencies in the reporting of STROBE items and their subcriteria in cohort studies focusing on chronic kidney disease [18]. Their study demonstrated weak evidence of improvement in the overall reporting quality of cohort studies in nephrology between the period before and after publication of the STROBE statement.

CONCLUSION AND RECOMMENDATIONS

In conclusion, risk can be presented both in relative and in absolute terms using either the relative risk or the absolute risk difference. The relative risk is often used, especially in studies showing the benefits of a treatment. However, relative risks may obscure the magnitude of the effect of an intervention and readers tend to overestimate the effect when it is presented in relative terms. Unless ratio measures are reported with the underlying actual risks per group, readers cannot judge the clinical significance of the effect. Reporting also the risk per group and the absolute risk difference gives a better representation of the actual situation, and also from the patient's point of view absolute risk measures often give more relevant information.

We therefore recommend the following when reporting measures of risk. Both the relative risk and the absolute risk difference with their 95% confidence intervals should be reported, as together they provide a complete picture of the effect and its implications. In general, it is important to keep in mind that one should always report the time period to which the risk applies.

CONFLICT OF INTEREST STATEMENT

None declared. The results presented in this article have not been published previously in whole or part.

REFERENCES

1. Rothman KJ. *Epidemiology. An Introduction*. New York, NY: Oxford University Press, 2002
2. Jager KJ, Zoccali C, Kramar R *et al.* Measuring disease occurrence. *Kidney Int* 2007; 72: 412–415
3. Noordzij M, Leffondre K, van Stralen KJ *et al.* When do we need competing risks methods for survival analysis in nephrology? *Nephrol Dial Transplant* 2013; 28: 2670–2677
4. van Dijk PC, Jager KJ, Zwinderman AH *et al.* The analysis of survival data in nephrology: basic concepts and methods of Cox regression. *Kidney Int* 2008; 74: 705–709
5. Andersen PK, Geskus RB, de Wiite T *et al.* Competing risks in epidemiology: possibilities and pitfalls. *Int J Epidemiol* 2013; 2: 861–870
6. Tripepi G, Jager KJ, Dekker FW *et al.* Measures of effect: relative risks, odds ratios, risk difference, and 'number needed to treat'. *Kidney Int* 2007; 72: 789–791
7. Vogelzang JL, van Stralen KJ, Noordzij M *et al.* Mortality from infections and malignancies in patients treated with renal replacement therapy: data from the ERA-EDTA registry. *Nephrol Dial Transplant* 2015; 30: 1028–1037
8. http://www.reuters.com/article/us-japan-nuclear-cancer-idUSBRE91R0D42 0130228 (10 June 2016, date last accessed)
9. Muzaale AD, Massie AB, Wang MC *et al.* Risk of end-stage renal disease following live kidney donation. *JAMA* 2014; 311: 579–586
10. van Diepen M, Ramspek CL, Jager KJ *et al.* Prediction versus aetiology: common pitfalls and how to avoid them. *Nephrol Dial Transplant* 2017; 32 (Suppl 2): ii1–ii5
11. Bucher HC, Weinbacher M, Gyr K. Influence of method of reporting study results on decision of physicians to prescribe drugs to lower cholesterol concentration. *BMJ* 1994; 309: 761–764
12. Hochman M, McCormick D. Endpoint selection and relative (versus absolute) risk reporting in published medication trials. *J Gen Intern Med* 2011; 26: 1246–1252
13. Schwartz LM, Woloshin S, Dvorin EL *et al.* Ratio measures in leading medical journals: structured review of accessibility of underlying absolute risks. *BMJ* 2006; 333: 1248
14. Schulz KF, Altman DG, Moher D *et al.* CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *BMJ* 2010; 340: c332
15. Moher D, Hopewell S, Schulz KF *et al.* CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. *BMJ* 2010; 340: c869

16. von Elm E, Altman DG, Egger M *et al.* The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Ann Intern Med* 2007; 147: 573–577
17. Vandenbroucke JP, von Elm E, Altman DG *et al.* Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. *Ann Intern Med* 2007; 147: W163–W194
18. Rao A, Bruck K, Methven S *et al.* Quality of reporting and study design of CKD cohort studies assessing mortality in the elderly before and after STROBE: a systematic review. *PloS One* 2016; 11: e0155078

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