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mengyu,shuyi

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Daza (2018) Causal Analysis of Self-Tracked Time Series Data using a Counterfactual Framework for N-of-1 Trials

General procedures

1.Design

Raw outcome is per-day average body weight and the constructed is average centered body weight(ACBW) per week(here centered body weight means the difference in body weight from empirical body weight taken over all 6 years).

Raw exposure is engaging in PA on a given day and PA includes multiple kinds of physical activities(running, weight lifting, cycling etc). Constructed exposure is the proportion of days per week when any PA was reported among days when body weight is reported.

The resulting constructed time series consists of 290-293 time points(weeks). Then, changepoint analysis is used to detect the possible period lengths, finding where the mean of an otherwise stationary series changes over time and then partition the series into a sequence of segments. For each segment, PA intensity is defined as high/low if the segment mean is greater/lower than 5/7(i.e, more/less than 5 days of PA per week)

2.Notation

Throughout the article, Daza used the following notations. Random variables and fixed values are written in upper-case and lower-case, respectively. Let $p(A = a)$ denote the probability mass or density of random variable A at a, with shorthand p(a). Let $\{(A)\}$ denote a stochastic process; i.e., a time series of random variables. For any index j, let $\{(j)\}$ denote a sequence. For any random variable B, let $B|A$ denote the event B conditional on A, with shorthand $B|a$ for $B|A = a$. Let $B \perp A$ denote statistical independence of B and A.

Under the setting of APTE, Daza made the following notations. Let$\{(X, Y)\}$ represent a stochastic process. In the basic N1RT, a two-level treatment X is randomized at each time period t, defined as a set of measurement time points. Let t(j) denote a time point within period t for $j = 1, ..., m_t$. Treatment level is randomized per period only at t(1). We will call a treatment administered in a period consisting of only one time point (i.e., $m_t = 1$) a point treatment, and write t instead of t(1) in such cases; otherwise, a treatment may be called a period treatment for clarification.

Since in Daza's case, the effect of X_t on Y_{t+1} is interested in, the pair $\{X_t, Y_{t+1}\}$ will be as an idiographic unit of observation. Let Y^a_{t+1} represent the counterfactual of Y_{t+1} corresponding to $X_t = a$, then the period treatment effect(PTE) will be a contrast between Y^a_{t+1} and $Y^{a'}_{t+1}$ and a contrast between $E(Y^a_{t+1})$ and $E(Y^{a'}_{t+1})$ is average period treatment effect(APTE).

3.Definition of causal effect

The causal effect is defined as the difference in potential outcomes within a period under different treatment levels.

4.Assumptions

5.The outcome model

Assumptions: 1. among a treatment level, only from unstable to stable, not destablization again
2. *washout subperiod* $\subset$ *stabilization subperiod* for any period
3. stability point k0

4. dummy variable k<k0 will be included
5. current outcome depends on previous outcome and this dependences vary by treatment level

Also, in standard N1RT(n-of-1 randomized trial), only the first treatment is randomized and then held constant for the rest of the period. i.e. $R_{t(0)} = 1$ and $R_{t(j-1)} = 0$ for $j \in (2, ..., m_t)$

Therefore, the outcome model is:

$$Y_{t(j+1)} = \beta_0 + \left\{1 - X_{t(j)}\right\}\left\{X_{t-1(1)} + \left(1 - X_{t-1(1)}\right) I\left(m_{t-1} < k_0 - 1\right)\right\} \sum_{k=1}^{k_0-1} \beta_{0k} I(j = k) + \beta_1 Y_{t(j)} + \left[\beta_2 + \left\{\left(1 - X_{t-1(1)}\right) + X_{t-1(1)} I\left(m_{t-1} < k_0 - 1\right)\right\} \sum_{k=1}^{k_0-1} \beta_{2k} I(j = k) + \beta_3 Y_{t(j)}\right] X_{t(j)} + \mathcal{E}_{t(j)}$$

where $k_{stable} = \{k : k_0 < k < m_t\}$ and $k_{unstable} = \{k : 0 < k < k_0\}$, all β are parameters need to be estimated. $X_{(t-1)(1)}$ means the treatment on previous period's first time point. $\sum_{k=1}^{k_0-1} \beta_{0k} I(j = k)$ simulate the process if the time point j is within the unstable period. $I(m_{t-1} < k_0 - 1)$ simulate the process if the period from 1 to m_t is shorter than k_0.

Then, the average baseline effect(i.e.,baseline average ACBW during weeks of low PA) is $E(Y^0_{t(k+1)}) = \beta_0 + \beta_1 E(Y_{t(k)})$ and apte is $E(Y^1_{t(k+1)}) - E(Y^0_{t(k+1)}) = \beta_2 + \beta_3 E(Y_{t(K)})$ for $k \in k_{stable}$. Here, Both $\{Y^a_{t(k+1)}\}$ for $a = 0/1$ are potential outcomes. One of them are actually observed and the other is the counterfactual.

3.Post-Hoc analysis:

1.Analysis1: model the change in outcome from the previous outcome, which is $\triangle^Y_{t(j+1)} = Y_{t(j+1)} - Y_{t(j)}$:

$$\Delta^Y_{t(j+1)} = \beta_0 + \left\{1 - X_{t(j)}\right\}\left\{X_{t-1(1)} + \left(1 - X_{t-1(1)}\right) I\left(m_{t-1} < k_0 - 1\right)\right\} \sum_{k=1}^{k_0-1} \beta_{0k} I(j = k) + \beta_1 \Delta^Y_{t(j)} + \left[\left\{\left(1 - X_{t-1(1)}\right) + X_{t-1(1)} I\left(m_{t-1} < k_0 - 1\right)\right\} \sum_{k=1}^{k_0-1} \beta_{2k} I(j = k)\right] X_{t(j)} + \mathcal{E}_{t(j)}$$

Then, $apte = \sum_{k=1}^{k_0-1} E(\triangle^{Y,1}_{t(k+1)} | x_{t-1(1)} = 0, k < k_0) - (k_0 - 1) E(\triangle^{Y,0}_{t(j+1)} | x_{t-1(1)} = 0, j \geq k_0) = \sum_{k=1}^{k_0-1} \beta_{2k}$

2.Analysis2: model the change in outcome from the preivous period's last outcome or the average of its stable outcomes(when $k_0 > m_{t-1}$), $\triangle_{t(j+1)} = Y_{t(j+1)} - Y^*_{t-1}$ and when $m_{t-1} \leq k_0$, Y^*_{t-1} is the previous last outcome; when $m_{t-1} \geq k_0$, Y^*_{t-1} is the average of its stable outcomes.

The model is:

$$\Delta_{t(j+1)} = \gamma_0 + \left\{1 - X_{t(j)}\right\}\left\{X_{t-1(1)} + \left(1 - X_{t-1(1)}\right) I\left(m_{t-1} < k_0 - 1\right)\right\} \sum_{k=1}^{k_0-1} \gamma_{0k} I(j = k) + \gamma_1 \Delta^Y_{t-1} + \left[\gamma_2 + \left\{\left(1 - X_{t-1(1)}\right) + X_{t-1(1)} I\left(m_{t-1} < k_0 - 1\right)\right\} \sum_{k=1}^{k_0-1} \gamma_{2k} I(j = k) + \gamma_3 \Delta^Y_{t-1}\right] X_{t(j)} + \mathcal{E}_{t(j)}$$

The abe(baseline average change in ACBW from Y^*_{t-1}) is $E(\triangle^0_{t(k+1)}) = \nu_0 + \nu_1 E(\triangle^Y_{t-1})$ and apte is $E(\triangle^1_{t(k+1)}) - E(\triangle^0_{t(k+1)}) = \nu_2 + \nu_3 E(\triangle^Y_{t-1})$ for $k \in k_{stable}$.

Daza (2019) Person as Population:. . .

The way he estimate the APTE in this paper is different.

- First predict the Potential Outcomes (PO) for each set of observed values (i.e., exposure and other causes) **at each time point**.
- Then take the **weighted average** over all non-exposure causes (lagged outcomes and exposures) at each time point to produce the **trajectory of estimated mean POs** for each exposure level, with weights derived from the empirical marginal CSC distribution as required by the **g-formula**.
- Report the estimated APTE as the trajectory of pre-defined **contrasts**. If desired, report the naively estimated mean POs and APTE by taking the simple rather than weighted average (i.e., conditional on treatment level at each time point).

From Table 1 in the article, APTE is calculated at 12 time points.

Formula from Linda

Assume that $X_{t(j)}$ precedes $Y_{t(j)}$

- Time point-wise treatment effect

$$E\left[Y_{t(j)}^{a=X_{t(j)}}\right] - E\left[Y_{t(j)}^{a^*=X^*_{t(j)}}\right]$$

* Cumulative treatment effect

$$\boldsymbol{a} = a_{t,1}, ..., a_{t,j}$$

$$\bar{X}_{t(j)} = (X_{t,1}, ..., X_{t,j})$$

$$E\left[Y_{t(j)}^{\boldsymbol{a}}\right] - E\left[Y_{t(j)}^{\boldsymbol{a}^*}\right]$$

The difference among the three ways to calculate the APTE

The definition and method of APTE estimation are different between Linda and Daza. The APTE mentioned in Daza (2018) is calculated condition on *previous period's exposure being equal to 0*, and estimate the β_{2k} which are the coefficients of exposure at the time point before stable point k_0. The final estimated APTE we get is the APTE average across 6 six years.

The APTE mentioned in Daza (2019) is not conditioned on the previous period's exposure level. Instead, each period is regard as an individual, and then, the weighted POs are estimated with weights derived from the empirical marginal CSC distribution as required by the **g-formula**. Plus, no stability point is mentioned, but the stationarity of confounder or simultaneous cause (CSC) need to be statisfied for the *APTE g-formula estimator* to be consistent for an effect-stable APTE. The final estimated APTE is for each time point (a trajectory of pre-defined contrast), and since each period is seen as an individual and have different length, the length of APTE is decided by the shortest period which is over at least 11 weeks (the analysis results from Daza (2018), saying that "estimated APTE may have been stable between 11 and 17 weeks of high PA").

As for Linda's APTE, the effect is considered within the current period (or including some of the the previous period time points if we change the defination of $\bar{X}_{t(j)}$), which means the Linda's cumulative effect include the *non-exposure causes* that defined in Daza (2019).

Modeling (state space model)

Shu Li (*Estimating heterogeneous treatment effects in nonstationary time series with state-space models*, 2020) proposed a method Causal Transfer to estimate the causal effect in non-stationary time series. Causal Transfer can be used to predict population and sample treatment efect, and we will use the sample version to calculate the $apte_j$ we defined before.

1. Estimate the unknown parameters with MLE and plug them into the model.
2. For all time points, smoothing distribution $N(s_{t(j)}, S_{t(j)})$ of the states $\theta_{t(j)}$ will be estimated by iterating the smoothing recursions (need to change notations)

$$s_t = m_t + C_t G'_{t+1} R^{-1}_{t+1}(s_{t+1} - a_{t+1})$$
$$S_t = C_t G'_{t+1} R^{-1}_{t+1}(R_{t+1} - S_{t+1}) R^{-1}_{t+1} G_{t+1} C_t.$$

3. Given the smoothing distribution, we estimate the distribution $N(\tilde{a}_j, \tilde{P}_j)$ of the **counterfactuals** with $\tilde{a}_j = \tilde{Z}_j s_j$ and $\tilde{P}_j = \tilde{Z}_j S_j \tilde{Z}'_j + H_j$. $\tilde{Z}_j$ is the same as Z_j except for X_j being replaced by $\tilde{X}_j = |X_j - 1|$.
4. Draw B sets of samples $(\tilde{y}_t^{(b)})_{b=1}^B$ from $N(\tilde{a}_j, \tilde{P}_j)$ to impute the missing outcome (counterfactuals).
5. The effect would be calcualted by $\hat{\tau}_t^{(b)} = (\tilde{y}_t^{(b)} - y_t)(\tilde{X}_j - X_j)$.
6. Finally, we will get the mean and interval of estimated effects by taking average and percentile of $(\tilde{y}_t^{(b)})_{b=1}^B$.