Determining Timing Effects of Microrandomized Trials Using Intensive Longitudinal Data and
the Differential Time-Varying Effect Model

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October 21, 2020

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Abstract

In the area of behavioral sciences, methods for delivering interventions within the context of daily life are developing rapidly, fueled by the development of microrandomized controlled trials and ecological momentary interventions. While intensive longitudinal data are often collected to evaluate the immediate effects of these interventions, the timing of these interventions on behavior has been given limited attention. The field of behavioral sciences would therefore benefit from an accessible and efficient tool to detect the time in which interventions impact their respective outcomes. In this paper, we propose an extension of the Differential Time-Varying Effect Model (DTVEM) that will detect and estimate the lagged effects of behavioral interventions on outcomes. Our extension of the DTVEM pairs the generalized additive mixed models with linear mixed model to identify optimal time lags of interventions and estimate their effects, respectively. The efficiency of this extended DTVEM was tested using extensive simulations, and the results showed promising power, reliable point estimates, and low type I error. Consequently, this extended DTVEM allows researchers to (1) perform power analyses regarding the timing of intervention effects and (2) detect the timing of interventions using intensive longitudinal data and microrandomized controlled trials.

Keywords: Microrandomized controlled trials, Timing, Ecological momentary interventions, Intensive longitudinal data, Ecological momentary assessments

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1 Introduction

In recent years, researchers have begun delivering interventions in repeated short bursts within the context of daily life. The effects of these interventions are often assessed via intensive longitudinal data, such as ecological momentary assessments. For example, text messages delivered via mobile phones are frequently used to deliver health behavior change interventions (Fjeldsoe, Marshall, & Miller, 2009). Understanding whether and how the frequency of these interventions affects certain targeted behaviors is critical (Thomas & Bond, 2015). Many technologies have been proposed as methods for delivering behavioral interventions, but the timing of these interventions has not yet been addressed (Riley et al., 2011). In the context of this paper, the timing of interventions can be understood as the time lags¹ that interventions display when affecting their outcome. For example, if we define one measurement interval as 1 hour, then the hourly intervention may have effects on outcome after some specific number of hours.

Researchers can use Microrandomized trials (MRTs), one type of experimental design, to understand whether behavioral interventions delivered within the context of daily life have achieved their intended effects—and if so, to what degree of efficacy (Klasnja et al., 2015). The main purpose of MRTs is to (1) randomize each intervention component for each person repeatedly, and then (2) analyze effects of intervention by statistical tools. This research design has the potential to facilitate causal inference within this setting and represents a major milestone in the ability to evaluate novel interventions delivered in real-time. Despite this, however, MRTs focus only on the proximal effects of interventions, i.e., the next one time period effects of interventions (or, equivalently, the lag-1 effects of interventions if the time interval is discrete). This paper proposes one method to detect and estimate the timing of interventions across all later

¹ Time lags here mean the number of backward shifts in the time. For example, a lag-0 intervention refers to the current intervention at time t , a lag-1 intervention refers to the intervention at time $t - 1$, and so on.

potential time points².

The importance of the timing of interventions is strongly supported by theories, particularly those concerning operant conditioning. In particular, operant conditioning often suggests that proximal outcomes may appear to be effective in a short time period, when it is in fact deleterious to these outcomes across larger time periods. Consider, for example, a researcher who is using an ecological momentary intervention to test the efficacy of avoidance as a treatment for fear for persons with an anxiety disorder. Current theory regarding the formation and maintenance of anxiety disorders would suggest both (1) that avoidance as an intervention would have a strong and immediate reduction on fear, and (2) that if the effects of avoidance on fear were investigated as a proximal outcome exactly one time period later, it would likely appear to be a very successful intervention (Robinaugh et al., 2019). However, across a longer time period, avoidance would be expected to increase and maintain higher levels of anxiety by preventing the individual's ability to directly encounter the fear and realize that these external stimuli are not harmful (Robinaugh et al., 2019).

One approach to assessing the timing aspect of interventions is to analyze the lag structure of interventions within MRTs data (or, equivalently, find all significantly time lags of interventions). Although several methods have been developed to estimate the timing of relationships between dynamic variables (e.g., if and when variable X influences variable Y at a later point in time, if there are cyclical patterns in data), these methods have not yet been tested or optimized to estimate treatment effects within intensive longitudinal data (ILD).

When analyzing MRTs with ILD, we can think of an intervention as an exogenous variable³, and then analyze this exogenous variable together with other types of variables. Accordingly, this paper attempts to determine the optimal intervention timing—or, equivalently, the optimal (significant) lags of exogenous variables. Then, based on the lag structure of exogenous variables,

² In this paper, we only consider time points whose time intervals between them are discrete.

³ Exogenous variables are determined outside one model and are not affected by other variables; endogenous variables are dependent on other variables within one model.

we can learn more about the effects of behavioral interventions to optimize their delivery further.

Many statistical models—including the state-space model (SSM), the vector autoregressive moving average model (VARMA), and the dynamical systems model (DSM)—can be used to fit ILD (Boker & Graham, 1998; Durbin & Koopman, 2012; Goldstein, Healy, & Rasbash, 1994; Schafer, 2006). However, these models are most beneficial when users already know the lag structure in their ILD (usually when users have theory to suggest which lags are likely to be significant). If users have no prior knowledge about the related lag structure concerning their ILD, typical suggestions might be to apply standard methods in time series analysis—such as plotting autocorrelation functions, partial autocorrelation functions, cross-correlation functions, and partial cross-correlation functions—to identify the structure of the time series model within their data (Chatfield & Xing, 2019; Politis & McElroy, 2019).

Unfortunately, however, previous studies have shown that these time series analysis methods are ineffective in discerning optimal lags of variables within data sets which include multiple-subject data and missing values (Jacobson, Chow, & Newman, 2019). It is therefore difficult to apply these analysis methods to a real-world context, which usually concerns group-level data with missing values (i.e., multiple-subject data with missing values). It should also be noted that these analysis methods were also developed in an effort to examine the relationships between variables with continuous values, and thus are not well suited to test intervention effects which are inherently discrete in nature (i.e., deliver the intervention or not). Therefore, these methods appear ill-suited to determine the lag structure within ILD which contain MRTs and ecological momentary interventions.

A recent modeling technique and R software package were created to address some of these problems. The novel Differential Time-Varying Effect Model (DTVEM) was created to estimate the optimal lag structure of endogenous variables within ILD (Jacobson et al., 2019). In other words, the DTVEM gives users an estimated vector autoregression–VAR (or autoregression–AR) model to depict the lag structure within multiple-subject data (or single-subject data).

The existing DTVEM is a hybrid model that consists of two stages. In the first stage, the

DTVEM narrows down the space of potentially optimal lag structure by fitting a generalized additive mixed model (GAMM). For achieving this goal, the DTVEM utilizes the R package “mgcv” to produce this estimation (Wood, 2017). This first stage attempts to resolve two primary issues before modeling the second stage. First, there are many potential lag structures related to endogenous variables to be estimated, and a large number of time lags can make confirmatory modeling of these time lags computationally inefficient. Second, interdependencies between different lags will influence the accuracy of final estimation results (Bottan & Truglia, 2011; Buckner, Crosby, Wonderlich, & Schmidt, 2012; Buysse et al., 2007; Carels et al., 2004; Starr & Davila, 2012). In the second stage, the DTVEM applies the SSM using the filtered lag structure—which is obtained from the first stage—in order to further optimize and estimate the lag structure. In this stage, the DTVEM utilizes the R package “OpenMx” to estimate SSM (Chow, Ho, Hamaker, & Dolan, 2010a; Harvey, 1990a; Neale et al., 2016). To detect all potential significant time lags, the DTVEM offers users the option to repeat the first stage and second stage iteratively. That is, users can pass the estimated lag structure from the stage 2 back to stage 1, set these detected significantly lagged terms as fixed effects in GAMM, and repeat running stage 1 and stage 2 until there is no new significant time lag identified.

Empirical tests and simulations results have shown that the existing DTVEM can both (1) detect significant time lags of endogenous variables with high power and low Type I error and (2) estimate the lag structure with high accuracy and reasonable standard errors across univariate and bivariate situations, even for data sets with a high percentage of missing values. This suggests a promising future for the DTVEM—both as a preliminary tool for identifying the lag structure within data and as a confirmatory tool for estimating the lag structure (Jacobson et al., 2019).

Despite these strengths, however, the current version of the DTVEM is designed for dealing with endogenous variables and fails to consider analyses of exogenous variables. Since the intervention itself can be seen as an exogenous variable, we attempt to build on the current DTVEM’s ability to handle exogenous variables in order to detect the timing of interventions within ILD. One potential approach is to use the current DTVEM to analyze the endogenous and

exogenous variables together (i.e., treating exogenous variables as endogenous variables). Before going any further, we must reemphasize that this method does not distinguish between endogenous variables and exogenous variables.

If we overlook the inability to distinguish between endogenous and exogenous variables, this approach is practical to some extent. The GAMM in the first stage of the DTVEM can handle exogenous variables by entering them as dummy-coded varying coefficient terms. In the second stage of the DTVEM, however, users need to modify the existing SSM so that it includes exogenous variables. Recall that the existing DTVEM gives users an estimated VAR or AR model after iterations of stage 1 and stage 2. In other words, the second stage of the DTVEM represents the VAR or AR model using the frame of SSM⁴ and then estimates parameters by optimizing the so-called “prediction error decomposition” (Chow, Ho, Hamaker, & Dolan, 2010b; Harvey, 1990b). The point to be made is that when exogenous variables are taken into account, we should adjust the second stage of the DTVEM to derive a state-space representation of vector autoregressive model with exogenous inputs (VARX) or autoregressive model with exogenous inputs (ARX) model.

As we will see later in this paper, the power⁵ of discerning the lagged exogenous variables (i.e., equivalent to exogenous inputs) using the existing DTVEM directly with simulated data⁶ is quite decent. But the coverage rate⁷ of coefficients corresponding to lagged exogenous variables becomes severely low. It seems reasonable to attribute this reduction in coverage rate—herein

⁴ There are different approaches to achieve this goal by using equivalent matrices within SSM (Lütkepohl, 2005; Shumway & Stoffer, 2017).

⁵ The power is defined as the proportion of parameter estimates for truly nonzero population parameters from the DTVEM across large number times of Monte Carlo runs whose 95% confidence intervals do not contain zero (Jacobson et al., 2019).

⁶ Generate data using VARX model to simulate the ILD with exogenous variables, details about this procedure will be given in the next section.

⁷ The coverage rate is defined as the proportion of 95% confidence intervals whose values include the simulated parameters across large number times of Monte Carlo runs (Jacobson et al., 2019).

referred to as the “underestimated phenomenon”—to a conceptually flawed SSM. Nevertheless, a conceptually flawed SSM is not the only explanation behind this low coverage rate, and this paper will show that the frame of SSM in stage 2 of the current DTVEM does not meaningfully influence the estimation of lag structure within ILD. In other words, the current SSM method is imperfect to handle exogenous variables since low coverage rates exist no matter which frame of SSM is used to perform estimations (i.e., using conceptually flawed or correct SSM). Therefore, this paper proposes an extension to the current DTVEM to solve the underestimated phenomenon that arises when exogenous variables are present.

The remainder of this article is organized as follows: Section 2 presents the method of the current DTVEM and describes what our proposed extension entails regarding the distinction between endogenous and exogenous variables. Section 3 analyzes extensive simulations to verify the utility of this DTVEM extension in discerning and estimating the coefficients of exogenous variables. Finally, Section 4 summarizes the conclusions of the paper and discusses future implications regarding the DTVEM and proposed extension.

2 Methods behind the DTVEM with exogenous variables

As mentioned earlier, the existing DTVEM is a hybrid model that combines the GAMM and SSM to find the optimal lag structure of endogenous variables within ILD. We will show the current DTVEM’s performance on estimating coefficients of lagged exogenous variables is poor, but neither the DTVEM’s first stage, which uses the GAMM, nor the DTVEM’s second stage, which uses the SSM, need to be amended or reconstructed in order to fix this problem. Instead, a better approach (described in detail later in this section) will be to add a third stage to solve the underestimated phenomenon mentioned earlier.

2.1 The DTVEM’s First Stage

The first stage of the DTVEM takes advantage of the GAMM to narrow down the space of potentially optimal lag structure and vividly presents how the coefficients of lagged variables

change with time. We present the GAMM using the same notation as the prior paper about the DTVEM (Jacobson et al., 2019).

$$\eta_i = \mathbf{X}_i \boldsymbol{\beta} + \sum_{k=1}^K f_{1,k}(x_{1,k,i}) + \sum_{o=1}^O \sum_{c=1}^C f_{2,c,o}(x_{2,o,i}) x_{2',c,i} + \sum_{q=1}^Q \sum_{s=1}^S f_{3,s,q}(x_{3,q,i}, x_{3',s,i}) + \mathbf{Z}_i \mathbf{b}_i \quad (1)$$

In Equation 1, i indexes the i th subject in the ILD and takes value from 1 to n ; n is the total number of subjects; and η_i is the outcome of the i th subject. On the right-hand side of Equation 1, the first term represents the fixed-effects component and the last term represents the random-effects component. The second, third, fourth terms are different types of nonparametric components (i.e., unknown functional forms). More specifically, $\mathbf{X}_i$ is a $1 \times n_\beta$ design vector that includes the person i 's fixed-effects component; $\boldsymbol{\beta}$ is the corresponding $n_\beta \times 1$ vector of fixed effects parameters; and $\mathbf{Z}_i$ is the $1 \times b$ random-effects design vector for the subject i . The $\mathbf{b}_i \sim N(0, \boldsymbol{\Sigma}_b)$ is a $b \times 1$ vector of random effects, assumed to obey a multivariate normal distribution with zero mean and positive-definite covariance matrix $\boldsymbol{\Sigma}_b$. The terms $x_{2,o,i}$, $x_{2',c,i}$, $x_{3,q,i}$ and $x_{3',s,i}$ refer to different covariates corresponding to person i . The terms $f_{1,k}(\cdot)$, $f_{2,c,o}(\cdot)$, and $f_{3,s,q}(\cdot)$ ⁸ represent nonparametric functions involving the covariates in different ways⁹. Moreover, the covariates that appear in each smooth function may be different, so we use different indices (i.e., 1,2,3) and different subscripts (i.e., k, c, o, s, q) to distinguish the covariates that appear in the three sets of smooth functions.

With the exception of the fixed and random effects of subjects, the DTVEM only considers two nonparametric functions: (1) $f_{1,k}(\cdot)$ which is used to remove the trend within data, and (2)

⁸ GAMM provides an approach to approximate these functions and resultant curves using different smoothers.

$f_{1,k}(\cdot) - f_{3,s,q}(\cdot)$ are typically referred to as smooth functions, and the curves or lines generated by these functions are denoted as smooths (Hastie & Tibshirani, 1990; McKeown & Sneddon, 2014). Note that because the number of basis functions applied with each covariate can generally be different, the nonparametric part can not be presented in matrix form because the dimensions of the basis coefficient vectors and basis function vectors are generally different among covariates.

⁹ $f_{1,k}(\cdot)$ approximates the unknown association (linear or nonlinear) between variable $x_{1,k,i}$ on outcome η_i across all subjects in the sample; $f_{2,c,o}(\cdot)$ allows the variable $x_{2,o,i}$ to interact with $x_{2',c,i}$; $f_{3,s,q}(\cdot)$ is a tensor product to depict the unknown but possibly jointly nonlinear effects of a pair of covariates on outcome.

$f_{2,c,o}(\cdot)$ which depicts the relationship between lagged effects and outcome as a smooth function of time differences. Therefore, the GAMM used in the first stage of the DTVEM can be simplified from the comprehensive Equation 1 to the following Equation 2¹⁰.

$$\eta_i = \mathbf{X}_i\boldsymbol{\beta} + f_{1,k}(x_{1,k,i}) + \sum_{c=1}^C f_{2,c,o}(x_{2,o,i})x_{2',c,i} \quad (2)$$

In Equation 2, the term $x_{2',c,i}$ represents different lagged effects generated by exogenous or endogenous variables; the $f_{2,c,o}(\cdot)$ is a smooth function for the covariate $x_{2,o,i}$ (i.e., time difference) to interact with covariates $x_{2',c,i}$, and the C is the total number of lagged effects which we want to consider; $f_{1,k}(\cdot)$ is a nonparametric function which depicts the association between variable $x_{1,k,i}$ (i.e., time points of observations) on outcome to remove the time trend. Therefore, we can also present the association between lagged exogenous effects and outcome using the nonparametric function $f_{2,c,o}(\cdot)$. When the ILD contains both endogenous and exogenous variables, users can only set endogenous variables as outcomes (i.e., making all endogenous variables be variables with time-varying coefficients and outcomes in the GAMM).

Suppose we have an ILD that possesses two variables: one endogenous (outcome) variable X and one exogenous variable U (such as one kind of behavioral intervention). Based on Equation 2, the GAMM of one specific subject i in the first time stage 1 of the DTVEM can be written as Equation 3, shown below.

$$X_{t,i} = f(t) + f_1(\Delta t)XonX_i + f_2(\Delta t)UonX_i \quad (3)$$

In Equation 3, i indexes the i th subject, and $f(t)$ is a smooth function of variable t (i.e., time points of observations), used to remove the time trend within the data; $X_{t,i}$ represents the current outcome of subject i ; Δt is the discrete time difference between lagged time point and current time. The $XonX_i$ and $UonX_i$ represent lagged effects of X and U on outcome, respectively.¹¹ The $f_1(\Delta t)$ means the time-varying coefficient of the $XonX_i$. Similarly, the $f_2(\Delta t)$ represents

¹⁰ We omit the subject-specific differences within ILD. Modeling the subject-specific differences can be the future extension of the DTVEM.

¹¹ If there are one exogenous variable U and two endogenous variables (outcomes) X and Y , then two equations are

the time-varying coefficient of the $UonX_i$. It is assumed that the interested lag order (i.e., maximum value of Δt) is less than the maximum time difference of observed time points¹². Note that the detected significant lagged variables will be added into Equation 3 as a fixed-effects component $X_i\beta$ after finishing the first iteration of the DTVEM.

To better illustrate this procedure, let us perform stage 1 of the DTVEM using simulated data. In this example, we still assume there are one endogenous variable X , and one exogenous variable U which obeys a Bernoulli distribution with probability $p = 0.5$. The simulation data was generated using a “dse” package based on the VARX model in R (Gilbert, 2009). We first set the X_{t-1} and the U_{t-7} to have significant effects on outcome (i.e., the endogenous variable X and exogenous variable U have significant effects on outcome at lag-1 and lag-7 time, respectively). In other words, we anticipate that the DTVEM can detect significantly non-zero coefficients of $XonX$ and $UonX$ at lag-1 and lag-7 time (i.e., $f_1(\Delta t = 1)$ and $f_2(\Delta t = 7)$ are not equal to 0). Next, we generate data that simulates ILD per a AR model, shown below.

$$X_{t,i} = \beta_1 X_{t-1,i} + \beta_2 U_{t-7,i} + \epsilon_i \quad (4)$$

In Equation 4, ϵ_i is the noise term for subject i , assumed to obey a standard normal distribution. The constants β_1 and β_2 can be used to measure the extent to which these two lagged terms (i.e., X_{t-1}, U_{t-7}) impact outcome of subject i . In this simulation, we will assume that $\beta_1 = 0.5$ and $\beta_2 = 0.8$ across all subjects. After using Equation 4 to generate 28 time points (i.e., corresponding to 1 month of data in a daily diary study) 100 times, we can simulate one ILD that possesses 100 subjects (each of which has 28 time points). Setting the maximum value of Δt as 10 which implies there are total 20 parameters—coefficients of lagged effects $XonX$ and $UonX$ at $\Delta t = 1, \dots, 10$ —should be estimated (i.e., equivalent to coefficients of lagged terms $X_{t-\Delta t}$ and

needed to depict the relationship among these three variables in the first time stage 1 of the DTVEM: (1) $X_i = f(t) + f_1(\Delta t)XonX_i + f_2(\Delta t)YonX_i + f_3(\Delta t)UonX_i$; (2) $Y_i = f(t) + f_1(\Delta t)XonY_i + f_2(\Delta t)YonY_i + f_3(\Delta t)UonY_i$.

Other multiple variable situations are similar.

¹² Users can set the value of Δt in the “DTVEM” R package.

$U_{t-\Delta t})^{13}$. Performing the first stage of the DTVEM with this data set yields the results shown in Figure 1.

Figure 1. These two figures depict results of applying the first stage of the DTVEM on simulated data possessing one endogenous variable and one exogenous variable. Solid lines show β_1 and β_2 changing with time, whereas dashed lines represent the confidence bands of β_1 and β_2

From Figure 1, we see that neither the confidence bands of β_1 at time difference 1, 2, and 3 nor the confidence bands of β_2 at times 6, 7, and 8 contain 0. This implies that lag-1, 2, and 3 are the significant lags of endogenous variable X and that lag-6, 7, and 8 are the significant lags of exogenous variable U . In other words, the lagged endogenous terms X_{t-1} , X_{t-2} and X_{t-3} and lagged exogenous terms U_{t-6} , U_{t-7} and U_{t-8} have meaningful effects on outcome. These results from the stage 1 show that the GAMM can discern time lags that are truly significant. It should be acknowledged that this first stage also (incorrectly) discerns some false time lags, but this lag structure will be refined in the stage 2 of the DTVEM. Note that the intent of deploying the first stage of the DTVEM is to identify significant lags in order to narrow down the search space, and the first stage is quite successful in this regard (i.e., allowing us to estimate a total of 6 potential parameters rather than a total of 20 parameters within a confirmatory framework). This suggests that it is reasonable to use the first stage of the DTVEM to handle exogenous variables directly. However, when we pass the preliminary significant lags from the stage 1 to stage 2, additional methodological issues arise.

¹³ Recall that we only consider discrete time differences in this context.

2.2 The DTVEM's Second Stage

In the stage 2 of the DTVEM, the SSM is utilized to refine the lag structure obtained from the stage 1 further. Continuing the illustration in the last section, we present the SSM using the notation in “OpenMx” R package as Equation 5 (Neale et al., 2016).

$$\begin{aligned} \mathbf{x}_t &= \mathbf{A}\mathbf{x}_{t-1} + \mathbf{B}\mathbf{u}_t + \mathbf{q}_t \\ \mathbf{y}_t &= \mathbf{C}\mathbf{x}_t + \mathbf{D}\mathbf{u}_t + \mathbf{r}_t \end{aligned} \quad (5)$$

The top equation in Equation 5 is called the State Equation, and the below equation is called the Observation Equation. $\mathbf{y}_t$ is a $k \times 1$ vector of outcome (endogenous) variables; $\mathbf{x}_t$ is an $n \times 1$ state vector; $\mathbf{u}_t$ is an $m \times 1$ vector of observable inputs (i.e., observable exogenous variables in this paper); $\mathbf{r}_t$ and $\mathbf{q}_t$ are independent $k \times 1$ and $n \times 1$ noise vector, assumed to obey normal distribution with mean zero and covariance matrices $\mathbf{Q}$ and $\mathbf{R}$, respectively; $\mathbf{A}_{n \times n}$ is sometimes called transition matrix; $\mathbf{B}_{n \times m}$ is sometimes called input matrix of state equation; $\mathbf{C}_{k \times n}$ is sometimes called measurement matrix; and $\mathbf{D}_{k \times m}$ is sometimes called input matrix of observation equation (Lütkepohl, 2005).

When the SSM of the current DTVEM is applied on estimating the lag structure of endogenous variables within ILD, the $\mathbf{B}$ and $\mathbf{D}$ matrices are set as zero matrices since the current DTVEM assumes that there is no exogenous input. In the previous section, we saw that the significant lags of endogenous variable X on outcome corresponded to lag-1, 2, and 3, and that the significant lags of exogenous variable U on outcome corresponded to lag-6, 7, and 8. If the SSM within the current DTVEM is used to present this lag structure, a VAR model is represented in the following matrix form, displayed in Equations 6 and 7.

Equations 6 and 7 refer to the state equation and the observation equation, respectively. $\beta_{1,1}, \beta_{1,2}$ and $\beta_{1,3}$ in $\mathbf{A}$ matrix represent the unknown coefficients corresponding to $XonX$ (i.e., equivalent to coefficients of lagged terms X_{t-1}, X_{t-2} and X_{t-3}); $\beta_{2,6}, \beta_{2,7}$ and $\beta_{2,8}$ in $\mathbf{A}$ matrix represent the unknown coefficients corresponding to $UonX$ (i.e., equivalent to coefficients of lagged terms U_{t-6}, U_{t-7} and U_{t-8}). It is clear that the $\mathbf{B}$ and $\mathbf{D}$ matrices are zero matrices in the setting of Equations 6 and 7. Additionally, lagged exogenous terms (i.e., $U_{t-1}, \dots, U_{t-9}$, derived

$$\begin{pmatrix} X_t \\ X_{t-1} \\ \vdots \\ X_{t-9} \\ U_t \\ U_{t-1} \\ \vdots \\ U_{t-9} \end{pmatrix}_{20 \times 1} = \begin{pmatrix} \beta_{1,1} & \beta_{1,2} & \beta_{1,3} & 0 & \cdots & \beta_{2,6} & \beta_{2,7} & \beta_{2,8} & \cdots & 0 \\ 1 & 0 & 0 & 0 & \cdots & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & \cdots & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & \cdots & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & \cdots & 0 & 0 & 0 & 0 & 0 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ 0 & 0 & 0 & 0 & \cdots & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & \cdots & 0 & 0 & 0 & 1 & 0 \end{pmatrix}_{A, 20 \times 20} \begin{pmatrix} X_{t-1} \\ X_{t-2} \\ \vdots \\ X_{t-10} \\ U_{t-1} \\ U_{t-2} \\ \vdots \\ U_{t-10} \end{pmatrix}_{20 \times 1} + \mathbf{q}_t \quad (6)$$

$$\begin{pmatrix} X_t \\ U_t \end{pmatrix} = \begin{pmatrix} 1_{1,1} & 0 \\ 0 & 0 \\ \vdots & \vdots \\ 0 & 0 \\ 0 & 1_{11,2} \\ 0 & 0 \\ \vdots & \vdots \\ 0 & 0 \end{pmatrix}_{C, 2 \times 20}^T \begin{pmatrix} X_t \\ X_{t-1} \\ \vdots \\ X_{t-9} \\ U_t \\ U_{t-1} \\ \vdots \\ U_{t-9} \end{pmatrix}_{20 \times 1} + \mathbf{r}_t \quad (7)$$

from the exogenous variable U) are integrated with lagged endogenous terms (i.e., $X_t, \dots, X_{t-9}$, derived from the endogenous variable X) together into the state vector $\mathbf{x}_t$. If Equation 6 is plugged into Equation 7, a VAR model will be obtained. In other words, the second stage of the DTVEM will estimate this VAR model to refine the lag structure within data (i.e., discarding some insignificant coefficients) and give a final estimation of left coefficients.

While it may appear that we can analyze exogenous variables in this way, this approach is conceptually flawed, because we need to present the lag structure with exogenous variables using a VARX model (i.e., putting all lagged exogenous terms $U_{t-1}, \dots, U_{t-9}$ into the vector $\mathbf{u}_t$ in Equation 5). One prior study showed that any VARX model can be represented by a general SSM frame (Lütkepohl, 2005). For example, if $\mathbf{x}_t$ is a $k \times 1$ vector of autoregressive variables (endogenous variables) and $\mathbf{u}_t$ is a $m \times 1$ vector of exogenous inputs (exogenous variables), then the VARX model will have the form listed in Equation 8.

$$\mathbf{x}_t = \Phi_1 \mathbf{x}_{t-1} + \cdots + \Phi_p \mathbf{x}_{t-p} + \Theta_0 \mathbf{u}_t + \cdots + \Theta_s \mathbf{u}_{t-s} + \epsilon_t \quad (8)$$

In Equation 8, the $\Phi_i, i = 1, \dots, p$ represent the $k \times k$ coefficient matrices for $\mathbf{x}_{t-i}$; the Θ_j ,

$j = 0, \dots, s$ represent the $k \times m$ coefficient matrices for u_{t-j} , and the ϵ_t represents one $k \times 1$ vector of noise. The corresponding SSM representation is given in Equations 9 and 10:

$$z_t = \begin{pmatrix} x_t \\ x_{t-1} \\ \vdots \\ x_{t-p+1} \\ u_t \\ u_{t-1} \\ \vdots \\ u_{t-s+1} \end{pmatrix}_{(kp+ms) \times 1} = \begin{pmatrix} \Phi_1 & \dots & \Phi_{p-1} & \Phi_p & \Theta_1 & \dots & \Theta_{s-1} & \Theta_s \\ I_k & \dots & 0 & 0 & 0 & \dots & 0 & 0 \\ \vdots & \ddots & \vdots & \vdots & \vdots & \ddots & \vdots & \vdots \\ 0 & \dots & I_k & 0 & 0 & \dots & 0 & 0 \\ 0 & \dots & \dots & 0 & 0 & \dots & 0 & 0 \\ 0 & \dots & \dots & 0 & I_m & \dots & 0 & 0 \\ 0 & \dots & \dots & 0 & \vdots & \ddots & \vdots & \vdots \\ 0 & \dots & \dots & 0 & 0 & \dots & I_m & 0 \end{pmatrix} z_{t-1} + \begin{pmatrix} \Theta_0 \\ 0 \\ \vdots \\ 0 \\ I_m \\ 0 \\ \vdots \\ 0 \end{pmatrix} u_t + \begin{pmatrix} \epsilon_t \\ 0 \\ \vdots \\ 0 \\ 0 \\ 0 \\ \vdots \\ 0 \end{pmatrix} \quad (9)$$

$$x_t = (I_k, 0, 0, \dots, 0)_{k \times (kp+ms)} z_t \quad (10)$$

In this case, Equation 9 is the state equation and Equation 10 is the observation equation. Equations 9 and 10 present a different frame of SSM compared with those in the existing DTVEM, since the u_t vector in Equation 5 has been redefined to contain lagged exogenous variables and the B matrix is not a zero matrix. Similarly, if Equation 9 is plugged into Equation 10, a VARX model will be obtained. Therefore, the second stage of DTVEM can estimate the lag structure within data as a VARX model by applying Equations 9 and 10 (conceptually correct SSM frame).

It should be acknowledged that the result of 500 Monte Carlo (MC) simulations—using simulated data based on Equation 4—show that these two frames (the current SSM frame in the existing DTVEM and the adjusted SSM frame described above) give nearly the same results. In evaluating results of these two approaches, the following metrics will be used: (1) the mean estimated values across simulations (i.e., mean $\hat{\beta}$); (2) the root mean square error (RMSE); (3) the mean bias of each estimated value; (4) the mean standard error across 500 MC runs (i.e., SD of $\hat{\beta}$); (5) the mean relative deviance of SE (RDSE), which is defined as $\frac{\text{Mean SE-SD of } \hat{\beta} \text{ across MC runs}}{\text{SD of } \hat{\beta} \text{ across MC runs}}$; (6) the coverage rate, which is defined as the proportion of 95% confidence intervals whose values include the simulated true β across MC runs; and (7) power, which is defined as the proportion of 95% confidence intervals for truly non-zero parameters whose values do not include zero (Jacobson et al., 2019).

Table 1 presents two MC simulation results of the DTVEM based on two different SSM frames. These two results are nearly identical and show very high power in detecting the lag

Table 1

Estimation results of using different SSM frames to perform the second stage of the DTVEM. Rows with the name “Existing SSM” refer to the results of using the existing DTVEM’s SSM; rows with the name “Adjusted SSM” refer to the results of using a conceptually correct SSM. The terms β_1 and β_2 represent the coefficients of X_{t-1} and U_{t-7} in Equation 4, respectively.

	Term	Simulated β	Mean $\hat{\beta}$	RMSE	Bias	SD of $\hat{\beta}$	Mean of SE	RDSE	Coverage rate	Power
Existing SSM	β_1	0.5	0.497	0.017	-0.003	0.017	0.016	-0.054	0.924	1
Existing SSM	β_2	0.8	0.692	0.113	-0.108	0.034	0.035	0.041	0.138	1
Adjusted SSM	β_1	0.5	0.497	0.016	-0.003	0.016	0.016	0.012	0.948	1
Adjusted SSM	β_2	0.8	0.69	0.116	-0.11	0.036	0.036	-0.018	0.146	1

structure of endogenous and exogenous variables (i.e., detecting the non-zero coefficients of X_{t-1} and U_{t-7} with power 1). Additionally, for both SSM frames, the coverage rates of β_2 are much lower than the power metrics and the mean of estimated values is lower than the true simulated value of 0.8. These results illustrate the strengths of both SSM frames (the great power to discern the lag structure of endogenous and exogenous variables) and the weaknesses of both SSM frames (the tendency to underestimate the coefficients of exogenous variables, yielding a low coverage rate)¹⁴. Therefore, we cannot conclude that using the adjusted SSM improves the overall performance of the DTVEM.

This underestimated phenomenon occurs in using both existing DTVEM’s SSM and adjusted SSM frames as the model of the second stage, engendering the need for another approach to fix this methodological flaw of applying the SSM. We will now propose a one-stage extension to the current DTVEM in order to correctly estimate the lag structure of exogenous and endogenous variables.

¹⁴ This underestimation problem prevails in our other simulation processes. We just present one example here.

2.3 Additional stage of the DTVEM

This additional stage should still be able to handle both group-level data and data with potential missing values. If the data is related to just one subject, we can use the least squares technique, one standard method in time series analysis, to estimate the single dimension time series data. But if the dataset is group-level such as ILD, this least squares method will not be suitable. In this situation, the linear mixed-effects model (LMM) can be used to estimate the lag structure. Moreover, the LMM can be presented as a linear model containing fixed effects (such as common parameters in the entire data across different individuals) and random effects (such as parameters which are correlated with each individual unit). This model is mainly used to analyze the relationship between an outcome variable and covariates in data that are grouped according to one or more classification factors (Pinheiro & Bates, 2000).

As mentioned earlier, the additional stage should also have the ability to deal with missing values, with the goal of preserving the distributional characteristics and functionalities of the variables of interest. Failing to adequately deal with missing values will result in incorrect statistical conclusions (Black, Harel, & Matthews, 2012). A common method of dealing with missing values is to simply remove them from the data set. However, this may ruin the structure of time series, and so we need a different method to deal with missing values. Here, we propose using the Multivariate Imputation by Chained Equations (MICE) to impute incomplete multivariate data (Buuren & Groothuis-Oudshoorn, 2010). When using MICE to perform this procedure, we should distinguish between level-1 variables and level-2 variables. If we ignore the hierarchical group structure in multilevel data and simply use a single level imputation method, standard errors will be underestimated, leading to confidence intervals that are too short (Van Buuren, 2018). The part of random effects in LMM (which is grouped by classification factors) can be seen as level-2 variables, necessitating the imputation of missing values on a different level. Note that imputation based on a different level is only needed when analyzing group-level data, not individual data. Combining the above LMM and MICE methods will allow us to build on this additional stage.

Applying the existing results from the DTVEM to refine this additional stage is also helpful. Recall that the existing DTVEM already has great power to discern the lag structure of both endogenous and exogenous variables. Using the advantage of this detected structure, we can specify the LMM in the additional stage of the DTVEM more compactly. Continuing the simulation example in Section 2.1, the existing DTVEM finally determined that the significant lag of the endogenous variable X is lag-1 and that the significant lag of the exogenous variable U is lag-7. Then, we can use one linear form expression to describe the fixed and random effects (Bates, Mächler, Bolker, & Walker, 2014). Take an informal but easily readable expression of LMM in R, for example:

$$\text{Outcome } X_t \sim \beta_1 X_{t-1} + \beta_2 U_{t-7} + (1 + X_{t-1} + U_{t-7} | \text{ID}) \quad (11)$$

On the right-hand side of Equation 11, the first two terms represent the fixed effects (the effects of X_{t-1} and U_{t-7} on current outcome X_t), and the terms in the brackets represent the random effects of the LMM. The constant 1 represents the intercept varying among X_{t-1} and U_{t-7} . The ID represents different subjects within the data and also serves as a grouping factor. We can use the “lmer” function in R to fit this specified LMM, and subsequently get estimations of β_1 and β_2 . If there are missing values in the data, our main idea is to: (1) use the MICE to impute missing values and get several (M) imputed data sets; (2) fit LMM based on these M datasets; (3) and then pool all of these estimations to get the final estimation (Grund, Lüdtke, & Robitzsch, 2018).

To show the power of this additional stage, we will build on the same simulation described before, adding this additional stage of the DTVEM to estimate the lag structure of exogenous and endogenous variables. We still apply two different SSM frames (the existing SSM and the adjusted SSM) to our extended DTVEM. After conducting 500 MC simulations, we obtained the results in Table 2. Both coverage rates of β_2 increase, and both mean $\hat{\beta}_2$ s are very close to the true simulated value of 0.8. This suggests that the additional stage possesses the potential to solve the problem of underestimation and consequently improve the coverage rate.

So far, we have used one simulation to show that while the existing DTVEM possesses great power to discern exogenous and endogenous variables, it underestimates the coefficients of

Table 2

Estimation results of combining the DTVEM with the additional stage. Rows with the name “Existing SSM” display the results of using the existing SSM frame in the DTVEM; rows with the name “Adjusted SSM” display the results of using conceptually correct SSM frame. The terms β_1 and β_2 represent the coefficients of X_{t-1} and U_{t-7} in Equation 4, respectively.

	Term	Simulated β	Mean $\hat{\beta}$	RMSE	Bias	SD of $\hat{\beta}$	Mean of SE	RDSE	Coverage rate	Power
Existing SSM	β_1	0.5	0.494	0.02	-0.006	0.018	0.017	-0.105	0.918	1
Existing SSM	β_2	0.8	0.806	0.037	0.006	0.036	0.035	-0.036	0.946	1
Adjusted SSM	β_1	0.5	0.494	0.019	-0.006	0.018	0.017	-0.064	0.944	1
Adjusted SSM	β_2	0.8	0.803	0.039	0.003	0.039	0.035	-0.094	0.926	1

lagged exogenous variables to some extent. By adding one more stage to the existing DTVEM, this underestimated phenomenon is eliminated.

But before going any further, there are three limitations of applying the additional stage that should be acknowledged. First, we did not assign missing values to data in the simulation setting before; additional simulation tests should therefore be conducted to check whether this additional stage will correctly estimate coefficients of lagged variables, even for data with missing values. Second, in the simulation example above, we only considered the significant lag of exogenous variable to be lag-7; the coefficient of this lag is 0.8. Therefore, we should also test the performance of the additional DTVEM stage using different settings of significant lags. Third, we need to check the performance of this method using varying sizes of ILD. Comprehensive simulations will be performed to check the efficiency of this method in the next section

3 Comprehensive simulation

In this section, based on the idea of MRTs, we will design one comprehensive simulation in order to verify the efficacy of our extended DTVEM in detecting and estimating optimal time lags of endogenous and exogenous variables. For clarity and simplicity, we will only consider one endogenous variable X and one exogenous variable U in this simulation (simulations with

multiple variables situation can be performed similarly). And there is a 50% chance that this exogenous variable (intervention) will occur at specific time lags.

3.1 Simulation setting

In formulating this comprehensive simulation, we created different VARX models to generate simulated data and assigned a different percentage of random missing values to outcomes in each data set. Recall that the primary goal of this article is to discern and estimate the optimal time lags of exogenous variables; the efficiency of DTVEM at detecting and estimating the lag structure of endogenous variables has already been proven (Jacobson et al., 2019). We can fix the endogenous variable to have significant effects on outcome at lag-1; and change the significant lag order of the exogenous variable. We chose to fix the endogenous variable to have a significant autoregressive effect at lag-1 because we assume that the data of X_{t-1} usually harness the greatest influence on outcome among all past data. This assumption is reasonable, since the correlation between past data and current data usually decreases as the lagged time order increases, underscoring the greater importance of lag-1 time data. Testing the efficiency of the DTVEM with different reasonable magnitudes of exogenous variables is also greatly needed. In generating variables with different magnitude, we can fix the coefficient of the X_{t-1} term to be 0.5 and take the values generated from distribution $N(0, 1)$ as the noise term in the VARX model. If we assume that the exogenous variable is binary, then we can control the magnitude of this exogenous variable by changing the coefficient of its term. In other words, the coefficient of this exogenous variable under this simulation setting can be seen as a Cohen's d value, which is one appropriate effect size measure. Concerning the coefficient of the lagged exogenous variable, we used three values, 0.2, 0.5, and 0.8, which correspond to small, medium, and large lagged effects, respectively.

In summary, we set (1) the Cohen's d values of the exogenous variable U to either 0.2, 0.5, or 0.8; (2) the choices of significant lag of the exogenous variable to either lag-1 or lag-7; and (3) the percentage of missing values in outcome data to either 20% or 50%. From this, we created 12

different settings to build different VARX models and generated data. In testing the performance of DTVEM with different sizes of data, we generated data with either 1, 10, 50, or 100 subjects. Each subject can possess either 14, 28, 50 or 300 time points. Note that when the number of subjects is 1, the data set is no longer group-level—but even so, the results will show that the extended DTVEM still gives great estimation results as long as the time points are sufficiently large. In total, we generated 16 different sizes of ILD for each of the 12 settings. Within each ILD for each of the 12 settings, we conducted 500 MC simulations to verify the performance of the extended DTVEM; in total, 96,000 simulations were performed. These results are summarized below.

3.2 Summary of simulation results

The extended DTVEM has great power to detect both lagged endogenous and exogenous variables. The underestimation phenomenon of estimating coefficients of lagged exogenous variables, derived from the second stage of the DTVEM, is solved.

From the bottom-left and bottom-right of Figures 2 and 3, we can see that the power of discerning the lagged endogenous variable under different simulated settings is perfect. From the bottom-left and bottom-right of Figures B1 and B2 in Appendix B, we can see that the coverage rates of the simulated term X_{t-1} 's coefficient have nearly identical color patterns with the power of discerning this term. In other words, the extended DTVEM can still detect and estimate coefficients of lagged endogenous variables very well in the context of exogenous variables presenting. Combine this result with conclusions from a previous paper about the DTVEM (Jacobson et al., 2019), two things become clear. First, the performance of the extended DTVEM in dealing with endogenous variables is unaffected by the existence of exogenous variables. Second, the extended DTVEM always shows high level of estimating accuracy on handling endogenous variables, even with an extremely high percentage of missing values.

Additionally, from the upper-right and upper-left corners of Figures 2 and 3, we see that the power of discerning the lagged exogenous variable increases as the Cohen's d value of this

variable becomes larger. If the Cohen's d value of this lagged exogenous variable is larger than 0.5, the power of discerning that variable is decent even with outcome data possessing 50 % missingness. If the Cohen's d value of this variable is 0.2, the power of discerning that is weak when the ILD size is small, but becomes acceptable if the ILD size is sufficiently large. Under the same ILD size and Cohen's d value for a particular lagged exogenous variable, a higher percentage of missingness corresponds to a lower power of discerning variables. Despite the fact that high percentages of missingness dampen the power of the extended DTVEM, if we increase the size of ILD to be large enough, this problem is eliminated. Another interesting conclusion is that the power of discerning U_{t-7} is slightly weaker than the power of discerning U_{t-1} . This means that it is more difficult for DTVEM to detect the high lag order of exogenous variables—but again, when we have enough large ILD, this negative effect caused by high lag order becomes negligible.

In analyzing the performance of estimating coefficients of lagged exogenous variables, we consider the upper-right and upper-left of Figures B1 and B2 in Appendix B. Here we see that the coverage rates of the simulated terms U_{t-1} and U_{t-7} 's coefficients have nearly identical color patterns with the corresponding color patterns of the power. This means that the extended DTVEM does not underestimate the coefficients of lagged exogenous variables, since the coverage rate of estimating one exogenous variable's coefficient is almost same with the power of detecting this term. This reinforces a high level of efficacy for the extended DTVEM. The types of variables in the data set are irrelevant; as long as the dataset is sufficiently large, the extend DTVEM will have great power to detect these variables and will return sound estimations of their coefficients.

Furthermore, the successful performance of the extended DTVEM in analyzing the simulated data suggests that this method can also be applied to real-world data. The most important application of this method is to detect the existence of optimal time lags of exogenous variables (interventions), and then estimate corresponding effects. For example, if users want to analyze the influence of one treatment on outcomes, taking the treatment as one exogenous binary

variable—and then running the extended DTVEM with data containing outcomes and treatment—can give useful inferences. If this treatment (exogenous variable) truly does have significant effects on outcomes, then the extended DTVEM can detect the optimal timing of this treatment. Additionally, the extended DTVEM can detect the presence of the autoregressive phenomena in outcomes data (i.e., whether outcomes depend linearly on their own previous values). One VARX model is fitted to depict the relationship among outcomes and this treatment. On the other hand, if the DTVEM returns results that do not suggest any significant lag of this treatment (even with a large data set), then we can safely conclude this treatment does not have significant effects on outcomes—or, equivalently, that this treatment does not result in a significant change on the behavioral outcomes. To do this, we wrote a function named “TreatmentLAG”. Users can apply this function to check the existence of optimal lags of exogenous variables. Additionally, example R code is given in the Appendix A.

Figure 2. The above four pictures display the results of simulations in which the significant lag of exogenous variable U is lag-1 and the percentage of missingness in outcome data is either 20% or 50%. The three planes in each subfigure represent the power of discerning the X_{t-1} and U_{t-1} terms under different Cohen's d values. The axis labeled N represents the number of subjects in ILD and the axis labeled T represents the number of time points. The colorbar on the top-right of each subfigure presents the correlation between color and the value of power.

Figure 3. The above four pictures display the results of simulations in which the significant lag of exogenous variable U is lag-7 and the percentage of missingness in outcome data is either 20% or 50%. The three planes in each subfigure represent the power of discerning X_{t-1} and U_{t-7} terms under different Cohen's d value setting. The axis labeled N represents the number of subjects in ILD and the axis labeled T represents the number of time points. The colorbar on the top-right of each subfigure presents the correlation between color and the value of power.

4 Discussion

This article develops one convenient and flexible method for detecting the existence of optimal time lags of exogenous variables based on the existing DTVEM. In the field of behavioral science, this method meets the great demand of discerning the timing aspect of interventions and gives users practical inferences when researching the efficiency of these interventions. Using this method, users can determine and verify the most possible optimal timing of interventions, adjust them accordingly based on the results of the DTVEM.

The existing DTVEM is a novel integrated method that combines the strengths of two well-known models, the GAMM and the SSM, in order to detect and estimate the lag structure of endogenous variables (Jacobson et al., 2019). However, using the existing DTVEM to handle exogenous variables leads to underestimation problems derived primarily from the second stage

of the existing DTVEM (which uses the SSM to estimate the lag structure of exogenous variables). Despite the fact that potential optimal lags of variables have been filtered by the GAMM in first stage of the DTVEM, using the SSM directly still brings this problem of underestimation. This phenomenon shows the inability of SSM to estimate coefficients of lagged exogenous variables, and we proposed one additional stage to combat this shortcoming. The additional stage of the DTVEM takes advantage of the LMM and uses MICE to deal with potential missing values in the data.

The extended DTVEM is a hybrid method that integrates three different models, each of which meets the requirements for analyzing group-level data with missing values. Importantly, the extended DTVEM also integrates these three models in optimal order. First, the extended DTVEM deals with exogenous and endogenous variables as time-varying variables, using the GAMM to describe how coefficients of these variables change with time. Vivid figures are plotted to make users discern potentially significant lags of variables. Second, based on the results obtained from the GAMM, the lag structure is refined and estimated by using the SSM again. These first two stages of the DTVEM, as noted earlier, can detect optimal lags of variables with high power. Third, the underestimation problem—which comes from second stage of the DTVEM—is resolved by utilizing the LMM.

Running GAMM, SSM, and LMM in this order will exhaust the strengths of each model and maximize the efficacy of the extended DTVEM. Although this article considers only data with one endogenous variable and one exogenous variable, data with multiple endogenous and exogenous variables can be handled similarly. When only one endogenous variable is analyzed, other endogenous and exogenous variables should be treated as exogenous inputs. Taking other endogenous variables as exogenous inputs is reasonable in this situation; because when users fix one endogenous variable, other endogenous variables may have “exogenous” cross-regressive effects on this fixed endogenous variable. Users can analyze any number of endogenous and exogenous variables using the R function “TreatmentLAG”. Based on this function, the extended DTVEM can estimate the lag structure of multiple endogenous and exogenous variables.

Again, the findings of this article are restricted to data with just one endogenous variable and one exogenous variable. But, given that ILD in a real world context usually contains large number of variables, performing more simulations with multiple endogenous and exogenous variables is needed to further verify the efficacy of the extended DTVEM (great performance of DTVEM on estimating lag structure of multiple endogenous variables has been shown (Jacobson et al., 2019)). Of course, there are other approaches that can be used to detect and estimate the lag structure of ILD. For example, some researchers use the Bayesian Information Criterion (BIC) to select a VAR(1) model (Ho, Shumway, & Ombao, 2006). This approach needs to fit all potential lag structures and calculates the BIC for all fitted models. It is feasible if users are estimating a VAR model with low lag order. If users want to estimate VAR model with high lag order, this method fails because 8.32×10^{81} models are needed even for a VAR(15) model with only two variables (Jacobson et al., 2019). Compared with this approach, the extended DTVEM method is more practical, since the computationally efficient GAMM method will narrow down the potential lag structure space. Fitting SSM and LMM are both feasible even with large datasets.

Despite the aforementioned strengths of the extended DTVEM, several limitations of this DTVEM method should be addressed. First, the coverage rate of estimating one optimal time lag in our simulation depends on the power of discerning this time lag (i.e., one optimal time lag would be estimated by the DTVEM only if it was discerned by the first stage of the DTVEM). The first stage of the DTVEM is beneficial because it narrows down the search space of the optimal lag structure, but it may also exclude true optimal time lags at the same time. This exclusion clearly decreases the coverage rate of optimal time lags, and so one limitation of the DTVEM is its heavy reliance on performance of the GAMM. If the GAMM excludes true optimal lags, the next stage of the DTVEM will be affected and these time lags will not be included in the final results. Therefore, the extended DTVEM can be further improved by finding a more efficient method to be the first stage, resolving this initial limitation while improving the overall performance of the extended DTVEM. Nevertheless, as shown in the simulations, the GAMM often is considerably well-powered in detecting true lagged occasions.

Second, the extended DTVEM is sound for detecting and estimating lag structure in discrete-time models. In the future, the extended DTVEM should be adjusted for satisfying continuous-time modeling variations or other hybrid continuous-discrete variations (Oud, 2004; Bar-Shalom, Li, & Kirubarajan, 2004; Jacobson et al., 2019). Although the continuous-time model still has some limitations, including convoluted computations and interpretations, it is still worthy to be researched (Jacobson et al., 2019).

Methods to analyze the timing effects of interventions are currently inadequate in the area of behavioral science. In this paper, we have shown a necessary extension to the existing DTVEM in order to deal with exogenous variables. Users can use the extended DTVEM to determine the significance of interventions and to further estimate the lag structure of their data. Based on extensive simulations, this method has satisfied performance and can be applied with individual data or group-level data even with extremely large percentages of missingness. Additionally, the extended DTVEM can analyze any number of endogenous and exogenous variables, making it a powerful and convenient tool for researchers to analyze MRTs and ecological momentary intervention data deployed within the context of daily life.

Data availability

At <https://github.com/KejinWu/TreatmentLAG.git>, all simulation results can be found. Additionally, the code of “TreatmentLAG” function and two example datasets are also available at there.

Open Practices

From <http://www.nicholasjacobson.com/project/dtvem/>, the existing DTVEM package can be downloaded. The analysis was not pre-registered.

Appendix A

Example R code to run “TreatmentLAG” function

```
library (DTVEM) #Load the DTVEM package
library (OpenMx); library (lme4); library (mice)#Load required packages
#Load example1dat_with_treatment.rda which contains one endogenous variable X, and one
  exogenous variable U
test1 = TreatmentLAG(“X”, “U”, exovariabesinuvector = FALSE, varnamesexo = c(“U”),
  differentialtimevaryingpredictors = c(“X”, “U”), outcome=c(“X”), data=example1dat
  _with_treatment, ID=“ID”, Time=“Time”, k=9, standardized =“centerALL”) #Run
  TreatmentLAG function
#Load example2dat_with_treatment.rda which contains two endogenous variables X and Y,
  one exogenous variable U
test2 = TreatmentLAG(“X”, “Y”, “U”, exovariabesinuvector = FALSE, varnamesexo = c
  ( “U”), differentialtimevaryingpredictors = c(“X”, “Y”, “U”), outcome=c(“X”, “Y”
  ), data=example2dat_with_treatment, ID=“ID”, Time=“Time”, k=9, standardized =“
  centerALL”) #Run TreatmentLAG function
```

Default setting of “TreatmentLAG” function

```
TreatmentLAG(..., exovariabesinuvector = FALSE, varnamesexo = NULL, MItimes = 10, model
  = “LMM”, differentialtimevaryingpredictors=NULL, outcome=NULL, controlvariables=
  NULL, data=NULL, ID=“ID”, Time=NULL, k=10, k2=10, k3=3, k4=3, controllag=NULL,
  standardized=TRUE, predictionstart=NULL, predictionsend=NULL, predictionsinterval=
  NULL, software=“OpenMx”, independentpredictors=FALSE, minimumpracticalsignificance=
  NULL, gamma=1, minN=30, debug=FALSE, OpenMxStartingValues=.3, ResidualAnalysis=“
  Group”, blockdata=FALSE, rounddecimals=TRUE, maxintermediaterounds=10,
  differntialtimevaryingpredictors=NULL)
```

Descriptions of additional options in “TreatmentLAG” function

Since the primary options in DTVEM have been illustrated before (Jacobson et al., 2019), we just describe some additional options in the “TreatmentLAG” function.

varnamesexo. This parameter represents names of treatment in data.

exovariablesinuvector. This parameter determines which “SSM” frame is used in the second stage of DTVEM.

Mltimes. The time of doing multiple imputation, default value is 10.

model. This parameter determines which model’s estimation results will be returned, default value is “LMM”. Choices are “SSM” and “LMM”.

Appendix B

Additional figures

Figure B1. The above four pictures display the results of simulations in which the significant lag of exogenous variable U is lag-1 and the percentage of missingness in outcome data is either 20% or 50%. The three planes in each subfigure represent the coverage rate of coefficients of X_{t-1} term and U_{t-7} terms under different Cohen's d value setting. The axis labeled N represents the number of subjects in ILD and the axis labeled T represents the number of time points. The colorbar on the top-right of each subfigure presents the correlation between color and the value of coverage rate.

Figure B2. The above four pictures display the results of simulations in which the significant lag of exogenous variable U is lag-7 and the percentage of missingness in outcome data is either 20% or 50%. The three planes in each subfigure represent the coverage rate of coefficients of X_{t-1} term and U_{t-7} terms under different Cohen's d value setting. The axis labeled N represents the number of subjects in ILD and the axis labeled T represents the number of time points. The colorbar on the top-right of each subfigure presents the correlation between color and the value of coverage rate.

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