Estimating the Causal Marginal Effect of a Continuous Exposure on an Ordinal Outcome in the Presence of Confounding and Covariate-Driven Monitoring Times

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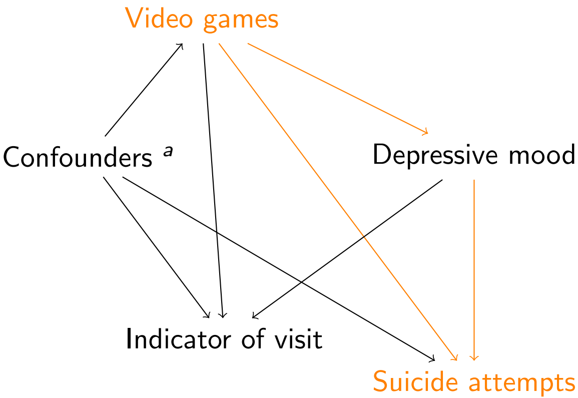
Background

- Causal inference and the marginal effect of exposure.
- Motivation: To assess the causal effect of the time spent playing video games weekly on the (categorized) number of suicide attempts in the *Add Health* study
- Data are subject to biasing imbalances (across exposure levels and across individuals who are/not monitored)
- Aim: To propose a general methodology meant for observational data subject to those imbalances
- Note: This work is a direct extension of previously proposed estimators (Coulombe et al., 2021)

Motivation: Add Health study



[a] Included age, sex, SES, ethnicity, different grades in school, trouble relaxing, grooming, seeming bored or impatient, frequency of hanging out with friends, feeling cared about, and no. of cigarettes smoked.

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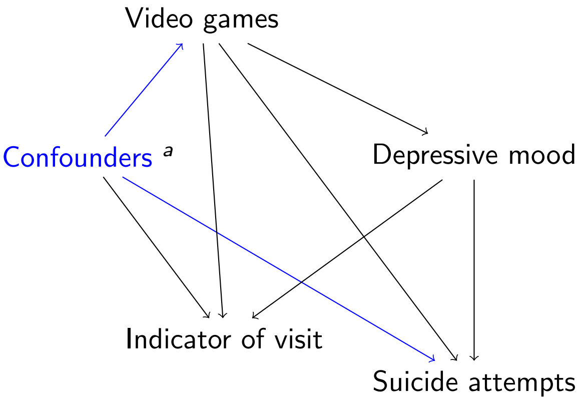

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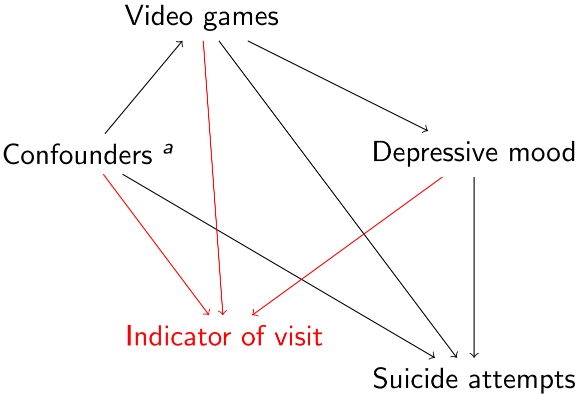

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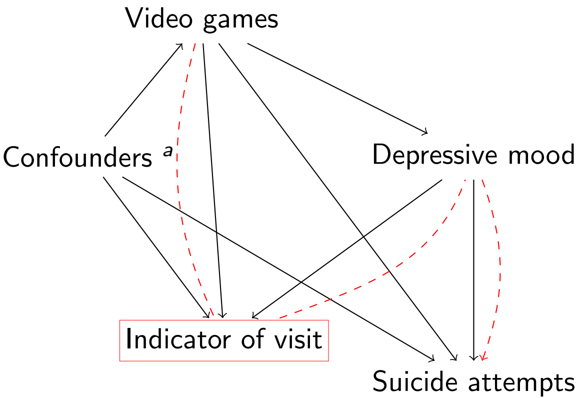

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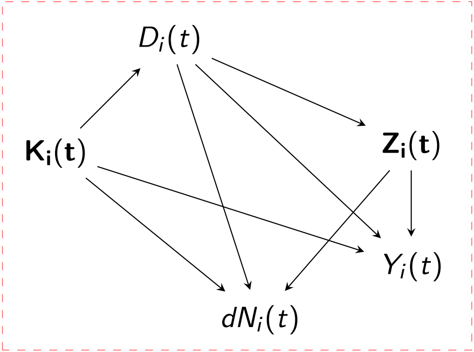
Notation, individual *i* at time *t*



$D_i(t)$ the exposure

$Y_i(t)$ the outcome

$\mathbf{K_i(t)}$ the confounders

$\mathbf{Z_i(t)}$ the mediators

$dN_i(t)$ a monitoring indicator

$$\mathbf{V_i(t)} = \{\mathbf{Z_i(t)}, D_i(t), \mathbf{K_i(t)}\}$$

$0 — 1 — 2 \quad \cdots \quad t \quad \cdots\cdot \quad C_i \leq \tau$

$$\xi_i(t) = \mathbb{I}(C_i \geq t)$$

Causal estimand

The potential outcome framework (Neyman, 1923; Rubin, 1974) is used to express the estimand of interest.

The marginal odds ratio (MOR) for a 1-unit increment in $\mathbf{D}(\mathbf{t})$:

$$MOR = \left(\frac{\mathbb{P}\left[Y_{id}(t) \leq j\right]}{1 - \mathbb{P}\left[Y_{id}(t) \leq j\right]} \right) \Big/ \left(\frac{\mathbb{P}\left[Y_{i(d+1)}(t) \leq j\right]}{1 - \mathbb{P}\left[Y_{i(d+1)}(t) \leq j\right]} \right)$$

where $Y_{id}(t)$ is a potential outcome under exposure d.

For each individual, at time t, only one of the infinitely many outcomes $Y_{id}(t)$ (d in $\mathbb{R}$) is observed.

Identifiability assumptions

Our goal is to construct a pseudo-population (Robins et al., 2000) in which there is no biasing imbalances due to confounding and the visit process.

Identifiability assumptions:

- Conditional exchangeability (augmented for the visit process)
- Stable unit treatment value assumption
- Positivity for the exposure and the monitoring models

Add to this the correct specification of the exposure, monitoring, and outcome models.

Pseudo-population: Monitoring process

The outcome is observed sporadically, at individual-specific visit times when $dN_i(\cdot) = 1$.

We postulate $dN_i(t) \perp Y_i(t) \mid \mathbf{V_i(t)}$ and a proportional rate model:

$$\mathbb{E}[dN_i(t)|\mathbf{V_i(t)}] = \xi_i(t) \exp\left(\boldsymbol{\gamma}'_{\mathbf{V}}\mathbf{V_i(t)}\right)\lambda_0(t)dt.$$

Parameters $\boldsymbol{\gamma}_{\mathbf{V}}$ are estimated using the Andersen and Gill model.

Weight 1: An inverse intensity of visit (IIV) weight (Lin et al., 2004; Bůžková and Lumley, 2009) given by

$$\varphi_i(t;\boldsymbol{\gamma}_V) = \exp\left(\boldsymbol{\gamma}'_V\mathbf{V_i(t)}\right).$$

Pseudo-population: Exposure process

There are infinitely many possible values for the exposure and the corresponding potential outcome. We assume Normality for $\mathbf{D}(\mathbf{t})$.

The continuous exposure is modeled as:

$$\mathbb{E}[D_i(t)|\mathbf{K_i}(\mathbf{t})] = \psi_0 + \boldsymbol{\psi}_{\mathbf{1}}'\mathbf{K_i}(\mathbf{t})$$
$$\mathbb{E}[D_i(t)] = \psi_m.$$

Denote by $h^{-1}(\widehat{D}_{l,i}(t)) = 1/\sqrt{2\pi\widehat{\sigma}_l^2}\exp\left(-\widehat{\epsilon}_{l,i}(t)^2/(2\widehat{\sigma}_l^2)\right)$ the Normal density evaluated at $\widehat{\epsilon}_{l,i}(t) = \left(D_i(t) - \widehat{D}_{l,i}(t)\right)$, and $\widehat{\sigma}_l^2 = var(\widehat{\epsilon}_{l,i}(t))$.

<u>**Weight 2**</u>: A generalized inverse probability of treatment weight:

$$e_i(t;\boldsymbol{\psi}) = \frac{h^{-1}(\psi_m)}{h^{-1}(\psi_0 + \boldsymbol{\psi}_1'\mathbf{K_i}(\mathbf{t}))}.$$

Extension with the proportional odds model

The proportional odds model (POM) (McCullagh, 1980) can account for the ordinal nature of the outcome:

$$\zeta_i(\mathbf{t}) = \begin{bmatrix} \mathbb{P}(Y_i(t) \leq 1 | D_i(t)) \\ \mathbb{P}(Y_i(t) \leq 2 | D_i(t)) \\ \dots \\ \mathbb{P}(Y_i(t) \leq J | D_i(t)) \end{bmatrix}, \text{ and } \mathbf{Q_i}(\mathbf{t}) = \begin{bmatrix} \mathbb{I}(Y_i(t) \leq 1) \\ \mathbb{I}(Y_i(t) \leq 2) \\ \dots \\ \mathbb{I}(Y_i(t) \leq J) \end{bmatrix}.$$

The estimating equation is given by:

$$\mathbb{E}\left[\int_0^\tau \frac{\mathbf{e}(\mathbf{t};\psi)(\mathbf{Q}(\mathbf{t}) - \zeta(\mathbf{t}))}{\varphi(\mathbf{t};\gamma_\mathbf{v})} \mathbf{dN}(\mathbf{t})\right] = \mathbf{0},$$

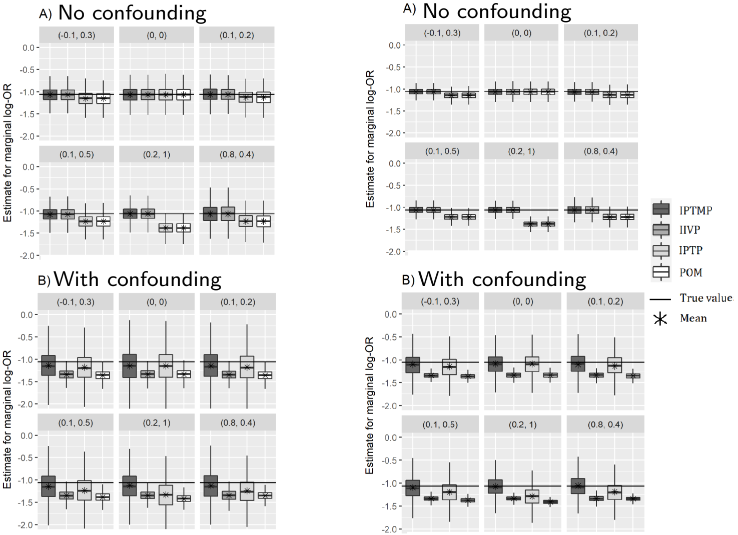
where $\zeta_{i,j}(t) = \text{expit}(\alpha_j - \beta_D D_i(t))$.

Simulation studies: Design

- Confounders: $K_1 \sim N(1,1)$, $K_2 \sim Bernoulli(0.55)$, and $K_3 \sim N(0,1)$
- Exposure: $D(t) \sim N(-0.5 + 0.5K_1 + 1K_2 - 0.05K_3; 0.5^2)$ or $D(t) \sim N(-0.5; 0.5^2)$
- Mediator: $Z(t) \sim Bernoulli(p_D(t))$ with $p_D(t) = 0.3$ if $D(t) > 0.5$ and $p_D(t) = 0.8$ otherwise
- Visits: $\lambda(t|D(t), Z(t)) = 0.01\eta \exp\left(\gamma_D D(t) + \gamma_Z Z(t)\right)$, η an individual random effect, simulated as a random Gamma variable
- Outcome: Random draw from logistic distribution with mean $\mu(t|D(t), Z(t), \mathbf{K(t)}) = -2D(t) + 5Z(t) + 0.4K_1 + 0.05K_2 - 0.6K_3$, and

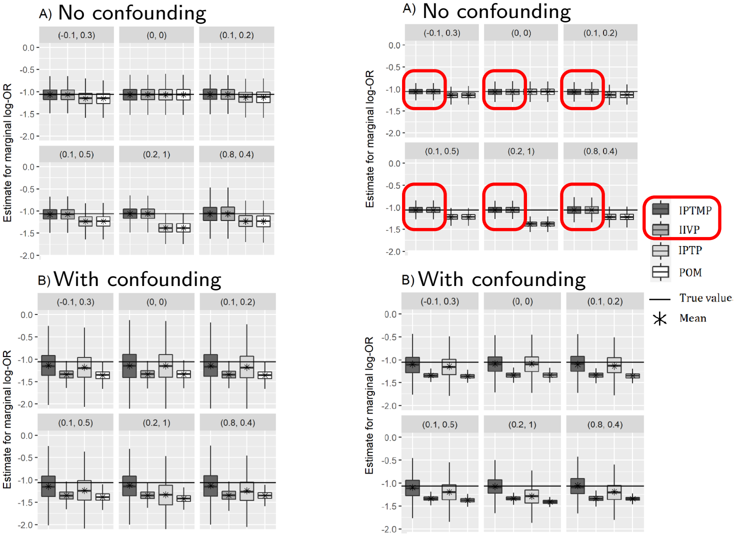
$$Y(t) = \begin{cases} 1 & \text{if draw} \leq 5 \\ 2 & \text{if } 5 < \text{draw} \leq 8 \\ 3 & \text{if draw} > 8 \end{cases}$$

Simulation studies: Results - Distribution of log-OR



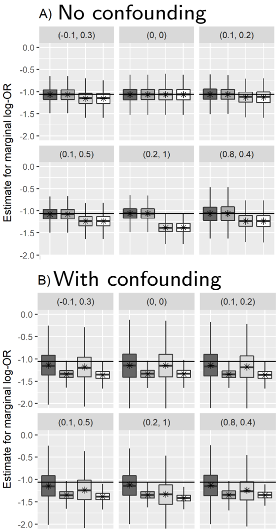
250 patients 1000 patients

Simulation studies: Results - Distribution of log-OR

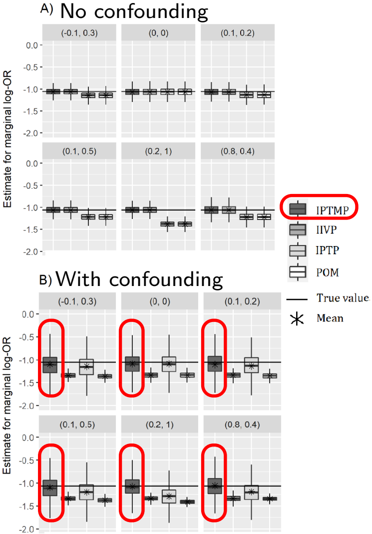


250 patients   1000 patients

Simulation studies: Results - Distribution of log-OR



250 patients



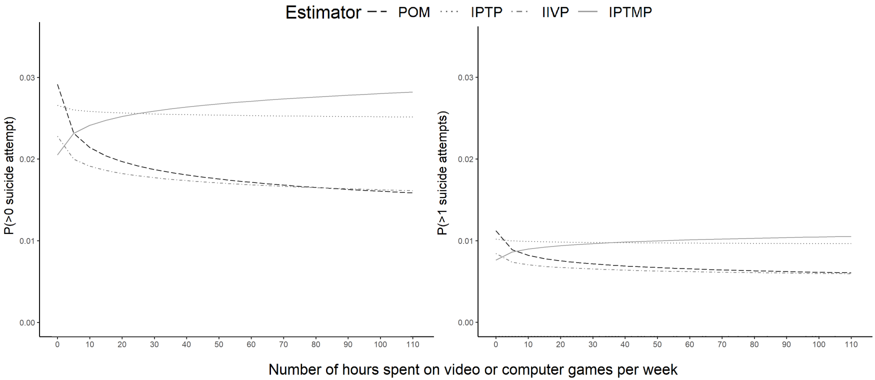
1000 patients

Application to the Add Health study: Effect of the time spent playing video games on suicide attempts

- Four-wave longitudinal study in the United States, adolescents followed until adulthood (Harris, 2013)
- Exposure distribution is highly skewed: log base 2 transformation and use of different IPT-weighting strategies (Naimi et al., 2014; Schulz et Moodie, 2021)
- Missingness in covariates affecting monitoring times: multiple imputation (Rubin, 1976)
- We found a few strong associations between the monitoring indicator and covariates (age, sex, ethnicity, SES)

Application to the Add Health study (cont'd)

Estimator	2-fold increase OR (95% CI)	8-fold increase OR (95% CI)
$\hat{\beta}_{POM}$	0.91 (0.83, 0.98)	0.76 (0.57, 0.96)
$\hat{\beta}_{IPTP}$	0.99 (0.89, 1.08)	0.98 (0.69, 1.28)
$\hat{\beta}_{IIVP}$	0.95 (0.85, 1.03)	0.86 (0.61, 1.09)
$\hat{\beta}_{IPTMP}$	1.05 (0.92, 1.15)	1.15 (0.78, 1.53)



Conclusion

- Our proposed estimator outperforms more “naive” estimators in simulation studies
- In the *Add Health* study, there are indications of confounding and covariate-driven monitoring times
- We have found a potential detrimental effect of the time spent playing video games on suicide attempts – is it clinically relevant?
- Limitations: Reliance on correctly specified models, identifiability assumptions, measurement mechanism
- (Correct) specification of the causal diagram is important

References

Bůžková, P, et Lumley, T (2009). "Semiparametric modeling of repeated measurements under outcome-dependent follow-up," *Statistics in Medicine*, 28(6), pp. 987–1003.

Coulombe, J, Moodie, E EM, et Platt, R W (2021). "Weighted regression analysis to correct for informative monitoring times and confounders in longitudinal studies," *Biometrics*, 77(1), pp. 162–174.

Harris, K M (2013). "The add health study: Design and accomplishments," Chapel Hill: Carolina Population Center, University of North Carolina at Chapel Hill, pp. 1-22.

Lin, H, Scharfstein, D O, et Rosenheck, R A (2004). "Analysis of longitudinal data with irregular, outcome-dependent follow-up," *Journal of the Royal Statistical Society: Series B (Statistical Methodology)*, 66(3), pp. 791-813.

McCullagh, P (1983). "Quasi-likelihood functions," *The Annals of Statistics*, 11(1), pp. 59-67.

Naimi, A I, Moodie, E EM, Auger, N, et al. (2014). "Constructing inverse probability weights for continuous exposures: a comparison of methods," *Epidemiology*, 25(2), pp. 292-299.

Neyman, J S (1923). "On the application of probability theory to agricultural experiments. Essay on principles. Section 9 (translation published in 1990)," *Statistical Science*, 5(4), pp. 472-480.

Robins, J M., Hernán, M A, et Brumback, B (2000). "Marginal structural models and causal inference in epidemiology," *Epidemiology*, 11(5), pp. 550-560.

Rubin, D B (1974). "Estimating causal effects of treatments in randomized and nonrandomized studies," *Journal of Educational Psychology*, 66(5), pp. 688-701.

Rubin, D B (1976). "Inference and missing data," *Biometrika*, 63(3), pp. 581-592.

Schulz, J et Moodie, E EM (2021). "Doubly robust estimation of optimal dosing strategies," *Journal of the American Statistical Association*, 116(533), pp. 256-268.

Back-up slides

Asymptotic variance

For $\hat{\boldsymbol{\beta}}_{\mathbf{TSE}}$ a two-step semiparametric estimator and $\boldsymbol{\beta}_{\mathbf{0}}$ the vector of true parameters, Newey and McFadden (1994) show that $\sqrt{n}(\hat{\boldsymbol{\beta}}_{\mathbf{TSE}} - \boldsymbol{\beta}_{\mathbf{0}}) \to N(\mathbf{0}, \boldsymbol{\Sigma})$, with

$$\boldsymbol{\Sigma} = \mathbf{G}_{\beta}^{-\mathbf{1}} \mathbb{E}\left[\left\{\mathbf{g}(\mathbf{o}; \beta_{\mathbf{0}}, \phi_{\mathbf{0}}) - \mathbf{G}_{\phi}\mathbf{M}^{-\mathbf{1}}\mathbf{m}(\mathbf{o}; \phi_{\mathbf{0}})\right\}^{\otimes 2}\right] \mathbf{G}_{\beta}^{-\mathbf{1}}$$

where

$$\begin{aligned}
\mathbf{G}_{\beta} &= \mathbb{E}(\nabla_{\beta}\mathbf{g}(\mathbf{o}; \beta_{\mathbf{0}}, \phi_{\mathbf{0}})) \\
\mathbf{G}_{\phi} &= \mathbb{E}(\nabla_{\phi}\mathbf{g}(\mathbf{o}; \beta_{\mathbf{0}}, \phi_{\mathbf{0}})) \\
\mathbf{M} &= \mathbb{E}(\nabla_{\phi}\mathbf{m}(\mathbf{o}; \phi_{\mathbf{0}}))
\end{aligned}$$

for $\mathbf{o}$ the data, and $\mathbf{m}(\mathbf{o}; \phi_{\mathbf{0}})$ and $\mathbf{g}(\mathbf{o}; \beta_{\mathbf{0}}, \phi_{\mathbf{0}})$ the estimating equations for the nuisance parameters $\boldsymbol{\phi}$ and the parameters of interest $\boldsymbol{\beta}$, respectively.

Weak Law of Large Numbers and CLT

Let the symbol $\xrightarrow{l}$ refers to convergence in law, and $\xrightarrow{p}$ refers to convergence in probability.

The Weak Law of Large Numbers
Let $Y_1, Y_2, Y_3, \ldots$ be an infinite sequence of random variables with mean μ, then

$$\bar{Y}_n \xrightarrow{p} \mu \text{ as } n \to \infty.$$

The Central Limit Theorem (CLT)
Let $Y_1, Y_2, Y_3, \ldots$ be an infinite sequence of random variables with mean μ and variance σ^2. Let $Y_1, Y_2, \ldots Y_n$ be a sample of size n, and $\bar{Y}_n$ be their sample average. Then

$$\sqrt{n}(\bar{Y}_n - \mu) \xrightarrow{l} \mathcal{N}(0, \sigma^2) \text{ as } n \to \infty.$$

Slutsky's theorem

Slutsky's theorem

Let X_n, X, and Y_n be random vectors or random variables, and let c be a constant. Suppose $X_n \xrightarrow{l} X$ and $\mathbb{P}(\lim Y_n) = c$. Then:

$$i) X_n + Y_n \xrightarrow{l} X + c$$

$$ii) X_n Y_n \xrightarrow{l} Xc$$

$$iii) Y_n^{-1} X_n \xrightarrow{l} c^{-1} X \text{ for } c \neq 0.$$

Generalized estimating equations

The score equations are given by

$$S_k(\boldsymbol{\beta}) = \sum_{i=1}^{n} \mathbf{D_i} \boldsymbol{\nu}_{\mathbf{i}}^{-1} (\mathbf{Y_i} - \boldsymbol{\mu}_{\mathbf{i}}) = \mathbf{0},$$

$\mathbf{D_i} = \partial \boldsymbol{\mu}_{\mathbf{i}} / \partial \beta_k$. Let $\mathbf{R_i}$ the correlation matrix between measurements of the same individual, $\mathbf{A_i}$ a diagonal matrix with the variance elements $g(\mu_{ij}) = \nu_{ij} \times \phi$ on its diagonal. Define $\mathbf{V_i} = \mathbf{A_i^{1/2}} \mathbf{R}(\alpha) \mathbf{A_i^{1/2}} \phi$ and plug it in the equation, to obtain

$$S_k'(\boldsymbol{\beta}) = \sum_{i=1}^{n} \mathbf{D_i} \mathbf{V_i}^{-1} (\mathbf{Y_i} - \boldsymbol{\mu}_{\mathbf{i}}) = \mathbf{0}. \tag{1}$$

GEE estimators are consistent and asymptotically normal (Liang and Zeger, 1986).

M-Estimators

If it exists, an M-estimator $\widehat{\boldsymbol{\beta}}_M$ solves the following vector equation for $\boldsymbol{\beta}$:

$$S_n(\boldsymbol{\beta}) = \sum_{i=1}^{n} \boldsymbol{\psi}(\mathbf{Y_i}, \boldsymbol{\beta}) = \mathbf{0}.$$

If the function $\psi(\cdot)$ is smooth, and if there is a unique solution $\boldsymbol{\beta}_0$, there exists a sequence of M-estimators that converges in probability to the true parameter (Huber, 1967).

The function S_n can be decomposed into a Taylor series expansion around the true value, as follows:

M-Estimators (continued)

$$S_n(\widehat{\boldsymbol{\beta}}_M) = S_n(\boldsymbol{\beta}_0) + \left.\frac{\partial S_n(\boldsymbol{\beta})}{\partial \boldsymbol{\beta}}\right|_{\boldsymbol{\beta}=\boldsymbol{\beta}_0} (\widehat{\boldsymbol{\beta}}_M - \boldsymbol{\beta}_0) + \mathcal{O}(n),$$

for $\mathcal{O}(n)$ a remainder term of order n.

Assuming that the matrix $\left.\frac{\partial S_n(\boldsymbol{\beta})}{\partial \boldsymbol{\beta}}\right|_{\boldsymbol{\beta}=\boldsymbol{\beta}_0}$ is non singular and, as such, that we can multiply by the inverse of that matrix on each side, and further rearranging the terms and multiplying by the square root of n, we obtain

$$\sqrt{n}(\widehat{\boldsymbol{\beta}}_M - \boldsymbol{\beta}_0) = \left[\left.\frac{\partial S_n(\boldsymbol{\beta})}{\partial \boldsymbol{\beta}}\right|_{\boldsymbol{\beta}=\boldsymbol{\beta}_0}\right]^{-1} \sqrt{n} S_n(\boldsymbol{\beta}_0) + \sqrt{n}\mathcal{O}^*(n).$$

M-Estimators (continued)

We then call upon all three theorems mentioned earlier (WLLN, CLT, Slutsky's theorem). We have

$$-\frac{\partial S_n(\boldsymbol{\beta})}{\partial \boldsymbol{\beta}}\bigg|_{\boldsymbol{\beta}=\boldsymbol{\beta}_0} \xrightarrow{p} \mathbb{E}\left[-\frac{\partial \psi(\mathbf{Y_1}, \boldsymbol{\beta})}{\partial \boldsymbol{\beta}}\bigg|_{\boldsymbol{\beta}=\boldsymbol{\beta}_0}\right],$$

$$\sqrt{n}S_n(\boldsymbol{\beta}_0) \xrightarrow{l} MVN(0, \mathbb{E}[\psi(\mathbf{Y_1}, \boldsymbol{\beta_0})\psi(\mathbf{Y_1}, \boldsymbol{\beta_0})^{\mathsf{T}}]).$$

Under further regularity conditions, we have

$$\widehat{\boldsymbol{\beta}}_M \xrightarrow{l} MVN\left(\boldsymbol{\beta}_0, \frac{\mathbf{V}(\boldsymbol{\beta}_0)}{n}\right) \text{ as } n \to \infty,$$

$$\mathbf{V}(\boldsymbol{\beta}_0) = \mathbb{E}\left[-\frac{\partial \psi(\mathbf{Y_1}, \boldsymbol{\beta})}{\partial \boldsymbol{\beta}}\bigg|_{\boldsymbol{\beta}=\boldsymbol{\beta}_0}\right]^{-1} \mathbb{E}[\psi(\mathbf{Y_1}, \boldsymbol{\beta_0})\psi(\mathbf{Y_1}, \boldsymbol{\beta_0})^{\mathsf{T}}] \left(\mathbb{E}\left[-\frac{\partial \psi(\mathbf{Y_1}, \boldsymbol{\beta})}{\partial \boldsymbol{\beta}}\bigg|_{\boldsymbol{\beta}=\boldsymbol{\beta}_0}\right]^{-1}\right)^{T}.$$

Identifiability assumptions

Exposure model:

- Conditional exchangeability: $\{Y_{i0}(t), Y_{i1}(t)\} \perp I_i(t) \,|\, \mathbf{K_i(t)}$
- Consistency (and SUTVA): $Y_i(t) = \begin{cases} Y_{i0}(t) & I_i(t) = 0 \\ Y_{i1}(t) & I_i(t) = 1 \end{cases}$
- Positivity: $0 < P(I_i(t)|\mathbf{K_i(t)}) < 1$ for $I_i(t) \in \{0,1\}$

Monitoring model:

- Conditional exchangeability: $\{Y_{i0}(t), Y_{i1}(t)\} \perp I_i(t) \,|\, \mathbf{K_i(t)}, dN_i(t), \mathbf{V_i(t)}$
- Positivity: $0 < P(dN_i(t)|\mathbf{V_i(t)}) < 1$ for $dN_i(t) \in \{0,1\}$

Variables in the exposure and monitoring models

Table 1: Variable definition

Variable (*question*)	Times of measurement	$D_i(t)$	$dN_i(t)$
Age	W1, W2, W3, W4	X	X
Sex, SES, ethnicity†	W1†	X	X
Frequency of having trouble relaxing (FHTR)	W1, W2	X	X
Level of grooming of the respondent (LGR)$^{\nu}$	W1, W2, W3, W4	X	X
Respondent seemed bored or impatient (RSBI)$^{\nu}$	W1, W2, W3, W4	X	X
Most recent grade in Mathematics (MATH)	W1, W2	X	X
Most recent grade in English/language arts (ENG)	W1, W2	X	X
Most recent grade in History/Social sciences (HSS)	W1, W2	X	X
Most recent grade in Science (GS)	W1, W2	X	X
Frequency of hanging out with friends (HOF)$^{\iota}$	W1, W2, W3	X	X
Feeling that friends care about you (FCA)	W1, W2	X	X
How many days of smoking cigarettes, past month	W1, W2, W3, W4	X	X
Number of hours spent on video/computer games	W1, W2, W3, W4		X
Frequency of feeling depressed	W1, W2, W3, W4		X

$\dagger$ Considered as remaining fixed throughout the study; ν Question answered by the researcher questioning the participant, rather than directly by the respondent; ι In the past week

Estimated rate ratios

Table 2: Estimated rate ratios (95% CI) for the monitoring model, *Add Health* study, United States, 1994-2008, $n = 6504$ individuals.

Variable	Rate ratio (Bootstrap 95% CI)
Number of hours spent on video or computer games	1.00 (1.00, 1.00)
Frequency of feeling depressed (Ref.= Never or rarely)	
Sometimes	1.00 (0.97, 1.02)
A lof of the time	0.99 (0.94, 1.03)
Most of the time or all the time	1.01 (0.94, 1.08)
Age	0.93 (0.93, 0.94)
Sex (Female)	1.11 (1.09, 1.13)
SES	1.01 (1.01, 1.02)
Race (Ref.= White)	
Black/African American	0.93 (0.91, 0.95)
American Indian/Alaskan Native	0.96 (0.87, 1.04)
Asian/Pacific Islander	0.92 (0.88, 0.97)
Other	0.90 (0.86, 0.94)

Estimated rate ratios (cont'd)

Table 2: Estimated rate ratios (95% CI) for the monitoring model, *Add Health* study, United States, 1994-2008, $n = 6504$ individuals.

Variable	Rate ratio (Bootstrap 95% CI)
FHTR	1.00 (0.99, 1.02)
LGR	0.99 (0.98, 1.00)
RSBI	0.98 (0.95, 1.02)
MATH	1.00 (0.99, 1.01)
ENG	1.00 (0.99, 1.01)
HSS	1.00 (0.99, 1.01)
GS	0.99 (0.98, 0.99)
HOF	1.00 (0.99, 1.02)
FCA	1.00 (0.98, 1.01)
How many days of smoking cigarettes over past month	1.00 (1.00, 1.00)

Visit process protocols (Pullenayegum and Lim, 2016)

According to the authors, there are 4 different case scenarios:

- Fixed visits
- History-dependent protocol visits
- Physician-driven visits
- Patient-driven visits.

The first and the third, if adhered perfectly, lead to the assumption of outcome being missing completely at random. Patient-driven visits are the ones likely to depend on unmeasured information.

Sensitivity analyses results

- S1: Continuous exposure and proposed IPT weight
- S2: Continuous exposure and binned IPT weight
- S3: Log base 2 exposure and binned IPT weight

Sensitivity analyses results (continued)

Table 3: **Analysis S1.** Comparison of four estimators for the marginal OR for 1-hour or 10-hour increases in the time spent playing video games per week, on the odds of suicide attempts (number of attempts categorized in 0, 1, or more), *Add Health* study, United States, 1994-2008, $n = 6504$.

Estimator	1-hour OR (95% CI)	10-hour OR (95% CI)
$\hat{\beta}_{POM}$	0.99 (0.97, 1.01)	0.93 (0.70, 1.06)
$\hat{\beta}_{IPTP}$	1.00 (0.97, 1.01)	1.01 (0.77, 1.15)
$\hat{\beta}_{IIVP}$	1.00 (0.97, 1.01)	0.97 (0.75, 1.09)
$\hat{\beta}_{IPTMP}$	1.01 (0.99, 1.02)	1.11 (0.88, 1.26)

Sensitivity analyses results (continued)

Table 4: **Analysis S2.** Comparison of four estimators for the marginal OR for 1-hour or 10-hour increases in the time spent playing video games per week, on the odds of suicide attempts (number of attempts categorized in 0, 1, or more), *Add Health* study, United States, 1994-2008, $n = 6504$.

Estimator	1-hour OR (95% CI)	10-hour OR (95% CI)
$\hat{\beta}_{POM}$	0.99 (0.97, 1.01)	0.93 (0.70, 1.07)
$\hat{\beta}_{IPTP}$	1.01 (0.98, 1.02)	1.07 (0.84, 1.20)
$\hat{\beta}_{IIVP}$	1.00 (0.97, 1.01)	0.97 (0.76, 1.09)
$\hat{\beta}_{IPTMP}$	1.01 (0.99, 1.02)	1.08 (0.87, 1.20)

Sensitivity analyses results (continued)

Table 5: **Analysis S3.** Comparison of four estimators for the marginal OR for a two-fold or 8-fold increases in the time spent playing video games per week, on the odds of suicide attempts (number of attempts categorized in 0, 1, or more), *Add Health* study, United States, 1994-2008, $n = 6504$.

Estimator	2-fold OR (95% CI)	8-fold OR (95% CI)
$\hat{\beta}_{POM}$	0.91 (0.82, 0.99)	0.76 (0.55, 0.98)
$\hat{\beta}_{IPTP}$	1.00 (0.88, 1.09)	0.99 (0.69, 1.30)
$\hat{\beta}_{IIVP}$	0.95 (0.85, 1.04)	0.86 (0.61, 1.11)
$\hat{\beta}_{IPTMP}$	1.03 (0.91, 1.13)	1.09 (0.74, 1.44)