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## Group-level symptom networks in depression

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*Published in:*  
Jama psychiatry

*DOI:*  
[10.1001/jamapsychiatry.2015.3103](https://doi.org/10.1001/jamapsychiatry.2015.3103)

**IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.**

*Document Version*  
Publisher's PDF, also known as Version of record

*Publication date:*  
2016

[Link to publication in University of Groningen/UMCG research database](#)

*Citation for published version (APA):*

Bos, E. H., & Wanders, R. B. K. (2016). Group-level symptom networks in depression. *Jama psychiatry*, 73(4), 411. <https://doi.org/10.1001/jamapsychiatry.2015.3103>

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# Letters

## COMMENT & RESPONSE

### Group-Level Symptom Networks in Depression

**To the Editor** About 8 years ago, network models entered the field of psychiatry.<sup>1</sup> In this approach, psychiatric disorders are conceptualized as a dynamic interplay between symptoms over time, contrasting the traditional disease model of an underlying common cause. With the intention to describe how symptoms give rise to each other, the network approach would deal with processes taking place at the level of the individual.<sup>1</sup> Nevertheless, almost all studies on networks have investigated this phenomenon at the group level.

The latest example is a study by van Borkulo et al.<sup>2</sup> This study showed that the sparse symptom network of a group of patients with persistent depression was more densely connected at baseline than the network of the remitted group. The authors argued that more strongly connected symptoms imply higher vulnerability to depression because of stronger feedback among the symptoms. Here they jump from the population to the individual level in their reasoning, without good arguments. Their group-level networks show whether symptoms co-occur across cases. The very fact that symptoms tend to co-occur does not imply that they influence each other over time within individuals. Symptoms may co-occur for several reasons including a common underlying cause. The fact that the difference in network connectivity largely disappeared when severity and level of functioning was partialled out is suggestive. Only in the minimally sparse networks was the difference preserved.

The authors did mention the limitation that their networks are based on between-subject variance, but suggest this is not problematic as long as the groups are homogenous. We think the problem is more fundamental because associations at the population level may be radically different from associations at the individual level even in the case of homogeneity. This phenomenon, called the *ecological fallacy* or *Simpson's paradox*,<sup>3</sup> may occur rather often, as was shown in an excellent review<sup>4</sup> (with 2 authors of the van Borkulo et al<sup>1</sup> article as coauthors). Therefore, drawing inferences from patterns observed between people to processes that occur within people is unwarranted. However, we have a natural tendency to do so, and the visually attractive network graphs enhance this tendency.

We think it is time to investigate networks at the proper level of investigation (ie, at the intraindividual level). As long as we keep investigating cross-sectional group-level networks, the results will remain compatible with a traditional disease model, will not be informative of symptom interactions within individuals, and will obscure scientific reasoning.

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**Published Online:** February 24, 2016. doi:10.1001/jamapsychiatry.2015.3103.

**Conflict of Interest Disclosures:** None reported.

1. Borsboom D. Psychometric perspectives on diagnostic systems. *J Clin Psychol*. 2008;64(9):1089-1108.
2. Van Borkulo C, Boschloo L, Borsboom D, Penninx BW, Waldorp LJ, Schoevers RA. Association of symptom network structure with the course of depression. *JAMA Psychiatry*. 2015;72(12):1219-1226.
3. Robinson WS. Ecological correlations and the behavior of individuals. *Am Sociol Rev*. 1950;15(3):351-357.
4. Kievit RA, Franke WH, Waldorp LJ, Borsboom D. Simpson's paradox in psychological science: a practical guide. *Front Psychol*. 2013;4:513.

**In Reply** In our publication in *JAMA Psychiatry*,<sup>1</sup> we reported that the structure of symptom networks is related to the course of depression. Our findings are based on a between-patients design. Although we agree with Bos and Wanders that this has implications for the interpretation of our results, we do not think their conclusions are warranted.

Bos and Wanders correctly point out that, in theory, associations identified through group-level analyses may differ radically across individuals (Simpson's paradox). However, we think that this is not very likely for the reported associations between depression symptoms in our study. First, it is hard to imagine that some patients become less depressed as a result of feeling worthless or get alert and focused when they feel slowed down. Associations between symptoms plausibly differ in degree, but not in kind, so that radical heterogeneity should not be expected for depression symptom networks. Second, our network parameters are partial correlations, not zero-order correlations: thus, each symptom-symptom connection in the network is already controlled for individual differences in all remaining symptoms, so that Simpson's paradox is ruled out with respect to these symptoms (and strong correlates of them). Third, recent research, which used intraindividual analyses for network estimation, showed that patients with depression had a more densely connected intraindividual network of negative mood states than healthy control individuals,<sup>2</sup> which parallels our result and suggests a positive answer to Bos and Wanders' question of whether our results generalize to the individual level.

Bos and Wanders further argue that the reported associations between symptoms could be the result of a common cause instead of causal associations between symptoms; they find it "suggestive" that the difference in network connectivity largely disappeared in certain analyses. However, we think this is merely the result of a loss of power due to a decrease in sample size (after matching on severity, the overall sample de-

creases from 515 to 344) and the strong regularization penalty; both networks lose almost all of their connections and, in that trivial sense, become more alike. As shown in our article,<sup>1</sup> when using procedures that have less effect on power (like partialling out general level of functioning or weakening the regularization parameter), differences between groups become more, rather than less, pronounced.

Although we believe that it is not very likely that the associations between symptoms are substantially different for individual patients, intraindividual analyses are needed to test this. In addition, intraindividual analyses are warranted to determine whether symptoms are associated over time within patients. Therefore, we gladly reveal that the Netherlands Study of Depression and Anxiety,<sup>3</sup> from which we drew our sample, recently started a new wave of measures in which 400 of its nearly 3000 participants are studied with Ecological Momentary Assessment<sup>4</sup> over 2 weeks. The aim of this study is to provide more insight into the association between intraindividual and interindividual differences, which will lead to an increased understanding of how nomothetic and idiographic analyses are related.

**Claudia D. van Borkulo, MSc**  
**Denny Borsboom, PhD**  
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**Published Online:** February 24, 2016. doi:10.1001/jamapsychiatry.2015.3157.

**Conflict of Interest Disclosures:** None reported.

**Additional Contributions:** We appreciate the thoughtful comments on this manuscript of Lynn Boschloo, PhD, at the University of Groningen, Groningen, the Netherlands. She did not receive compensation for her contributions.

1. van Borkulo C, Boschloo L, Borsboom D, Penninx BW, Waldorp LJ, Schoevers RA. Association of symptom network structure with the course of depression. *JAMA Psychiatry*. 2015;72(12):1219-1226.

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3. Penninx BWJH, Beekman ATF, Smit JH, et al; NESDA Research Consortium. The Netherlands Study of Depression and Anxiety (NESDA): rationale, objectives and methods. *Int J Methods Psychiatr Res*. 2008;17(3):121-140.

4. van der Rot M, Hogeneelst K, Schoevers RA. Mood disorders in everyday life: a systematic review of experience sampling and ecological momentary assessment studies. *Clin Psychol Rev*. 2012;32(6):510-523.

## CORRECTION

**Error in Title:** In the Original Investigation titled "Association of Symptom Network Structure With the Course of Longitudinal Depression," published online November 11, 2015, and also in the December 2015 print issue of *JAMA Psychiatry*,<sup>1</sup> there was an error in the title. The title should read as follows: "Association of Symptom Network Structure With the Course of Depression." This article was corrected online.

1. van Borkulo C, Boschloo L, Borsboom D, Penninx BWJH, Waldorp LJ, Schoevers RA. Association of symptom network structure with the course of longitudinal depression. *JAMA Psychiatry*. 2015;72(12):1219-1226.

**Error in Affiliation:** In the Original Investigation titled "Type 2 Diabetes Mellitus in Youth Exposed to Antipsychotics: A Systematic Review and Meta-analysis," published online January 20, 2016, in *JAMA Psychiatry*,<sup>1</sup> there was an error in the affiliation for Dr Arango. The affiliation CIBERSAM was inadvertently placed in the Conflict of Interest Disclosures for Dr Arango. The affiliation for Dr Arango should read as follows: "Child and Adolescent Psychiatry Department, Instituto de Investigación Sanitaria Gregorio Marañón, Hospital General Universitario Gregorio Marañón, School of Medicine, Universidad Complutense, CIBERSAM, Madrid, Spain." This article was corrected online.

1. Galling B, Roldán A, Nielsen RE, et al. Type 2 diabetes mellitus in youth exposed to antipsychotics: a systematic review and meta-analysis [published online January 20, 2016]. *JAMA Psychiatry*. doi:10.1001/jamapsychiatry.2015.2923.

**Error in Text and Table:** In the Original Investigation titled "Euthanasia and Assisted Suicide of Patients With Psychiatric Disorders in the Netherlands 2011 to 2014," published online February 10, 2016, in *JAMA Psychiatry*,<sup>1</sup> there was an error in the text and Table 2. The first sentence of the second paragraph of the Results section should read as follows: "Most patients had more than 1 condition, with 36 having at least 2 conditions, 11 having at least 3 conditions, and 4 having at least 4 conditions (Table 2)." In Table 2, the No. (%) for Bipolar depression should read 7(6). This article was corrected online.

1. Kim SYH, De Vries RG, Peteet JR. Euthanasia and assisted suicide of patients with psychiatric disorders in the Netherlands 2011 to 2014 [published online February 10, 2016]. *JAMA Psychiatry*. doi:10.1001/jamapsychiatry.2015.2887.

**Incorrect Definition in Abstract:** In the Original Investigation entitled "Heterogeneity in 10-Year Course Trajectories of Moderate to Severe Major Depressive Disorder: A Danish National Register-Based Study" published online March 2, 2016, and in this issue of *JAMA Psychiatry*,<sup>1</sup> an error occurred in the Results portion of the Abstract. In the second sentence, the parenthetical definition of brief contact, which read "(characterized by probability of contact after 2 years)," should be replaced with "(characterized by low probability of contact after 2 years)." This article was corrected online.

1. Musliner KL, Munk-Olsen T, Laursen TM, Eaton WW, Zandi PP, Mortensen PB. Heterogeneity in 10-year course trajectories of moderate to severe major depressive disorder: a Danish national register-based study [published online March 2, 2016]. *JAMA Psychiatry*. doi:10.1001/jamapsychiatry.2015.3365.