Defining ratio effects in randomized controlled trials using a stochastic theory of causal effects

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Motivation

- Effectiveness of interventions is of interest in many disciplines,. . .
- When the outcome variable is binary (e.g., success/no success) or a count variable (e.g, number of depressive symptoms), the effect of a treatment or intervention is often expressed as ratio (e.g., risk ratio, odds ratio)
- It is relatively straightforward to estimate some kind of ratio effect based on a logistic regression or Poisson regression
- There are multiple options how to quantify an (average) effect in this case
- It is not trivial which ratio effect measures should be considered and if yes, how they can be interpreted and which assumptions need to be fulfilled in order for them to have a causal interpretation.
- For example, a ratio effect based on group averages does not necessarily resemble an average over individual effect measures, not even in randomized controlled trials (non-collapsibility)

$\Rightarrow$ The different types of effects require different causality assumptions and have a different meaning, which only becomes clear when building on theories of causal effects.

Kiefer, C., Lugauer, B. & Mayer, A. (in press). Definition and identification of causal ratio effects. *Psychological Methods*.

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Illustrative Example

- Y: Binary outcome success with values 1 (yes) and 0 (no)
- X: Treatment variable with values 1 (treatment group) and 0 (control group)
- Z: Precondition covariate with values 1 (yes) and 0 (no)

	$Z=0$		
	$Y=0$	$Y=1$	
$X=0$	56	94	150
$X=1$	7	148	155
	63	242	305

	$Z=1$		
	$Y=0$	$Y=1$	
$X=0$	77	65	142
$X=1$	145	8	153
	222	73	295

$\Rightarrow$ Admittedly, this is a fairly extreme example with a strong interaction.

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Illustrative Example

This is what we get from statistical software when we estimate a logistic regression:

```
Coefficients:
            Estimate Std. Error z value Pr(>|z|)
(Intercept)   0.5179     0.1688   3.068  0.00215 **
X1            2.5334     0.4220   6.003 1.93e-09 ***
Z1           -0.6874     0.2385  -2.882  0.00395 **
X1:Z1        -5.2612     0.5817  -9.045  < 2e-16 ***
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

(Dispersion parameter for binomial family taken to be 1)
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$\Rightarrow$ But which effect should we consider?

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Different Options for Average Effects

There are different types of average effects that we can consider in this illustrative example

- Average effect on logit scale
- Difference of average risk in treatment and control group (ATE1)
- Ratio of average risk (SRA)
- Odds ratio of average risk (ORA)
- Average of conditional risk differences (ATE2)
- Average of conditional risk ratios (ASR)
- Average of conditional odds ratios (AOR)

$\Rightarrow$ In real examples, there can be lots of (unobserved) covariates in randomized controlled trials

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Some Effects in the Illustrative Example

	Group-level		Average over Z	
Effect	Estimate	95% CI	Estimate	95% CI
$\widehat{\text{ATE}}_{10}$	-0.038	$[-0.118,\ 0.042]$	-0.033	$[-0.023,\ 0.024]$
$\widehat{\text{SRA}}_{10}$	0.930	$[0.789, 1.072]$	0.940	$[0.833,\ 1.047]$
$\widehat{\text{ORA}}_{10}$	0.858	$[0.583, 1.134]$	0.878	$[0.661,\ 1.094]$
$\widehat{\text{ASR}}_{10}$	–	–	0.831	$[0.724,\ 0.973]$
$\widehat{\text{AOR}}_{10}$	–	–	6.435	$[1.139,\ 11.731]$

$\Rightarrow$ SRA and ORA suggest no ratio effect, aligning with the ATE, while the ASR and AOR imply a ratio effect with conflicting directions.

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Average Effects

Questions:

- Which of these effects are always identical (in theory)?
- Which of these effects always point in the same direction?
- Which of these effects always have a causal interpretation in randomized experiments?
- Which assumptions need to hold for the others to also have a causal interpretation?
- Which of these effects are always collapsible in randomized experiments?
- Which assumptions need to hold for the others to be collapsible?
- What if there are more (unobserved) covariates?

$\Rightarrow$ We need formal theories to help us with these questions.

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Definitions of Causal Effects

(Simplified) Definitions of Some Causal Effects

- True outcome variable under treatment x: $\tau_x = E(Y \mid X = x, U)$
- Expectation of true outcome variable: $E(\tau_x) = E[E(Y \mid X = x, U)]$
- Average treatment effect: $ATE_{10} = E(\delta_{10}) = E(\tau_1 - \tau_0) = E(\tau_1) - E(\tau_0)$
- Average ratio effect: $ASR_{10} = E(\rho_{10}) = E(\tau_1/\tau_0)$
- Average odds ratio effect: $AOR_{10} = E(o_{10}) = E[(\tau_1/(1-\tau_1))/(\tau_0/(1-\tau_0))]$
- Ratio of averages: $SRA_{10} = E(\tau_1)/E(\tau_0)$
- Odds ratio of averages: $ORA_{10} = (E(\tau_1)/(1-E(\tau_1))/(E(\tau_0)/(1-E(\tau_0))$

$\Rightarrow$ We define effects starting at the person level.

$\Rightarrow$ Potential outcomes cannot be used for defining these effects (division by zero).

Steyer, R., Mayer, A., & Fiege, C. (2014). Causal Inference on total, direct, and indirect Effects. In A. C. Michalos (Ed.), *Encyclopedia of Quality of Life and Well-Being Research* (pp. 606–630). Springer Netherlands..

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Causality Conditions

Causality Conditions

- Independent cause condition: $CC1$: $P(X = 1|U) = P(X = 1)$
- Conditional independent cause condition: $CC2$: $P(X = 1|U) = P(X = 1|Z)$
- Regressively independent outcome condition: $CC3$: $E(Y|X, U) = E(Y|X)$
- Conditional regressively independent outcome condition: $CC4$: $E(Y|X, U) = E(Y|X, Z)$

$\Rightarrow$ CC1 and CC2 hold under randomization
$\Rightarrow$ CC3 is oftentimes not plausible

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What are the Implications for Ratio Effects

ATE, SRA, and ORA:

- In a randomized experiment (CC1 holds), the ATE, SRA, and ORA are identified (i.e., have a causal interpretation based on true outcomes)
- They are also identified if one of the other causality conditions (CC2, CC3, or CC4) holds
- They always point in the same direction
- They are collapsible in the sense that the group-level effects are equal to the effects based on the risks averaged over Z (except for sampling variability)
- Their confidence intervals are more narrow if estimated based on the regression with Z (more power)
- ATE1 and ATE2 are identical by definition
- SRA and ASR are not identical in randomized experiments (same holds for ORA and AOR)
- That means that SRA and ORA cannot be interpreted as average over individual effects (even though they have a causal interpretation as (odds) ratios of unbiased expectations/risks)

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What are the Implications for Ratio Effects

ASR and AOR:

- Randomization (gold standard) is not sufficient to identify ASR and AOR (neither is ignorability)
- If CC3 holds (rarely realistic), ASR and AOR are identified
- If CC3 holds, ASR and AOR are collapsible (because the expected risk does not depend on the person at all and thus all individual treatment effects are the same and actually equal the group-level effect)
- If covariates are selected such that CC4 holds, ASR and AOR are identified
- In this case they can be interpreted as average over individual effects
- However, they are still not collapsible
- In rare cases (as in our illustrative example), both SRA/ORA and ASR/AOR have (different) causal interpretations and point in different directions

⇒ Conclusion: There is value in considering all types of causal effects but be aware of the assumptions/properties

⇒ Full explanations, implications and proofs in Kiefer, Lugauer & Mayer (in press).

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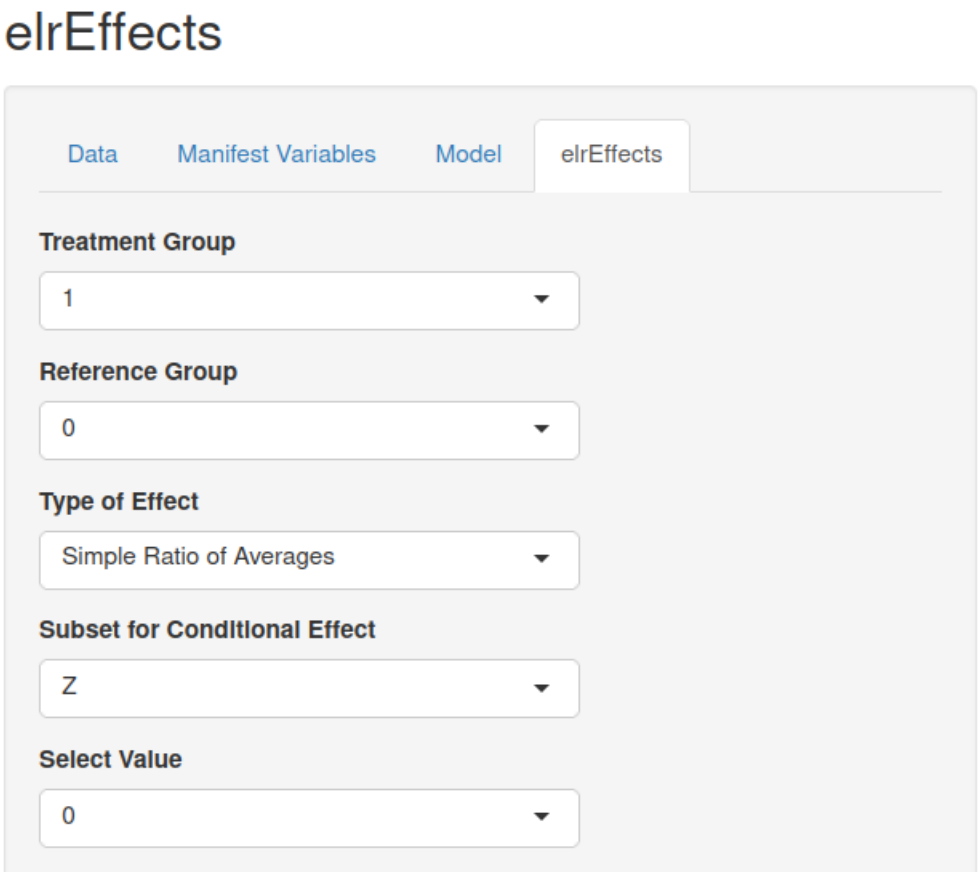
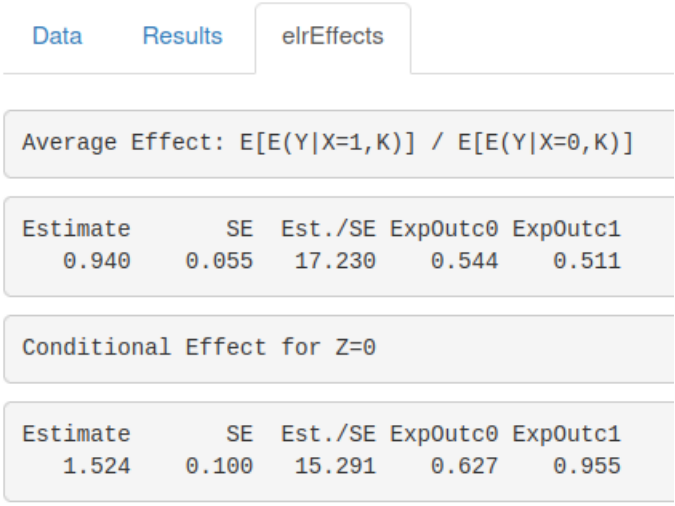
EffectLiteR, the elrEffects() Function and the elrEffectsGUI()





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Thank you!

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