Understanding and Communicating Risk: Assessing Both Relative and Absolute Risk Is Absolutely Necessary

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TO THE EDITOR

Clinicians make medical decisions that require risk assessment on a daily basis. Ordering a test, prescribing a medication, and performing a procedure are examples of decisions that involve risk–benefit assessments. Making the best decisions requires the ability to quantify risk; unfortunately, both patients and clinicians have showed suboptimal performance in this ability (Koo et al., 2017). Furthermore, how risks are presented has a significant effect on how they are understood (Stone et al., 2017, 2015; Zipkin et al., 2014).

Risks are often expressed in relative terms using ORs or risk ratios/relative risks. Although these two measures are not the same, ORs are often interpreted in the same way as risk ratios (Table 1). This is not a poor approximation when the outcome of interest is uncommon (<10% frequency) but is inaccurate when the outcome is common. Odds (often used in gambling) are calculated by dividing the number of events by the number of nonevents in a population, whereas risk is calculated by dividing the number of events by the total population. For example, one could equally state that the odds of losing a contest are 3:1 or that the risk of losing is 3 in 4 (0.75). An OR is the quotient of two odds, and a risk ratio is the quotient of two risks. When the number of events or outcome of interest is <10%, the number of nonevents is very close to the total population, making both measures very similar in magnitude. For example, older age, especially age >75 years, has been identified as a risk factor for an adverse outcome of COVID-19 (Booth et al., 2021). In the >75 years age group, the estimated OR of an adverse outcome is 2.65. If adverse outcomes occur in 100 of every 100,000 people in the ≤75 years age group, this OR corresponds to adverse events occurring in 265 of every 100,000 people in the >75 years age group or a relative risk of 265/100 = 2.65—just as the OR (Table 2). But if adverse outcomes occur in 30,000 of every 100,000 people in the ≤75 years age group, the same OR corresponds to adverse events occurring in 53,200 of every 100,000 in the >75 years age group or a relative risk of 1.77—quite different from the OR of 2.65 (Table 3). Figure 1 illustrates the change in relative risk as a function of the prevalence of adverse outcomes in the control population.

Table 1. Summary of Risk Measures

Measure	Definition	Formula
Risk	Number of events divided by the total population at risk	$Risk = \frac{\#\ events}{total\ population\ at\ risk}$
Odds	Number of events divided by the number of nonevents in a population	$Odds = \frac{\#\ events\ in\ population\ A}{\#\ nonevents\ in\ population\ A}$ $Odds = \frac{x}{1-x}$
RD or ARR	Difference between two comparable risks, which is attributed to an exposure or treatment	$Risk\ difference = Risk\ in\ exposed - Risk\ in\ unexposed$
NNT	Number of people who need to receive an intervention or treatment to prevent an adverse outcome	$NNT = \frac{1}{AR}$
Risk ratio or RR	Quotient of two risks comparing exposed and unexposed individuals	$RR = \frac{Risk\ in\ exposed}{Risk\ in\ unexposed}$
OR	Quotient of two odds comparing exposed and unexposed individuals	$OR = \frac{Odds\ in\ exposed}{Odds\ in\ unexposed}$

Abbreviations: AR, absolute risk; ARR, absolute risk reduction; NNT, number needed to treat; RD, risk difference; RR, relative risk.

This leads to the key principle that one cannot fully understand risk without reporting both the absolute risk and the relative risk. Absolute risk can be expressed as the **risk difference**, also known as **absolute risk reduction**, which represents the absolute difference in the incidence of an event between an exposed and an unexposed group. From the example mentioned earlier, in the first scenario, adverse events occur in 100 of every 100,000 people or 0.1% of people aged ≤75 years with COVID-19, whereas 265 of every 100,000 people or 0.265% of people aged >75 years experience adverse events. The risk difference here is 0.265−0.1% or 0.165%. In the second scenario mentioned earlier, the risk difference is 53.2−30% or 23.2%. This means that in the first scenario, there are 165 more deaths per 100,000 people in the ≥75 years age group, whereas in the second scenario a

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Table 2. Table (2 × 2) for Adverse Outcomes at a Prevalence of 0.1%

Age	Adverse Outcome	No Adverse Outcome	Total
<75 years	100	99,900	100,000
≥75 years	X	100,000 − x	100,000

Abbreviations: RR, relative risk.

1. Calculation of absolute number of adverse outcomes for population aged ≥75 years on the basis of OR

$$OR = \frac{Odds\ of\ an\ adverse\ outcome\ in\ people\ 75\ years\ and\ older}{Odds\ of\ an\ adverse\ outcome\ in\ people\ under\ 75\ years\ old}$$

$$2.65 = \frac{Odds\ of\ adverse\ outcome\ in\ people\ 75\ years\ and\ older}{\frac{100}{99,900}}$$

$$Odds\ of\ adverse\ outcome\ in\ people\ 75\ years\ and\ older = 2.65\ x\frac{100}{99\ 900}$$

$$\frac{x}{1-x} = 0.00265265$$

$$x = 0.00264563 = 264.5\ per\ 100\ 000$$

2. Calculation of RR

$$RR = \frac{Risk\ of\ an\ adverse\ outcome\ in\ people\ 75\ years\ and\ older}{Risk\ of\ an\ adverse\ outcome\ in\ people\ under\ 75\ years\ old}$$

$$RR = \frac{\frac{265}{100,000}}{\frac{100}{100.000}}$$

$$RR = 2.65$$

higher prevalence of an adverse outcome in the control group translates into 23,200 more deaths per 100,000 people (Table 4). A frequently presented measurement derived from the absolute risk reduction is the number needed to treat, which is the inverse of the absolute risk reduction. The number needed to treat is generally applied to therapeutic interventions and represents the theoretical number of people who would need to receive an intervention, on average, for one person to benefit. Therefore, if a new COVID-19 treatment was associated with an absolute risk reduction of 0.165% compared with placebo, the number needed to treat would be 1 of 0.00165 or 606. The converse of the number needed to treat is the number needed to harm, which represents the theoretical

Table 3. Table (2 × 2) for Adverse Outcomes at a Prevalence of 30%

Age	Adverse Outcome	No Adverse Outcome	Total
<75 years	30,000	70,000	100,000
≥75 years	y	100,000 − y	100,000

Abbreviations: RR, relative risk.

1. Calculation of absolute number of adverse outcomes for population aged ≥75 years on the basis of OR

$$OR = \frac{Odds\ of\ an\ adverse\ outcome\ in\ people\ 75\ years\ and\ older}{Odds\ of\ an\ adverse\ outcome\ in\ people\ under\ 75\ years\ old}$$

$$2.65 = \frac{Odds\ of\ adverse\ outcome\ in\ people\ 75\ years\ and\ older}{\frac{30,000}{70,000}}$$

$$Odds\ of\ adverse\ outcome\ in\ people\ 75\ years\ and\ older = 2.65\ x\frac{30,000}{70,000}$$

$$\frac{y}{1-y} = 1.1357$$

$$y = 0.53177 = 53,177\ per\ 100,000$$

2. Calculation of RR

$$RR = \frac{Risk\ of\ an\ adverse\ outcome\ in\ people\ 75\ years\ and\ older}{Risk\ of\ an\ adverse\ outcome\ in\ people\ under\ 75\ years\ old}$$

$$RR = \frac{\frac{53,177}{100,000}}{\frac{30,000}{100,000}}$$

$$RR = 1.77$$

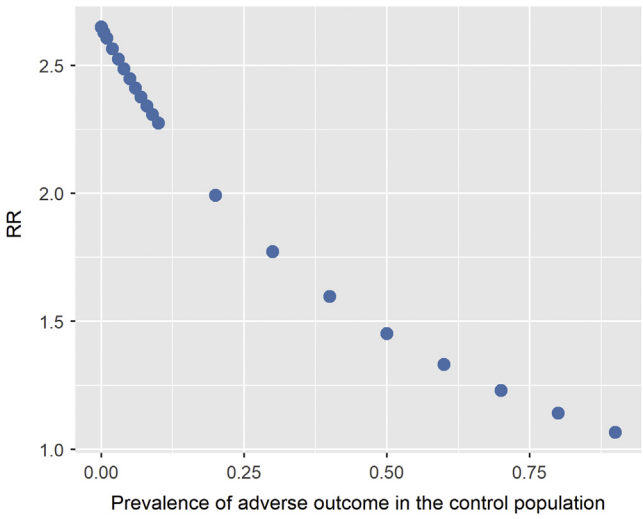

Figure 1. Change in RR for a given OR with changing outcome prevalence. Change in RR for an adverse outcome given a fixed OR of 2.65 (experimental: control populations) as the prevalence of the adverse outcome. Note that at low outcome prevalence in the control population, the OR is fairly close to the RR, whereas at high outcome prevalence, the OR and RR are quite different. RR, relative risk.

number of people who would receive an intervention, on average, for one person to experience a specific adverse event. From an individual's perspective, generally an absolute risk gives values that are easily interpreted into what risks they can expect when deciding between possible options (Noordzij et al., 2017), and presentation of the absolute risk has been shown to be more effective in communicating with patients (Zipkin et al., 2014). A recent study examining the risk of adverse outcomes after COVID-19 mRNA vaccines illustrates this point (Klein et al., 2021). The relative risk of thrombotic thrombocytopenic purpura in the first 21 days after mRNA vaccination was 2.60 (albeit statistically not different from the control interval), which at first glance would seem alarming. However, the number of events in the 21-day risk interval was 9.1 per million person-years, whereas the number of events in the comparison interval (22–42 days after the most recent dose) was 5.5 per million person-years. The absolute risk difference was 3.6 cases of thrombotic thrombocytopenic purpura per million person-years, slightly more than half the risk of death by lightning strike in the population of the South African Highveld (Blumenthal, 2005), which is a more reassuring figure.

Risk–benefit and cost–benefit analyses, which are frequently used for decision-making, rely on absolute risks rather than relative risks. An important recent example of a risk–benefit analysis involved was the emergence of thrombotic events associated with the administration of the Janssen COVID-19 vaccine (MacNeil et al., 2021). On 13 April 2021, the Centers for Disease Control and Prevention and the Food and Drug Administration recommended pausing of the administration of this vaccine after six cases of cerebral venous sinus thrombosis with thrombocytopenia were reported. By 21 April 2021, approximately 7.98 million doses of the Janssen COVID-19 vaccine had been administered in the United States, and a total of 12 cases of cerebral venous thrombosis had been reported (See et al., 2021). If the at-risk period is assumed to be about 3 weeks after vaccination, this corresponds to an approximate incidence of 26 cases of cerebral venous thrombosis per million person-years. To put this in context, the background incidence of cerebral venous thrombosis has been estimated at between 2 and 5 cases per million population per year, although some studies have reported as high as 15.7 cases per million per year (Devasagayam et al., 2016). Thus, the relative risk of cerebral venous thrombosis among Janssen vaccine recipients (using the background population figure of five per million for comparison) was 26 of 5 or 5.2, which is alarming. Examination of only the relative risk here would likely have completely halted administration of this vaccine.

However, the Advisory Committee on Immunization Practices used the absolute risks and benefits and calculated the number of hospitalizations, intensive care unit admissions, and deaths prevented per million Janssen COVID-19 vaccine doses administered (Centers for Disease Control and Prevention, 2021). Comparing the risk of hospitalization, intensive care unit admission, and death due to COVID-19 for females aged 18–49 (the highest risk group for this thrombosis syndrome), for every expected case of vaccine-associated thrombosis, 297 hospitalizations, 56 intensive care unit admissions, and six deaths would be prevented by administering the vaccine. These comparisons were even more dramatic for women aged ≥50 years because there would be an expected 2,454 hospitalizations, 661 intensive care unit admissions, and 394 deaths prevented for every expected case of vaccine-associated thrombosis. The benefit of vaccination clearly outweighed the risk, and the use of the Janssen vaccine resumed in the United States.

Understanding common measurements of risk presented in medical literature is essential for placing the risks of diagnostic and therapeutic interventions into context and for communicating those risks with

Table 4. Risk Difference in Absolute and Relative Numbers

Age Category	Absolute Risk	Risk Difference
Prevalence of an adverse outcome of 0.1%		
Adverse outcome in people aged ≥75 years	265 of every 100,000	165 per 100,000
Adverse outcome in people aged <75 years	100 of every 100,000	or 0.165%
Prevalence of an adverse outcome of 30%		
Adverse outcome in people aged ≥75 years	53,200 of every 100,000	23,200 per 100,000 or 23.2%
Adverse outcome in people aged <75 years	30,000 of every 100,000	

patients. Relative and absolute risk measures are complementary, and both should be presented when medical decisions are made.

Data availability statement

No datasets were generated or analyzed during this study.

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AUTHOR CONTRIBUTIONS

Conceptualization: SZ, JES; Supervision: JES; Writing - Original Draft Preparation: SZ; Writing - Review and Editing: SZ, JES

CONFLICT OF INTEREST

The authors state no conflict of interest.

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