A Clinical PREMISE for Personalized Models: Toward a Formal Integration of Case Formulations and Statistical Networks

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Over the past decade, the idiographic approach has received significant attention in clinical psychology, incentivizing the development of novel approaches to estimate statistical models, such as personalized networks. Although the notion of such networks aligns well with the way clinicians think and reason, there are currently several barriers to implementation that limit their clinical utility. To address these issues, we introduce the Prior Elicitation Module for Idiographic System Estimation (PREMISE), a novel approach that formally integrates case formulations with personalized network estimation via prior elicitation and Bayesian inference. PREMISE tackles current implementation barriers of personalized networks; incorporating clinical information into personalized network estimation systematically allows theoretical and data-driven integration, supporting clinician and patient collaboration when building a dynamic understanding of the patient's psychopathology. To illustrate its potential, we estimate clinically informed networks for a patient suffering from obsessive–compulsive disorder. We discuss open challenges in selecting statistical models for PREMISE, as well as specific future directions for clinical implementation.

General Scientific Summary
Personalized networks estimated from intensive longitudinal data are a promising tool to inform case formulations in clinical practice. This paper addresses current implementation barriers and proposes a new Bayesian framework that formally integrates personalized networks with the case formulation approach via prior elicitation.

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In recent years, the idiographic approach received significant attention in psychopathology research (Barlow & Nock, 2009; Fisher et al., 2018; Molenaar, 2004; Molenaar & Campbell, 2009). Proponents of this approach emphasize that individuals differ considerably in their symptomatology and etiology, even within the same diagnosis. It follows that findings from group-level studies can only be generalized to within-person processes under very strong, potentially unreasonable assumptions. The idiographic approach therefore calls for a stronger focus on processes at the *individual* level (Hayes et al., 2019; Hofmann & Hayes, 2019; Zuidersma et al., 2020), one that aims to identify *the right treatment for the right patient at the right time*. This call for personalization in psychopathology research has incentivized the development of new statistical approaches that allow clinicians to estimate personalized models (Piccirillo & Rodebaugh, 2019; Wright & Woods, 2020).

Statistical Advances in Idiographic Research: Personalized Networks

An increasingly popular example in the area of idiographic modeling is the use of personalized networks (Epskamp, van Borkulo, et al., 2018; Wild et al., 2010) estimated from Ecological Momentary Assessment (EMA) data (Myin-Germeys et al., 2018; Shiffman et al., 2008). Such networks aim to display dynamic interactions between personalized variables and may guide tailored intervention planning (Henry et al., 2020; Rubel et al., 2018). One commonly used approach to estimate idiographic networks is based on the Vector Auto-Regressive (VAR) model (Bringmann, 2021), predicting the current score of each variable by (a linear combination of) the scores of all variables at one (or multiple) previous measurement occasion(s). The VAR model can be used to derive *temporal* relationships (indicating predictive effects over time), as well as *contemporaneous* relationships (indicating effects within the same time frame). Figure 1 shows a schematic example of estimating temporal and contemporaneous networks from EMA data of a patient.

Idiographic networks have been applied to a vast range of psychological disorders, such as personality disorders (Dotterer et al., 2020), eating disorders (Levinson et al., 2020, 2021), depression (Wichers et al., 2021), and anxiety disorders (Fisher et al., 2017; Lutz et al., 2018).[1] Van Os and colleagues (2013) emphasized that the use of precision diagnoses via EMA derived personalized networks can increase empowerment in patients, and Kaiser and Laireiter (2018) suggested that these models can provide insight into the interaction between symptoms and therapy processes. Another particularly relevant application of personalized networks is the identification of tailored interventions (Epskamp, van Borkulo, et al., 2018; Henry et al., 2020; Rubel et al., 2018). It should be noted, however, that these methods to identify intervention targets are heuristic and require further scrutiny. This is because network models are statistical models that, by themselves, do not allow for causal inference (Dablander & Hinne, 2019; Pearl et al., 2016; Ryan et al., 2019).

From Personalized Networks to Case Formulations: The Inference Gap

Idiographic reasoning is not new to therapeutic practice. Indeed, the *case formulation approach to cognitive behavioral therapy* (Kuyken et al., 2009; Persons, 2012, 2006; Persons & Talbot,

2019) provides a concrete framework to extrapolate individual models from nomothetic theories and tailor evidence-based interventions to the patient's specific psychopathology, thinking patterns, and resources. Page and Stritzke (2014) formulated a science-informed model for clinical practice that embeds case formulations within the therapeutic process (see also Page et al., 2008), which we will draw on in this paper.

Constructing case formulations can be challenging, and personalized networks could therefore provide supportive exploratory insights into dynamic relationships between variables (von Klipstein et al., 2020). Current efforts to implement personalized networks into clinical practice are primarily focused on using the resulting statistical models to investigate patient-specific dynamics. Although the *content* of the EMA items is grounded in clinical considerations, the *relationships* between the items–the connections in the network–are most commonly established using data-driven routines that disregard clinical theory and expertise. For this reason, we here refer to these routines as *agnostic estimation*. In this data-driven approach, clinician and patient determine a personalized set of EMA items, the patient collects data in between sessions, typically repeatedly throughout the day, and personalized networks are subsequently estimated from the collected data. The resulting networks can then be used to stimulate a dialogue between clinician and patient regarding the identified dynamics, and may provide a rationale for tailored interventions (Rodebaugh et al., 2020; von Klipstein et al., 2020). In doing so, personalized networks promise to provide a powerful tool that can inform the construction of case formulations and therefore overcome the therapist's dilemma–the challenge to tailor nomothetic principles and treatment indications to the circumstances faced by a specific patient (Piccirillo & Rodebaugh, 2019; Piccirillo et al., 2019; Rodebaugh et al., 2020).

This promise to use personalized networks in practice has experienced a tempered response in both the clinical and technical literature. In the following, we will summarize some of the main theoretical, technical, and practical limitations to the agnostic approach.

Limitation 1: Lack of Clinical Considerations

Clinicians may not see utility in using personalized networks if these fail to acknowledge their intuitions or fail to capture the patient's experience (Burger et al., 2020). Indeed, the central aim of constructing case formulations is to integrate these considerations by connecting the patient's presenting psychopathology with clinical theory, empirical literature, and clinical expertise. As discussed above, personalized networks are in most cases estimated *agnostically*, that is, their parameters are based on a data-driven algorithm that lacks the flexibility to incorporate clinically relevant prior information.

Limitation 2: Inaccurate Estimation

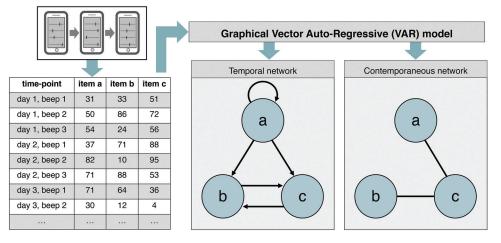Statistical networks usually consist of many parameters that need to be estimated, which in turn requires a large number of

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[1] Some of these references use multi-level approaches (Bringmann et al., 2013; Epskamp et al., 2019) that are not truly idiographic in the sense that data from only one individual are used for network estimation (Piccirillo & Rodebaugh, 2019; Wright & Woods, 2020).

Figure 1
Illustrating the Process of Estimating Vector Auto-Regressive (VAR)-b Assessment (EMA) Data (Burger et al., 2022)

Note. EMA = Ecological Momentary Assessment. Temporal and contemporaneous relationships can be calculated via components of the VAR model, which predicts the current score of a variable from previous scores of all variables. The resulting model can be used to construct temporal networks (left, directed conditional relationships) and contemporaneous networks (right, undirected conditional relationships). See the online article for the color version of this figure.

observations to arrive at reliable estimates. For a relatively simple network of five variables, a graphical VAR network model contains 35 parameters. Note that the number of variables included in personalized EMA assessment is typically much higher, at least 20 (von Klipstein et al., 2020), which would lead to a total of 590 parameters. Reliably estimating such complex models requires a minimum number of observations that is often not realistic to achieve in idiographic research designs. Simulation studies indicate that the length of commonly obtained EMA time series in psychiatric settings lead to networks with low sensitivity, potentially leaving relationships undetected (Mansueto et al., 2020).

Limitation 3: Practical Considerations and Technical Skills

Statistical skills to estimate and interpret personalized networks are not routinely taught in training programs for health care psychologists. This barrier makes it hard for these models to be used by practitioners directly and would require additional statistical consultation and collaboration with researchers. Although such collaborations may be desirable because they stimulate interdisciplinary exchange, they are also time-intensive and might therefore hamper implementation.

A Formal Integration of Case Formulation and Personalized Networks

The main objective of this paper is to address these limitations by presenting an approach that formally integrates case formulation with personalized network estimation, and to offer an intuitive and user-friendly tool to apply the presented approach in clinical practice. We introduce the Prior Elicitation Module for Idiographic System Estimation (PREMISE) as a first step toward a systematic incorporation of clinical considerations in estimating personalized networks.

The core idea of the PREMISE approach is to use an initial case formulation ("working hypothesis") as the fundament for further statistical modeling routines. The integration of such clinical information with technical estimation routines requires that the case formulation first needs to be translated into a computational model using mathematical equations, a process referred to as the *formalization* of the case formulation. A new line of literature highlights the benefits of such computational accounts of theories for psychological science generally (Borsboom et al., 2021; Fried, 2020a; Guest & Martin, 2021; Haslbeck et al., 2019; Robinaugh et al., 2021; Robinaugh et al., 2019; van Rooij & Baggio, 2021), and also specifically for case formulations as an example of theories on the individual level (Burger et al., 2020; Schiepek, 2003; Stoger-Schmidinger et al., 2016; Schiepek et al., 2016). Once formalized, it is possible to investigate the precise implications of a case formulation through computer simulations. This allows one to evaluate to what extent the simulated implications of the case formulation align with clinical observations and to investigate the effects of formalized interventions (Burger et al., 2020). *Verbal* accounts of case formulations (and theories in general), on the other hand, tend to be rather imprecise in their specifications and are therefore fallible in terms of accurate predictions and intervention testing (Fried, 2020a).

The process of formalization is complicated and entails making many technical decisions. To increase accessibility, tutorial papers have been published that guide researchers in formalizing verbal theories (Smaldino, 2020; van Rooij & Blokpoel, 2020). In this paper, we draw on principles of *prior elicitation* (O'Hagan, 2006, 2019; Stefan et al., 2020) as one approach to make the formalization of case formulations more accessible for clinical practice. Prior elicitation refers to "the process of extracting expert knowledge about some unknown quantity or quantities, and formulating that information as a probability distribution" (O'Hagan, 2006). The experts, in our case clinician and patient, can formalize case

formulations without specifying probability distributions themselves, circumventing the technical limitation of implementing formalization techniques in clinical practice. Prior literature focused on similar approaches to eliciting perceived relationships, for instance using Perceived Causal Relations (Deserno et al., 2020; Frewen et al., 2012), and Perceived Symptom Relations (Schumacher et al., 2021). These approaches have been extended to the idiographic context, referred to as Perceived Causal Problem Networks (Klintwall et al., 2021). Furthermore, there are new approaches that use EMA data to assess relationships within functional analysis (Scholten et al., 2021).
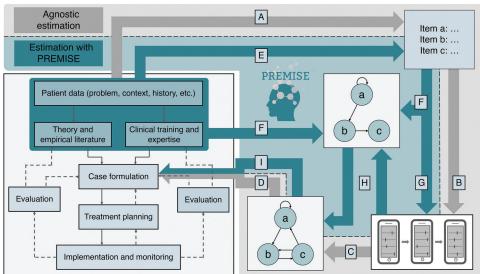
Figure 2 schematically illustrates differences in the process between the *agnostic estimation* of personalized networks (online version: highlighted in gray, print version: highlighted in light gray), and the *estimation with PREMISE* (online version: highlighted in cyan, print version: highlighted in dark gray). In both approaches, items are established in collaboration with the patient (paths A and E in Figure 2). The core difference lies in the way these approaches estimate relationships between the EMA items: Whereas agnostic estimation calculates relationships directly from EMA data in a data-driven manner (paths B and C), estimation with PREMISE formalizes an initial working hypothesis via prior elicitation (path F). This clinical prior model is then subsequently updated using EMA data (paths G and H). Finally, the resulting networks of both approaches can be used to inform case formulation (paths D and I).

The Prior Elicitation Module for Idiographic System Estimation (PREMISE)

In the following, we introduce a first step toward implementing the approach outlined in the previous section. In its current implementation, PREMISE extracts expert information on linear relationships between the selected EMA items via prior elicitation. Depending on the processes of interest, expert information can be extracted for temporal or contemporaneous relationships (Epskamp, van Borkulo, et al., 2018). The extracted information are then used as so-called *informative prior,* representing the perceived distributions of putative relationships, for the subsequent estimation of a Bayesian VAR model. Doing so allows one to systematically integrate clinical considerations with further statistical modeling. Once EMA data have been collected, the priors can be updated using Bayesian inference. This entails shifting the clinical prior model (i.e., the prior probability distributions derived via prior elicitation in PREMISE) according to the pattern found in the data.

Two principles are important here: First, the more data points are used, the more the initial estimates will shift toward the signal in the data. This means that if only little data are available, the updated model will be largely based on the initial specification of the clinician and patient, whereas with the number of observations increasing, the model will more and more converge to the effects driven by the data. Second, prior information can be assigned weights which determine how much data is required to override

Figure 2

Relating Two Different Approaches to Estimating Personalized Networks to the Process Model of Constructing Case Formulations Proposed by Page and Stritzke (2014)

Note. In the agnostic estimation, Ecological Momentary Assessment (EMA) items are derived from patient data, theory, literature and clinical expertise and training (A). Once items are established, the patient collects data in their daily life (B), which can subsequently be used to calculate personalized networks (C). Such networks can stimulate conversations between patient and clinician and inform the construction of case formulations (D). In the estimation with PREMISE (the Prior Elicitation Module for Idiographic System Estimation), EMA items are also first derived from the patient data (E). In contrast to the agnostic approach, however, PREMISE formalizes prior beliefs regarding the relationships between items, based on patient data, theory, literature, and clinical expertise (F). Once data is collected (G), these clinical networks can then systematically be updated (H) via Bayesian inference. The resulting network can be used to inform case formulation (I). See the online article for the color version of this figure.

the prior information. This means that strong priors (i.e., priors with a narrow distribution) will take more data to be ruled out as compared to weak priors (i.e., priors with a wide distribution).

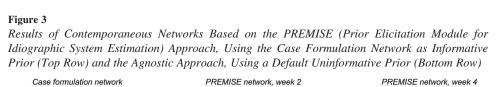## Clinical Example: Patient With Obsessive-Compulsive Disorder

To illustrate the principles of PREMISE, we describe the data and case formulation of a 31-year-old patient diagnosed with obsessive–compulsive disorder. In this example, the clinical prior was derived from a verbal patient report, and the models have been estimated with different amounts of available data (i.e., after 2 weeks and 4 weeks), mimicking the updating of personalized networks during biweekly therapy sessions. Another example on eating disorders has recently been published elsewhere (Burger et al., 2022).
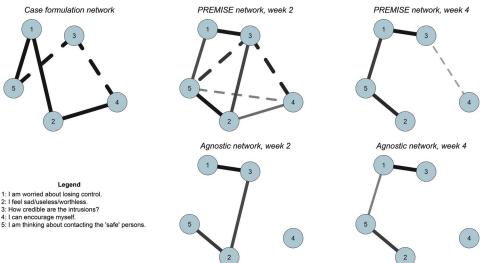
Method

Data on personalized EMA items have been collected three times a day over a period of almost one year, starting in 2017. During this period, the patient followed a cognitive–behavioral therapeutic program, which included exposure therapy with response prevention. Data collection was exempted from formal ethical assessment (METc 2015/140). For a more extensive description of the dataset, see the paper by Bringmann et al. (2020).

Formalizing Initial Case Formulations via PREMISE

During the initial stages of therapy, clinician and patient discussed a working hypothesis regarding interaction and maintenance of symptoms. The patient reported the following: "Having *intrusions* (a), I can *encourage* (b) myself that they are harmless. This is something I must be able to do myself, independent of others. I can keep doing this but it exhausts me, and it becomes less and less effective, until I come to the point where I can no longer hold on to what I am telling myself. I become increasingly *sad and hopeless* (c). Passing this certain threshold, I panic and become extremely afraid to *lose control* (d) over myself." The clinician additionally observed that once this fear of losing control became unmanageable, the patient usually *contacted* (e) their "safe persons" at the hospital and asked for admission, which made them feel safe from acting out on their intrusions. Other than their reaching out to safe contacts, the patient showed no behavioral compulsions. The absence of other overt behavioral compulsions is the result of previous (thus partly effective) intensive cognitive behavioral treatments.

Using this report, we constructed a prior network based on the five EMA items (translated from Dutch): (a) *intrusions* ("How credible are the intrusions?"), (b) *encourage* ("I can encourage myself."), (c) *sad* ("I feel sad/useless/worthless."), (d) *control* ("I am worried about losing control."), and (e) *contact* ("I am thinking about contacting the 'safe' persons."). The structure of the established prior network can be seen in the top left panel of Figure 3 As the reported process unfold relatively fast, and therefore likely occur in between consecutive assessments, contemporaneous networks are the more appropriate choice (Epskamp, van Borkulo, et al., 2018).

Sampling Observations and Data Preparation

Over the course of one year, the patient experienced several relapses. In this example, we therefore focus on a sample of the data that did not coincide with a relapse period, because the VAR model assumes that its parameters do not change over time, an assumption referred to as *stationarity*. For this example, we selected four weeks worth of data collected between June 1st 2017

Figure 3
Results of Contemporaneous Networks Based on the PREMISE (Prior Elicitation Module for Idiographic System Estimation) Approach, Using the Case Formulation Network as Informative Prior (Top Row) and the Agnostic Approach, Using a Default Uninformative Prior (Bottom Row)

Legend
1: I am worried about losing control.
2: I feel sad/useless/worthless.
3: How credible are the intrusions?
4: I can encourage myself.
5: I am thinking about contacting the 'safe' persons.

Note. Solid edges denote positive relationships, dashed edges denote negative relationships. The thickness of each edge corresponds to strength of the relationship. See the online article for the color version of this figure.

and June 28th 2017. We estimated a temporal model using the psychonetrics package (Epskamp, 2020), and proceeded to use the residuals as observations for the estimation of contemporaneous networks. Prior to estimating the networks, we conducted several preprocessing steps that are common for time series analyses. For details on preprocessing and statistical estimation, see the R code in the online supplemental materials.

Estimation With PREMISE Versus Agnostic Estimation

The prior network structure derived from the patient report served as a formalized working hypothesis that was systematically updated in two steps. This resulted in three networks: First, the prior network based on the patient report (without EMA data), second, the updated network after two weeks (23 data points; 39 scheduled assessments), and third, the updated network after four weeks (53 data points; 84 scheduled assessments) of data collection. We will refer to these three networks as the PREMISE networks. Additionally, we estimated networks without the report-derived prior information, which we will refer to as the agnostic networks. These networks are representative for the VAR-based network models that are estimated without clinical input and serve as a comparison point between the two approaches.

As is common in the field of undirected networks, edges represent the partial correlation structure of the variables (Epskamp, Waldorp, et al., 2018). Here, we used the STAN implementation in R (Stan Development Team, 2022) to model the variance-covariance matrix of the residuals via an inverse-Wishart distribution.[2] In the PREMISE approach, we used the case formulation network matrix as informative prior for the inverse-Wishart distribution (the so-called scale matrix). Furthermore, the degrees of freedom of the inverse-Wishart distribution, here set to 30, determine how strongly the prior matrix will be weighed in during the updating process, with larger degrees of freedom centering more probability mass around the prior. In the agnostic approach, we used an uninformative prior set-up further described in a paper by Schuurman et al. (2016). Edges were thresholded by only including them if the respective 95% credibility interval did not include zero (Jongerling et al., 2022).

Transparency and Openness Promotion (TOP)

The paper follows level 2 of the TOP-guidelines on all fundamental aspects of research planning and reporting (i.e., the paper shares materials when legally and ethically permitted). We share all relevant computer code, and provide references that further describe the dataset, including research material specifications (Bringmann et al., 2020). The example analyses in this paper were not preregistered.

Results

All networks are visualized using the qgraph package in R (Epskamp et al., 2012), and can be seen in Figure 3. The goal of the PREMISE estimation (top row) is to investigate changes to an initially established prior network (the "case formulation network"), which may advance the understanding of the patient's psychopathology. In this example, updating the model with two weeks worth of EMA data removes one edge (control–sad), but

includes additional edges (control–intrusions; sad–intrusions; encourage–contact [negative]). After four weeks, further edges are removed (intrusions–contact [negative]; encourage–contact [negative]; sad–intrusions; sad–encourage). In this updated model, the patient experiences worries about losing control when intrusions are currently very credible. In turn, they think about contacting the "safe" persons, which makes them feel increasingly sad, useless, and worthless. At the same time, they manage to regulate the credibility of intrusions through self-encouragement.

The agnostic networks (bottom row), on the other hand, are sparser and miss links specified in the case formulation. For example, in the agnostic approach, the relationship between them being worried about losing control and thinking about contacting the "safe" persons is only detected after four, but not after two weeks. This is most likely because there is not enough evidence (data) yet to establish this relationship after two weeks. In the PREMISE network, this relationship is part of the case formulation network, and is therefore retained throughout the updating process. Furthermore, other features relevant to the case formulation cannot be found in the agnostic network, such as the patient's ability to decrease the credibility of intrusions through self-encouragement. Generally, it is important to note that (unexpected) modifications need to be interpreted with caution. These could also arise due to artifacts of the timing of EMA assessment (i.e., there are effects, but they are not captured by the assessment, see the discussion), or unmeasured variables that are obscuring effects.

Discussion

In this paper, we contrasted different ways in which personalized networks can be used to inform case formulations. We discussed that current approaches to estimating personalized networks are primarily data-driven ("agnostic") and thus lack options to systematically incorporate clinically relevant information, result in models with low sensitivity, and require a level of technical expertise that might hamper clinical implementation. Based on these considerations, we proposed that a formal integration of case formulation and personalized networks, in combination with an intuitive user-interface, could advance clinical utility and implementation. In the following, we provide future directions on how the PREMISE approach can be used to advance our understanding of an individual's psychopathology, and different considerations for implementing it in practice.

Using PREMISE to Gain Insight Into the Patient's Psychopathology

One main question in the context of the PREMISE approach pertains to what we can learn from discrepancies between the clinical prior model and the statistical model based on EMA data. It is unclear at present which of these models better represent the *ground truth* of the patient's personalized systems. Bayesian inference conceptualizes the strength of evidence as the amount of information that points toward a certain effect; the more we learn

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[2] Networks are based on the standardized precision matrix, rather than the variance-covariance matrix. The former represents partial correlations, and can be computed by taking the inverse of the variance-covariance matrix, followed by standardization.

about the patient (i.e., more data), the stronger the evidence for the presence or absence of certain symptom relations. As such, in the context of PREMISE, the ground truth reflects a (hypothetical) model that is based on the maximum amount of data that can be collected within a stationary time unit (in the case of the classic VAR model). If a personalized model then veers away from the prior model in the updating process, this can be attributed to (a) the learning about new aspects of a patient's psychopathology that were previously unknown, (b) a mismatch between the type of prior information that is specified and the assumptions of the statistical model that are imposed (e.g., if prior edges reflect a different time scale compared to the EMA sampling scheme, or if prior edges represent nonlinear relationships but are applied to a linear model), or both.

It is impossible to infer which of these two explanations can account for discrepancies between prior and posterior model by merely observing them in PREMISE. However, behavioral and thought experiments (e.g., Waller, 2009) may help to identify the source of discrepancies, and therefore investigate if changes in the model indeed reflect new insights into the patient's psychopathology. If changes to the initial model seem inappropriate or unreasonable following these experiments, clinician and patient may discuss different aspects to the EMA data collection, such as changes to the sampling scheme or the inclusion or exclusion of items. Of note, both outcomes help us to learn more about the individual's psychopathology, either by directly providing insight into their experienced symptom relations (explanation a), or by indirectly pointing toward changes in the research design that may in turn reveal more valid inferences in the future (explanation b).

To give a clinical example, suppose a clinician and their patient establish a positive relationship between them staying in bed and experiencing depressed mood in the prior model, but the updated model does not contain this relationship. Given theory and experience, this seems surprising, and clinician and patient therefore decide to manipulate this pathway in a small experiment: The patient is instructed to purposefully stay in bed versus get out of bed on different days, and to specifically monitor the effects on depressed mood throughout the day. If outcomes of this experiment support the pathway *staying in bed–depressed mood*, changes to the sampling scheme should be discussed (ruling out explanation a, support for explanation b). In this example, *depressed mood* potentially operates at a different time scale compared to *staying in bed*, which can only be assessed once a day, and changing the sampling frequency for this variable would therefore not solve the problem. An alternative could be to collect data on related variables that can vary throughout the day, such as feeling tired.

The fact that clinical and statistical predictions may differ, and, indeed, compete with one another (Meehl, 1954), does not mean that one model is generally preferable over the other. The different assessment strategies discussed in this paper have their unique benefits: The clinical prior models can be established relatively quickly (about 22.7 minutes were needed for a comparable method by Klintwall et al., 2021), because they are based on a combination of readily available information, such as clinical literature, reported patient experiences, and clinical training (Page & Stritzke, 2014). Furthermore, the process of establishing a prior model as collaborative effort between clinician and patient may also stimulate a more active discussion on symptom relations

compared to solely examining statistical output (see also section On the Importance of Collaboration below). As such, clinical models may be preferable in the initial stages of data collection when insufficient EMA data are available, because they provide an intuitive framework to efficiently formalize symptom relations. The statistical models, on the other hand, provide particular benefits in the exploration of symptom relations (Rodebaugh et al., 2020; von Klipstein et al., 2020) that may have been missed (or overestimated) in the prior model. They are therefore valuable especially in later stages when more EMA data are available, allowing new evidence to suggest potential modifications to the clinical model. The PREMISE approach ties together these unique benefits in a systematic way using Bayesian inference. We hypothesize that these models therefore result in more actionable insights for clinical practice compared to either model alone, because they systematically balance clinical judgment with new evidence.

On the Importance of Collaboration

Although there are no gold standards, the case formulation approach to CBT emphasizes the importance of collaboration between clinician(s) and patient (Kuyken et al., 2009; Persons, 2012). Nomothetic theories and treatment guidelines are usually the starting point of a case formulation, but the ultimate goal is to extrapolate an idiographic model by integrating these theories interactively with clinical expertise, observations, and patient experience (Zuidersma et al., 2020). This approach has further benefits, for example in regard to compliance and the therapeutic relationship. Specifically in the context of PREMISE, another benefit to collaboration is the fact that interactive reasoning (*explorative talk*) has been found to improve judgment over individual results (Mercier & Sperber, 2018; Resnick et al., 1993; Wegerif et al., 1999). We therefore suggest that PREMISE should be used as a tool to aid interactive reasoning about symptom relations that should involve both clinician and patient. PREMISE may help to make the process of interactive reasoning explicit by formalizing expertise and experiences into a prior model that can flexibly be integrated with EMA data.

Choosing a Statistical Model for PREMISE

The PREMISE approach is not tied to the specific elicitation method (i.e., estimates on temporal or contemporaneous relationships) or statistical model (i.e., Bayesian VAR) used in this paper. As such, it is important to distinguish the general approach as highlighted in Figure 2 from the current statistical implementation of PREMISE. The key idea of PREMISE as an approach to establishing personalized models survives issues of the specific statistical model because these can be replaced by other implementations, should they offer a more intuitive and valid elicitation of clinical prior information. The VAR model currently takes a prominent role in the literature of personalized networks (Bringmann, 2021), which is why we opted for including it in PREMISE. Other statistical models can be used that are simpler or more sophisticated, which impacts how nuanced and intuitive the implications of the model are.

We see three criteria that are relevant to evaluate the utility of a statistical model for implementation in PREMISE: (a) Can the model describe relevant clinical phenomena? (b) Does the model contain quantities that can intuitively assessed via prior elicitation?,

and (c) Can the model provide actionable insights relevant for psychotherapy? Below we discuss these points in regard to the current implementation and alternative models.

Capturing Relevant Clinical Phenomena

A common criticism of VAR-based networks is that they rely on strong and potentially unfeasible assumptions, such as *stationarity*, i.e., the properties of the time series do not change over time. Generally, it is advisable to specifically examine the collected data in light of the research question and related modeling goals. For example, stationarity can be investigated by visualizing the time series, by performing formal tests such as the Dickey-Fuller test (Dickey & Fuller, 1979), and by employing change point detection algorithms (Aminikhanghahi & Cook, 2017). Although specific deviations from assumptions can be accounted for by transformations (e.g., removing time-related trends; Burger et al., 2022), some research questions explicitly aim at understanding mechanisms related to change, for example modeling the effects of interventions. In such cases, it may be possible to use the VAR model, including the priors discussed in this paper, for data collected within stationary time-periods (e.g., prior to the start of an intervention); however, the VAR model does not allow one to model shifts between disorder states typically following interventions (Henry et al., 2020).

In addition to nonstationarity, the VAR model should not be used to answer research questions that aim at capturing higher-order interactions between variables from different levels (Haslbeck et al., 2019), or dynamics between variables that operate at time scales different to the frequency at which EMA is administered (Haslbeck & Ryan, 2021). More sophisticated modeling approaches may be better at capturing these clinical phenomena (Bringmann, 2021; Haslbeck et al., 2019); such as nonlinear (Schiepek et al., 2016; Schiepek et al., 2017; Scholler et al., 2019), time-varying (Haslbeck et al., 2021), and continuous time series models (Driver et al., 2017; Ryan & Hamaker, 2020; Ryan et al., 2018).

Intuitive Prior Elicitation

Prior elicitation techniques infer probability distributions based on quantities that can intuitively be provided by an expert. As such, prior elicitation can benefit clinical implementation because clinician and patient do not need to specify technical aspects of statistical models themselves. On the other hand, bias can arise when the elicitation technique imposes additional assumptions which do not align with the expert's intuition. This could be the case if the model in question is too technically advanced.

In the current implementation of PREMISE, clinicians specify estimates for temporal or contemporaneous relationship. It is currently unclear if the specifications provided by the clinician indeed align with the assumptions and specifications of the VAR model. For example, at this moment we do not know whether the elicited quantity is understood by the clinician to be a marginal effect or a conditional effect, whether clinicians consider the specified time lag when indicating a relationship, or how to precisely specify distributions for edges that are not indicated by the clinician. Bias may be reduced if less sophisticated–but more intuitive–approaches such as means or marginal correlations between items are used. These could inform case formulation in a more basic yet

potentially very insightful manner. The more sophisticated models discussed in the previous section, on the other hand, would potentially require assessment of quantities that are not very intuitive for the expert, and therefore could be a potential source of bias in establishing prior distributions. Another approach to reducing potential bias in more complex models could be to ask for concrete estimates on the item-level (i.e., symptom scores), rather than estimates on the parameter-level (i.e., edges between symptoms). In the current implementation, we opted for eliciting information on the parameter-level, as this aligns conceptually well with the process of establishing case formulations, where clinician and patient discuss dynamic relationships (i.e., parameters) between the different items.

Actionable Insights for Psychotherapy

All statistical models–no matter their level of sophistication–are "wrong" in that they are incomplete approximations of reality (Meehl, 1990), and one statistical model is not necessarily more useful than another one simply because it features more sophistication in its modeling approach. The utility of a model for clinical inference is also determined by its ability to provide actionable insights (Fried, 2020b) for psychotherapy, which means that simpler, more abstract models could be at least equally meaningful if they qualify as useful thinking tools for clinical practice. Indeed, VAR-based networks have been suggested to serve as a first step toward informing case formulation in an exploratory fashion (von Klipstein et al., 2020). Future research should aim to investigate what model would indeed provide the most useful, intuitive, and actionable insights for case formulations and treatment selection, for instance through focus groups and utility studies.

Clinical Implementation via Sequential Case Designs

One of the core aims of PREMISE is to advance the implementation of personalized networks in clinical practice, by embedding the statistical estimation into the context of case formulations. However, integrating personalized models with clinical reasoning is only one aspect relevant for implementation. Another aspect is that these models should be seamlessly integrated with the therapeutic process, answering questions such as "When should we update our networks with EMA data?" and "What can we learn about the individual's psychopathology?" As these questions are inherently idiographic and answers will differ from patient to patient, they are best addressed using case designs.

In the future, we propose that PREMISE should be implemented using sequential case designs, such as within-person adaptations of the leapfrog design (Blackwell et al., 2019). The leapfrog design compares the efficacy of interventions against the currently most effective treatment (or a waitlist or other control condition, if no treatment has been established yet), by quantifying the evidence of improvement via Bayes Factors. If interventions derived from previously established personalized networks do not lead to substantive improvements (anymore), this could be a sign that the networks should be updated with new EMA data, which in turn may result in a shift in intervention targets and new knowledge on the individual's pathology. In the future, we hope that such implementations will lead to a more systematic dialogue between assessment, statistical modeling, personalized therapy, and the advancement of understanding the individual's psychopathology.

Conclusion

Formally integrating case formulation and personalized networks could potentially help overcoming current problems in personalized models, such as inaccurate estimation of networks and a disconnect with clinical theory, expertise, and practice. If combined with an intuitive tool for prior elicitation, this approach has promise to bring the benefits of personalized models into clinical practice. Future research should aim to investigate which statistical models are best suited for this approach, work toward providing concrete practical recommendations for implementation, and test if resulting networks can indeed improve therapy outcomes as evaluated by clinicians and patients.

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