THE AUTHORS REPLY

We thank Drs. Poole and Kaufman (1) for their interest in our paper (2). It seems that Drs. Poole and Kaufman agree with the main conclusion of our paper, which is that the well-known and robust inverse association between tobacco use and Parkinson’s disease (PD) is unlikely to result from reverse causation or confounding, and thus most likely
reflects a genuine protective effect of some component of tobacco. This conclusion has important consequences for research on PD treatment, because the potential therapeutic effects of tobacco have so far been little investigated. Strong evidence of a possible protective effect may help to overcome the understandable resistance of most investigators to pursuing research on the possible beneficial effects of tobacco, considering the multitude of people who die because of its unquestionable harmful effects.

In their letter (1), Poole and Kaufman propose 6 possible states of nature, which we will refer to as scenarios 1–6, according to the order in which they appear in Poole and Kaufman’s Table 1. Scenario 1 follows Figure 3 in our paper (2), with the addition of a direct effect of parental smoking on offspring PD. This scenario, like that of Figure 3, supports our causal interpretation. Scenario 2, as Drs. Poole and Kaufman point out, is rather implausible, because it implies that passive exposure to parental smoking has stronger biologic effects than active smoking. For this reason, in our figures where offspring smoking did not directly affect offspring PD, we intentionally omitted a direct effect of parental smoking on PD. Poole and Kaufman ask whether scenario 3 is worth considering (1); we would argue that it is most likely implausible, for the same reason as scenario 2.

Our use of directed acyclic graphs (DAGs) was meant to illustrate several important logical arguments that support the above conclusion rather than to provide a single “right” DAG. Among never smokers, the pooled relative rate of PD among participants whose parents both smoked was 0.87 (95% confidence interval: 0.55, 1.37; \( P = 0.6 \)).

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REFERENCES

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