

Investigators' Corner

Effect Modification and Interaction Terms: It Takes Two to Tango



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ABSTRACT

In this Investigators' Corner I look more deeply into the previously discussed phenomenon of effect modification. I revisit an explanation and examples of the phenomenon and then examine how to account for it statistically. Specifically, I show, in detail, how to write a regression equation that includes interaction terms that account for the effect modification. Finally, I look at interpretation of regression coefficients both with and without the presence of effect modification, and the associated interaction terms.

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In previous Investigators' Corners (1–3), I examined effect modification and confounding, and in those discussions, I cursorily addressed the appropriate analyses to be carried out in the presence

of these phenomena. Here, I take a more in-depth look at the occurrence of effect modification. Specifically, after reviewing the definition of effect modification, drawing some pictures of it, and describing some examples, I show, in detail, how to write a regression equation that accounts for the effect modification. I explain how to interpret regression coefficients in models accounting for the presence of effect modification and how this contrasts with their interpretation in situations where there is no coefficient for effect modification. Finally, I will hint at the topic to be discussed in my next Investigators' Corner: random effects, with which we can account for variation between sites when considering multisite studies.

Effect Modification and Confounding

Very briefly, *effect modification* and *confounding* arise when 1 variable under study impacts the relationship between 2 other variables. Generally, the relationship being impacted is that between a main predictor variable of interest and a main outcome variable of interest, and the confounder or effect modifier variable is often, although not always, of secondary interest. A simple example is the relationship between surgeon salary and work experience, as modified by gender: If I posit that, in addition to the main effect of experience on salary, there is also gender discrimination in the way in which raises are given, I would expect that the rate at which salaries increase with experience differs by gender.

More precisely, *effect modification* arises when the relationship between the predictor and outcome is different at different levels of the effect modifier. There are situations in which the effect differs in magnitude but not direction between the levels of the modifier; alternately, there are situations in which the direction of effect differs between the levels of the modifier. In order to have confounding, the purported confounder must be associated with the predictor in the sample being examined, and the confounder must be associated with the outcome, either in fact or in the sample being examined. The

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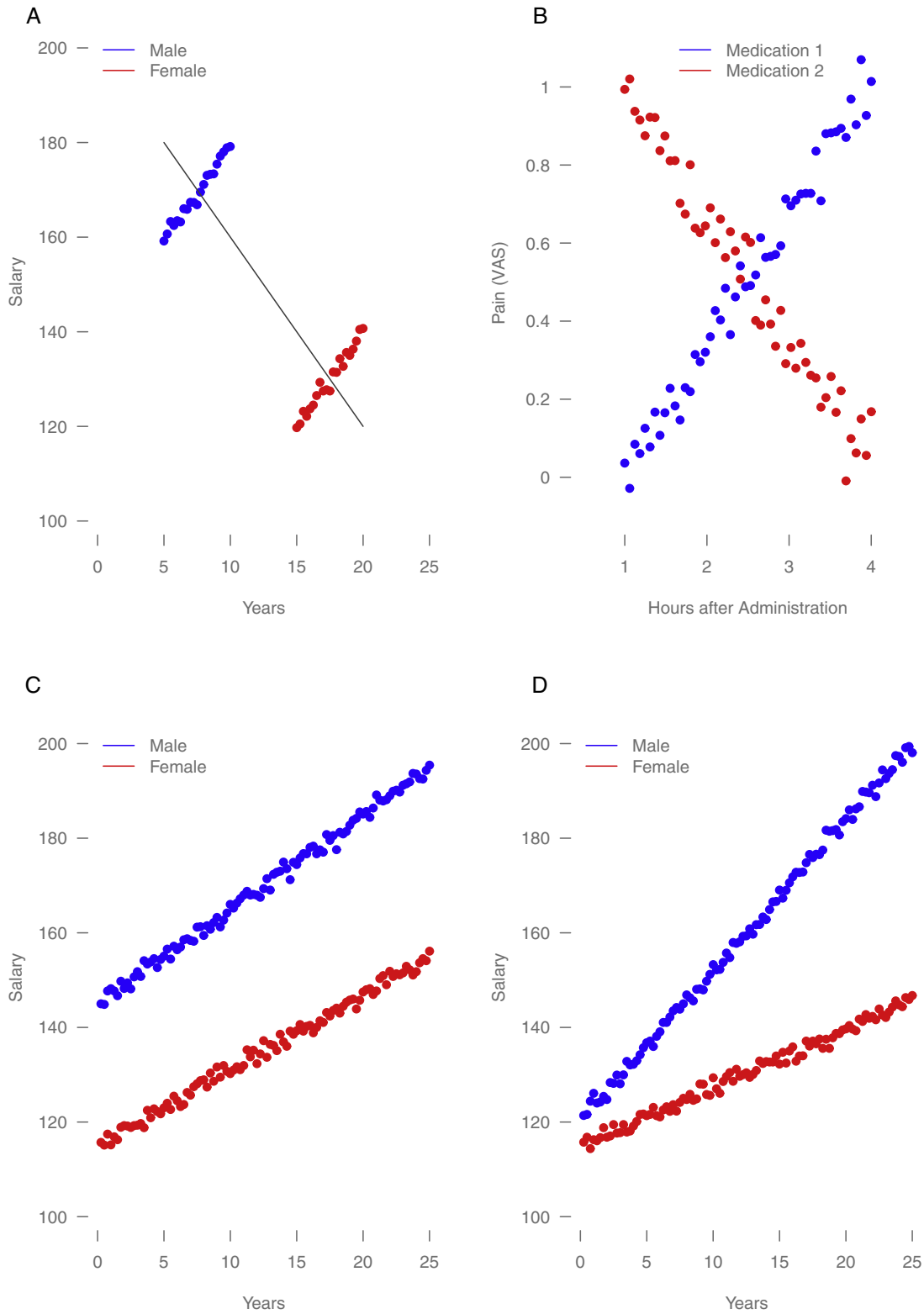


Fig. 1. (A) Confounding in the absence of effect modification. (B) Confounding in the presence of effect modification. (C and D) Effect modification in the absence of confounding, differing only in the magnitude of the effect.

confounder cannot be on the causal pathway between the predictor and outcome.

These relationships are more easily understood with the aid of diagrams. Shown are examples of *confounding in the absence of effect*

modification (Fig. 1A), *confounding in the presence of effect modification* (Fig. 1B), and *effect modification without confounding* (Fig. 1C and D). Fig. 1 shows some examples of the ways in which confounding and effect modification can appear in data, but this is by no means an

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