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EDITORIAL

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Relative vs absolute risk and odds: Understanding the difference

1 | INTRODUCTION

Improving the two key pillars of clinical research, efficacy and safety, is the primary focus of the vast majority of all trials conducted. However, confusion often arises when attempting to quantify such outcomes. Consider the following examples. The US Centers for Disease Control and Prevention's report detailing deaths in 2015 was published in November 2017. For those 35 to 44 years of age, the probability of dying in 2015 due to atherosclerosis was 0.1 in 100 000 (equivalent to one in a million or 0.0001%).[1] Consider, therefore, the following scenario involving a pharmacological treatment for atherosclerosis. Suppose a new treatment was being developed for the disease and a two-arm randomized clinical trial enrolling only 35- to 44-year-old participants was conducted to compare the new treatment with a placebo. Suppose further that, upon analysis of the study results, those in the treatment arm were found to have fully half the chance of death due to atherosclerosis as compared with those in the placebo arm in this hypothetical study. Would you be impressed? Should you be?

Now consider a second scenario, based on the observation by Blood Pressure UK that 80% of people with type II diabetes have hypertension.[2] Suppose a new treatment was being developed for hypertension and a two-arm randomized clinical trial enrolling those with type II diabetes was conducted to compare the new treatment with a placebo. Following the analysis of this hypertension study's data, those in the treatment arm were found to have fully half the chance of hypertension as compared with those in the placebo arm.

In the first example, death due to atherosclerosis was reduced by 50%, while in the second example the chance of hypertension was reduced by 50%. However, are these 50% reductions equivalent? That is, is half of 0.0001% comparable to half of 80%? Stated another way, the question of interest that arises by considering both scenarios together is as follows: Is the 50% decrease in hypertension any more or less significant or clinically relevant compared with the 50% decrease in atherosclerosis? And if so, why is that the case?

These examples highlight a common misconception that often erroneously presented (and occasionally taken advantage of by unscrupulous authors) in the scientific literature, namely the statistical concepts of *relative* vs *absolute* risk. Further complicating the delineation between these concepts is confusion surrounding the difference between risk and odds. As explained in the examples above, the chance (risk) of death due to atherosclerosis and the chance (risk) of hypertension decreased by 50%. What do these decreases imply for the odds in each scenario? This paper clarifies these terms and their meaning to provide readers with a solid foundation from which to consider any research results based in these concepts. To facilitate simultaneous untangling of the concepts of "relative" and "absolute" for both risk and odds, it is helpful to clarify the distinction between risk and odds.

2 | DIFFERENTIATING RISK AND ODDS

While risk tends to be associated with an outcome involving danger or harm, statistically speaking, risk and probability are defined identically. The risk of an event occurring is simply defined as its probability. In the present context, this is the number of individuals with an event of interest out of the total number in the group or population under consideration. Using our examples from the introduction, the risk of a 35- to 44-year-old individual dying in 2015 due to atherosclerosis was found to be 0.1 divided by 100,000 (ie, 1 in million, 0.000001, or 0.0001%). The risk of someone with type II diabetes having hypertension is 80%, for example, 800 000 in a million, 800 in 1 000 or 4 out of 5. Of note, as risk is a probability, risk is limited to the range of 0 (an impossible occurrence) to 1 (a certain occurrence). Further, as a probability is by definition some part of a whole, terms such as "chance" and "likelihood" can be used interchangeably when interpreting results ("The probability [or risk or chance or likelihood] of a 35- to 44-year-old individual dying in 2015 due to atherosclerosis was 1 in a million."). The intuitive nature of these terms, along with their utility in everyday life, provides an inherent "feel" for their intended meaning.

Odds, on the other hand, are a bit less intuitive to use and interpret. The origin of the idea of odds goes back centuries and was presumably derived to more directly relate positive outcomes with negative outcomes. For a given group, the odds of an outcome are the number of individuals in the group with the event of interest divided by the number of individuals without the event. Again using the examples from the introduction, the odds of death due to atherosclerosis for individuals 35 to 44 years old are 1-to-999 999 (one person out of a million 35- to 44-year-old people dying from atherosclerosis and the remaining 999 999 not dying), while given the previously cited statistic that "80% of people with type II diabetes have hypertension," the odds of hypertension are four. This number is calculated as follows. If 80% (say 8 out of 10) have hypertension, then 20% (2 out of 10) do not. Thus, the number of individuals with an event (in this case, hypertension) in the group divided by the number of individuals with no event is 8 divided by 2, that is, 4. This calculation is consistent for a group of any size for the given percentage with the event of interest (eg, 80 vs 20 out of 100, 800 vs 200 out of 1000, and 16 vs 4 out of 20).

Odds can range between zero and infinity. Unlike risk, odds are not a fraction of a whole, but are instead a ratio of the number of elements with the outcome of interest to the number of elements without the outcome of interest, which is what creates the zero-to-infinity range of this ratio. Thus, terms such as chance, likelihood, and probability cannot be used to interpret odds.

Given that we cannot describe odds with terms such as chance, likelihood, and probability, remaining descriptor choices are somewhat inelegant. In our two examples, we would simply say that the odds of death from atherosclerosis in 2015 for 35- to 44-year-old individuals are 1 to 999 999, while the odds of hypertension for those with type II diabetes are 4 to 1. That is, there was one death from atherosclerosis in 2015 among 35- to 44-year-old individuals for every 999 999 that did not die due to that cause, while among those with type II diabetes, four times as many people have hypertension as not.

The relationship between risk and odds is interesting due to the difference in their upper bounds. As shown in Table 1, the two are very similar for values near 0 (the lower bound common to each) but diverge quickly as we move away from 0 and approach a risk of 1 (risk's upper limit). This divergence and the odds' infinite upper limit play a meaningful role in the non-intuitive nature of odds. Most people have a better feel for a risk of 95% than the comparable odds of 19. Why, then, do we employ the concept of odds at all? In much of research, interest lies in the comparison of one group to another. While risk restricts the quantification of an outcome relative to the total number involved, odds explicitly facilitate the comparison of two groups directly. So, while the divergence between risk and odds can unfortunately be exploited, considering each column of the table individually leads us back to the question with which we began this paper: should one be impressed by the 50% reductions in risk of our atherosclerosis and/or hypertension examples?

TABLE 1 The divergence of risk and odds

When the risk is as shown in this column…	…the respective odds are as shown in this column
0.000	0.000
(1/1000) 0.001	(1/999) 0.001
(1/100) 0.010	(1/99) 0.010
(1/10) 0.100	(1/9) 0.111
(1/5) 0.200	(1/4) 0.250
(1/4) 0.250	(1/3) 0.333
(1/3) 0.333	(1/2) 0.500
(1/2) 0.500	(1/1) 1.000
(2/3) 0.667	(2/1) 2.000
(4/5) 0.800	(4/1) 4.000
(9/10) 0.900	(9/1) 9.000
(95/100) 0.950	(95/5) 19.000
(99/100) 0.990	(99/1) 99.000
(999/1000) 0.999	(999/1) 999.000

3 | RELATIVE VS ABSOLUTE RISK (ODDS)

Now that we have delineated the distinction between risk and odds, we will address a second point of confusion concerning these calculations: absolute and relative risk. (Note that "odds" can replace "risk" in each instance discussed in this paragraph and also in the Concluding Comments section). When comparing two groups, absolute risk is most simply thought of as the *difference* between two risks, while relative risk is the *ratio* between two risks. Relative risk is more correctly thought of as a "risk ratio" due to the nature of the mathematical ratios involved. For the sake of convenience, we will assume that the placebo arms in each of our hypothetical clinical trials were found to have same result as the background statistics cited from the literature. That is, those in the placebo arm in the atherosclerosis study were found to have experienced atherosclerosis at a rate of 0.1 in 100 000, and 80% of those in the placebo arm in the hypertension study were in fact found to have hypertension.

A word of caution. The atherosclerosis and hypertension facts initially stated in the introduction were given in terms of chance (probability), that is, risk. It is important to note that the question then proffered in each case was in regard to a 50% reduction in the risk of each. As we will demonstrate next, a 50% reduction in risk is not equivalent to a 50% reduction in odds. We will determine the comparable reduction in odds while framing the relative vs absolute considerations.

With a risk of dying due to atherosclerosis of 0.1 in 100 000, that is, one in a million, in the placebo arm and a 50% decrease in the risk of atherosclerosis for those in the treatment arm, the risk of atherosclerosis would drop to one in two million. That is, while the *relative* risk decreased by 50%—1/2 000 000 divided by 1/1 000 000 is equal to 0.5—the *absolute* risk only changed from 1/1 000 000 to 1/2 000 000, that is, a difference of 0.00005%. In such a situation, the relative risk (risk ratio) will often be reported/interpreted as "those in the treatment arm were 0.5 times as likely (ie, 50% less likely) than those in the placebo arm to die from atherosclerosis." What is all too often omitted from such reported results is the absolute risk, an omission attempting to make inauspicious results sound more impressive. The reality of this example is that despite this 50% reduction in relative risk, the new treatment leads to only one less person out of two million being afflicted with this disease. In stark contrast to the 50% reduction in relative risk, this is a miniscule reduction in absolute risk.

A similar argument can be made for the odds. Recall that the odds of an outcome are the number of individuals with the event of interest divided by the number of individuals without the event. Thus, the one-in-a-million risk in the placebo arm of the atherosclerosis study means that the odds are 1 in 999 999 (out of the one million individuals, 1 has atherosclerosis and 999 999 do not). Considering the 50% decrease in the *risk* of atherosclerosis for those on the treatment arm, the risk (as just demonstrated) drops to 1/2,000,000 and hence the odds change to 1 in 1 999 999. That is, while the relative odds (odds ratio) are 1/1 999 999 divided by 1/999 999 (equal to 0.50000025), the absolute odds only changed from 1 in 999 999 to 1 in 1 999 999, a difference of 0.0000005 (the same difference we found for risk, to the number of significant digits presented). This odds ratio could then be interpreted as "those in the treatment arm had 0.5 times the odds (50% of the odds) of those in the placebo arm to die from atherosclerosis." As with risk, the miniscule absolute difference in odds makes the at-first-glance impressive sounding odds ratio entirely trivial. The 50% relative decrease (improvement) in both the odds and risk masks the reality that such a small number of people have actually been helped due to the simple fact that that this particular outcome (atherosclerosis) is so unlikely in this age group in the first place.

Contrast the atherosclerosis example with our hypertension example. In that case, 80% of people with type II diabetes in the placebo arm were found to have hypertension while those in the treatment arm were found to have a 50% decrease in the risk of hypertension. Using the same denominator as the previous example for the sole purpose of comparison, for a cohort of one million people with type II diabetes, 800 000 would be expected to have hypertension, a risk of 0.8 or 80% (odds: 4.0). The 50% reduction in this risk attributable to the new treatment would lead to only 400 000 with hypertension, a risk of 0.4 or 40%. However, the 50% decrease in the risk of hypertension would reduce the odds from 4.0 to 0.67 (the same reduction to 400,000 with hypertension and thus now 600 000 of the million without, but with the odds computed as 400 000/600 000 = 0.67). Thus, while the *relative* odds (odds ratio) are 0.67/4.0 = 0.1675, the *absolute* odds changed from 4.0 to 0.67, that is, a difference of 3.33. We would interpret this odds ratio as those in the treatment arm had 0.1675 times the odds (83.25% lower odds) than those in the placebo arm to have hypertension. That is, 80% vs 40% in relative risk (50% reduction) translates to 4.0 vs 0.67 in relative odds (83.25% reduction). Reductions of 50% and 83.25%, the latter being 66.5% greater than the former, are dramatically different.

4 | CONCLUDING COMMENTS

To fully appreciate the importance of distinguishing between relative and absolute risk (odds), contrast the number of people helped by the new treatment in each study. Despite a 50% relative reduction in risk in each, only one less person in two million would die from atherosclerosis, regardless of whether we consider risk or odds. In contrast, 400 000 less people out of million would have hypertension with a 50% relative reduction in risk (equivalent to an 83.25% reduction in the corresponding odds).

These numbers suggest a couple of important take-home messages. The first is the notable divergence between odds and risk when computing the relative change *as the absolute change increases*. The 50% relative change in atherosclerosis between the study arms yielded essentially no difference between the risk and odds because the absolute percentage with the condition was so low (0.0001% vs 0.00005%). However, the 50% relative change in the risk of hypertension between that study's arms (80% vs 40%) yielded a dramatic difference between the resulting odds and risk because of the large absolute percentage with the condition. This demonstrates the need for researchers to carefully choose the more relevant metric (risk or odds) to most accurately and informatively represent their result(s).

Secondly, *relative* risk increases in importance and meaning as the underlying *absolute* risk increases. Stating a 50% relative change is misleading when the known absolute risk is miniscule, particularly to the layperson. It is only when the known absolute risk becomes clinically meaningful that one is justified in reporting the relative risk. A determination of when absolute risk becomes clinically meaningful across any-and-all subjects to whom risk can be applied is unlikely to be agreed upon. As such, we propose and strongly endorse a simple, but powerful, solution to eliminate confusion; authors should always report both absolute and relative risk (or if one is reporting odds instead, both absolute and relative odds). This will allow the reader improved context with which to better assess whether the relative risk or odds is in fact meaningful.

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Michael R. Jiroutek DrPH, MS[1]
J. Rick Turner PhD, DSc[2]
[1]*Clinical Research, Campbell University College of Pharmacy & Health Sciences, Buies Creek, North Carolina*
[2]*Pharmacy Practice, Campbell University College of Pharmacy & Health Sciences, Buies Creek, North Carolina*

Correspondence
J. Rick Turner, Pharmacy Practice, Campbell University College of Pharmacy & Health Sciences, P.O. Box 1090, 180 Main Street, Buies Creek, NC. 27506.
Email: j.rick.turner123@outlook.com

ORCID

Michael R. Jiroutek https://orcid.org/0000-0002-0136-1305
J. Rick Turner https://orcid.org/0000-0003-0302-2902

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