

Letters to the Editor

The Implications of Using Binary Outcomes in Mediation Analysis



To the Editor:

We were interested to read the study by Carriere and colleagues¹ in the December 2015 issue of *The Journal of Pain* that tested a theory of the psychological processes that underlie the development of poor outcome in patients with whiplash injuries. Because these processes have been largely untested, the findings hold significant potential to improve our understanding of this difficult to manage patient group. The results showed that expectancies mediated the pathway from pain catastrophizing to return-to-work status, and fear of movement to return-to-work status. The authors concluded that expectancies should be targeted by interventions that aim to improve return-to-work rates.

Carriere et al conducted their mediation analysis using the product of coefficients method.⁷ Although this is a common method,⁵ it relies on a specific statistical model (linear regression) that does not accommodate nonlinear relationships between the exposure, mediator, and outcome.^{4,12} Therefore, using the product of coefficients method to model binary outcomes (that might require logistic or log linear models) is likely to lead to biased estimates in which the total effect does not accurately decompose into an indirect and direct effect.¹² That is, the sum of the indirect and direct effect should equal the total effect. We therefore were not surprised to see that the total effects reported by Carriere et al¹ did not accurately decompose into indirect and direct effects (Figure 2 in Carriere et al) because they used a binary outcome—'return-to-work status.' We think that this might be due to the limitations of the product of coefficients approach. Because it is important to know not only whether but also how much of the effect of catastrophizing on pain, and fear on pain is mediated via expectancies, it is critical that the mediation analysis accurately decomposes the total effect.

Recent advances in 'causal mediation analysis' have developed counterfactual definitions of total, indirect, and direct effects that do not rely on specific statistical models.^{4,8,11} This flexible approach allows the use of generalized linear models to model linear, logistic, or Poisson distributions. Practically, this allows the investigator to accurately decompose the total effect into indirect and direct effects, even with binary outcomes. These approaches can be implemented in common statistical packages including: Stata,² R,⁹ SPSS,¹⁰ and SAS.¹⁰ An alternative approach that can also accommodate categorical variables has been proposed by Iacobucci,³ and MacKinnon and Cox.⁶

Although it is unclear whether taking a different analytical approach would result in substantively different conclusions, using contemporary methods that can accurately model binary outcomes would make the findings of Carriere et al¹ more tenable. Thus, we humbly urge the authors to reanalyze their data using one of the approaches listed previously. This should allow for an accurate decomposition of the total effect that can show what proportion of the effect of catastrophizing and fear on pain is mediated through expectancy. These results would further contribute to our empirical evidence for theoretical models that underpin how we might adapt treatments to allow patients with whiplash to return to work. The use of mediation analyses is growing in the pain field. Attention to the nuances of analytical approaches to mediation deserves attention.

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References

1. Carriere JS, Thibault P, Milioto M, Sullivan MJ: Expectancies mediate the relations between pain catastrophizing, fear of movement and return to work outcomes following whiplash injury. *J Pain* 16:1280-1287, 2015
2. Hicks R, Tingley D: Causal mediation analysis. *Stata J* 11:1-15, 2011

3. Iacobucci D: Mediation analysis and categorical variables: The final frontier. *J Consum Psychol* 22:582-594, 2012
4. Imai K, Keele L, Tingley D: A general approach to causal mediation analysis. *Psychol Methods* 15:309-334, 2010
5. Lee H, Hübscher M, Moseley GL, Kamper SJ, Traeger AC, Mansell G, McAuley JH: How does pain lead to disability? A systematic review and meta-analysis of mediation studies in people with back and neck pain. *Pain* 156:988-997, 2015
6. MacKinnon D, Cox M: Commentary on "Mediation analysis and categorical variables: the final frontier" by Dawn Iacobucci. *J Consum Psychol* 22:600-602, 2012
7. Preacher KJ, Hayes AF: SPSS and SAS procedures for estimating indirect effects in simple mediation models. *Behav Res Methods Instrum Comput* 36:717-731, 2004
8. Robins JM, Greenland S: Identifiability and exchangeability for direct and indirect effects. *Epidemiology* 3:143-155, 1992
9. Tingley D, Yamamoto T, Hirose K, Keele L, Imai K: Mediation: R package for causal mediation analysis. *J Stat Softw* 59:1-38, 2014
10. Valeri L, VanderWeele TJ: Mediation analysis allowing for exposure-mediator interactions and causal interpretation: Theoretical assumptions and implementation with SAS and SPSS macros. *Psychol Methods* 18:137-150, 2013
11. VanderWeele TJ: *Explanation in causal inference: Methods for mediation and interaction*, Oxford University Press, 2015
12. VanderWeele TJ, Vansteelandt S: Odds ratios for mediation analysis for a dichotomous outcome. *Am J Epidemiol* 172:1339-1348, 2010