University of Sheffield
NIHR | Applied Research Collaboration Yorkshire and Humber

Depicting patient-reported outcome measures within directed acyclic graphs: practice and implications for causal reasoning

Matthew Franklin[1], Tessa Peasgood[1], and Peter WG Tennant[2]
[1] Uni. of Sheffield, Sheffield, UK; [2] Uni. of Leeds, Leeds, UK

UNIVERSITY OF LEEDS

MSR159

SUMMARY. We introduce the practice and implications of depicting patient-reported outcome measures (PROMs) within directed acyclic graphs (DAGs) to support causal analyses and subsequent result interpretation.

OBJECTIVES. Estimating causal effects of an exposure (e.g., health condition or treatment) on a PROM can have complications depending on the relationship between the PROM's indicators (i.e. items) and construct(s). Using DAGs as visual tools (**Fig. 1**), we show how to represent a PROM's potential internal causal relationship between its indicators and latent construct(s), then explain the implications when also accounting for external variables when estimating causal effects within observational data.

METHODS. Measurement theory suggests a PROM's relationship between its items/indicators and latent construct(s) is reflective (construct causes the indicators) or formative (indicators cause the construct). We present DAGs under reflective and formative model assumptions when the PROM is unidimensional (e.g., Patient Health Questionnaire-9 [PHQ-9] representing depression severity) or multidimensional (e.g., EQ-5D representing health-related quality-of-life [HRQoL]) (**Fig. 2**). We use a hypothetical example of estimating the causal effect of cognitive behavioural therapy (CBT) compared to counselling on depression severity (i.e., PHQ-9 score) or HRQoL (i.e., EQ-5D value set score) to explain some considerations.

RESULTS. Unidimensional PROMs like the PHQ-9 under a reflective model can be analysed like other unidimensional outcomes (e.g., mortality) to estimate causal effects, thus don't require additional consideration (**Fig. 3**). In comparison, we suggest the EQ-5D represents a multidimensional construct under a formative model (**Fig. 4**). As such, each EQ-5D item needs specific consideration to ensure relevant external variables are appropriately conditioned to estimate causal effects. The ability to estimate causal effects may be further complicated depending on if the EQ-5D items are assumed to arise in parallel or serially overtime (**Fig. 4**). In any case, DAGs transparently show such hypotheses to support causal analyses.

CONCLUSION. Using multidimensional outcome constructs formed under a formative model increases the complexity of causal analyses. We visually show this complexity using DAGs. As interest in real-world evidence grows, conducting causal analyses using PROMs in observational data will become more prominent. We have taken important initial steps by showing how PROMs can be incorporated into DAGs to inform such causal analyses.

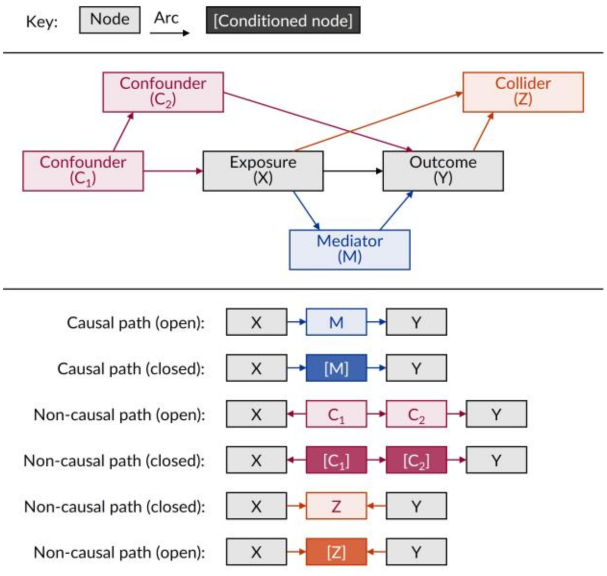

Figure 1: Simple illustration showing the main features of a DAG

Footnote. Variables within a DAG are represented by nodes. A unidirectional arrow (or 'arc') path signifies the first variable (i.e., parent node) is thought to cause the second (i.e., child node). Paths may be open (transmitting an association) or closed (not transmitting an association). Causal paths flow in the same direction, while non-causal paths do not. The average causal effect of a specified *exposure (X)* on a specified *outcome (Y)* is the combination of all causal paths between X and Y. In theory, this may be estimated from the conditional association between X and Y, if an appropriate set of variables are conditioned so all causal paths are open and all non-causal paths are closed. This requires conditioning on *confounders* (C_1, C_2), but not conditioning on *mediators* (M) or *colliders* (Z). Conditioning can be done using methods such as multivariable regression; conditioning in Fig 1 is depicted using [Conditioned node], e.g., [C_1] closes a non-causal path; [M] closes a causal path.

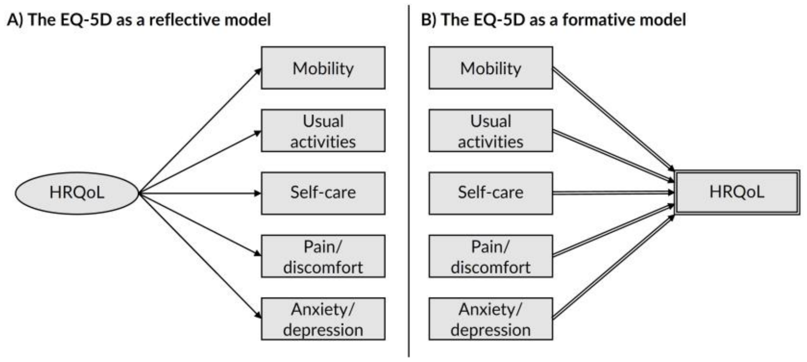

Figure 2: The EQ-5D depicted within a DAG under reflective (A) and formative (B) models

Footnote: Under the reflective model (panel A), health-related quality of life (HRQoL) is depicted as a latent variable by drawing the node as an ellipse; it is shown to probabilistically cause the indicator variables using ordinary arcs. Under a formative model (panel B), HRQoL is depicted as a composite derived variable by drawing the node as a double-outlined rectangle; it is shown to be mathematically determined by its parent items using double-lined arcs.

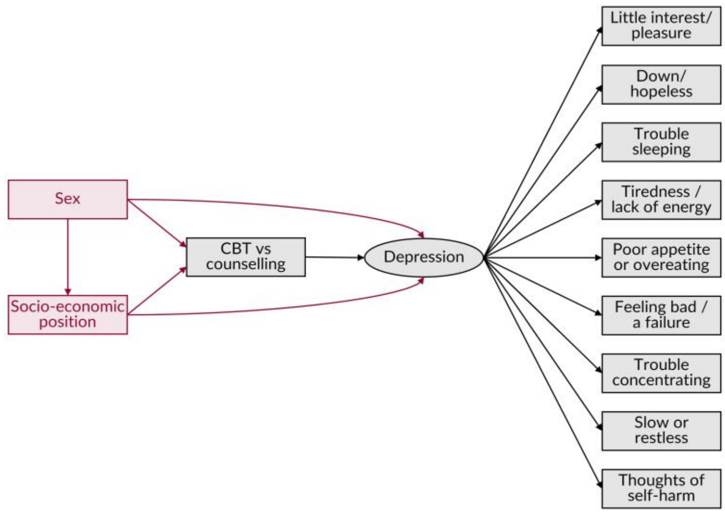

Figure 3: Illustrative DAG showing the relationship between CBT and depression measured using the PHQ-9 under a reflective model

Footnote: Under a reflective model, the items that we use to measure the outcome are assumed to be downstream of it. Although essential for measuring the outcome, in this case for depression based on the PHQ-9 whereby the construct is hypothesised to cause the indicators, the items are hence incidental to the DAG and can arguably be omitted entirely. Confounders (i.e., sex & socio-economic position) and confounding pathways are presented as red nodes and arcs.

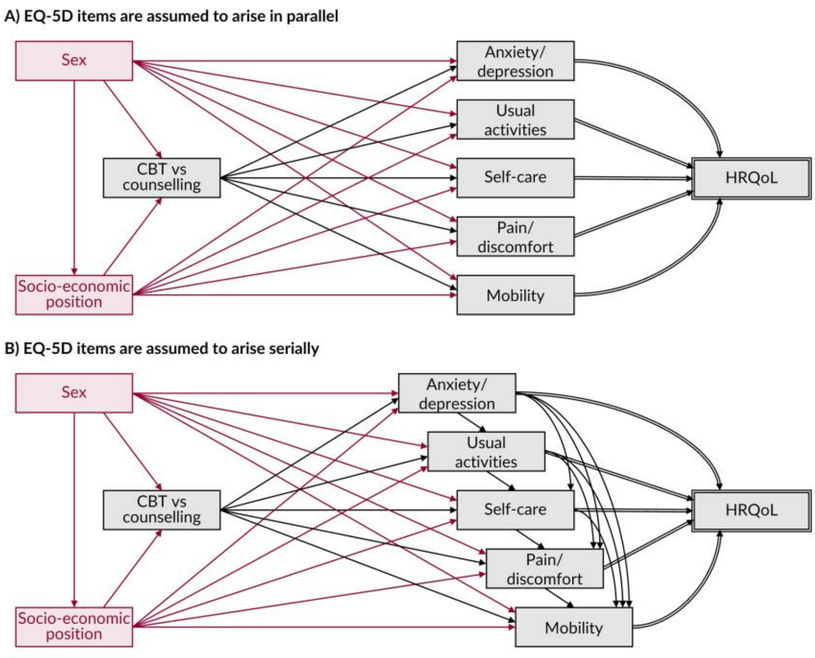

Figure 4: Illustrative DAGs showing the relationship between CBT and HRQoL, as measured using the EQ-5D under a formative model

Footnote. In Panel A, the items are assumed to occur in parallel while in Panel B they are assumed to occur serially, i.e. with each item arising in turn and potentially influenced by previous items. Confounders (i.e., sex & socio-economic position) and confounding pathways are presented as red nodes and arcs.

Corresponding author's email: matt.franklin@sheffield.ac.uk