

**eAppendix for "On the distinction between interaction and effect modification" by T.J. VanderWeele. Formal Identification Arguments for Joint and Conditional Causal Effects in Figure 4.**

In this eAppendix, we show that for the causal DAG given in Figure 4, it is possible to identify the joint effects,  $\mathbb{E}[D_{eq}]$ , of  $E$  and  $Q$  on  $D$  and thus to assess interaction but that it is not possible to identify conditional causal effects of the form  $\mathbb{E}[D_e|Q = q]$  and thus not in general possible to assess effect modification in Figure 4.

We first use Result 2 in Appendix 2 to show that the joint effects,  $\mathbb{E}[D_{eq}]$ , of  $E$  and  $Q$  on  $D$  are identified in the example represented by Figure 4. If, in Result 2, we choose  $A_1 = E$ ,  $A_2 = Q$  and  $W = \emptyset$ , we can see that all backdoor paths from  $E$  to  $D$  are blocked in the graph with the arrows into  $Q$  removed. Furthermore, if we select  $V = X$  then we can easily verify that all backdoor paths from  $Q$  to  $D$  on the original graph are blocked by  $(E, X)$ ; the backdoor paths  $Q - U_2 - E - D$  and  $Q - U_2 - E - X - D$  are both blocked by  $E$ ; the backdoor path  $Q - U_1 - X - D$  is blocked by  $X$ ; and the backdoor path  $Q - U_1 - X - E - D$  is not blocked by  $X$  (since  $X$  is a collider on this path) but it is nevertheless blocked by  $E$ . Thus we can apply Result 2 to Figure 4 to identify the joint effects,  $\mathbb{E}[D_{eq}]$ , of  $E$  and  $Q$  on  $D$  and thus to assess interaction between the effects of  $E$  and  $Q$  on  $D$ .

We now show that quantities of the form  $\mathbb{E}[D_e|Q = q]$  are not identified in causal DAG given in Figure 4. The argument is subtle and uses a number of technical results concerning causal DAGs.<sup>28,31</sup> First we note that there is a backdoor path from  $Q$  to  $D$  in the graph corresponding to Figure 4 with the node  $E$  removed, namely  $Q - U_1 - X - D$ ; from Theorem 6 of Shpitser and Pearl<sup>28</sup> we have that  $P(D_e|Q = q)$  is identified if and only if  $P(D_e, Q_e)$  is identified. Since  $E$  has no effect on  $Q$  in Figure 4, it follows that  $P(D_e|Q = q)$  is identified if and only if  $P(D_e)$  is identified. Now, in Figure 4, there is path from  $E$  to  $X$  which consists entirely of consecutive confounding

arcs, namely  $E - U_2 - Q$  and  $Q - U_1 - X$ ;  $X$  is a child of  $E$  and from Theorem 3 of Tian and Pearl<sup>31</sup> it follows that  $P(D_e)$  and thus that  $P(D_e|Q = q)$  is not identified.

Intuitively, one might reason that if we are interested in estimating the effect of  $E$  on  $D$  conditional on  $Q$  we must use data on  $E$ ,  $Q$  and  $D$ . However, if one controls for  $X$ , then control is being made for an effect of  $E$  and this will bias the estimate. If control is not made for  $X$  then there is an unblocked backdoor path from  $E$  to  $D$ , namely,  $E - U_2 - Q - U_1 - X - D$  (note that this path is unblocked because  $Q$  is a collider on this path and one is conditioning on  $Q$ ). The situation may seem analogous to the classical time-dependent confounding issue (that marginal structural models handle) in which a confounder of a subsequent exposure is on the causal pathway between prior exposure and the outcome. However, in Figure 4, unlike in the time-dependent confounding case, marginal structural models cannot help in the identification of the effect of interest,  $\mathbb{E}[D_e|Q = q]$ . The argument given above using the results of Shpitser and Pearl<sup>28</sup> and Tian and Pearl<sup>31</sup> demonstrates that the  $P(D_e|Q = q)$  is not identified; no method of adjustment can be used to identify  $\mathbb{E}[D_e|Q = q]$ . The distinction is that in the time-dependent confounding case, data is available to identify the causal effects of interest but simple adjustment approaches like regression and stratification do not suffice; inverse-probability-of-treatment weighting techniques are needed. In Figure 4 the issue does not concern the method of adjustment but rather the fact that the data available are insufficient to identify the conditional causal effect of interest.