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# A reply to the letter on 'Directed acyclic graphs for clinical research: a tutorial'

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Dear Editor.

We thank the editor for the opportunity to respond to this letter [1], which makes knowledgeable comments about our tutorial [2]. The letter discusses three points, which we address one by one in this reply.

The letter's first point is that we should emphasize more the aspect that the validity of a directed acyclic graph (DAG) analysis depends entirely on the assumed causal structure. Basically, we agree with the aspect. In general, a DAG encodes domain knowledge about causal structure rather than establishing a new causal structure. An incorrect DAG can lead a biased causal effect estimate. Therefore, it is important to construct DAG after conducting literature review and reflecting on expert opinions. In our tutorial, we mentioned that DAGs are useful tools for visualizing the "hypothesized" causal structure (page 1), have been widely used to visualize "the domain knowledge" (page 2), represent the causal structure of research variables based on subject matter knowledge (page 3), and tell researchers what they must do and not do based on the "hypothesized" causal structure (page 9). We believe that these statements, to some extent, encapsulate the essence of the letter's first point.

The letter's second point states that colliders are not always

problematic, arguing that, in many cases, conditioning on a collider has no deleterious effects. We think that the second point needs further scrutiny. It is true that colliders are not always a problem. However, that fact does not necessarily make the collider issue less important. Confounders also are not always a problem. Still, no researcher appears to take confounding lightly in observational studies. It is more important to understand under what circumstances confounding causes significant issues. If ignored in data analysis, conditioning on a collider can make for a disaster. Typically, the sample selection bias issue is the case. When discussing a research problem's severity, it is crucial to provide the specific context. For example, the importance of conditioning on a collider should be understood in connection with the outcome type, exposure type, and reported risk measures. Without this context, it is hazardous to claim that, in many cases, conditioning on a collider has no deleterious effects. We recommend that researchers discern when collider bias is significant rather than blindly assuming it is negligible.

The final point references the availability of other tools for dealing with DAGs. When introducing software, we believe it is important to consider the trade-offs between user-friendliness

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and functionalities. Due to space limitations, we selected DAGitty for our tutorial because it is one of the most user-friendly programs while still providing necessary functionalities, even though it is not the most flexible. As mentioned in the letter, other software options offer more flexibility. However, researchers should consider the learning curve associated with their use.

#### **Notes**

#### **Conflict of interest**

The author has no conflicts of interest to declare.

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# **Data availability**

The data presented in this study are available on request from the corresponding author.

# **REFERENCES**

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