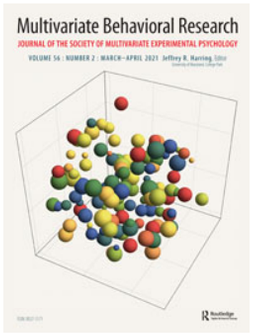

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Bridge Centrality: A Network Approach to Understanding Comorbidity

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ABSTRACT

Recently, researchers in clinical psychology have endeavored to create network models of the relationships between symptoms, both within and across mental disorders. Symptoms that connect two mental disorders are called "bridge symptoms." Unfortunately, no formal quantitative methods for identifying these bridge symptoms exist. Accordingly, we developed four network statistics to identify bridge symptoms: *bridge strength*, *bridge betweenness, bridge closeness*, and *bridge expected influence*. These statistics are nonspecific to the type of network estimated, making them potentially useful in individual-level psychometric networks, group-level psychometric networks, and networks outside the field of psychopathology such as social networks. We first tested the fidelity of our statistics in predicting bridge nodes in a series of simulations. Averaged across all conditions, the statistics achieved a sensitivity of 92.7% and a specificity of 84.9%. By simulating datasets of varying sample sizes, we tested the robustness of our statistics, confirming their suitability for network psychometrics. Furthermore, we simulated the contagion of one mental disorder to another, showing that deactivating bridge nodes prevents the spread of comorbidity (i.e., one disorder activating another). Eliminating nodes based on bridge statistics was more effective than eliminating nodes high on traditional centrality statistics in preventing comorbidity. Finally, we applied our algorithms to 18 group-level empirical comorbidity networks from published studies and discussed the implications of this analysis.

KEYWORDS

Graph theory; network analysis; psychopathology; bridge nodes; node centrality linear models; comorbidity

Mental disorders are common and co-occur at high rates. American adults have a 17% chance of qualifying for at least one mental disorder (Park-Lee, Lipari, Hedden, Copello, & Kroutil, 2016), and if an individual qualifies for one disorder, there is a 45% chance that he or she qualifies for at least one more (Kessler, Chiu, Demler, & Walters, 2005). Having multiple mental disorders predicts poorer prognosis, greater demand for professional help, greater trouble dealing with everyday life, and higher suicide rates (Albert, Rosso, Maina, & Bogetto, 2008; Brown, Antony, & Barlow, 1995; Schoevers, Deeg, Van Tilburg, & Beekman, 2005).

An emerging approach to psychopathology and comorbidity is the network model (Borsboom, 2017; Borsboom & Cramer, 2013; Cramer, Waldorp, van der Maas, & Borsboom, 2010; McNally, 2016). Network models are used within a wide variety of scientific fields (Barabási, 2012). Networks consist of nodes (components of a system) and edges (relationships between these components). The edges in a network may or may not be *directed* (having a specific direction from one node to another) and may or may not be *weighted* (edges are assigned a value to represent the strength of relationships).

Network models of psychopathology describe mental disorders as an interacting web of symptoms. Mental disorder networks may also include other important nodes, such as cognitive and biological variables (Jones, Heeren, & McNally, 2017). Network theorists hold that mental disorders are emergent phenomena arising from direct causal interactions among their constituent symptoms; they are not underlying entities that cause the emergence of symptoms. The accurate characterization of these interactions is an essential key to elucidating the mechanisms of psychopathology and developing focused intervention strategies. Many researchers have recently endeavored to use empirical data to model networks of mental disorders (for reviews, see Fried et al., 2017; McNally, 2016). More recently, an emphasis has been placed on estimating networks at the level of the individual (Epskamp, Borsboom, & Fried, 2018; Fried & Cramer, 2017).

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Network models provide a new understanding of comorbidity (Cramer et al., 2010). Symptoms are often shared among mental disorders; sleep disturbance and difficulty concentrating appear as symptoms in many psychiatric syndromes, for example, and features of certain disorders figure as risk factors for other disorders. Social isolation, common in social anxiety disorder, is a risk factor for other mental and physical health problems (Cornwell & Waite, 2009; Lim, Rodebaugh, Zyphur, & Gleeson, 2016). Symptoms of obsessive-compulsive disorder (OCD) are linked to guilt, which is a risk factor for depression (Kim, Thibodeau, & Jorgensen, 2011). In other words, the symptoms of mental disorders spread: having certain symptoms of one disorder can put one at risk for other disorders, thereby producing diagnostic comorbidity. Those symptoms that increase risk of contagion to other disorders are "bridge symptoms" (Cramer et al., 2010). To treat or to prevent comorbidity, clinicians may wish to therapeutically target these bridge symptoms.

Psychometric network terminology

Network methods are used in a variety of fields, and the terminology and application of these methods differ somewhat by discipline. In this article, we use psychometric network terminology, especially as it pertains to clinical psychology (e.g., Borsboom, 2017). We cover basic terminology of network psychometrics here; for extensive discussions see McNally (2016) and Epskamp et al. (2018).

Networks in clinical psychology are typically estimated from datasets containing information about mental disorder symptoms. Datasets may be binary indicators of symptom presence or absence, but more frequently consist of Likert-style ratings of symptom severity. These datasets can be conceptualized as forming a two-mode affiliation network—in this case, a network where one mode is the respondents and the other mode is the symptoms, with edges drawn between respondents and symptoms when a respondent endorses that symptom (Wasserman & Faust, 1994). Psychometric network analysis (Epskamp et al., 2018) involves collapsing this two-mode structure into a one-mode structure of symptoms only. Edges are drawn between symptoms based on psychometric properties calculated from the two-mode information (e.g., correlation)[1]. Because this type of collapse involves calculating psychometric information such as correlations or linear regressions, it makes the assumption that responses arise from a meaningful underlying population.

In the simplest of cases, the estimated networks consist of *association* networks based on cross-sectional datasets, where the nodes represent symptoms and the edges correspond to zero-order correlations between the symptoms. Researchers also estimate *concentration* networks, where the edges correspond to partial correlations. Because such estimation methods often generate many small, potentially spurious edges, researchers frequently use regularization methods such as a graphical least absolute shrinkage and selection operator (graphical LASSO or GLASSO; Friedman, Hastie, & Tibshirani, 2014) to shrink small edges in concentration networks to zero, resulting in a sparse network. Some researchers have used thresholding of edges to achieve a similar purpose. Edge weights in psychometric networks typically have a sign (negative or positive). A positive sign indicates that the connected nodes covary in the same direction, and a negative sign indicates that they covary inversely (e.g., as node A increases, node B decreases).

There are other techniques for estimating edges based on cross-sectional data, such as relative importance networks and directed acyclic graphs (DAGs). A relative importance network is a directed network relying on multiple regression where edges estimate the contribution of a given node in the prediction of another node (e.g., Grömping, 2006). DAGs are directed graphs that disallow feedback loops among nodes. DAGs can be estimated via several techniques (e.g., Kalisch, Mächler, Colombo, Maathuis, & Bühlmann, 2012; Scutari, 2010). When intensive longitudinal data are available, researchers may estimate temporally directed networks, including vector autoregressive models (VARs) and multilevel vector autoregressive models (mlVARs). In VAR models a network is constructed for a single individual over time where each variable is modeled as a linear function of all variables at previous time points, with edges representing regression coefficients (Chatfield, 2003). Multilevel VARs (mlVARs) expand upon the VAR approach by using data across multiple individuals measured longitudinally to simultaneously estimate temporal, contemporaneous, and between-subjects networks (Epskamp, Deserno, & Bringmann, 2017).

Psychometric networks are often analyzed by calculating *node centrality* statistics, such as *strength centrality, betweenness centrality, closeness centrality,* and *expected influence*, computed via the R packages *qgraph* (Epskamp, Cramer, Waldorp, Schmittmann, &

[1]The resultant one-mode structures are typically termed "dependence graphs" in the statistical literature, rather than "psychometric networks."

Borsboom, 2012) or *bootnet* (Epskamp et al., 2018). For weighted graphs, these packages rely on the node centrality formulas outlined by Opsahl, Agneessens, and Skvoretz (2010). *Strength centrality* sums the absolute values of the weights on the edges connected to a node and is a measure of overall connectedness. *Betweenness centrality* counts the number of times a node lies on the shortest path between any other two nodes and is used to infer which nodes might frequently act as "middlemen" in network transactions. *Closeness centrality* measures how close, in terms of edge distance, a node is on average to all other nodes. *Expected influence centrality* is similar to strength centrality but does not take the absolute value of edges before summing, therefore providing a measure of overall *positive* connectivity in networks with both positive and negative edges (Robinaugh, Millner, & McNally, 2016). Strength and expected influence have been most emphasized within the context of psychopathology networks, whereas betweenness centrality and closeness centrality are less applicable (Epskamp et al., 2018; Forbes, Wright, Markon, & Krueger, 2017). Although betweenness and closeness are somewhat less emphasized within psychometric networks, they remain useful in other types of networks.

In this article, we use the term *community* to indicate a theoretically based group of nodes which correspond to a psychiatric disorder based on clinical criteria, not based on any network analytic procedure (e.g., community detection analyses; see Blanken et al., 2018; Hoffman, Steinley, Gates, Prinstein, & Brusco, 2018). In other words, communities are based on information independent of the network structure itself. A useful parallel in social network analysis would be examining individuals in communities of various ethnicities. Although the actual network structure of friendships among individuals may not be split along ethnic lines, ethnic communities are still meaningful groups in which individuals may be categorized.

Bridge centrality

Psychometric researchers in psychopathology have relied on visual inspection of networks to identify bridge symptoms (Beard et al., 2016; Jones et al., 2017; Levinson et al., 2017; McNally, Mair, Mugno, & Riemann, 2017). Unfortunately, this informal approach is untenable for large, complex networks, and may be misleading even in small networks (Jones, Mair, & McNally, 2018). Accordingly, one of us devised four statistics that formally identify nodes high on *bridge centrality*, implementing them in the R package *networktools* (Jones et al., 2017; R Core Team, 2017). As extensions of extant centrality measures, we call them *bridge strength, bridge betweenness, bridge closeness,* and *bridge expected influence*.

For each statistic, we consider a network consisting of multiple predefined disorders, deemed *communities*. To illustrate each statistic, we consider a highly simplified toy network consisting of three communities: depression, generalized anxiety disorder (GAD), and OCD (see Figure 1).

We introduce the following notations that apply to all of the statistics found below.

Let a network consisting of a set of V nodes and E edges be noted as $G(V, E)$. Let C be a set of nodes in a community in this network, $C \subset V$. We will define each of the bridge centrality statistics with respect to a node a, where $a \in C$. We use $N(a)$ to denote the set of nodes adjacent to a. Let w_{ab} denote the weight on each edge $ab \in E$.

Bridge strength indicates a node's total connectivity with other disorders. Consider the node *sadness* in the depression community. We can find its bridge strength by summing the absolute value of every edge which connects *sadness* to symptoms of GAD or to symptoms of OCD. In a directed network, bridge strength can be separated into bridge in-strength (the sum of absolute inter-community edges directed toward the node) and bridge out-strength (the sum of absolute inter-community edges issuing from a node).

$$bridge\,strength = \sum_{b \in (N(a) - C)} |w_{ab}|$$

Bridge betweenness assesses the number of times a node lies on the shortest path between any two nodes

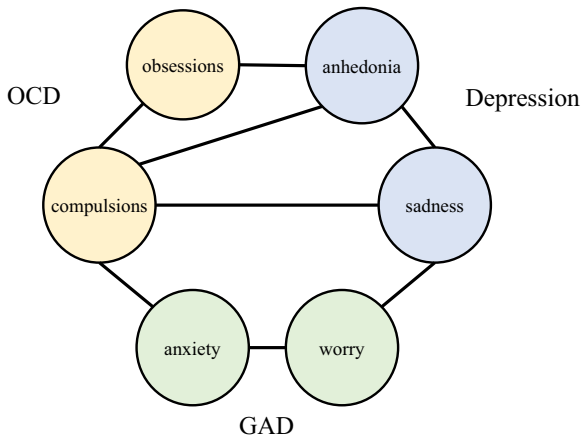

Figure 1. An example figure to illustrate bridge centrality calculations. If all edge weights are equal to 1, the bridge strength of the sadness node is 2, the bridge betweenness is 4 (all ties counting), and the bridge closeness is 0.75.

from two distinct disorders. For example, we would count the number of times in which the node *sadness* lies on the shortest path between other depression nodes and GAD nodes, depression nodes and OCD nodes, and GAD nodes and OCD nodes.

Let P_{ij} be a shortest path between $i \in V$ and $j \in V$, where node i and node j are in different communities.

Define x such that

$$x = \begin{cases} 0.5, & \text{if } a \in P_{ij} \\ 0, & \text{otherwise} \end{cases}$$

Then the *bridge betweenness* of $a \in A$ is

$$bridge\ betweenness = \sum_{i \in V} x_i$$

Bridge closeness reflects the average distance from a node to all nodes outside of its own disorder. In an unweighted network, distance is simply the shortest possible number of edges that separate one node from another (e.g., the distance between worry and compulsions is 2). In a weighted network, distance is based upon the inverse of the edge weights (edges with higher weights indicate nodes that are "closer" together). For the *sadness* node, we would first find the distance between *sadness* and each node of OCD and GAD. Then, we would determine the average of these distances. Finally, to convert the statistic into a measure of closeness, where higher values represent closer nodes, we take the inverse of the average distance.

Let $a \in C$ and $b \notin C$. Let P_{ab} be a shortest path between a and b, consisting edges $E(P_{ab}) = \{e_1, \ldots, e_k, \ldots, e_n\}$ where each edge has weight w_k for $1 \leq k \leq n$.

The *bridge closeness* of a is

$$bridge\ closeness = \frac{|V - C|}{\sum_{b \in (V-C)} \sum_{e_k \in E(P_{ab})} \frac{1}{w_k}}.$$

Bridge expected influence, much like bridge strength, indicates a node's sum connectivity with other disorders. However, in the case of bridge expected influence, we do not take the absolute value of edges before summing them. Accordingly, this statistic is useful for networks that have negative as well as positive edges (Robinaugh et al., 2016). In correlation-based networks, an edge with a positive value indicates that an increase in activation of one node is associated with an increase in activation of the node connected to it. In contrast, a negative edge indicates that an increase in the first node is associated with a *decrease* in the second node. Therefore, attention to the signs of edge weights is essential if one wishes to calculate a centrality statistic signifying an overall *increase* in node activation (expected influence) rather than a statistic signifying the absolute value of the summed connection weights. This is especially important when clinical researchers aim to target certain symptoms for therapeutic deactivation (Robinaugh et al., 2016). In a directed network, bridge expected influence sums only those edges issuing from a node.

$$bridge\ expected\ influence = \sum_{b \in (N(a) - C)} w_{ab}$$

Extant statistics related to bridge centrality

The idea that certain nodes play a key role in connecting groups of nodes to one another has been explored by researchers in the past. As mentioned above, *betweenness* is commonly regarded as a statistic that signifies the extent to which a node might play a key role in serving as a connection point between other nodes. Another example is Hwang, Kim, Ramanathan, and Zhang's (2008) *bridging centrality* statistic that combines betweenness with a bridging coefficient that determines the extent to which the node is located between high-degree nodes. The names are similar, but the concepts are not. *Bridging centrality* is an extension of betweenness centrality and is based solely on network structure whereas *bridge centrality* denotes a set of novel network statistics based on theoretically defined community structures.

Identifying bridges across theoretically important communities

The main difference between extant centrality statistics and bridge centrality is the specification of communities via a *guiding theory*, rather than by network structures. In other words, bridge centrality depends on how the researcher defines communities. All the aforementioned statistics, on the other hand, do not take into account any theoretically determined community structure

Consider the toy example in Figure 2. Suppose that a researcher is interested in the comorbidity of social anxiety and depression. Because node SA1 highly connects many nodes to each other, it would score high on betweenness centrality or on Hwang et al.'s bridging centrality. However, such measures would not address the question of bridge symptoms driving comorbidity between the social anxiety community and the depression community.

Theoretically defined communities figure in fields other than clinical psychology. For example, social scientists examining bridge nodes (individual persons) connecting groups distinguished by race or ethnicity, or a personality psychologist examining characteristics of extroversion and agreeableness traits may usefully compute bridge centrality statistics. Such communities are defined by features external to network structure per se.

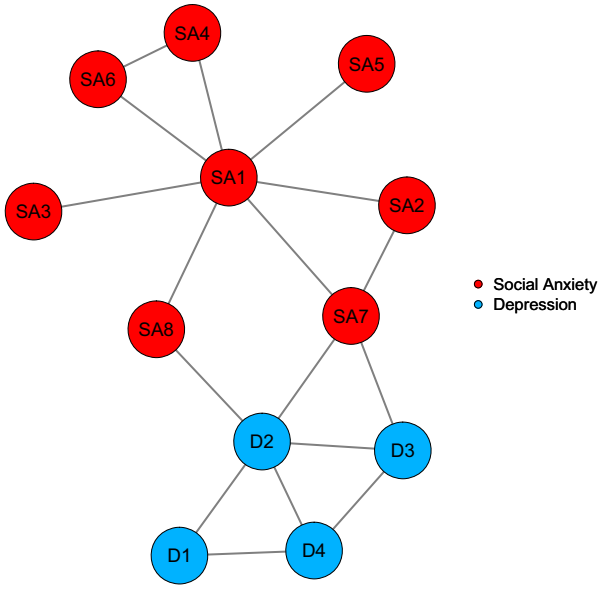

Figure 2. A toy example for differentiating general bridgeness from bridge centrality with specified communities.

Study 1: Sensitivity and specificity of bridge centrality in detecting known bridges

First, we tested whether the statistics accurately identified bridge symptoms. To accomplish this aim, we created artificial networks consisting of communities connected by bridge symptoms. We then applied our statistics across diverse networks under various conditions to test their accuracy in identifying the "true" bridge nodes.

Using the *igraph* R package (Csardi & Nepusz, 2006; R Core Team, 2017), we simulated networks and applied the *bridge* function in the *networktools* R package (Jones et al., 2017) to calculate bridge centrality statistics. The structure of the networks was designed to reflect empirical network studies on diagnostic comorbidity using network psychometrics; a representative simulated network appears in Figure 3a. In each network, we randomized the number of network communities between 2 and 5 inclusive, representing the number of comorbid disorders. In each community, we generated a random number of nodes between 6 and 21 inclusive, representing the number of symptoms in each disorder. Furthermore, we generated a random number, between 1 and 5 inclusive, of bridge nodes and assigned them to random communities. Edges were added such that each node was connected to 75–100% of nodes in its own community, with weights randomly assigned to each edge from a uniform distribution between 0 and 1. Bridge nodes were connected to 75–100% of nodes in their own

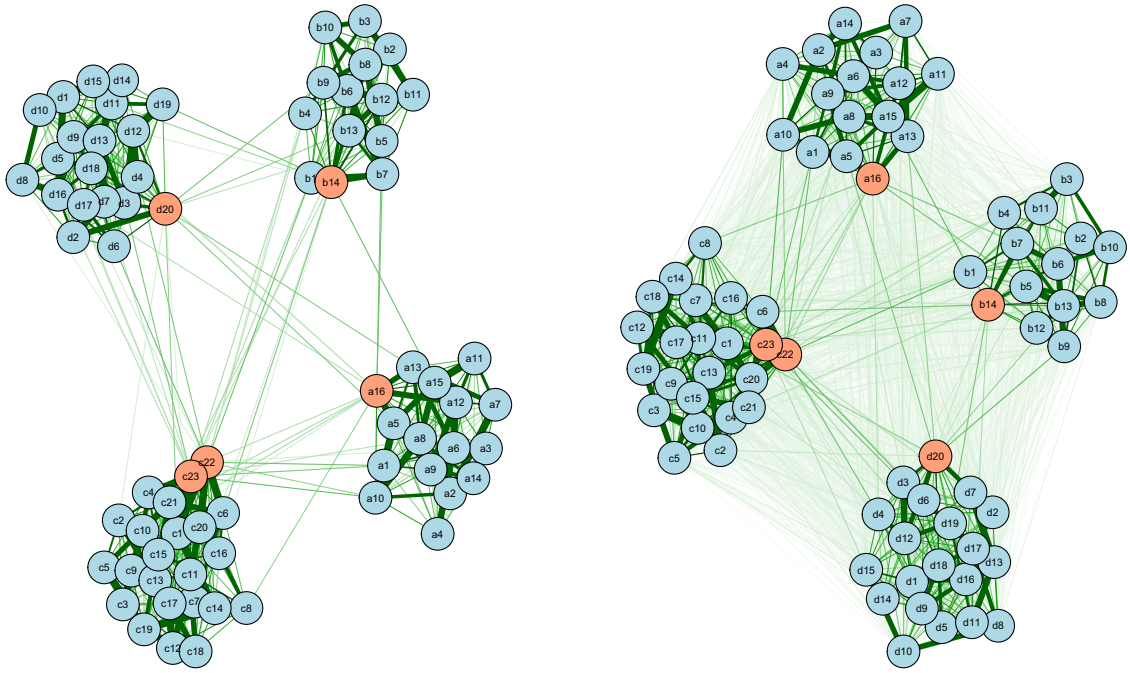

Figure 3. (Left) a simulated comorbidity network with no noise, (right) a simulated comorbidity network with noise added.

communities, and connected to 0–25% of random nodes in other communities, with weights randomly assigned from uniform distributions between 0.5–1 and 0–0.5, respectively. Networks were simulated as either *directed* or *undirected*. In the case of directed networks, edge direction was determined randomly. For each network, we recorded which node belonged to which community. To render the simulation especially challenging for the algorithm, we added random noise to some of the simulated networks, creating another condition: *noiseless* vs. *noisy*. To generate noise, we combined each edge with a noise parameter generated from a normal distribution with mean 0 and standard deviation 0.05 to simulate random errors that may occur in real measurements. A network with noise added appears in Figure 3b.

Because there are many types of psychometric networks, it is impossible to design a simulation paradigm representative of all of them. For example, association networks depict undirected zero-order correlation matrices, whereas this simulation paradigm does not produce networks which approximate the structure of correlations, and some of its networks are directed. Graphical LASSO networks are typically sparse, and this simulation paradigm will produce dense networks in conditions where noise is added. However, the conditions generated by this paradigm are broad and represent a wide variety of network structures and number of communities, increasing confidence that bridge centrality statistics function well in a wide variety of situations.

Finally, we used bridge strength, bridge betweenness, and bridge closeness to detect bridge nodes. After calculating the bridge centrality values for each network, we selected the top 20% scoring nodes on a given statistic and selected these as predicted bridge nodes. We do not recommend using a specific cutoff for empirical analyses: instead, one should carefully analyze distributions and select bridge nodes based on distributional tendencies in combination with one's own disciplinary expertise. In the case of our simulated networks, 20% produced an acceptable balance between sensitivity and specificity.

In summary, our simulation involved a $2 \times 2 \times 3$ approach for a total of 12 simulation conditions on 500 networks each (*directed* vs. *undirected; noiseless* vs. *noisy; strength* vs. *betweenness* vs. *closeness*). After using our algorithms to predict bridge nodes, we compared these predictions to the true patterns of bridge nodes, thereby assessing their sensitivity and specificity. Sensitivity (true positive rate) indicates the percentage of bridge nodes correctly detected by the algorithm. Specificity (true negative rate) indicates the percentage of non-bridge nodes correctly excluded by the algorithm. Code in the supplementary materials includes additional simulations on networks that include negative edges, motivating the use of the bridge expected influence statistic.

Study 1: Results

The results for averages of sensitivity and specificity across various conditions are presented in Table 1. An expanded table with results for all simulation conditions is available in the supplementary materials (supplementary materials can be accessed at http://osf.io/c5dkj/). The grand mean across all conditions yielded a sensitivity of 92.7% and a specificity of 84.9%. In other words, across all conditions, the algorithms detected 92.7% of true bridges in the networks and misidentified 15.1% of ordinary nodes as bridge nodes. Our relatively low threshold for bridge node selection erred on the side of sensitivity across conditions; a slightly higher cutoff would have yielded a higher specificity at the expense of sensitivity.

Sensitivity and specificity were extremely stable across all conditions (total range of sensitivity 89.5–96.9%, specificity 84.1–86.5%). *Undirected* vs. *directed* networks showed very minimal differences in both sensitivity and specificity (<1%) across conditions. Unsurprisingly, networks without noise had greater sensitivity than did those with noise added (difference of ~2% sensitivity). We were surprised that added noise had only a minor effect on sensitivity and specificity. Notably, adding noise also altered the

Table 1. Sensitivity and specificity of bridge detection algorithms.

Directedness	Noise	Criterion	Sensitivity	Specificity
–*	–	–	**0.927**	**0.849**
Undirected	–	–	0.928	0.849
Directed	–	–	0.927	0.849
–	Yes	–	0.917	0.845
–	No	–	0.938	0.853
–	–	Strength	0.946	0.854
–	–	Betweenness	0.937	0.851
–	–	Closeness	0.899	0.842
Undirected	No	Strength	0.969	0.863
Undirected	No	Betweenness	0.943	0.852
Undirected	No	Closeness	0.902	0.842
Undirected	Yes	Strength	0.927	0.845
Undirected	Yes	Betweenness	0.932	0.850
Undirected	Yes	Closeness	0.895	0.841
Directed	No	Strength	0.969	0.865
Directed	No	Betweenness	0.942	0.852
Directed	No	Closeness	0.903	0.842
Directed	Yes	Strength	0.919	0.844
Directed	Yes	Betweenness	0.932	0.850
Directed	Yes	Closeness	0.895	0.841

*The symbol "–" indicates a mean score across conditions.
Grand means are in bold typeface.

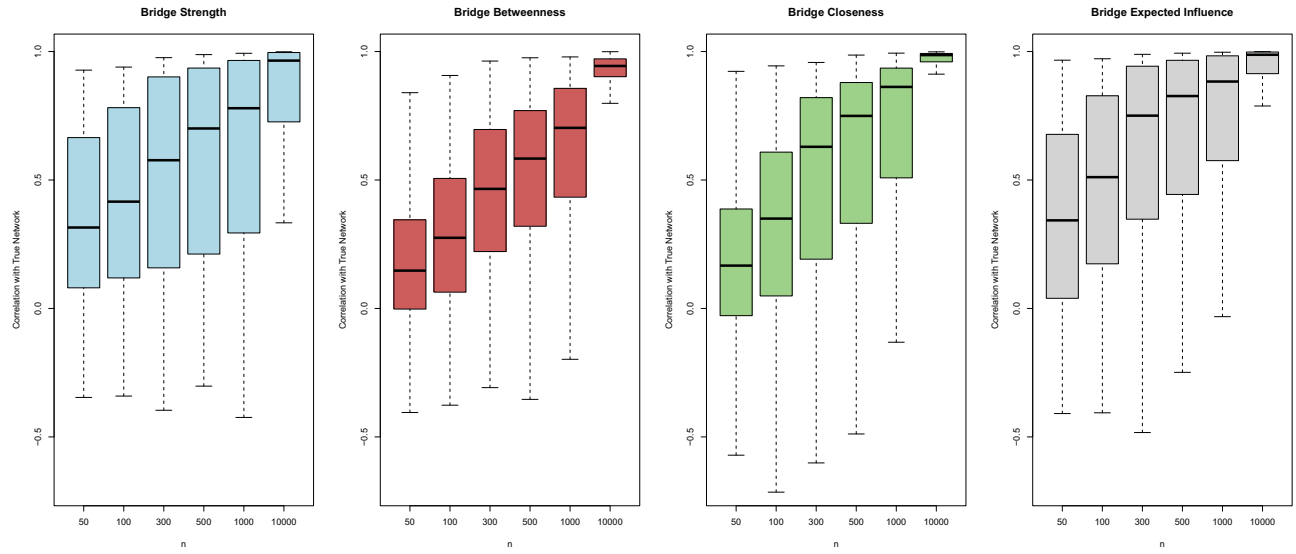

Figure 4. Accuracy in retrieving each type of bridge centrality in simulations.

density of the networks, such that networks with added noise had a density of 100%. This density change seemingly had little effect on the sensitivity and specificity of the statistics. Of the three algorithmic criteria, bridge strength, and bridge betweenness were the most accurate in terms of sensitivity, with bridge closeness lagging slightly behind. This is somewhat unsurprising, given that our simulation approach focused on direct connections between bridge nodes and other nodes, a situation most closely aligned to bridge strength.

Study 2: Robustness of bridge centrality statistics in estimated networks

In practice, psychometric networks are estimated from datasets of varying sample sizes. Estimated networks may or may not approximate the true network structure underlying the data. To determine the robustness of our bridge centrality statistics in estimated networks, we simulated datasets of varying sample size and estimated psychometric networks based on the simulated data. For the "true networks" used to generate the data structures, we used 12 empirical psychometric networks from published studies. This allows us to test whether our simulation paradigm works well in applied settings. More information on the identification and collection of these empirical psychometric networks is reported in Study 4.

We simulated datasets consisting of 50, 100, 300, 500, 1000, or 10,000 observations. For each possible sample size in each of the 12 viable empirical correlational network structures, we estimated 100 datasets (i.e., a 6×12 simulation with 100 datasets in each cell). For each dataset, we generated a psychometric network consisting of partial correlation values, and subsequently calculated each of the four bridge centrality statistics (bridge strength, bridge betweenness, bridge closeness, and bridge expected influence). We then correlated those recovered bridge centrality statistics with the bridge centrality statistics as calculated in the underlying true network structures. We define adequate robustness as a large correlation ($r > 0.5$) between the true bridge statistics and the estimated bridge statistics.

Study 2: Results

The results of Study 2 are visualized as box plots in Figure 4. As expected, bridge centrality statistics were substantially more accurate in recovering the true network structure when the sample size was large. Notably, the median correlation of the recovered bridge centrality statistics consistently remained below 0.5 when the sample size was 100 or below. With a sample of 10,000, bridge centrality statistics were consistently recovered with a large correlation, whereas sample sizes between 100 and 1000 had a broad range of recovery. Median correlations above 0.5 were typically observed when the sample size was equal to or greater than 300. We were surprised that robustness seemed relatively consistent across the different statistics, although bridge expected influence and bridge strength showed a modest advantage over bridge betweenness and bridge closeness, with bridge expected influence showing the greatest robustness at high sample sizes.

Table 2. Simulation of mental disorder symptom contagion over time.

Removed nodes	Noise	Direction	Contagion (Iteration 3)	Contagion (Iteration 5)	Contagion (Iteration 10)
Bridge strength	Noiseless	Undirected	0.001*	0.002	0.007
Strength	Noiseless	Undirected	0.012	0.028	0.086
Betweenness	Noiseless	Undirected	0.003	0.007	0.021
Bridge strength	Noiseless	Directed	0.001	0.002	0.007
Strength	Noiseless	Directed	0.013	0.030	0.093
Betweenness	Noiseless	Directed	0.003	0.008	0.024

**Contagion* represent the total activation of symptoms in all disorders other than the original activated disorder.

Study 3: Efficacy in prevention of contagion

We also tested whether deactivating (successfully "treating") a node high on bridge centrality would be an especially potent means of thwarting the spread of activation, thereby preventing the emergence of comorbid psychopathology, as Cramer et al. (2010) hypothesized. Indeed, clinical interest in bridge symptoms arises from their promise as targets of therapeutic intervention.

It should be noted that empirical cross-sectional and even individual psychometric networks in the literature *do not* represent validated causal models of how activation might spread from node to node. This simulation therefore rests on assumptions made in network theory (Borsboom, 2017) that nodes do indeed spread activation through causal patterns and represents a simulation of important bridges being detected *given a causal network structure*. Thus, any results of this simulation will *not* demonstrate that psychometric networks are causal in any way but will rather show that if a causal network were known, bridge centrality statistics would accurately capture nodes that are important in bridging communities within this causal network.

To investigate this issue, we followed Robinaugh et al. (2016) method of simulating network activity in each of 1000 simulated networks by allowing activation to "spread" across symptoms over a process of 10 iterations (Robinaugh et al., 2016). We first assigned a value of 0.5 to each node in a single community, thereby activating all its symptoms. For the subsequent iterations, the activated symptoms increased the value of their neighbors by a rate proportional to their current value multiplied by the edge weight between them. For example, if node A had an initial value of 0.5, and had an edge of weight 0.8 with its neighbor node B, then after the first step, node B would increase by a value proportional to 0.4 (0.5×0.8). Because the networks primarily consisted of positive edges, consecutive steps lead to higher total network activation.

We simulated this network activity in two control conditions and one experimental condition. In the first control condition, the five nodes in the network with the highest *strength* centrality were permanently set to 0 before running the simulation. In the second control condition, the five nodes with the highest *betweenness* centrality were fixed at 0. In the experimental condition, the five nodes with the highest *bridge strength* centrality were fixed at 0. Simulations were run across 500 undirected networks and 500 directed networks generated via the process described in Study 1. Because this simulation was designed to assess contagion in true mental disorder networks, we did not include the generation of random noise.

We measured the network activation of all communities excepting community A at each step in the process. We hereafter refer to this network activation as the *contagion*, as it represents the total amount of activation spread from the first disorder to all other disorders.

Study 3: Results

Results for the Study 3 simulation are presented in Table 2. As expected, the experimental condition of turning off bridge nodes as detected by the bridge strength algorithm was the most successful method for preventing contagion across all conditions, with bridge strength performing more than three times as well than either control condition in preventing contagion by the last iteration. Results were consistent across both directed and undirected networks. Figure 5 presents a visualization of contagion over time in the undirected condition.

These results were unsurprising, given the strong conceptual foundation for bridge nodes and the evidence from Study 1 that bridge nodes could be accurately predicted. However, it should be noted that the findings were based upon representative networks that consisted of semi-connected communities, and may not apply to all networks (e.g., when communities are very closely intertwined). In contrast, eliminating bridges may sometimes be more effective than shown in this simulation if communities are only connected by a few edges (e.g., DAG in McNally et al., 2017).

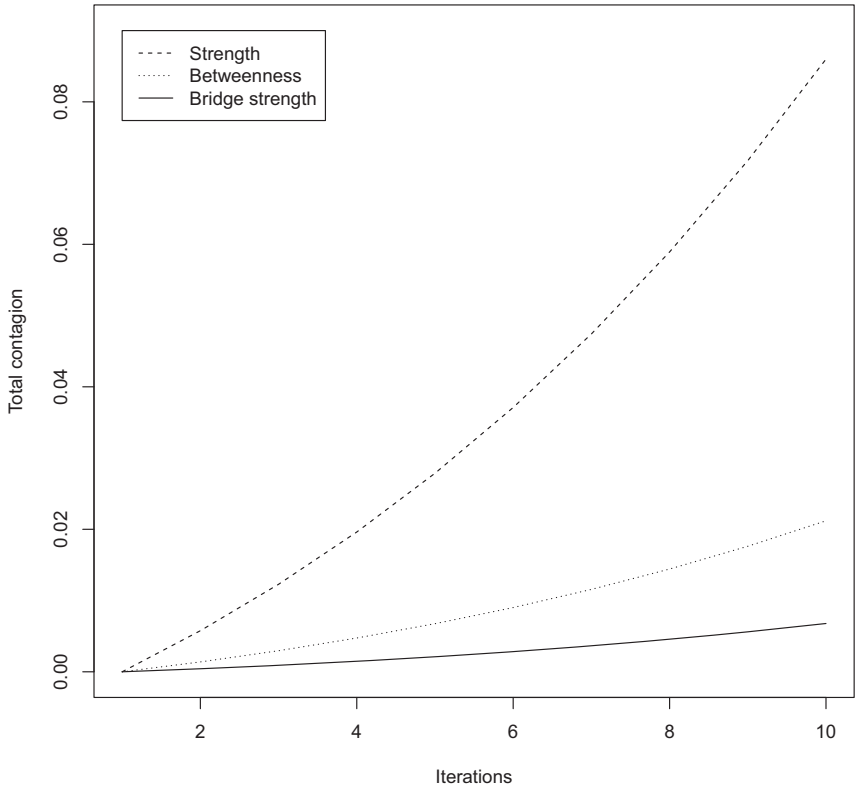

Figure 5. Eliminating nodes with high bridge strength was more effective compared to control conditions in limiting contagion of symptom activation over successive iterations.

Study 4: Application to clinical datasets

Our final aim was to evaluate the bridge centrality indices in networks based on empirical data. Through a literature search, we were able to identify nine publications examining the comorbidity between multiple mental disorders (Beard et al., 2016; Borsboom & Cramer, 2013; Boschloo, Schoevers, van Borkulo, Borsboom, & Oldehinkel, 2016; Boschloo, van Borkulo, Rhemtulla, Keyes, Borsboom, & Schoevers, 2015; Jones, Mair, Riemann, Mugno, & McNally, 2018; Levinson et al., 2017; McNally et al., 2017; Robinaugh et al., 2016; Ruzzano, Borsboom, & Geurts, 2015). These articles contained a total of 18 unique psychometric networks. After using supplementary materials and contacting authors for additional data, we were able to completely reproduce 17 of the networks, and partially reproduce 1 network (due to small instabilities in Bayesian estimation techniques).

After reproducing these 18 networks, we used the *bridge* function in the *networktools* packaged to analyze bridge centralities. Bridge centralities were visualized in each case, and likely bridges were colored and presented in a network graph. A representative analysis is presented in Figure 6 (completed analyses for each of the 18 networks can be accessed at osf.io/c5dkj/). Although the brevity of this article precludes a full discussion of all networks, each analysis provides useful insight into how comorbidity might function in each of the relevant disorders.

Networks were calculated with diverse methods. Six networks were association networks comprising zero-order correlation values as edges. Six networks used a graphical LASSO approach estimating a sparse network comprising regularized partial correlations. These twelve networks were used in Study 2, as their structures provide sufficient information for simulating data from a partial correlation approach. Four networks were DAGs, two which were generated with a Bayesian approach (for details see McNally et al., 2017), and two generated with a PCalg approach (Kalisch et al., 2012). Two networks were generated with eLASSO, which involves a shrinkage approach toward a sparse network as with the graphical LASSO approach but uses a regression approach rather than partial correlation values. The authors of these studies apparently identified bridge symptoms via visual inspection as they did not mention any statistical approaches for identifying bridges.

Because many studies included a discussion of potential bridge symptoms, we sought to analyze the overall concordance between our statistics and the authors' reports of potential bridge symptoms. We

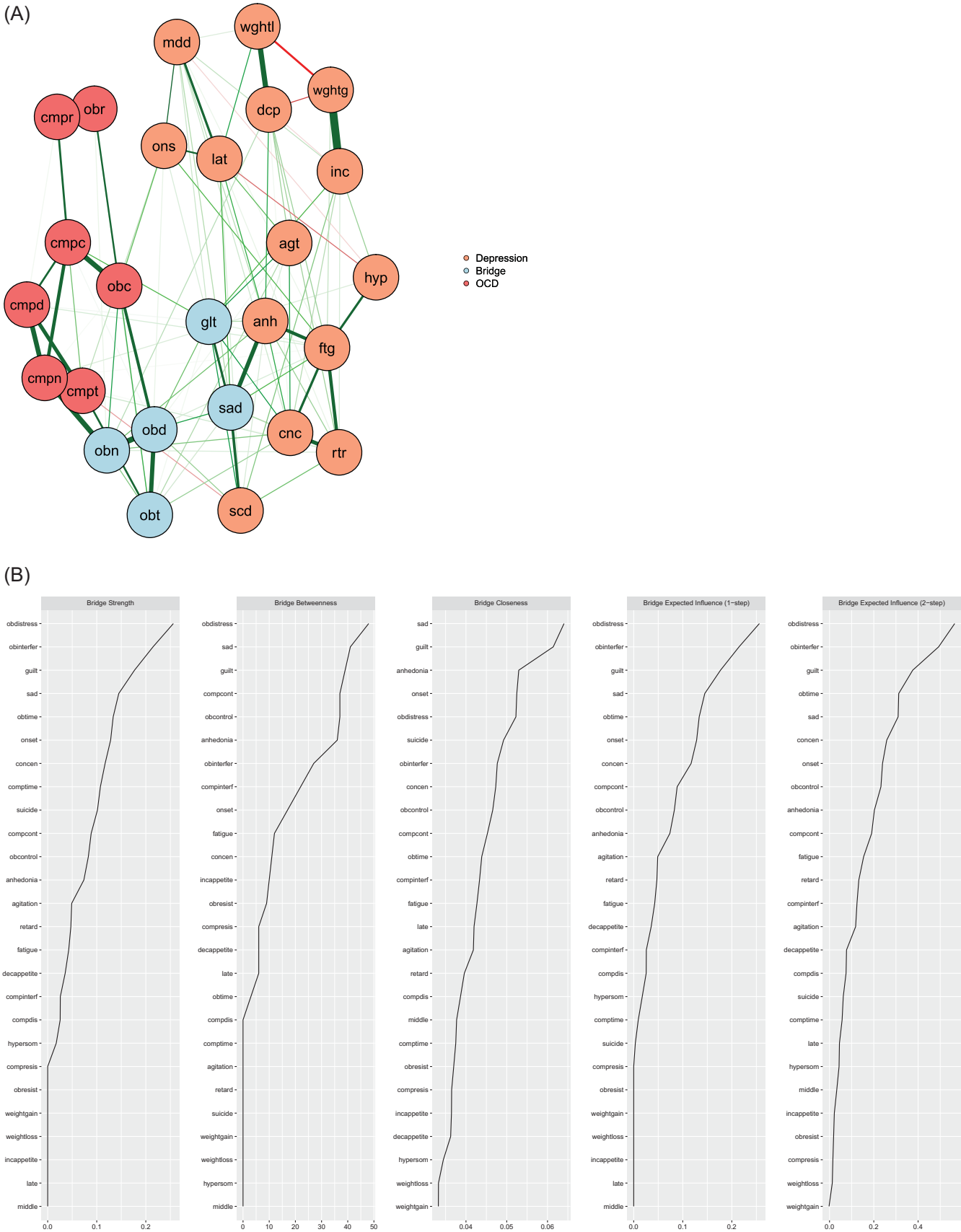

Figure 6. (A) A graphical LASSO model of symptoms of OCD and depressions among 408 adults with primary OCD. Nodes identified as bridge symptoms are colored in blue. (B) Bridge centrality estimates for each node in the network, ordered by highest value.

selected bridge nodes by using a blind 80th percentile cutoff on the scores of bridge strength to avoid confirmation biases in our interpretation of bridge centrality statistics. We then compared these selected bridge nodes with the bridge nodes reported in each study (if any). The results of this analysis can be viewed in Table 3.

Several trends emerged from our analysis of these 18 networks. First, concordance between algorithmic predictions and researcher insight was high when networks were sparse, but diverged for dense networks and when considerable overlap occurred between communities. This observation converged with our initial aim in developing bridge centrality: to aid researchers and clinicians in the objective identification of bridge nodes, especially when networks are large, complex, or difficult to interpret visually.

Another interesting observation was that several symptoms emerged as bridge symptoms across multiple analyses. For example, concentration problems emerged as bridge symptoms in seven out of the thirteen networks that included depression as a comorbid disorder, and sadness/sad mood emerged in six, even though the other comorbid disorder varied among studies (GAD, OCD, complicated grief, and bulimia nervosa). The emergence of these bridge symptoms in multiple analyses was further surprising given that studies used unique, heterogeneous symptom scales (Fried, 2017). These findings suggest that sad mood and concentration problems are important transdiagnostic problems related to diagnostic comorbidity.

To demonstrate the usefulness of each individual analysis, we focus on the graphical LASSO network involving OCD and depression symptoms appearing in the article by McNally et al. (2017; see Figure 6). Comorbidity between OCD and depression is extremely common, with 62.7–78.2% lifetime rates for those who have been diagnosed with OCD (Millet et al., 2004; Pinto, Mancebo, Eisen, Pagano, & Rasmussen, 2006). This comorbidity is associated with several problematic outcomes, including suicide attempts (Kamath, Reddy, & Kandavel, 2007; Torres et al., 2011), functional disability (Storch, Abramowitz, & Keeley, 2009), and increased OCD symptom severity (Brown, Lester, Jassi, Heyman, & Krebs, 2015) among those with comorbid depression. This comorbidity may impede treatment in some cases (Foa, 1979; Rickelt et al., 2016). Thus, an understanding of the symptoms that bridge these disorders could be highly useful to provide focus to treatments of this comorbidity.

McNally et al. (2017) presented a regularized partial correlation network displaying the overlap between OCD and depression. However, because of the complexity of this network, they were unable to report on which symptoms are most likely to play a role as bridge symptoms. Our re-analysis indicated that distress associated with obsessions, interference due to obsessions, time spent obsessing, guilt, and sadness were the likely bridge symptoms in this network. This information should guide clinicians to focus on obsessional (rather than compulsion-related) concerns as well as guilt and sadness when attempting to treat or reduce the likelihood of this dangerous comorbidity.

Each individual analysis of bridge symptoms is similarly useful in elucidating the mechanisms by which disorders are interconnected. We encourage researchers to use the information provided in Table 3 as well as additional information on individual analyses available in the supplementary materials to guide future research on the bridges between the various mental disorders presented.

Discussion

There are several limitations to our approach. First, bridge centrality statistics are based upon existing centrality statistics which already exist in network science. Each of these statistics comes with certain limitations: for instance, strength centrality may not apply well to psychometric networks with many negatives edges (Robinaugh et al., 2016), and betweenness and closeness may have limited stability in certain psychometric networks (Epskamp et al., 2018; Forbes et al., 2017). However, although we have focused on the validation of these statistics in the field of network psychometrics, the statistics could potentially be used in fields such as physics or ecology as well as in psychology. Some types of centrality may be best suited for limited applications: bridge betweenness, for instance, may be particularly attractive in social networks, but unattractive in cross-sectional psychometric networks.

Comorbidity is a core issue in the prevention and treatment of mental disorders. Prevention and reduction of comorbidity is an important goal for mental health professionals, and a deeper understanding of how comorbidity functions in psychopathology is needed to address this important issue.

The network approach to psychopathology suggests that bridge symptoms may play a role in the development and maintenance of comorbid mental disorders (Cramer et al., 2010). Consequently, when one disorder presents, treating potential bridge symptoms

Table 3. A literature search revealed seven empirical articles examining the comorbidity between various mental disorder networks.

Author(s)	Disorders examined	Specific network	Number of nodes	Bridges reported in original	Bridges predicted using *bridge strength*
Borsboom and Cramer (2013)	GAD and Depression	Undirected (Association)	18	*Not reported*	Concentration problems, depressed mood, loss of interest, sleep problems
		DAG (PCalg)	18	*Concentration problems*, fatigue, sleep problems*	*Concentration problems, fatigue,* psychomotor disturbances, *sleep problems*
Robinaugh, LeBlanc, Vuletich, and McNally (2014)	Persistent Complex Bereavement Disorder and Depression	Wave 1 (Association)	19	*Depressed mood*, disbelief or emotional numbness, emotional pain, feeling that life is empy or meaningless, *loneliness*	*Depressed mood*, everything feels like an effort, restless sleep, sadness
		Wave 2 (Association)	19		*Depressed mood*, everything feels like an effort, restless sleep, sadness
		Wave 3 (Association)	19		*Depressed mood, loneliness*, restless sleep, sadness
Ruzzano et al. (2015)	Autism and OCD	Association	17	*Not reported*	Compulsions/rituals, repeatedly doing things until they feel just right, unusual sensory interests, verbal rituals
		DAG (PCalg)	17	*Compulsions/rituals*, repeatedly doing things until they feel just right, verbal rituals	*Compulsions/rituals*
Boschloo et al. (2015)	Multiple disorders/problems	eLASSO	120	*Not reported*	Depressive episode 3, 4, 5, 6, 7, 12; Dysthymia 2, 3, 4, 5; GAD 8; Social anxiety 1; Phobia 1, 2, 3, 4, 5; Panic 1, 3; Agoraphobia 1, 2, 3, 4
Beard et al. (2016)	GAD and Depression	GLASSO	16	Feeling nervous, guilt, psychomotor retardation/agitation, restlessness, *too much worry*, sad mood	*Too much worry*, trouble relaxing
Boschloo et al. (2016)	Multiple disorders/problems	eLASSO	95	*Not reported*	Attention problems 5, 7, 9; Externalizing symptoms 3, 9, 11, 12; Internalizing symptoms 3, 4, 7, 15, 20; Thought problems 1, 2; Social problems 2, 4, 5, 8, 9
McNally et al. (2017)	OCD and Depression	GLASSO	26	*Not reported*	Distress associated with obsessions, guilt, interference due to obsessions, sadness, time spent obsessing
		DAG (Bayesian)**	26	*Distress associated with obsessions, sadness*	*Distress associated with obsessions, sadness*
Levinson et al. (2017)	Bulimia nervosa and Anxiety	GLASSO	48	*Avoidance of eating, avoidance of social eating*, eating in secret, *fear of losing control*, feelings of unsteadiness, feelings of wobbliness, *terrified*, guilt over eating	*Avoidance of eating, avoidance of social eating*, dieting rules, *fear of losing control*, fear of dying, *feelings of unsteadiness*, hands trembling, overevaluation of shape, *terrified*
	Bulimia nervosa and Depression	GLASSO	48	*Binge eating, change in appetite, desire to have an empty stomach, crying*, guilty feelings, lack of interest in sex, overevaluation of shape, overevaluation of weight, *preoccupation with shape*, preoccupation with weight, *self-criticalness*, self-dislike, thinking of suicide	*Binge eating, change in appetite, crying, desire to have an empty stomach*, discomfort with exposure, disliking self, food avoidance, loss of interest in sex, *preoccupation with shape*, *self-criticalness*
	Bulimia nervosa, Anxiety, and Depression	GLASSO	69	*Not reported*	Concentration problems, crying, difficulty making decisions, discomfort with exposure, disliking self, fear of the worst happening, feeling agitated and restless,

(*Continued*)

Table 3. Continued.

Author(s)	Disorders examined	Specific network	Number of nodes	Bridges reported in original	Bridges predicted using *bridge strength*
					feeling nervous, numbness or tingling, sadness, self-criticalness, sleep problems, terrified, unable to relax
Jones et al. (2018)	OCD and Depression	Association	26	*Concentration problems, distress associated with obsessions, lack of control over obsessions*, guilt, sadness	*Concentration problems, distress associated with obsessions, interference due to obsessions*, lack of control over obsessions, time spent obsessing
		GLASSO	26	*Concentration problems, distress associated with obsessions*, lack of control over obsessions, guilt, *sadness, time spent obsessing*	*Concentration problems, distress associated with obsessions, sadness, time spent obsessing*
		DAG (Bayesian)	26	*Concentration problems, guilt, lack of control over obsessions, time spent obsessing*	*Concentration problems, guilt, lack of control over obsessions, time spent obsessing*

For each of 18 networks reported in these papers, we algorithmically identified bridge nodes using a blind, 0.8 percentile cutoff for values of bridge strength centrality, and further compared these nodes to the bridge nodes reported by the authors (if any). Articles are sorted in order of the year of publication.
*Symptoms reported in both the original reports and the algorithmic analyses are italicized.
**Network did not perfectly replicate due to small instabilities in the *bnlearn* package.

may prevent comorbidity. *Bridge strength*, *bridge betweenness*, *bridge closeness*, and *bridge expected influence* are effective tools to detecting bridge symptoms. Furthermore, in a simulation approach, detecting bridges with these statistics and focusing treatment on the detected nodes is effective in preventing the contagion of comorbid disorders. Each of these statistics can be computed via application of the *networktools* R package (Jones et al., 2017); we provide a brief tutorial in our supplementary materials (osf.io/c5dkj/). We encourage the use of these statistics as well as other innovations in network science for the identification of bridge symptoms to improve research and practice regarding mental disorder comorbidity.

In conclusion, our bridge centrality statistics provide an objective, quantitative index to identify symptoms likely to foster diagnostic comorbidity. Our measures converge with informal clinical impressions of what symptoms likely function as bridges between syndromic communities of symptoms when networks are sparse, and likely outperform clinical impressions when networks are complex and dense.

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