The perils of conducting meta-analyses of observational data

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Accessibility
Dear Editors,

We read with interest Li and colleagues’ recent article in this journal [1], which conducted a systematic review and meta-analysis of the literature on associations between intimate partner violence (IPV) and HIV infection in women. The authors found a significant positive association between various types of IPV and HIV, concluding that “physical violence, sexual violence, a combination of physical and sexual violence, and any type of IPV were associated with HIV infection in women (p. 7)” [1].

The authors noted in their Table 1 that a past study of which we were co-authors reported no significant association between IPV and HIV in 10 Demographic and Health Surveys conducted between 2003 and 2007 [2]. We were therefore surprised to see that, in conducting their meta-analysis, the authors report that our data show significant positive relationships between HIV and several types of IPV (Figures 2 and 3 in authors’ Figures 2 and 3 is likely to represent a lower bound.

Second, the conduct of meta-analyses using non-randomized data — particularly in the context of an association that may vary by time and place — is always subject to the risk of confounding by either measured or unmeasured factors [5,6]. Meta-analysis aims to combine experimental data from several small but comparable studies with similar scope, and homogeneous designs and patient populations, to achieve more precise effect estimates [7]. Ideally, meta-analyses use RCT data to avoid confounding and bias. Since this meta-analysis used observational data, and given the fact that we do not believe that individuals are randomly exposed to IPV or HIV, there is a strong likelihood that any unadjusted analyses of this relationship are confounded. Although Li and colleagues evaluated how well each included study identified and adjusted for confounding in their study, they themselves did not then adjust for such confounding in their meta-analysis, thus reopening the possibility of confounding in their results. Indeed, we show (again, in Table 3 of [2]), adjusting for conceptually precedent, individual-level covariates leaves no significant association between IPV and HIV in any of the countries we study.

The Cochrane Handbook for Systematic Reviews of Interventions notes that a systematic review need not include a meta-analysis and “(I)f there is considerable variation in results, and particularly if there is inconsistency in the direction of effect, it may be misleading to quote an average value for the intervention effect.” (Section 9.5.3 of [8]). We believe that this paper highlights the potential hazards of using aggregate data to conduct meta-analysis of observational data, particularly when the data extracted from published papers are not adjusted for possible confounding variables. Even when literature is identified through an exhaustive systematic review, it may not be feasible or responsible to conduct a meta-analysis if the identified papers are not deemed comparable, or heterogeneity across trials and populations is detected [3]. Should the authors still wish to conduct an analysis, alternative approaches, such as using fully individual-level data [9], meta-regressions, or a combination of
aggregated and individualized data [10], may also prove fruitful in generating trustworthy effect measures.

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References