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Rejoinder: Re: Some Thoughts on Consequential Epidemiology and Causal Architecture

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We would like to thank Professor Charles Poole for his views¹ on our commentary;² we are always glad to see interest in our work. We would, however, like to take the opportunity to reply to some of Poole's comments. Our read is that Poole's commentary suggests some misunderstanding about the positions we outlined in our own comment. We highlight here our five main concerns.

First, we are not asking anyone to “abandon [their] interests in internal validity”. We agree that internal validity is vitally important to scientific inference, and emphasize this view here and in our original commentary. We refer readers who are skeptical of our position on internal validity to Chapter 12 of our textbook “Epidemiology Matters”,³ which outlines the stages of validity that have formed a foundation of modern scientific inquiry for many decades. Rather than suggesting that we abandon internal validity, instead we argue that too often the goal of estimating an internally valid effect becomes the research agenda itself, rather than the process through which we engage in important public health research.

Second, Poole suggests that we “hail” the ratio measure over the difference measure; we do not do so. We are in agreement with Poole that difference measures provide much more informative evidence regarding the magnitude of public health impact of exposures than ratio measures. While this may be the epidemiologic and public health “mainstream”, most of the papers published in medical as well as epidemiologic journals continue to use ratio measures. Our comment was on the field as it is, not on as it should be. Further, our argument about the limitations of risk-factor epidemiology are not germane to the merits of differences versus ratios; the same issues apply regardless of the measure. More specifically, in our commentary we focus on the limitations of studying exposure-outcome relations agnostic to the underlying distributions of causes that vary within and across populations. Difference measures often highlight these underlying distributions as they are, rightfully so, more sensitive to base rates and co-occurring causes. Yet our contention remains that more

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expansive theorizing and interrogation about the ways in which these measures vary across populations would benefit the field of epidemiology.

Third, Poole asks “What’s wrong with restricting first and studying interaction later?” We respond with the question “What’s wrong with laying out a series of hypotheses about causal interactions first, and testing all of them simultaneously to build a series of testable, high-stakes hypotheses?” It is the latter question, and its difference with the question that Poole posed, that forms the foundation of what we mean by causal architecture. To answer Poole’s question more directly, nothing is wrong with restricting first and studying interaction later. However, we argue that the inherent questions that lead to methods that involve restriction are often not the pertinent questions to engage. Poole’s question on restriction leads to his comments that complex systems models rely on parameter estimates from the literature, and therefore internally valid risk ratios and risk differences from single exposures form the bedrock of the validity of the complex systems model. That is true, but experience from agent-based modeling approaches has taught us that what can be parameterized is based on summary ratio measures of single exposures because those are what is available in the literature, rather than a broad array of interactions, which would be much more informative for our models. If the causal architecture approach were adopted, rather than making our complex systems models untenable, as Poole suggests, our models would be more rigorous and flexible.

Fourth, Poole finds our claim that representative sampling enhances the assessment of interaction “dubious”. We agree the representative sampling is not necessary to assess interaction; our point was that we can better understand how the estimates that we obtain translate into actionable public health impact when we inquire about the distributions of other causes of the outcomes we are interested in within the populations for which we would like to intervene. Recent debates about the importance of representativeness have been presented recently in the pages of other journals, and we refer readers to these commentaries.^{4–14} We agree with Poole that our studies are always set in the past so it is impossible to know how applicable they will be to populations of the future, and yet, we argue that some thought and consideration to how causes will distribute in populations can aid in our endeavor to use our data to improve public health. Representative sampling is one method (among others) that requires us to engage in that thought process, which is why we recommend it.

Fifth, Poole provocatively asks whether causal architecture is “antithetical to much of social epidemiology”. Poole claims that there is no place in causal architecture, or more broadly in the systems sciences within which many causal pathways are parameterized, for researchers aiming to estimate net, total, and direct effects of single exposures. Poole also suggests that this has been the bedrock of social epidemiology. We disagree with both these statements. First, with regard to the place of total or net effects in causal architecture, such estimates are critical, as are estimates of mechanisms and ‘opening the black box’. The role of causal architecture is not specifically to understand mechanisms, but to more broadly consider the underlying distributions of causes and generating processes across populations across which our estimates may vary. When McMichael chastised us for being ‘prisoners of the proximate’,¹⁵ he did not suggest that we should never examine proximate causes, only that

we do too much of it and should also focus on structural causes. We align ourselves similarly; total and net effects are necessary to estimate, but total and net effects of what? We argue that the field can be more expansive in the total and net effects that are estimated, and consider joint distributions of many causes simultaneously in order to provide more comprehensive total and net effects. Second, with regard to the point that total and net effects are the bedrock of social epidemiology, Poole provides only one example, that of neighborhood effects. In fact, social epidemiology has for decades been a field that utilizes theory-driven investigations into social structures and systems, as well as mechanisms that create distributions of disease. It is also a subfield in which rigorous multi-disciplinary methods have been developed to assess the ways in which these systems become embedded, far beyond traditional total and net effect estimates.¹⁶

Finally, we note that scientific disagreements provide much of the grist for methodologic innovation, and we hope that this disagreement is no different, regardless of the side taken by the readers of this journal. In arguing for change we have tried to balance a firm criticism of current approaches with respect for the scholarship and innovation that has come before us. We close by underscoring that epidemiologic investigations of risk factors have provided a wealth of understanding of the pathogenesis of disease, and an array of methods that are critical to the success of our field. It is only because of generations of scholarship before us that we are able to cast a critical eye on the state of the field and suggest new directions. Our intentions in our commentary were to open a discussion that pushes the field forward. We are grateful to Poole for his return volley and hope that our comment is taken in the spirit in which it is intended: as an engagement with difficult issues, in the spirit of inquiry and respectful disagreement.

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