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On the “proportion eliminated” for risk differences versus excess relative risks

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In the January 2013 issue, VanderWeele¹ discussed the concept of “proportion eliminated” by fixing intermediates as a policy-relevant proportion for direct effects.² In the present letter, we discuss the interpretations of and relations between the proportion eliminated for a risk difference and excess relative risk (i.e., relative risk minus 1) and an erratum for the letter of VanderWeele.³

Let X denote a binary exposure of interest, Y a binary outcome, and M a potential mediator. Then, we let $Y_x(\omega)$ denote the potential outcomes for individual ω if, possibly contrary to fact, there had been interventions to set X to x . We also let $Y_{xm}(\omega)$ denote the potential outcomes for individual ω if, possibly contrary to fact, there had been interventions to set X to x and to set M to m .

VanderWeele¹ defined the proportion eliminated as $(TE - CDE(m))/TE$, where TE represents the total effect of the exposure on the outcome and $CDE(m)$ represents the controlled direct effect of the exposure on the outcome, intervening to set the intermediate to some fixed level m , where TE and $CDE(m)$ are on the risk different scale. Thus, by using the notations of potential outcomes, the proportion eliminated can be written as $\{RD(TE) - RD(CDE(m))\}/RD(TE) = E[Y_1 - Y_0] - (Y_{1m} - Y_{0m})/E[Y_1 - Y_0]$, where RD stands for a risk difference. Note that this measure, although called a “proportion”, is not constrained between 0 and 1. Trivially, this measure is equal to 0 when the risk difference remains identical before and after the intervention on the intermediate (i.e., $E[Y_1 - Y_0] = E[Y_{1m} - Y_{0m}]$) whereas it is equal to 1 when one achieves perfect equality between the exposed and unexposed groups by the intervention on the intermediate (i.e., $E[Y_{1m}] = E[Y_{0m}]$). It is notable that the numerator of this measure can be interpreted as a differential in risk reduction due to the intervention between the exposed and the unexposed groups because it can be rewritten as $E[(Y_1 - Y_{1m}) - (Y_0 - Y_{0m})]$.

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VanderWeele¹ further explained that the “proportion eliminated can also be calculated if a risk ratio scale (or odds ratio scale with a rare outcome) is used to estimate the effects”, providing the following formula $\{RR(TE) - RR(CDE(m))\} / \{RR(TE) - 1\}$, where RR stands for a risk ratio. Contrary to the letter of VanderWeele,¹ this does not give the PE on the risk difference scale but rather on the excess relative risk scale.³ The two are not equivalent for the proportion eliminated. This can be seen as follows:

$$\begin{aligned}
 & \frac{\{RR(TE) - RR(CDE(m))\}}{\{RR(TE) - 1\}} \\
 &= \frac{\{RR(TE) - 1\} - \{RR(CDE(m)) - 1\}}{\{RR(TE) - 1\}} \\
 &= \frac{\{E[Y_1 - Y_0]/E[Y_0]\} - \{E[Y_{1m} - Y_{0m}]/E[Y_{0m}]\}}{E[Y_1 - Y_0]/E[Y_0]} \\
 &\neq \frac{E[(Y_1 - Y_0) - (Y_{1m} - Y_{0m})]}{E[Y_1 - Y_0]} (\because E[Y_0] \neq E[Y_{0m}]) \\
 &= \frac{\{RD(TE) - RD(CDE(m))\}}{RD(TE)}.
 \end{aligned}$$

Thus, the formula yields the PE on the risk difference scale only when $E[Y_0] = E[Y_{0m}]$, which will not be the case in general.^{4,5} One can still interpret the formula as the proportion eliminated on an excess relative risk scale (i.e., by what proportion is the excess relative risk reduced by fixing M to m). Trivially, this measure is equal to 0 when the risk ratio remains identical before and after the intervention on the intermediate (i.e., $E[Y_1]/E[Y_0] = E[Y_{1m}]/E[Y_{0m}]$) whereas it is equal to 1 when one achieves perfect equality between the exposed and unexposed groups by the intervention (i.e., $E[Y_{1m}] = E[Y_{0m}]$). See the eAppendix for some further relations.

Finally, it is worth noting that one can still calculate the PE on the risk difference scale from ratio measures.⁶ The formula that applies when intervening to set a binary intermediate to 0 is:

$$\frac{(RERI)P(M=1|X=1) + (RR_{01} - 1)\{P(M=1|X=1) - P(M=1|X=0)\}}{(RR_{10} - 1) + (RERI)P(M=1|X=1) + (RR_{01} - 1)\{P(M=1|X=1) - P(M=1|X=0)\}},$$

where $RR_{xm} = E[Y_{xm}]/E[Y_{00}]$ is a risk ratio comparing category $X = x$, $M = m$ to the reference category $X = 0$, $M = 0$, and where RERI or “relative excess risk due to interaction” is a measure of additive interaction using ratios (i.e., $RR_{11} - RR_{10} - RR_{01} + 1$). See VanderWeele⁶ for other settings of m and for formulae that are applicable to arbitrary exposures and intermediates.

Applying these different formulae of proportions of effect eliminated by fixing intermediates will enhance interpretation of the estimated effect of actual policy interventions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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