Depressive Symptoms as a Heterogeneous and Constantly Evolving Dynamical System: Idiographic Depressive Symptom Networks of Rapid Symptom Changes among Persons with Major Depressive Disorder

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Abstract

Major depressive disorder (MDD) is the leading cause of global disease burden. Diagnostically, major depressive episodes are conceptualized as a series of individual symptoms occurring most of the day for at least two weeks. Despite this operationalization, among those meeting criteria for MDD, symptoms are highly variable, showing greater variation within and across days than across weeks. Moreover, MDD is highly heterogeneous, varying considerably across people in both function and form. Recent efforts have examined this heterogeneity by studying MDD as a system where symptoms influence one another over time across individuals. In studying MDD symptom dynamics, however, most studies have made a strong assumption: that the symptom dynamics themselves are static and do not dynamically change over time. Nevertheless, there is a possibility that the individual MDD system dynamics change continuously across time. As a part of the Tracking Depression Study, funded by the National Institute of Mental Health and the National Institute of General Medical Sciences, participants (N = 105) completed ratings of MDD depressive symptoms three times a day for 90 days. In the current manuscript, we conducted time-varying vector autoregressive models to investigate the idiographic symptom networks of the entire sample of participants collected to date, and illustrate the finding with a case series of five persons with MDD. Aligned with prior research, the results indicate that there is high heterogeneity across persons, such that the individual network composition is unique from person to person. Moreover, the results suggest that for most persons, individual MDD symptom networks change rather dramatically across the 90 days. This is supported by the fact that 86% of individuals experienced at least one change in their most influential symptom with the median number of shifts being three over the 90 days. Additionally, the majority of individuals had at least one symptom that acted as both the most and least influential symptom at any given point over the 90-day tracking period. Our findings offer further insight into short-term symptom dynamics, suggesting that the composition and driving factors of MDD are not only heterogeneous across persons but also within-persons across time.

Keywords: major depressive disorder, ecological momentary assessment, time-series, network analysis, symptom dynamics

General Scientific Summary

In the current study, we conducted a case-series on five individuals with current major depressive disorder who responded to a depression questionnaire three times a day and used time-series methodology to determine, for each person, how each of the symptoms changed and influenced each other over the course of 90 days. Our findings indicate that major depressive disorder is not only heterogeneous in its manifestation between persons, but can also be highly variable in presentation within an individual over time. As such, individuals with major depressive disorder who experience a more variable symptom presentation may benefit from personalized, time-sensitive clinical interventions.

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Major depressive disorder (MDD) is one of the most common mental disorders and the leading cause of global disease burden (Smith, 2014). Unfortunately, current diagnostic conceptualizations are faced with several difficulties. Firstly, MDD is a complex, heterogeneous system with over 1,000 unique symptom presentations (Cramer et al., 2016; Fried & Nesse, 2015a). However, current diagnostic conceptualizations of MDD treat different MDD symptoms as interchangeable (e.g., meeting 5 of 9 diagnostic criteria or using sum scores of individual symptoms of MDD occurring most of the day, nearly every day for at least two weeks to create a total score, reflecting overall depression severity). This conceptualization falls short of accurately capturing an individual's MDD given that presentations can vary substantially from person to person (Fried & Nesse, 2015a, 2015b). Indeed, conceptualizing MDD as a sum score leaves out crucial information as to which symptoms are the most important and influential in a person's overall diagnostic presentation (Beard et al., 2016). A second problem with diagnostic conceptualizations is the assumption that within a major depressive episode, MDD is assumed to be chronic and unwavering (e.g., occurring "most of the day nearly every day for two weeks"). However, when persons with MDD are measured intensively within persons' daily lives, their symptoms are far from stable across days or weeks, but rather vary more substantially across hours within days as opposed to across weeks or months (Ebrahimi et al., 2021; Fried et al., 2022; Lorenz et al., 2020; Wichers et al., 2016, 2020).

Rather than using traditional diagnostic conceptualizations, MDD may be better conceptualized as a constantly evolving, complex system for individual persons. As such, MDD symptoms dynamically interact with each other such that one symptom can influence the development and maintenance of other MDD symptoms, thus contributing to the overall, complex system of how MDD presents (Beard et al., 2016; Cramer et al., 2016). Moreover, symptom dynamics can vary from person to person, and, importantly, can highly vary within a single day for an individual person due to both internal (e.g., negative cognitions) and external factors (e.g., stressful life events; (Bringmann et al., 2018). Thus, it is important to utilize methodological and statistical approaches to accurately capture the dynamic system of MDD.

Current Network Approaches to Symptom Variability

Ecological momentary assessments (EMAs) allow for researchers to collect several assessments throughout a single day for a longitudinal period and can be used to investigate short-term changes in symptom variability. Vector autoregressive (VAR) modeling is a statistical analysis that uses repeated measures regression to examine the temporal relationships between symptoms in psychopathology, including MDD (Jordan et al., 2020), and often include data from EMAs. More recently, VAR modeling has been applied to network science to examine MDD as a symptom and investigate how symptoms change and influence each other over time (Epskamp et al., 2018; Jordan et al., 2020). When applied to network analysis, VAR models are able to detect whether certain symptoms at one time point (e.g., insomnia) directly lead to increases or decreases of other symptoms (e.g., anhedonia) or the same symptom (e.g., insomnia) at the next time point. Prior research that has investigated the dynamics of symptom networks within MDD with VAR models have commonly employed graphical ($N = 1$) or multilevel ($N > 1$) methods.

Utilization of these types of VAR models for network analysis, however, may not provide an accurate picture of how symptoms dynamically fluctuate over time. First, the multilevel VAR model takes a group-level approach to examine network structures over time, and cannot provide information as to how symptoms change at an individual level. Alternatively, graphical VAR takes an idiographic approach, although relatively few studies have utilized this modeling for depression (de Vos et al., 2017; Kaiser & Laireiter, 2018; Wichers et al., 2016, 2020, 2021), so further research is needed to investigate how symptoms change over time within single individuals. Second, graphical and multilevel VAR models assume that the relationships between variables (e.g., insomnia and anhedonia) are static across time, and assume dynamic changes do not occur between variables across time (Bringmann et al., 2015; Haslbeck et al., 2021; Jordan et al., 2020; Lütkepohl, 2005), neglecting the possibility that MDD symptom networks themselves change over time. Thus, prior work has not yet been able to accurately capture the complex, dynamic system of MDD and has instead investigated MDD as a complex, static system.

Time-Varying Vector Autoregressive Modeling

To address this deficiency in capturing the dynamic nature of MDD symptoms over time, a time-varying auto and cross regressive modeling framework can be applied. The major benefit of this approach is it allows for both autoregressive and cross-regressive relationships to change with time (i.e., model nonstationary processes). This better reflects the reality of MDD in that it is still capable of capturing static symptom dynamics over time (which may be the case for some individuals), but can also model fluctuating dynamics as both internal and external factors arise.

Generalized additive models (GAMs) are uniquely poised to handle this modeling framework as they allow for non-linear smooths to estimate changing coefficients over time (Hastie & Tibshirani, 1995). When applied in a single-lag auto and cross regressive approach, this methodology allows us to estimate the changing relationship between each symptom of MDD, as measured by the PHQ-9, and every other symptom (including the symptom of interest) at the next time point. For example, the relationship between anhedonia and itself (autoregressive) at the prior time point can be different on day two than it is on day nine, and there is a smoothed trajectory for this changing association over time. This same idea can also be applied to any cross-regressive association (e.g., the association between concentration difficulties and psychomotor difficulties at the time-point prior can be quite large at time-point 15 and quite small at time-point 30). This changing association may be due to changing external or internal factors, and importantly, using this approach we are able to capture these changing dynamics.

Rationale

As noted above, prior research has investigated MDD symptoms over time using a stationary approach (e.g., graphical and multilevel VAR), thus potentially leaving out important information about the heterogeneity of MDD symptoms and how they can dynamically change and influence each other over time. Moreover, relatively few studies have examined MDD symptoms with an idiographic network analysis approach. Thus, the purpose of the current case series is to examine the dynamics of MDD symptoms within individual persons using a time-varying VAR approach and validate the findings through a qualitative analysis of individuals' written accounts.

Method

Procedure

As a part of the Tracking Depression Study, an R01 study funded by the National Institute of Mental Health and the National Institute of General Medical Sciences, individuals

over 18 years of age with current major depressive disorder (MDD) were recruited remotely across the United States via Google Ads. Participants were required to use an Android-based phone as their primary mobile device. They were screened for current MDD and exclusion criteria through online surveys and virtual interviews, allowing for mental health assessments and for collection of demographic information. The mental health assessment included a clinician-administered Structured Clinical Interview for DSM-5 (SCID-5). Individuals were excluded from participation if, at any point during the screening process, they endorsed active suicidality, current or past psychotic symptoms, or bipolar disorder, or if they did not meet criteria for a major depressive episode within the past 30 days. This study was approved by the Dartmouth College Institutional Review Board (the Committee for the Protection of Human Subjects (STUDY00032081)) and participants were asked to provide both written and verbal consent prior to taking part in study.

Following screening, qualifying participants were asked to install the smartphone application, MLife, on their Android device. MLife is a mobile sensing application developed to collect passive sensing and ecological momentary assessment (EMA) data (R. Wang et al., 2014). Participants were instructed to keep MLife running throughout the 90-day study period, and were prompted three times a day by the application to answer an EMA (i.e. a short survey), which included questions about depressive symptoms and a diary entry. EMA notifications were delivered starting four hours after participant self-reported wake time (morning EMA), and at four-hour intervals thereafter (afternoon and evening EMAs), with a total of 270 EMA prompts per participant over the 90 days. Upon study completion, participants were compensated $1 per EMA completed.

Patient Health Questionnaire-9 (PHQ-9)

At each EMA, participants completed a modified version of the Patient Health Questionnaire-9 (PHQ-9), a validated measure used to assess depression severity (Kroenke & Spitzer, 2002; Torous et al., 2015). In the current study, we utilized a modified PHQ-9 to make the EMA questions more mobile-friendly (see Supplemental Materials). Participants were asked to use a sliding scale (rather than the original 4-item Likert-scale) to select a value ranging from 0 to 100 that best reflected how they felt, as done in prior work (Torous et al., 2015). Participants were asked to think of the sliding scale as ranging from a day in their past when the relevant question was not an issue at all (i.e., “0” or “Not at All”) to a day in their past when the relevant question was the most applicable (i.e., “100” or “Constantly”), and to assess how they had felt over the past four hours within this range.

Diary Entry Question

The optional diary entry question prompted participants to describe how they had felt over the past four hours and why. Participants were provided the option of responding through either video, audio, or text, and were encouraged to use this space to provide any other relevant information including changes in medication or therapy.

Participants

At the time of this analysis, the Tracking Depression Study had a total of 105 participants that had completed the EMA portion of the larger trial and were included in the present analyses. The five participants included in the current analyses were selected as a representative sample based on overall symptom variability and number of diary entries. Participants with the greatest number of diary entries were selected in order to allow for qualitative validation of model findings. The five illustrative participants met criteria for MDD via the SCID-5 and were between the ages of 20-40 years old, with the majority of participants identifying as female (80%

female, *n* = 4) and Non-Hispanic White (48%, *n* = 3) (see Table 1 for individual demographic data).

Data Preparation

The first step of data processing was to select those individuals with the most daily diary entries as described above. Using these subjects allowed for thorough qualitative validation of the modeling outputs. Data used for this analysis consisted of all PHQ-9 EMA data collected over the course of the 90-day study except for the question related to sleep difficulties, which we excluded as it was only presented to each participant once a day rather than three times per day. EMA entries were either fully completed or did not exist, and thus there were no EMAs that contained partial data. Across the five participants they each answered 277, 266, 273, 216, and 168 EMAs respectively,[1] and no participant went more than three days without answering a survey across the 90 days of the study.

From this EMA data, eight data tables were generated per person, with each data table representing one MDD symptom as the outcome and all eight symptoms at a lag of one EMA as the predictors. These data tables had (t-1) rows with one row for each EMA excluding the first because there are no lag one predictors at t=1.

Modeling Approach

Following the data preparation, eight GAM models, representing each of the eight MDD symptoms as an outcome, were fit per person (*N* = 5) included in the case series, resulting in 40 total GAM models. An example GAM model formula looks as follows for the prediction of PHQ-9 Question 1 (Q1): Having little interest or pleasure. The rest of the PHQ-9 questions Q1-Q8 (excluding the sleep question) at the time prior to the outcome (t-1) are the predictors.

$$Q1_t = \beta_0 + f(t) * Q1_{t-1} + f(t) * Q2_{t-1} + \ldots + f(t) * Q8_{t-1} + \epsilon, \epsilon \sim N(0, \sigma^2)$$

In this formula, we evaluate the linear relationship between each MDD symptom as it predicts every other MDD symptom as a (non)linear smooth function (*f*) of time. Additionally, we add an L1 penalty term allowing predictors to be penalized to zero (Wood, 2017). This penalization was put in place to prevent spurious results from estimates with high variability. From each of these models, we were able to obtain a coefficient for each lagged predictor at each time point (each EMA). These changing coefficients represented the dynamic, directional relationship between the lagged predictor and the outcome for a given symptom.

Model Outputs and Evaluation

Given the aforementioned modeling approach, the per-person outputs consisted of a coefficient for each symptom as it predicted every other symptom, including itself, at the next time point. These results were then constructed into an adjacency matrix of coefficients for each time-point (EMA). From these adjacency matrices, directed networks could be generated with nodes representing symptoms and edges representing the association for how well the starting node predicted the receiving node at the next time point. The primary outcome of interest was the changing outdegree for each node in the network. In this case, outdegree is essentially just the sum of the absolute value of the coefficient for a given lag one predictor across each outcome. This value represents how influential a given symptom is on all other symptoms,

1 Note that surveys beyond the 270 required were due to participants' entering surveys before the official start date or completing more than the required number of surveys in a given day.

including itself at the next time point. With this, we can evaluate the changing influence over time of any given symptom on all other PHQ-9 measured components of MDD.

This approach is similar to what would typically be seen in a Gaussian Graphical Model (GGM) where nodes are represented by symptoms and edges are represented as partial correlations between symptoms across persons (Epskamp et al., 2018; Yuan & Lin, 2007). Typically these models are validated via bootstrapping to assess whether the partial correlations persist over bootstrap iterations. Unfortunately, with the idiographic approach, there is no appropriate method to bootstrap over time points and thus a quantitative validation becomes implausible. To address this issue, we chose to complete a qualitative evaluation using written diary entries from the participants. A trained predoctoral clinical psychology intern read through each participant's diary entries while qualitatively evaluating how well they corresponded to the dynamic symptom fluctuations. Entries that corresponded temporally to shifts in symptomatology were noted and mapped back to the model outputs to qualify the modeling results.

Results

The primary results of this analysis are the changing symptom dynamics across the five participants selected for this case series. These are represented in Figures 1-5, which display the changing outdegree for each symptom as it predicts all other symptoms at the next time point. Through this we can evaluate the changing influence of a given symptom on their depression profile as well as the overall variability of an individual's depression dynamics and presentation. Note, an even more nuanced representation of symptom dynamics is reported in Supplemental Materials. These animated gifs are able to capture all symptom to symptom relationships over time instead of simply taking the sum of a symptom's influence.

Participant 1

Participant 1 is a White, non-Hispanic transgender female in the 20-40 age range. Of the five participants, Participant 1 had the most variable symptom profile in this case series as evidenced by their top influential symptom changing seven times (see Figure 1). Across the eight measured symptoms, this participant had four unique symptoms that were the most influential, each for a given period of time. Of note, Participant 1 seemed to experience a periodic effect for "lack of concentration" where this symptom varied from high to low importance in an oscillatory manner. In addition, anhedonia and fatigue seemed to maintain relatively high importance, and were the most influential symptom profile components when prior high impact symptoms had dampened effects.

Participant 2

Participant 2 is an Asian, non-Hispanic female in the 20-40 age range. The majority of this participant's symptom profile was influenced by anhedonia and fatigue, and they demonstrated only one change in their top influential symptom (see Figure 2). Towards the end of the 90-day period, psychomotor difficulties quickly became a larger influence on other symptoms despite starting as a symptom with the lowest amount of influence. Remaining PHQ-9 symptoms were relatively static with respect to their influence on this participant's MDD dynamics.

Participant 3

Participant 3 is a White, non-Hispanic female in the 20-40 age range. Their top influential symptom changed three times (see Figure 3). For the first two months of the study, the symptom of psychomotor difficulties was the primary contributor to their symptom dynamics, increasing in influence for the first month, and, while still dominant over the influence of other symptoms,

slowly decreasing in importance for the second month. Both anhedonia and feeling down and depressed maintained a constant influence to start with, and then both fell off in their influence in the second month alongside the psychomotor difficulties. Across the 90-days, the symptom of feeling bad about the self remained a relatively constant influence. In the final month, psychomotor difficulties returned as an important driver of other symptoms, but was not nearly as influential as it had been previously. In addition, anhedonia also returned as the third most important symptom, while feeling down and depressed remained low.

Participant 4

Participant 4 is a White, Hispanic male in the 20-40 age range. This participant had the least variable depression profile with no changes in their top influential symptom, concentration difficulties, which was maintained throughout the duration of the study (see Figure 4). Beyond this, however, all other symptoms also exhibited a relatively static level of predictiveness across the study with psychomotor difficulties and feeling down and depressed as the next two most important features. Participant 4's symptom variability profile exemplifies how MDD has been broadly defined in the past as a relatively static combination of symptoms. In context with the four other participants studied, this finding highlights the inherent flexibility of this methodology to capture not only dynamic MDD symptom fluctuations, but also more consistent MDD experiences.

Participant 5

Participant 5 is a White, non-Hispanic female in the 20-40 age range. Their top influential symptom changed three times (see Figure 5). At the outset of the study, the symptom of concentration difficulties seemed to drive their overall depression characterization. Over the first half of the study, however, this symptom influence decreased, followed by a sustained lack of impact starting midway into the study. Instead, fatigue and weight/appetite difficulties became the primary drivers of this participant's symptom profile across the second part of the study.

Comparisons Between Time-Varying Networks and Qualitative Data

We also included selective diary entries to further validate the changes in symptom networks and investigate internal and external factors that may have influenced these changes. When examining this qualitative data (i.e., diary entries), a common theme emerged such that participants often wrote about symptoms, thoughts, or behaviors that were related to the most influential depressive symptom at the time instead of directly writing about the actual depressive symptom. Thus, it is likely that some of these depressive symptoms are capturing more than the symptom itself, including anxiety and somatic symptoms. For example, Participant 1 provided more diary entries about having headaches when difficulties concentrating was the most influential symptom in the network. Specifically, 20% of their diary entries included a headache between Oct-30 and Nov-11, compared to 4% of their diary entries from Oct-16 to Oct-29. Participant 2 endorsed having COVID-19 around Dec-20, which is when the influence of tired/no energy on other symptoms of the network increased. Participant 3 provided more diary entries regarding her physical activity (e.g., exercising more) and medical problems (e.g., blood sugar decreasing) and increased anxiety throughout her 90 days. Participant 4 did not have any changes in outdegree in the network as difficulties concentrating remained the most influential symptom in the network across the 90 days. However, they may have consistently endorsed concentration difficulties due to them ruminating daily on negative aspects of their life, including a recent breakup, hopelessness, and worthlessness.

All Participants

In addition to the primary case-series participants, we also used this modeling approach to analyze the 105 participants that had completed the larger study. This was done in order to evaluate the distribution of symptom dynamic variability as assessed by this method. In this broader analysis, and as a means of simplifying a more complex set of results, symptom dynamic variability was defined as "the number of times the most influential feature changes" (see Figure 6 for symptom dynamic variability distribution). The average number of times the most predictive feature changed for an individual was 2.817 times with a median of three times. Furthermore, 90 out of the 105 individuals included in the study had their most influential symptom change at least once over the 90 day study period.

Discussion

In the current study, we conducted a novel investigation of the dynamics of depressive symptoms within 105 participants over the course of 90 days using EMA data and a time-varying VAR approach and used five individuals as exemplars to illustrate the approach. In line with prior research, our results indicate that there is high heterogeneity across persons, such that the individual network composition is unique from person to person (de Vos et al., 2017; Kaiser & Laireiter, 2018). Moreover, our results show that for most persons, individual depressive symptom networks can change dramatically in form across a three-month period, as evidenced by some participants exhibiting significant variability within their symptom networks. Further investigation of symptom changes in the larger sample (N = 105) also revealed heterogeneity across persons, as evidenced by variability across the sample in the number of times that the most influential sample changed for a given individual (i.e., 0-8 times). Within the larger sample, 86% of individuals had their top symptom change at least once and 72% had this occur more than once. Furthermore, 52% of individuals had at least one symptom be both the most influential and least influential at some point over the course of the 90 days, and 82% of individuals had their most influential symptom fall into the bottom half. Taken together, our findings suggest that the dynamics of depressive symptom networks vary from person to person and are highly variable across time.

Clinical Implications

Our findings hold important clinical implications for treatment as well. The field of network science has thus far provided important information about the development and maintenance of depressive symptoms. If reflecting causal relationships, centrality measures (e.g., outdegree) can give us information about which depressive symptoms are the most influential over others in a network and potentially suggest which symptoms can serve as important targets for clinical interventions. For example, for individuals where anhedonia emerges as the most impactful symptom, interventions targeting this symptom (e.g., positive affect treatments) may be more beneficial than other treatments (Wichers et al., 2021). As currently explored with graphical and multilevel VAR models, the symptom that emerges as the most impactful may indicate that this symptom is a risk factor and an important intervention target overall, but these models do not assess time-sensitive changes in symptom dynamics and intervention needs. As evidenced by our findings, MDD is better represented as a heterogeneous, dynamic system, given that, for some individuals, symptoms and symptom dynamics change dramatically across time. Moreover, symptoms also dynamically change during treatment, often as a result of direct therapeutic change. Thus, investigating depressive symptoms with a dynamic, time-varying approach may provide better information as to how the symptoms dynamics change over time in response to psychological and pharmacological therapies (Bringmann, 2021; Bringmann et al.,

2017). This approach may help to bridge the gap between network science and clinical practice for providing personalized therapeutic care based on person-specific networks.

Based on the differences between the five case studies presented here and prior research (Fisher, 2015; Jacobson & Nemesure, 2021), individuals likely benefit from different treatments depending on their initial presentation. For example, anhedonic depressed individuals may benefit more from positive affect treatments, and primarily depressed individuals may benefit more from cognitive-behavioral therapy. Thus, taking a "one size fits all" treatment approach across individuals can be potentially problematic and ineffective. Additionally, our findings indicate that the dynamic nature of depressive symptoms may be better suited for interventions that are more time-sensitive and fluid rather than traditional, weekly in-person interventions. Thus, a "one size fits all" treatment approach within an individual may also be potentially problematic as a patient's therapeutic needs will most likely fluctuate over time in response to treatment or other internal (e.g., negative cognitions) or external factors (e.g., stressful life events).

Fortunately, digital interventions represent a growing field in the literature, with several interventions currently in use for MDD (Moshe et al., 2021). Digital interventions offer an advantage over traditional in-person interventions as they are often cheaper, less time consuming, and available in the moment to individuals (Wilhelm et al., 2020). Given the range in variability of symptom changes from person to person, those who experience greater fluctuations in symptoms may benefit more from digital interventions that can be used in the moment than weekly in-person interventions. Just-in-time, adaptive interventions (JITAI) in particular can be utilized for those individuals whose symptoms tend to change dynamically over the course of hours or days (Teepe et al., 2021; L. Wang & Miller, 2020). Thus, being able to monitor individuals' symptom dynamics over time, and implement JITAIs in response to specific symptom changes, may help advance personalized treatment.

Limitations

Although our findings provide important, novel information as to how depressive symptom networks vary on an idiographic level, there are several limitations of the current study. First, due to space constraints, we were unable to include all of the participants in the current presentation and consequently only selected the five individuals with the most written diary entries to include in our qualitative analyses and illustration. While these individuals were more inclined to write diary entries and may not have been representative of the broader population, we picked them specifically so that we could validate whether the modeling approach was accurately detecting symptom changes. Moreover, given the time-series nature of the data, a quantitative validation would not have worked given that bootstrapping is not suitable with an idiographic approach. However, despite the selection process as a potential limitation, the symptom variability for these five individuals proved representative of the range of variability for all participants in the sample (i.e., Participant 1 had significant variability in symptoms over time and Participant 4 had no variability).

Second, given the nature of the time-varying vector autoregressive model, we were unable to include the symptom related to sleep difficulties as this symptom was only measured once per day (compared to three times per day for all other symptoms). Thus, it is possible that excluding this item impacted the variability of symptoms overall for some individuals. For example, sleep difficulties could indeed be the most influential for some individuals; however, we were unable to capture this phenomenon with the current sampling framework and inherent missingness (Bringmann, 2021).

Third, we recruited participants online via Google Ads, allowing us to sample participants more representative of the general population within the United States than had we used a community or clinical sample (e.g. from a local hospital). Given that we did not recruit from patients in a hospital or outpatient clinic, it is unclear whether our sample extends to a more specific clinical, treatment-seeking sample of depressed individuals. However, three participants endorsed receiving treatment for MDD (i.e., psychotherapy and/or psychotropic medication) at some point during their 90 days in the study, thus, it is possible that we would see similar results if investigated within a clinical setting.

Finally, the MLife app utilized for the current study was developed for use on Android devices. Thus, participants were required to own and use an Android phone as their primary device, resulting in exclusion of participants who used smartphones other than an Android (e.g. iPhones). Given that Android devices constitute 44% of smartphone usage in the United States (statcounter, 2022), our sample does not accurately reflect the larger United States population with regards to smartphone usage.

Conclusions

In the current study, we conducted the first case series investigating the symptom dynamics of major depressive disorder using time-varying vector autoregressive models. Our findings support prior research that MDD is a dynamic, constantly-evolving system and suggest that the dynamics of depressive symptoms are person-specific and can dramatically change over time in response to both internal and external factors. Moreover, our findings suggest that digital interventions may be promising toward providing personalized, in-the-moment treatment for depressed individuals. Thus, monitoring depressive symptoms with intensive, longitudinal data may allow for better detection of symptom changes and for implementation of time-sensitive interventions.

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Table 1

Participant Demographics

	Participant 1	Participant 2	Participant 3	Participant 4	Participant 5
Gender	Transgender Female	Female	Female	Male	Female
Race	White	Asian	White	White	White
Ethnicity	Non-Hispanic	Non-Hispanic	Non-Hispanic	Hispanic	Non-Hispanic
Treatment	None	None	None[a]	Psychotherapy/ Antidepressant[b]	Antidepressant

Note. Psychotherapy indicates that the participant was seeing a mental health clinician for therapy (i.e., not medication management). Antidepressant indicates that the participant was taking a psychotropic medication for MDD (i.e., SSRI or SNRI).

[a]Participant 3 started an SSRI in April

[b]Participant 4 started esketamine in March

Figure 1

Changes in Symptom Dynamics for Participant 1

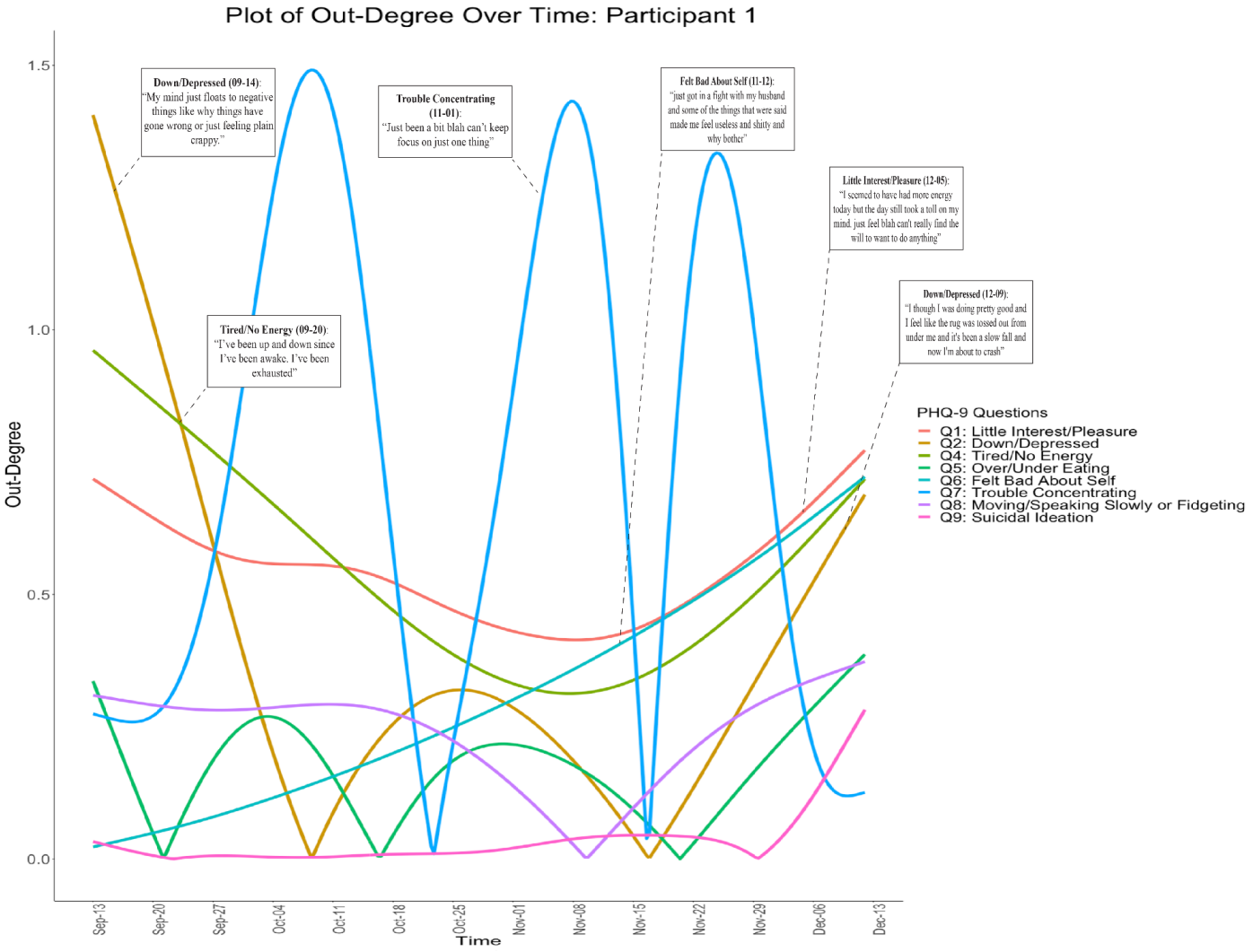

Figure 1. This figure shows the sum of the absolute value of out-degree for each symptom as it predicts every other symptom at the next time point. As an example, the value for Q1 (Little Interest/Pleasure) for the last survey on September 13th is the sum of how predictive it is for all measured symptoms of the first survey on September 14th.

Figure 2

Changes in Symptom Dynamics for Participant 2

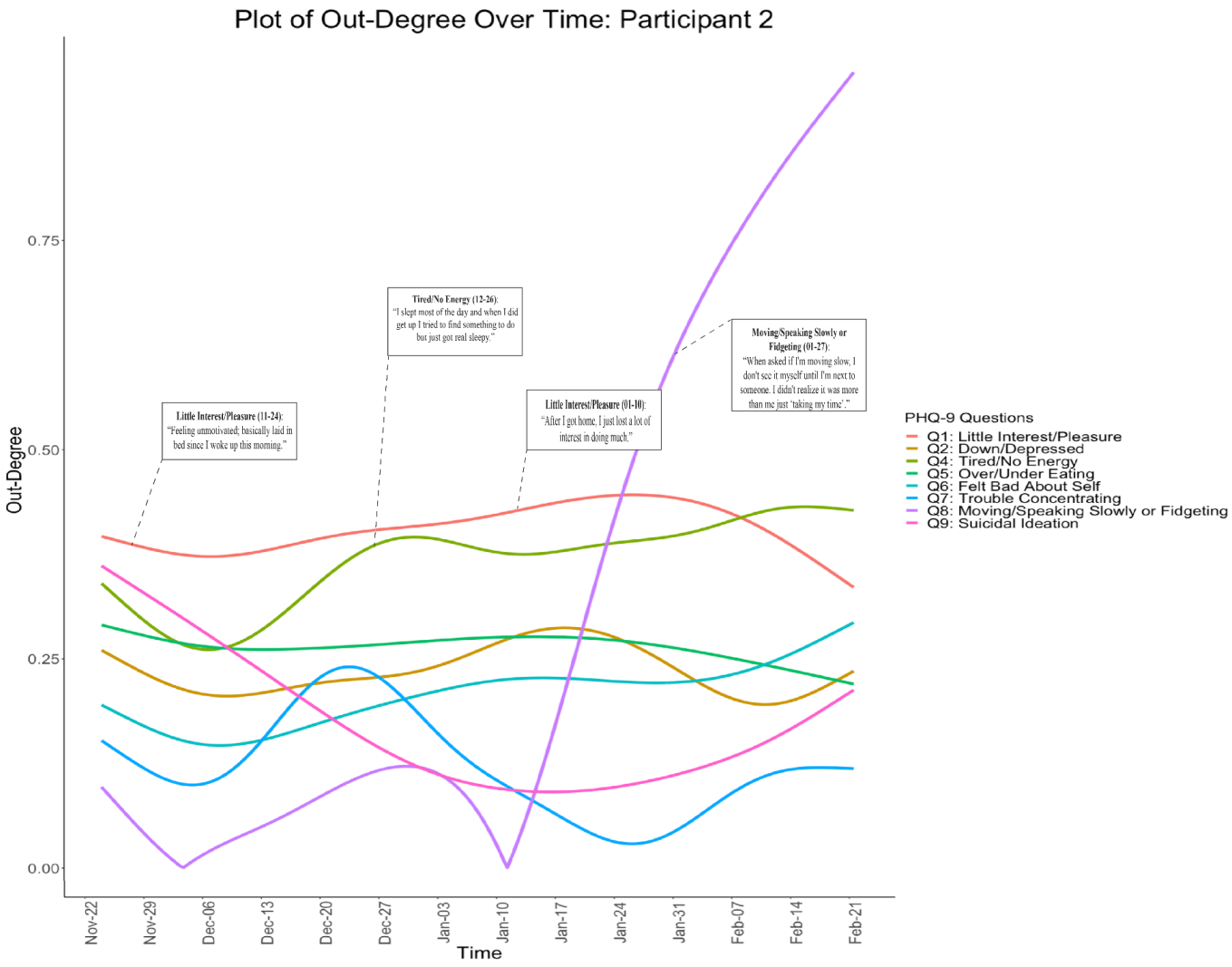

Figure 2. This figure shows the sum of the absolute value of out-degree for each symptom as it predicts every other symptom at the next time point. As an example, the value for Q1 (Little Interest/Pleasure) for the last survey on November 29th is the sum of how predictive it is for all measured symptoms of the first survey on November 30th.

Figure 3

Changes in Symptom Dynamics for Participant 3

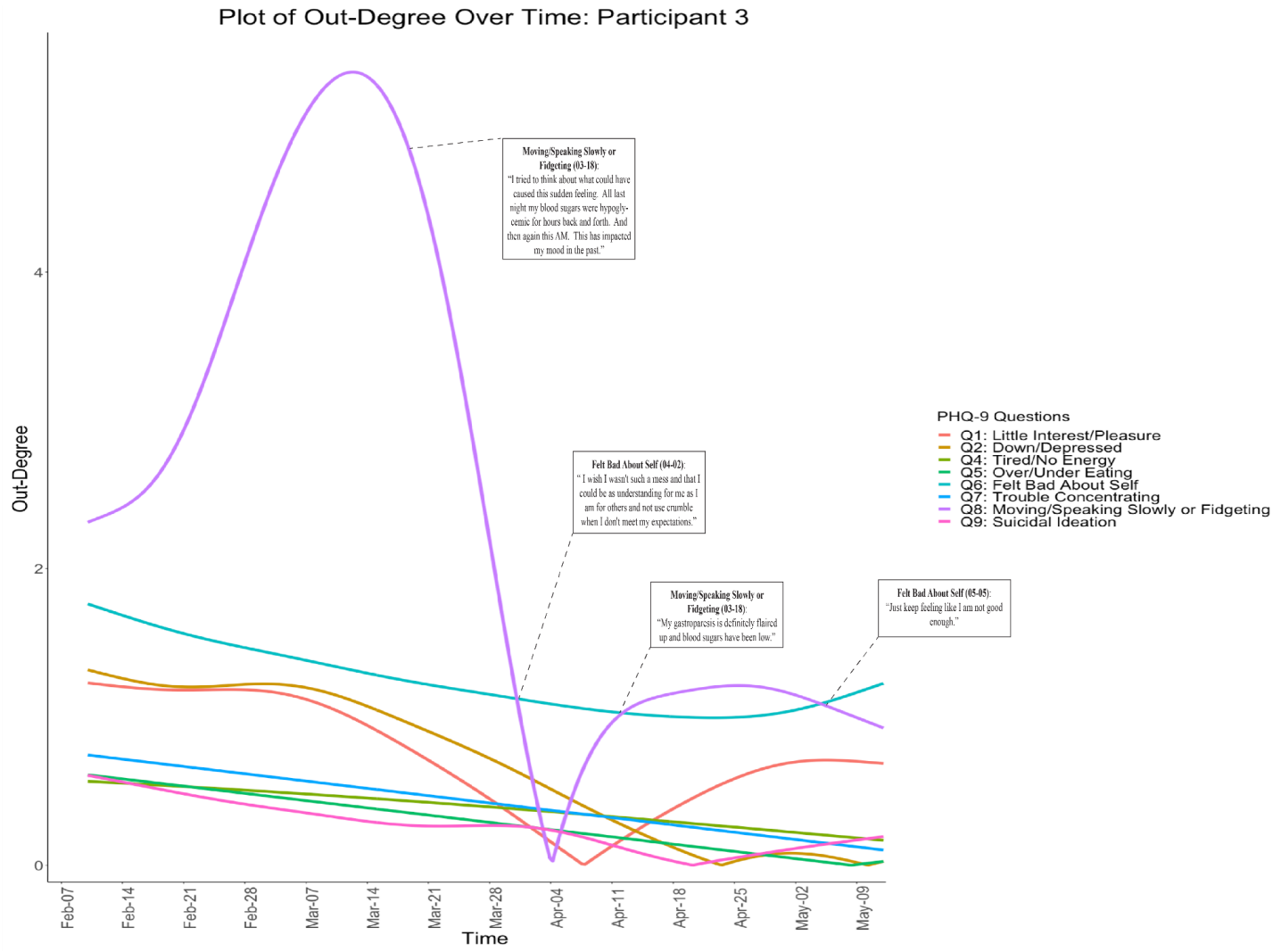

Figure 3. This figure shows the sum of the absolute value of out-degree for each symptom as it predicts every other symptom at the next time point. As an example, the value for Q1 (Little Interest/Pleasure) for the last survey on February 21st is the sum of how predictive it is for all measured symptoms of the first survey on February 22nd.

Figure 4

Changes in Symptom Dynamics for Participant 4

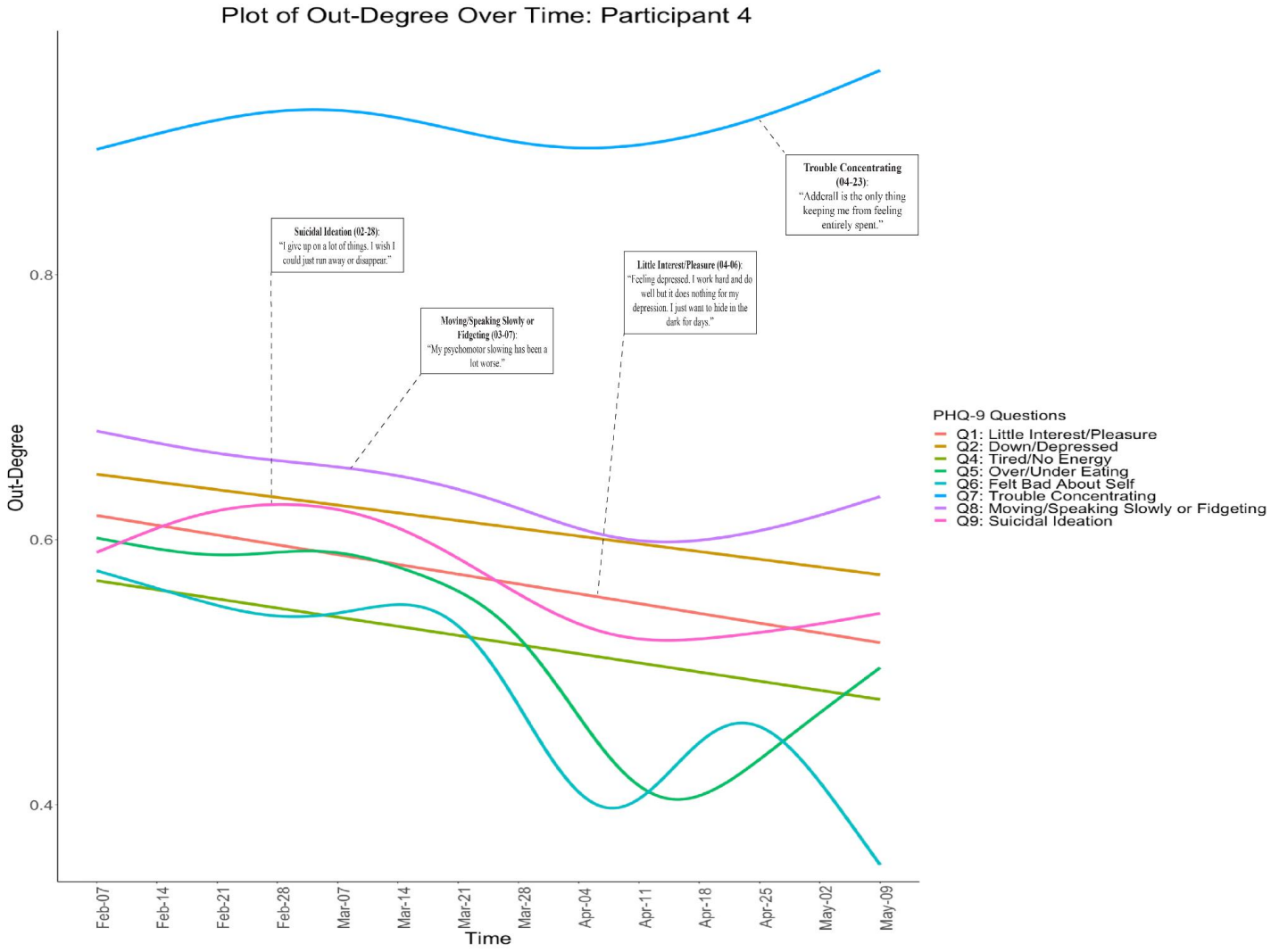

Figure 4. This figure shows the sum of the absolute value of out-degree for each symptom as it predicts every other symptom at the next time point. As an example, the value for Q1 (Little Interest/Pleasure) for the last survey on February 21st is the sum of how predictive it is for all measured symptoms of the first survey on February 22nd.

Figure 5

Changes in Symptom Dynamics for Participant 5

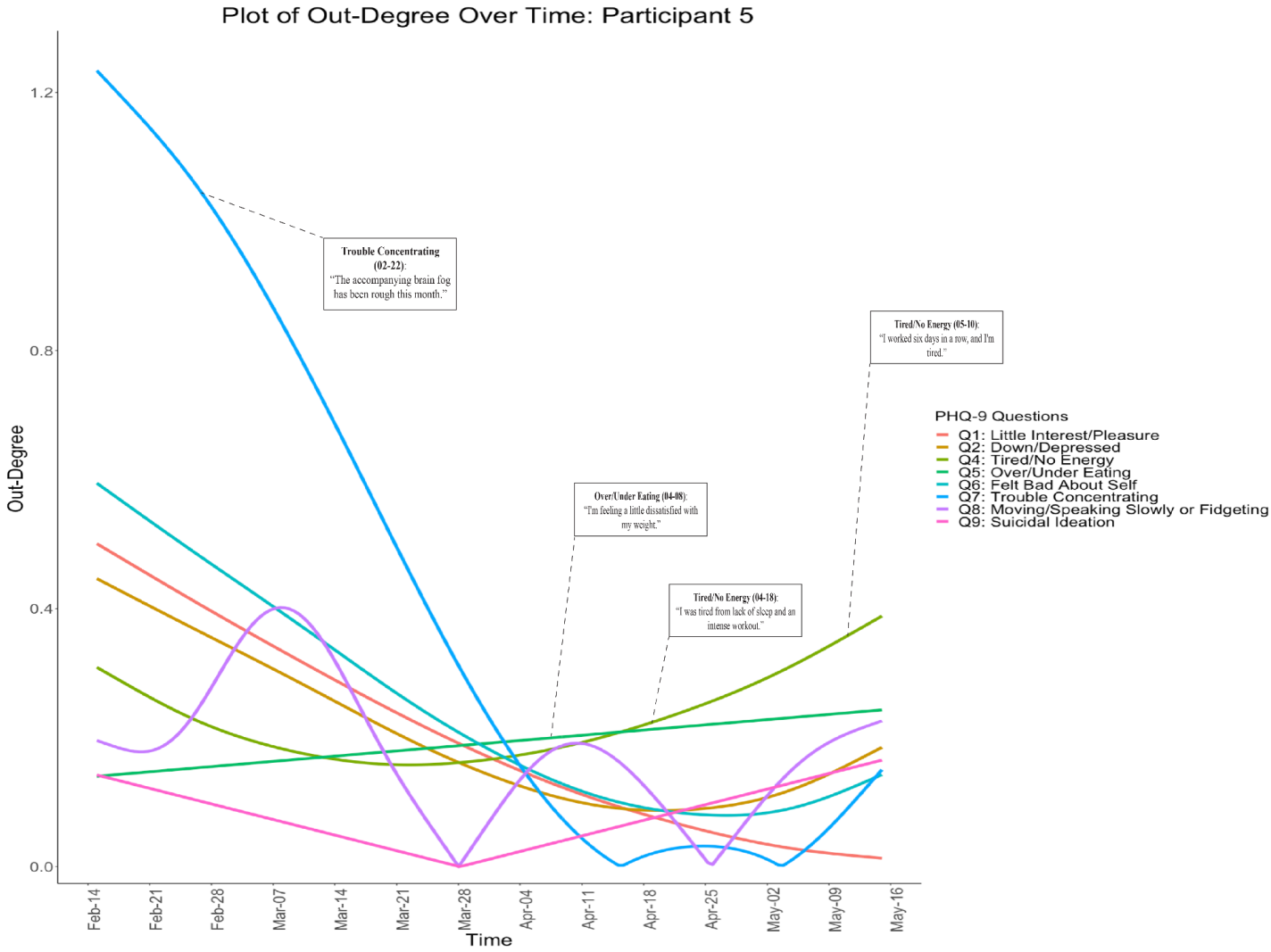

Figure 5. This figure shows the sum of the absolute value of out-degree for each symptom as it predicts every other symptom at the next time point. As an example, the value for Q1 (Little Interest/Pleasure) for the last survey on February 21st is the sum of how predictive it is for all measured symptoms of the first survey on February 22nd.

Figure 6

Distribution of Symptom Dynamic Variability for Larger Study (N = 105)

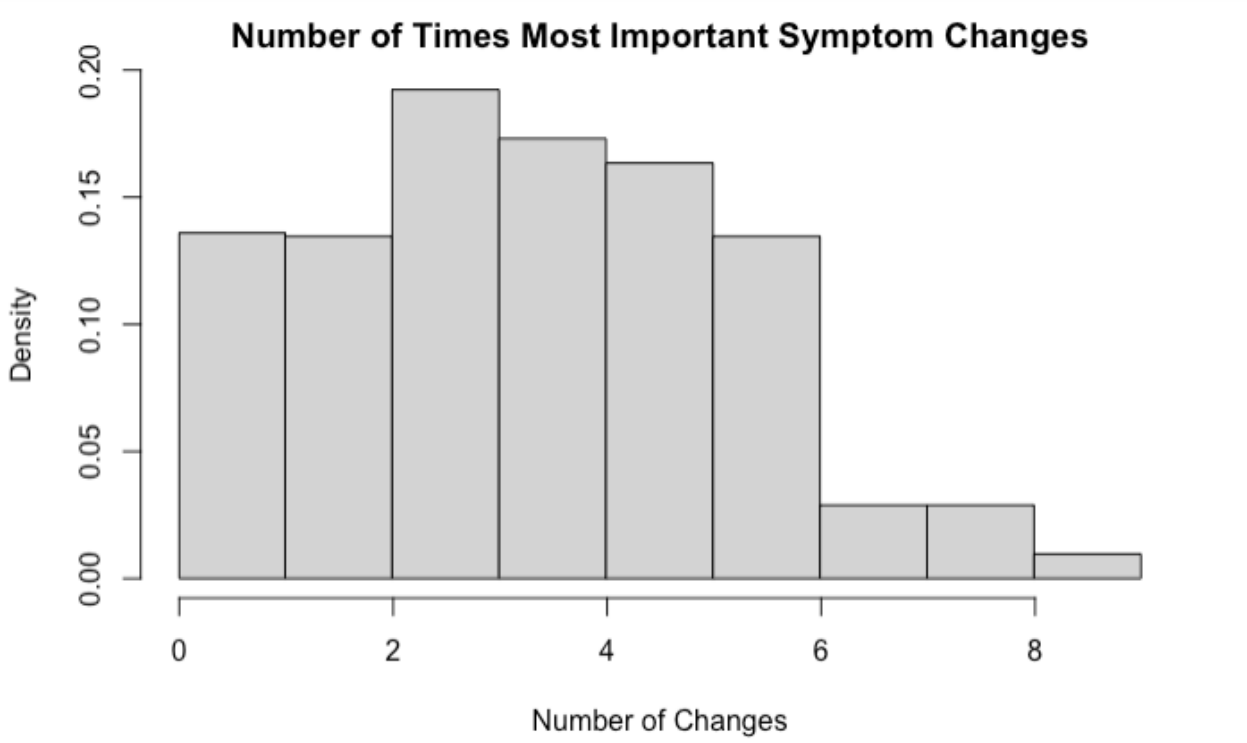

Figure 6. This histogram shows the distribution for the number of times the top most predictive symptom changed over the course of the study for the first 105 individuals to complete the study.

Supplemental Figures

https://github.com/mnemesure/Tracking_Depression_TV-Var-GIFS