Assumption-Lean Quantile Regression

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Supplementary Material

The supplementary material includes details on the construction of adjusted estimators based on parametric quantile regression with variable selection, proofs, additional simulation results, a sensitivity analysis for the data analysis, and a generalization of the estimand with link function.

S1 Proof that $\Psi_\tau(L) = \beta_\tau(L)$ under model (1.2)

Model (1.2) states that $Q_\tau(Y|A,L) = \beta_\tau(L)A + Q_\tau(Y|A=0,L)$. Plugging this into the expression for $\Psi_\tau(L)$ yields

$$\begin{aligned}
\Psi_\tau(L) &= \frac{\text{Cov}\{A, Q_\tau(Y|A,L)|L\}}{\text{Var}(A|L)} \\
&= \frac{\text{Cov}\{A, \beta_\tau(L)A + Q_\tau(Y|A=0,L)|L\}}{\text{Var}(A|L)} \\
&= \frac{\beta_\tau(L)\text{Cov}\{A, A|L\}}{\text{Var}(A|L)} + \frac{\text{Cov}\{A, Q_\tau(Y|A=0,L)|L\}}{\text{Var}(A|L)} \\
&= \beta_\tau(L)\frac{\text{Var}(A|L)}{\text{Var}(A|L)} + 0 \\
&= \beta_\tau(L).
\end{aligned}$$

S2 Proof that the estimand (2.2) minimizes loss (2.1) and equals Ψ_τ

The minimizer of

$$E\left[\int \left\{Q_\tau(Y^{A+a}|A,L) - Q_\tau(Y^A|A,L) - \Psi_\tau a\right\}^2 f_{A|L}(A+a)da\right]$$

is

$$\begin{aligned}
\Psi_\tau &= \frac{E\left[\int a\left\{Q_\tau(Y^{A+a}|A,L) - Q_\tau(Y^A|A,L)\right\} f(A+a|L)da\right]}{E\left[\int a^2 f(A+a|L)da\right]} \\
&= \frac{E\left[\iint a\left\{Q_\tau(Y^{\tilde{a}+a}|A=\tilde{a},L) - Q_\tau(Y^{\tilde{a}}|A=\tilde{a},L)\right\} f(\tilde{a}+a|L)f_A(\tilde{a}|L)da d\tilde{a}\right]}{E\left\{\iint a^2 f(\tilde{a}+a|L)f_A(\tilde{a}|L)da d\tilde{a}\right\}} \\
&= \frac{E\left[\iint a\left\{Q_\tau(Y^|A=\tilde{a}+a,L) - Q_\tau(Y|A=\tilde{a},L)\right\} f(\tilde{a}+a|L)f_A(\tilde{a}|L)da d\tilde{a}\right]}{E\left\{(A-A^*)^2\right\}} \\
&= \frac{E\left[(A-A^*)\{Q_\tau(Y|A,L) - Q_\tau(Y|A^*,L)\}\right]}{E\left\{(A-A^*)^2\right\}}
\end{aligned}$$

Now, we rewrite its numerator:

$$\begin{aligned}
&E[(A-A^*)\{Q_\tau(Y|A,L) - Q_\tau(Y|A^*,L)\}] \\
&= E[\{A - E(A|L) + E(A|L) - A^*\}\{Q_\tau(Y|A,L) - Q_\tau(Y|A^*,L)\}] \\
&= E[\{A - E(A|L)\}\{Q_\tau(Y|A,L) - Q_\tau(Y|A^*,L)\}] \\
&\quad + E[\{A^* - E(A|L)\}\{Q_\tau(Y|A^*,L) - Q_\tau(Y|A,L)\}] \\
&= 2E[\{A - E(A|L)\}Q_\tau(Y|A,L)] - E[\{A - E(A|L)\}Q_\tau(Y|A^*,L)] \\
&\quad - E[\{A^* - E(A^*|L)\}Q_\tau(Y|A,L)].
\end{aligned}$$

We made use of the fact that A and A^* follow the same distribution conditional on L. Moreover, the last two terms are zero because of the (assumed) conditional independence of A and A^* given L:

$$\begin{aligned}
E[\{A - E(A|L)\}Q_\tau(Y|A^*, L)] &= E\big(E[\{A - E(A|L)\}Q_\tau(Y|A^*, L)|L]\big) \\
&= E\big(E[\{A - E(A|L)\}|L]E\{Q_\tau(Y|A^*, L)|L\}\big) \\
&= E\big[0E\{Q_\tau(Y|A^*, L)|L\}\big] \\
&= 0.
\end{aligned}$$

Thus, we have

$$\begin{aligned}
E[(A - A^*)\{Q_\tau(Y|A, L) - Q_\tau(Y|A^*, L)\}] &= 2E[\{A - E(A|L)\}Q_\tau(Y|A, L)] \\
&= 2E\left(\{A - E(A|L)\}\left[Q_\tau(Y|A, L) - E\{Q_\tau(Y|A, L)|L\}\right]\right).
\end{aligned}$$

To prove that the minimizer equals (2.2), it remains to show that $E\left\{(A - A^*)^2\right\} = 2E[\{A - E(A|L)\}^2]$. This can be done as follows:

$$\begin{aligned}
E\{(A - A^*)^2\} &= E[\{A - E(A|L) + E(A|L) - A^*\}^2] \\
&= E[\{A - E(A|L)\}^2 + \{E(A|L) - A^*\}^2 - 2\{A - E(A|L)\}\{A^* - E(A|L)\}] \\
&= 2E[\{A - E(A|L)\}^2] - 2E[\{A - E(A|L)\}\{A^* - E(A|L)\}] \\
&= 2E[\{A - E(A|L)\}^2] - 2E\big(E[\{A - E(A|L)\}\{A^* - E(A|L)\}|L]\big) \\
&= 2E[\{A - E(A|L)\}^2] - 2E\big(E[\{A - E(A|L)\}|L]E[\{A^* - E(A|L)\}|L]\big) \\
&= 2E[\{A - E(A|L)\}^2].
\end{aligned}$$

S3 Proof that $\Psi_\tau = \beta_\tau$ and $\Phi_\tau = 0$ if model (2.3) holds.

Model (2.3) states that $Q_\tau(Y|A,L) = \beta_\tau A + Q_\tau(Y|A=0,L)$. From the calculation in S1 it is clear that under this model $\Psi_\tau(L) = \beta_\tau$, such that $\Psi_\tau = E\{w(L)\beta_\tau\} = \beta_\tau$ because the weights have mean 1. Consequently, we have that $\Phi_\tau = E\left[w(L)\left\{\beta_\tau - \beta_\tau\right\}^2\right] = 0$.

S4 Proof of Theorem 1

To calculate the efficient influence function of (2.2), we follow the strategy described in Hines et al. (2022) as well as the notation. Consider the one-dimensional parametric submodel $\mathcal{P}_t = (1-t)\mathcal{P} + t\widetilde{\mathcal{P}}$, where $\mathcal{P}$ is the true data-generating law and $\widetilde{\mathcal{P}}$ is a point mass data generating distribution, such that the density of $\mathcal{P}_t$ is given by $f_t(y,a,l) = (1-t)f(y,a,l) + t\mathbb{1}_{(\tilde{y},\tilde{a};\tilde{l})}(y,a,l)$, where $\mathbb{1}_{(\tilde{y},\tilde{a};\tilde{l})}(y,a,l)$ is a Dirac delta function and $f(y,a,l)$ is the joint density of Y, A and L. In the same way, we also define all other functions, e.g. $f_t(a|l) = f_t(a,l)/f_t(l)$. To calculate the efficient influence function, we first give some intermediate results.

Lemma 1.

$$\frac{d}{dt}Q_{\tau,t}(Y|A,L)\Big|_{t=0} = \frac{\mathbb{1}_{\tilde{a},\tilde{l}}(A,L)}{f\{Q_\tau(Y|A,L),A,L\}}\Big[\tau - I\{\tilde{y} \le Q_\tau(Y|A,L)\}\Big]$$

Proof. Starting from

$$\tau = \int_{-\infty}^{Q_\tau(Y|A,L)} f(Y|A,L)\,dY = \int_{-\infty}^{Q_\tau(Y|A,L)} \frac{f(Y,A,L)}{f(A,L)}\,dY$$

and using the Leibniz integral rule, one can find

$$\begin{aligned}
0 &= \frac{d}{dt}\left(\int_{-\infty}^{Q_{\tau,t}(Y|A,L)} \frac{f_t(Y,A,L)}{f_t(A,L)}\,dY\right)\Bigg|_{t=0} \\
&= \frac{f(Q_\tau(Y|A,L),A,L)}{f(A,L)}\frac{d}{dt}Q_{\tau,t}(Y|A,L)\Big|_{t=0} + \int_{-\infty}^{Q_\tau(Y|A,L)} \frac{\mathbb{1}_{\tilde{y},\tilde{a},\tilde{l}}(Y,A,L) - f(Y,A,L)}{f(A,L)}\,dY \\
&\qquad - \int_{-\infty}^{Q_\tau(Y|A,L)} \frac{[\mathbb{1}_{\tilde{a},\tilde{l}}(A,L) - f(A,L)]f(Y,A,L)}{f(A,L)^2}\,dY
\end{aligned}$$

$$
\begin{aligned}
&= \frac{f(Q_\tau(Y|A,L),A,L)}{f(A,L)} \frac{d}{dt} Q_{\tau,t}(Y|A,L)\Big|_{t=0} + \int_{-\infty}^{Q_\tau(Y|A,L)} \frac{\mathbb{1}_{\tilde{y},\tilde{a},\tilde{l}}(Y,A,L)}{f(A,L)}\, dY \\
&\qquad - \int_{-\infty}^{Q_\tau(Y|A,L)} \frac{\mathbb{1}_{\tilde{a},\tilde{l}}(A,L) f(Y,A,L)}{f(A,L)^2}\, dY \\
&= \frac{f(Q_\tau(Y|A,L),A,L)}{f(A,L)} \frac{d}{dt} Q_{\tau,t}(Y|A,L)\Big|_{t=0} + \frac{\mathbb{1}_{\tilde{a},\tilde{l}}(A,L)}{f(A,L)} \int_{-\infty}^{Q_\tau(Y|A,L)} \mathbb{1}_{\tilde{y}}(Y)\, dY \\
&\qquad - \frac{\mathbb{1}_{\tilde{a},\tilde{l}}(A,L)}{f(A,L)} \int_{-\infty}^{Q_\tau(Y|A,L)} f(Y|A,L)\, dY \\
&= \frac{f(Q_\tau(Y|A,L),A,L)}{f(A,L)} \frac{d}{dt} Q_{\tau,t}(Y|A,L)\Big|_{t=0} + \frac{\mathbb{1}_{\tilde{a},\tilde{l}}(A,L)}{f(A,L)} I\{\tilde{y} \le Q_\tau(Y|A,L)\} \\
&\qquad - \frac{\mathbb{1}_{\tilde{a},\tilde{l}}(A,L)}{f(A,L)} \tau.
\end{aligned}
$$

This leads to

$$
\frac{d}{dt} Q_{\tau,t}(Y|A,L)\Big|_{t=0} = \frac{\mathbb{1}_{\tilde{a},\tilde{l}}(A,L)}{f(Q_\tau(Y|A,L),A,L)} \Big(\tau - I\{\tilde{y} \le Q_\tau(Y|A,L)\}\Big).
$$

□

Lemma 2.

$$
\begin{aligned}
&\frac{d}{dt}\{A - E_t(A|L)\}\left[Q_{\tau,t}(Y|A,L) - E_t\{Q_{\tau,t}(Y|A,L)|L\}\right]\Big|_{t=0} \\
&= -\frac{\mathbb{1}_{\tilde{l}}(L)}{f(L)}(\tilde{a} - E(A|L))\left[Q_\tau(Y|A,L) - E\{Q_\tau(Y|A,L)|L\}\right] \\
&+ \{A - E(A|L)\}\left[\mathbb{1}_{\tilde{a},\tilde{l}}(A,L)\frac{\tau - I\{\tilde{y} \le Q_\tau(Y|A,L)\}}{f(Q_\tau(Y|A,L),A,L)}\right. \\
&\qquad \left. - \frac{\mathbb{1}_{\tilde{l}}(L)}{f(L)}\left[Q_\tau(Y|A=\tilde{a},L) - E\{Q_\tau(Y|A,L)|L\}\right]\frac{\mathbb{1}_{\tilde{l}}(L)}{f(L)}\frac{\tau - I\{\tilde{y} \le Q_\tau(Y|A=\tilde{a},L)\}}{f(Q_\tau(Y|A=\tilde{a},L)|A=\tilde{a},L)}\right]
\end{aligned}
$$

Proof.

$$
\frac{d}{dt}\{A - E_t(A|L)\}\left[Q_{\tau,t}(Y|A,L) - E_t\{Q_{\tau,t}(Y|A,L)|L\}\right]\Big|_{t=0}
$$

$$
\begin{aligned}
&= \frac{d}{dt}(A - E_t(A|L))\Big|_{t=0} \left[Q_\tau(Y|A,L) - E\{Q_\tau(Y|A,L)|L\}\right] \\
&\quad + (A - E(A|L))\frac{d}{dt}\left[Q_{\tau,t}(Y|A,L) - E_t\{Q_{\tau,t}(Y|A,L)|L\}\right]\Big|_{t=0} \\
&= -\frac{\mathbb{1}_{\tilde{l}}(L)}{f(L)}(\tilde{a} - E(A|L))\left[Q_\tau(Y|A,L) - E\{Q_\tau(Y|A,L)|L\}\right] \\
&\quad + \{A - E(A|L)\}\left[\mathbb{1}_{\tilde{a},\tilde{l}}(A,L)\frac{\tau - I\{\tilde{y} \le Q_\tau(Y|A,L)\}}{f(Q_\tau(Y|A,L),A,L)}\right. \\
&\qquad \left. -\frac{\mathbb{1}_{\tilde{l}}(L)}{f(L)}\left[Q_\tau(Y|A=\tilde{a},L) - E\{Q_\tau(Y|A,L)|L\}\right] - \frac{\mathbb{1}_{\tilde{l}}(L)}{f(L)}\frac{\tau - I\{\tilde{y} \le Q_\tau(Y|A=\tilde{a},L)\}}{f(Q_\tau(Y|A=\tilde{a},L)|A=\tilde{a},L)}\right]
\end{aligned}
$$

□

Lemma 3.

$$
\frac{d}{dt}(A - E_t(A|L))^2\Big|_{t=0} = -2\{A - E(A|L)\}(\tilde{a} - E(A|L))\frac{\mathbb{1}_{\tilde{l}}(L)}{f(L)}
$$

Proof.

$$
\begin{aligned}
\frac{d}{dt}(A - E_t(A|L))^2\Big|_{t=0} &= -2\{A - E(A|L)\}\frac{d}{dt}E_t(A|L)\Big|_{t=0} \\
&= -2\{A - E(A|L)\}(\tilde{a} - E(A|L))\frac{\mathbb{1}_{\tilde{l}}(L)}{f(L)}
\end{aligned}
$$

□

Taking the derivative of $\Psi_\tau(\mathcal{P}_t)$ with respect to t, evaluated at $t = 0$, results in

$$
\begin{aligned}
&\frac{d}{dt}\Psi_\tau(\mathcal{P}_t)\Big|_{t=0} \\
&= \frac{\frac{d}{dt}E_t[(A - E_t(A|L))\left[Q_{\tau,t}(Y|A,L) - E_t\{Q_{\tau,t}(Y|A,L)|L\}\right]]\Big|_{t=0}}{E[\{A - E(A|L)\}^2]} \\
&\qquad - \frac{\Psi_\tau}{E[\{A - E(A|L)\}^2]}\frac{d}{dt}E_t[(A - E_t(A|L))^2]\Big|_{t=0}
\end{aligned}
$$

$$= \frac{(\tilde{a} - E(A|L=\tilde{l}))[Q_\tau(Y|A=\tilde{a}, L=\tilde{l}) - E\{Q_\tau(Y|A,L)|L=\tilde{l}\}]}{E[\{A-E(A|L)\}^2]} - \Psi_\tau$$
$$+ \frac{E\left[\frac{d}{dt}(A - E_t(A|L))\left[Q_{\tau,t}(Y|A,L) - E_t\{Q_{\tau,t}(Y|A,L)|L\}\right]\Big|_{t=0}\right]}{E[\{A-E(A|L)\}^2]}$$
$$- \frac{\Psi_\tau}{E[\{A-E(A|L)\}^2]}\left[(\tilde{a} - E(A|L=\tilde{l}))^2 - E[\{A-E(A|L)\}^2] + E\left(\frac{d}{dt}(A - E_t(A|L))^2\Big|_{t=0}\right)\right]$$

$$= \frac{1}{E[\{A-E(A|L)\}^2]}\Bigg[(\tilde{a} - E(A|L=\tilde{l}))[Q_\tau(Y|A=\tilde{a}, L=\tilde{l}) - E\{Q_\tau(Y|A,L)|L=\tilde{l}\}]$$
$$- \iint \frac{\mathbb{1}_{\tilde{l}}(L)}{f(L)}(\tilde{a} - E(A|L))[Q_\tau(Y|A,L) - E\{Q_\tau(Y|A,L)|L\}]f(A,L)\,dA\,dL$$
$$+ \iint \{A - E(A|L)\}\mathbb{1}_{\tilde{a},\tilde{l}}(A,L)\frac{\tau - I\{\tilde{y} \le Q_\tau(Y|A,L)\}}{f(Q_\tau(Y|A,L),A,L)}f(A,L)\,dA\,dL$$
$$- \Psi_\tau\left((\tilde{a} - E(A|L=\tilde{l}))^2 - 2\iint \{A-E(A|L)\}(\tilde{a} - E(A|L))\frac{\mathbb{1}_{\tilde{l}}(L)}{f(L)}f(A,L)\,dA\,dL\right)\Bigg]$$

$$= \frac{1}{E[\{A-E(A|L)\}^2]}\Bigg[(\tilde{a} - E(A|L=\tilde{l}))[Q_\tau(Y|A=\tilde{a}, L=\tilde{l}) - E\{Q_\tau(Y|A,L)|L=\tilde{l}\}]$$
$$- (\tilde{a} - E(A|L=\tilde{l}))\left[\int Q_\tau(Y|A, L=\tilde{l})f(A|L=\tilde{l})\,dA - E\{Q_\tau(Y|A,L)|L=\tilde{l}\}\right]$$
$$+ (\tilde{a} - E(A|L=\tilde{l}))\frac{\tau - I\{\tilde{y} \le Q_\tau(Y|A=\tilde{a}, L=\tilde{l})\}}{f(Q_\tau(Y|A=\tilde{a}, L=\tilde{l})|A=\tilde{a}, L=\tilde{l})}$$
$$- \Psi_\tau\left((\tilde{a} - E(A|L=\tilde{l}))^2 - 2(\tilde{a} - E(A|L=\tilde{l}))\int (A - E(A|L=\tilde{l}))f(A|L=\tilde{l})\,dA\right)\Bigg]$$

$$= \frac{\tilde{a} - E(A|L=\tilde{l})}{E[\{A - E(A|L)\}^2]} \Bigg[Q_\tau(Y|A=\tilde{a}, L=\tilde{l}) - E\Big(Q_\tau(Y|A, L=\tilde{l})\big|L=\tilde{l}\Big) + \frac{\tau - I\{\tilde{y} \le Q_\tau(Y|A=\tilde{a}, L=\tilde{l})\}}{f(Q_\tau(Y|A=\tilde{a}, L=\tilde{l})|A=\tilde{a}, L=\tilde{l})} - \Psi_\tau\Bigg((\tilde{a} - E(A|L=\tilde{l})) - 2E\big(A - E(A|L=\tilde{l})|L=\tilde{l}\big)\Bigg)\Bigg]$$

$$= \frac{\tilde{a} - E(A|L=\tilde{l})}{E[\{A - E(A|L)\}^2]} \Bigg[Q_\tau(Y|A=\tilde{a}, L=\tilde{l}) - E\Big(Q_\tau(Y|A, L=\tilde{l})\big|L=\tilde{l}\Big) + \frac{\tau - I\{\tilde{y} \le Q_\tau(Y|A=\tilde{a}, L=\tilde{l})\}}{f(Q_\tau(Y|A=\tilde{a}, L=\tilde{l})|A=\tilde{a}, L=\tilde{l})} - \Psi_\tau(\tilde{a} - E(A|L=\tilde{l}))\Bigg],$$

where we use Lemma 2 and Lemma 3 in the third equation. Going back to the random variables, this results in the following efficient influence function:

$$\frac{A - E(A|L)}{E[\{A - E(A|L)\}^2]} \Bigg[Q_\tau(Y|A, L) - E\left\{Q_\tau(Y|A, L)|L\right\} + \frac{\tau - I\{Y \le Q_\tau(Y|A, L)\}}{f\{Q_\tau(Y|A, L)|A, L\}} - \Psi_\tau\{A - E(A|L)\}\Bigg].$$

S5 Proof of Theorem 2

Using a von Mises expansion (see e.g. van der Vaart (1998)), we have

$$\hat{\Psi}_\tau - \Psi_\tau = \frac{1}{n}\sum_{i=1}^{n} \frac{A_i - E(A_i|L_i)}{E[\{A - E(A|L)\}^2]} \Bigg[Q_\tau(Y_i|A_i, L_i) - E\left\{Q_\tau(Y|A, L)|L\right\} + \frac{\tau - I\{Y_i \le Q_\tau(Y_i|A_i, L_i)\}}{f\{Q_\tau(Y_i|A_i, L_i)|A_i, L_i\}} - \Psi_\tau(A_i - E(A_i|L_i))\Bigg] + R_1 + R_2.$$

Here, the first term is $O_p(n^{-1/2})$ and

$$R_1 = \frac{1}{n}\sum_{i=1}^{n}\Bigg[\frac{A_i - \hat{E}(A_i|L_i)}{\hat{E}[(A_i - \hat{E}(A_i|L_i))^2]}\Bigg\{\hat{Q}_\tau(Y_i|A_i,L_i) - \hat{E}\Big(\hat{Q}_\tau(Y_i|A_i,L_i)\big|L_i\Big) + \frac{\tau - I\{Y_i \le \hat{Q}_\tau(Y_i|A_i,L_i)\}}{\hat{f}\{\hat{Q}_\tau(Y_i|A_i,L_i)|A_i,L_i\}} - \hat{\Psi}_\tau(A_i - \hat{E}(A_i|L_i))\Bigg\}$$
$$- \frac{A_i - E(A_i|L_i)}{E[\{A - E(A|L)\}^2]}\Bigg\{Q_\tau(Y_i|A_i,L_i) - E\left\{Q_\tau(Y|A,L)|L\right\} + \frac{\tau - I\{Y_i \le Q_\tau(Y_i|A_i,L_i)\}}{f\{Q_\tau(Y_i|A_i,L_i)|A_i,L_i\}} - \Psi_\tau(A_i - E(A_i|L_i))\Bigg\}\Bigg]$$
$$- \mathbb{P}\Bigg[\frac{A - \hat{E}(A|L)}{\hat{E}[(A - \hat{E}(A|L))^2]}\Bigg\{\hat{Q}_\tau(Y|A,L) - \hat{E}\Big(\hat{Q}_\tau(Y|A,L)\big|L\Big) + \frac{\tau - I\{Y \le \hat{Q}_\tau(Y|A,L)\}}{\hat{f}(\hat{Q}_\tau(Y|A,L)|A,L)} - \hat{\Psi}_\tau(A - \hat{E}(A|L))\Bigg\}$$
$$- \frac{A - E(A|L)}{E[\{A - E(A|L)\}^2]}\Bigg\{Q_\tau(Y|A,L) - E\left\{Q_\tau(Y|A,L)|L\right\} + \frac{\tau - I\{Y \le Q_\tau(Y|A,L)\}}{f\{Q_\tau(Y|A,L)|A,L\}} - \Psi_\tau\{A - E(A|L)\}\Bigg\}\Bigg]$$

and

$$R_2 = \hat{\Psi}_\tau - \Psi_\tau + \mathbb{P}\Bigg[\frac{A - \hat{E}(A|L)}{\hat{E}[(A - \hat{E}(A|L))^2]}\Bigg\{\hat{Q}_\tau(Y|A,L) - \hat{E}\Big(\hat{Q}_\tau(Y|A,L)\big|L\Big) + \frac{\tau - I\{Y \le \hat{Q}_\tau(Y|A,L)\}}{\hat{f}(\hat{Q}_\tau(Y|A,L)|A,L)} - \hat{\Psi}_\tau(A - \hat{E}(A|L))\Bigg\}\Bigg].$$

The term R_1 can be shown to be $o_p(n^{-1/2})$ by using sample-splitting. A detailed elaboration of this can be found along the lines of the Supplementary Material of Vansteelandt and Dukes (2022). In what follows we take a deeper look into R_2 to understand under what conditions it is $o_p(n^{-1/2})$. From the definition of R_2, it follows

that

$$
\begin{aligned}
R_2 &= \hat{\Psi}_\tau - \Psi_\tau - \hat{\Psi}_\tau \frac{\mathbb{P}[(A-\hat{E}(A|L))^2]}{\hat{E}[(A-\hat{E}(A|L))^2]} \\
&\quad + \mathbb{P}\left[\frac{A-\hat{E}(A|L)}{\hat{E}[(A-\hat{E}(A|L))^2]}\left\{\hat{Q}_\tau(Y|A,L) - \hat{E}\Big(\hat{Q}_\tau(Y|A,L)\Big|L\Big) + \frac{\tau - I\{Y \le \hat{Q}_\tau(Y|A,L)\}}{\hat{f}(\hat{Q}_\tau(Y|A,L)|A,L)}\right\}\right] \\
&= (\hat{\Psi}_\tau - \Psi_\tau)\left[1 - \frac{\mathbb{P}[(A-\hat{E}(A|L))^2]}{\hat{E}[(A-\hat{E}(A|L))^2]}\right] \\
&\quad + \mathbb{P}\left[\frac{A-\hat{E}(A|L)}{\hat{E}[(A-\hat{E}(A|L))^2]}\left\{\hat{Q}_\tau(Y|A,L) - \hat{E}\Big(\hat{Q}_\tau(Y|A,L)\Big|L\Big)\right.\right. \\
&\qquad\qquad \left.\left. + \frac{\tau - I\{Y \le \hat{Q}_\tau(Y|A,L)\}}{\hat{f}(\hat{Q}_\tau(Y|A,L)|A,L)} - \Psi_\tau(A-\hat{E}(A|L))\right\}\right].
\end{aligned}
$$

Here, the first term is $o_p(|\hat{\Psi}_\tau - \Psi_\tau|)$, and thus a lower order term. To understand the behaviour of the remaining terms, we make use of

$$
\Psi_\tau = \mathbb{P}\left[\frac{A-E(A|L)}{\mathbb{P}[(A-E(A|L))^2]}\left\{Q_\tau(Y|A,L) - E\Big(Q_\tau(Y|A,L)\Big|L\Big) + \frac{\tau - I\{Y \le Q_\tau(Y|A,L)\}}{f\{Q_\tau(Y|A,L)|A,L\}}\right\}\right].
$$

To simplify the notation in the following calculations, let $\zeta = Q_\tau(Y|A,L)$. Then the remaining terms can be written as

$$
\begin{aligned}
&\frac{1}{\hat{E}[(A-\hat{E}(A|L))^2]}\left(\mathbb{P}\left[(A-\hat{E}(A|L))\Big\{\hat{\zeta} - \hat{E}(\hat{\zeta}|L) + \frac{\tau - I\{Y \le \hat{\zeta}\}}{\hat{f}(\hat{\zeta}|A,L)}\Big\}\right]\right. \\
&\qquad \left. - \mathbb{P}\left[(A-E(A|L))\Big\{\zeta - E(\zeta|L) + \frac{\tau - I\{Y \le \zeta\}}{f(\zeta|A,L)}\Big\}\right]\frac{\mathbb{P}[(A-\hat{E}(A|L))^2]}{\mathbb{P}[(A-E(A|L))^2]}\right) \\
&= \frac{1}{\hat{E}[(A-\hat{E}(A|L))^2]}\left(\mathbb{P}\left[(A-\hat{E}(A|L))\Big\{\hat{\zeta} - \hat{E}(\hat{\zeta}|L) + \frac{\tau - P(Y \le \hat{\zeta}|A,L)}{\hat{f}(\hat{\zeta}|A,L)}\Big\}\right]\right. \\
&\qquad \left. - \mathbb{P}\left[(A-E(A|L))\Big\{\zeta - E(\zeta|L) + \frac{\tau - P(Y \le \zeta|A,L)}{f(\zeta|A,L)}\Big\}\right]\frac{\mathbb{P}[(A-\hat{E}(A|L))^2]}{\mathbb{P}[(A-E(A|L))^2]}\right)
\end{aligned}
$$

$$= \frac{1}{\hat{E}[(A-\hat{E}(A|L))^2]}\left(\mathbb{P}\left[(A-\hat{E}(A|L))\Big\{\hat{\zeta}-\hat{E}(\hat{\zeta}|L)+\frac{\tau-P(Y\leq\hat{\zeta}|A,L)}{\hat{f}(\hat{\zeta}|A,L)}\Big\}\right]\right.$$
$$\left.-\,\mathbb{P}\left[(A-E(A|L))\Big\{\zeta-E(\zeta|L)\Big\}\right]\frac{\mathbb{P}[(A-\hat{E}(A|L))^2]}{\mathbb{P}[(A-E(A|L))^2]}\right).$$

Next, using a Taylor expansion around τ, one can write

$$P(Y\leq\hat{\zeta}|A,L)=\tau+f(\zeta|A,L)(\hat{\zeta}-\zeta)+O_p\{(\hat{\zeta}-\zeta)^2\}.$$

This reduces the remaining terms to

$$\frac{1}{\hat{E}[(A-\hat{E}(A|L))^2]}\left(\mathbb{P}\left[(A-\hat{E}(A|L))\Big\{\hat{\zeta}-\hat{E}(\hat{\zeta}|L)-\frac{f(\zeta|A,L)}{\hat{f}(\hat{\zeta}|A,L)}(\hat{\zeta}-\zeta)+O_p\{(\hat{\zeta}-\zeta)^2\}\Big\}\right]\right.$$
$$\left.-\,\mathbb{P}\left[(A-E(A|L))\Big\{\zeta-E(\zeta|L)\Big\}\right]\frac{\mathbb{P}[(A-\hat{E}(A|L))^2]}{\mathbb{P}[(A-E(A|L))^2]}\right)$$
$$= \frac{1}{\hat{E}[(A-\hat{E}(A|L))^2]}\left(\mathbb{P}\left[(A-\hat{E}(A|L))\Big\{\zeta-\hat{E}(\hat{\zeta}|L)-\left(\frac{f(\zeta|A,L)}{\hat{f}(\hat{\zeta}|A,L)}-1\right)(\hat{\zeta}-\zeta)+O_p\{(\hat{\zeta}-\zeta)^2\}\Big\}\right]\right.$$
$$\left.-\,\mathbb{P}\left[(A-E(A|L))\Big\{\zeta-E(\zeta|L)\Big\}\right]\frac{\mathbb{P}[(A-\hat{E}(A|L))^2]}{\mathbb{P}[(A-E(A|L))^2]}\right)$$
$$= \frac{1}{\hat{E}[(A-\hat{E}(A|L))^2]}\left(\mathbb{P}\left[(A-E(A|L))\Big\{\zeta-\hat{E}(\hat{\zeta}|L)-\left(\frac{f(\zeta|A,L)}{\hat{f}(\hat{\zeta}|A,L)}-1\right)(\hat{\zeta}-\zeta)+O_p\{(\hat{\zeta}-\zeta)^2\}\Big\}\right]\right.$$
$$+\,\mathbb{P}\left[(E(A|L)-\hat{E}(A|L))\Big\{\zeta-\hat{E}(\hat{\zeta}|L)-\left(\frac{f(\zeta|A,L)}{\hat{f}(\hat{\zeta}|A,L)}-1\right)(\hat{\zeta}-\zeta)+O_p\{(\hat{\zeta}-\zeta)^2\}\Big\}\right]$$
$$-\,\mathbb{P}\left[(A-E(A|L))\Big\{\zeta-E(\zeta|L)\Big\}\right]$$
$$\left.+\left(1-\frac{\mathbb{P}[(A-\hat{E}(A|L))^2]}{\mathbb{P}[(A-E(A|L))^2]}\right)\mathbb{P}\left[(A-E(A|L))\Big\{\zeta-E(\zeta|L)\Big\}\right]\right)$$
$$= \frac{1}{\hat{E}[(A-\hat{E}(A|L))^2]}\left(\mathbb{P}\left[(A-E(A|L))\Big\{-\hat{E}(\hat{\zeta}|L)-\left(\frac{f(\zeta|A,L)}{\hat{f}(\hat{\zeta}|A,L)}-1\right)(\hat{\zeta}-\zeta)+O_p\{(\hat{\zeta}-\zeta)^2\}\Big\}\right]\right.$$
$$\left.+\,\mathbb{P}\left[(E(A|L)-\hat{E}(A|L))\Big\{\zeta-\hat{E}(\hat{\zeta}|L)-\left(\frac{f(\zeta|A,L)}{\hat{f}(\hat{\zeta}|A,L)}-1\right)(\hat{\zeta}-\zeta)+O_p\{(\hat{\zeta}-\zeta)^2\}\Big\}\right]\right.$$

$$
\begin{aligned}
&\quad - \mathbb{P}\left[(A - E(A|L))\Big\{ - E(\zeta|L)\Big\}\right] \\
&\quad + \left(1 - \frac{\mathbb{P}[(A - \hat{E}(A|L))^2]}{\mathbb{P}[(A - E(A|L))^2]}\right) \mathbb{P}\left[(A - E(A|L))\Big\{\zeta - E(\zeta|L)\Big\}\right] \Bigg) \\
&= \frac{1}{\hat{E}[(A - \hat{E}(A|L))^2]} \Bigg(\mathbb{P}\left[(A - E(A|L))\Big\{O_p\{(\hat{\zeta} - \zeta)^2\} - \left(\frac{f(\zeta|A,L)}{\hat{f}(\hat{\zeta}|A,L)} - 1\right)(\hat{\zeta} - \zeta)\Big\}\right] \\
&+ \mathbb{P}\left[(E(A|L) - \hat{E}(A|L))\Big\{\zeta - \hat{E}(\hat{\zeta}|L) + E(\zeta|L) - E(\zeta|L) - \left(\frac{f(\zeta|A,L)}{\hat{f}(\hat{\zeta}|A,L)} - 1\right)(\hat{\zeta} - \zeta) + O_p\{(\hat{\zeta} - \zeta)^2\}\Big\}\right] \\
&\quad + \left(1 - \frac{\mathbb{P}[(A - \hat{E}(A|L))^2]}{\mathbb{P}[(A - E(A|L))^2]}\right) \mathbb{P}\left[(A - E(A|L))\Big\{\zeta - E(\zeta|L)\Big\}\right] \Bigg) \\
&= \frac{1}{\hat{E}[(A - \hat{E}(A|L))^2]} \Bigg(\mathbb{P}\left[(A - E(A|L))\Big\{O_p\{(\hat{\zeta} - \zeta)^2\} - \left(\frac{f(\zeta|A,L)}{\hat{f}(\hat{\zeta}|A,L)} - 1\right)(\hat{\zeta} - \zeta)\Big\}\right] \\
&\quad + \mathbb{P}\left[(E(A|L) - \hat{E}(A|L))\Big\{\zeta - E(\zeta|L) - \left(\frac{f(\zeta|A,L)}{\hat{f}(\hat{\zeta}|A,L)} - 1\right)(\hat{\zeta} - \zeta) + O_p\{(\hat{\zeta} - \zeta)^2\}\Big\}\right] \\
&\quad + \mathbb{P}\left[(E(A|L) - \hat{E}(A|L))\Big\{E(\zeta|L) - \hat{E}(\hat{\zeta}|L)\Big\}\right] \\
&\quad + \left(1 - \frac{\mathbb{P}[(A - \hat{E}(A|L))^2]}{\mathbb{P}[(A - E(A|L))^2]}\right) \mathbb{P}\left[(A - E(A|L))\Big\{\zeta - E(\zeta|L)\Big\}\right] \Bigg) \\
&= \frac{1}{\hat{E}[(A - \hat{E}(A|L))^2]} \Bigg(\mathbb{P}\left[(A - E(A|L))\Big\{O_p\{(\hat{\zeta} - \zeta)^2\} - \left(\frac{f(\zeta|A,L)}{\hat{f}(\hat{\zeta}|A,L)} - 1\right)(\hat{\zeta} - \zeta)\Big\}\right] \\
&\quad + \mathbb{P}\left[(E(A|L) - \hat{E}(A|L))\Big\{O_p\{(\hat{\zeta} - \zeta)^2\} - \left(\frac{f(\zeta|A,L)}{\hat{f}(\hat{\zeta}|A,L)} - 1\right)(\hat{\zeta} - \zeta)\Big\}\right] \\
&\quad + \mathbb{P}\left[(E(A|L) - \hat{E}(A|L))\Big\{E(\zeta|L) - \hat{E}(\hat{\zeta}|L)\Big\}\right] \\
&\quad + \left(1 - \frac{\mathbb{P}[(A - E(A|L) + E(A|L) - \hat{E}(A|L))^2]}{\mathbb{P}[(A - E(A|L))^2]}\right) \mathbb{P}\left[(A - E(A|L))\Big\{\zeta - E(\zeta|L)\Big\}\right] \Bigg) \\
&= \frac{1}{\hat{E}[(A - \hat{E}(A|L))^2]} \Bigg(\mathbb{P}\left[(A - \hat{E}(A|L))\Big\{O_p\{(\hat{\zeta} - \zeta)^2\} - \left(\frac{f(\zeta|A,L)}{\hat{f}(\hat{\zeta}|A,L)} - 1\right)(\hat{\zeta} - \zeta)\Big\}\right]
\end{aligned}
$$

$$
\begin{aligned}
&+ \mathbb{P}\left[(E(A|L) - \hat{E}(A|L))\Big\{E(\zeta|L) - \hat{E}(\hat{\zeta}|L)\Big\}\right] \\
&- \frac{\mathbb{P}[2(A - E(A|L))(E(A|L) - \hat{E}(A|L)) + (E(A|L) - \hat{E}(A|L))^2]}{\mathbb{P}[(A - E(A|L))^2]} \\
&\quad \times \mathbb{P}\left[(A - E(A|L))\Big\{\zeta - E(\zeta|L)\Big\}\right]\Bigg) \\
= \frac{1}{\hat{E}[(A - \hat{E}(A|L))^2]}&\Bigg(\mathbb{P}\left[(A - \hat{E}(A|L))O_p\{(\hat{\zeta} - \zeta)^2\}\right] + \mathbb{P}\left[(A - \hat{E}(A|L))\left(1 - \frac{f(\zeta|A,L)}{\hat{f}(\hat{\zeta}|A,L)}\right)(\hat{\zeta} - \zeta)\right] \\
&+ \mathbb{P}\left[(E(A|L) - \hat{E}(A|L))\Big\{E(\zeta|L) - \hat{E}(\hat{\zeta}|L)\Big\}\right] \\
&- \frac{\mathbb{P}[(E(A|L) - \hat{E}(A|L))^2]}{\mathbb{P}[(A - E(A|L))^2]}\mathbb{P}\left[(A - E(A|L))\Big\{\zeta - E(\zeta|L)\Big\}\right]\Bigg) \\
= \frac{1}{\hat{E}[(A - \hat{E}(A|L))^2]}&\Bigg(\mathbb{P}\left[(A - \hat{E}(A|L))O_p\{(\hat{\zeta} - \zeta)^2\}\right] + \mathbb{P}\left[(A - \hat{E}(A|L))\left(1 - \frac{f(\zeta|A,L)}{\hat{f}(\hat{\zeta}|A,L)}\right)(\hat{\zeta} - \zeta)\right] \\
&+ \mathbb{P}\left[(E(A|L) - \hat{E}(A|L))\Big\{E(\zeta|L) - \hat{E}(\hat{\zeta}|L)\Big\}\right] - \mathbb{P}[(E(A|L) - \hat{E}(A|L))^2]\Psi_\tau\Bigg).
\end{aligned}
$$

Assuming $A - \hat{E}(A|L) = O_p(1)$ and using the Cauchy-Schwarz inequality, the term R_2 is $o_p(n^{-1/2})$ under the following conditions:

$$
\begin{aligned}
\mathbb{P}\left[(\hat{Q}_\tau(Y|A,L) - Q_\tau(Y|A,L))^2\right] &= o_p(n^{-1/2}), \\
\mathbb{P}\left[\left(1 - \frac{f\{Q_\tau(Y|A,L)|A,L\}}{\hat{f}(\hat{Q}_\tau(Y|A,L)|A,L)}\right)^2\right]^{1/2} \mathbb{P}\left[(\hat{Q}_\tau(Y|A,L) - Q_\tau(Y|A,L))^2\right]^{1/2} &= o_p(n^{-1/2}), \\
\mathbb{P}\left[(E(A|L) - \hat{E}(A|L))^2\right]^{1/2}\mathbb{P}\left[\Big(E(Q_\tau(Y|A,L)|L) - \hat{E}(\hat{Q}_\tau(Y|A,L)|L)\Big)^2\right]^{1/2} &= o_p(n^{-1/2}), \\
\mathbb{P}\left[(E(A|L) - \hat{E}(A|L))^2\right] &= o_p(n^{-1/2}).
\end{aligned}
$$

Note that if $\Psi_\tau = 0$, the final condition is redundant.

S6 Sketch of a proof that the sum in (3.6) is $o_P(n^{-1/2})$

Here, we give a sketch of a proof that

$$\frac{1}{n}\sum_{i=1}^{n}\Big(A_i - \hat{E}(A_i|L_i)\Big)\left[\frac{\tau - I\{Y_i \leq \widetilde{Q}_\tau(Y_i|A_i,L_i)\}}{\hat{f}(\widetilde{Q}_\tau(Y_i|A_i,L_i)|A_i,L_i)}\right] = o_P(n^{-1/2}).$$

We consider

$$\widetilde{Q}_\tau(Y|A,L) = \hat{Q}_\tau(Y|A,L) + \epsilon w(\hat{Q}_{\tau,i}),$$

with $w(\hat{Q}_{\tau,i})$ defined as in (3.7). Thus, the aim is to prove that

$$\frac{1}{n}\sum_{i=1}^{n} w(\hat{Q}_{\tau,i})\Big[\tau - I\{Y_i \leq \hat{Q}_\tau(Y_i|A_i,L_i) + \epsilon w(\hat{Q}_{\tau,i})\}\Big] \tag{S6.1}$$

is $o_P(n^{-1/2})$.

One can control the sign of (S6.1) by changing the value of ϵ. Indeed, for $\epsilon \to +\infty$ and $w(\hat{Q}_{\tau,i}) \geq 0$, we have

$$w(\hat{Q}_{\tau,i})\Big[\tau - I\{Y_i \leq \hat{Q}_\tau(Y_i|A_i,L_i) + \epsilon w(\hat{Q}_{\tau,i})\}\Big] = w(\hat{Q}_{\tau,i})(\tau - 1) \leq 0.$$

For $\epsilon \to +\infty$ and $w(\hat{Q}_{\tau,i}) \leq 0$, we have

$$w(\hat{Q}_{\tau,i})\Big[\tau - I\{Y_i \leq \hat{Q}_\tau(Y_i|A_i,L_i) + \epsilon w(\hat{Q}_{\tau,i})\}\Big] = w(\hat{Q}_{\tau,i})\tau \leq 0,$$

such that

$$\lim_{\epsilon\to+\infty}\frac{1}{n}\sum_{i=1}^{n} w(\hat{Q}_{\tau,i})\Big[\tau - I\{Y_i \leq \hat{Q}_\tau(Y_i|A_i,L_i) + \epsilon w(\hat{Q}_{\tau,i})\}\Big] \leq 0.$$

Analogously, one can show

$$\lim_{\epsilon\to-\infty}\frac{1}{n}\sum_{i=1}^{n} w(\hat{Q}_{\tau,i})\Big[\tau - I\{Y_i \leq \hat{Q}_\tau(Y_i|A_i,L_i) + \epsilon w(\hat{Q}_{\tau,i})\}\Big] \geq 0.$$

By slightly adjusting the value of ϵ, terms from the summation can change from $w(\hat{Q}_{\tau,i})(\tau-1)$ to $w(\hat{Q}_{\tau,i})\tau$ or vice versa. Changing one term leads to a change of (S6.1) of magnitude $\frac{w(\hat{Q}_{\tau,i})}{n}$. This implies that we can get (S6.1) within a distance $|\frac{w(\hat{Q}_{\tau,i})}{n}|$ of 0. In Theorem 2 we assume that $A - \hat{E}(A|L) = O_p(1)$ and $\hat{f}(Q_\tau(Y|A,L)|A,L) > \sigma$ with probability 1 for some $\sigma > 0$, which implies that $w(\hat{Q}_{\tau,i}) = O_P(1)$. Consequently, we have that (S6.1) is $O_P(1/n)$ and thus $o_p(n^{-1/2})$. Potentially, multiple terms change at the same time. However, as we implicitly assume Y_i to be absolutely continuous w.r.t. the Lebesgue measure, the same holds for $\{Y_i - \hat{Q}_\tau(Y_i|A_i,L_i)\}/w(\hat{Q}_{\tau,i})$. Thus the event that multiple terms change at the same time occurs with probability zero.

S7 More details about the TMLE estimator

To estimate $E\{Q_\tau(Y|A,L)|L\}$, one would first need to estimate $Q_\tau(Y|A,L)$. Then, based on these estimates, one can estimate $E\{Q_\tau(Y|A,L)|L\}$ by taking the quantile estimates as the outcome for a model that predicts its conditional expectation given L. However, when the exposure A is binary, this conditional expectation reduces to

$$Q_\tau(Y|A=1,L)E(A|L) + Q_\tau(Y|A=0,L)\{1-E(A|L)\}. \tag{S7.2}$$

This allows us to estimate this nuisance parameter without additionally modeling the conditional expectation of $Q_\tau(Y|A,L)$ given L, because $Q_\tau(Y|A,L)$ and $E(A|L)$ need to be modeled anyway. Furthermore, targeted learning with cross-fitting can easily be applied in this case, as

$$\hat{E}\{\widetilde{Q}_\tau(Y|A,L)|L\} = \widetilde{Q}_\tau(Y|A=1,L)\hat{E}(A|L) + \widetilde{Q}_\tau(Y|A=0,L)\{1-\hat{E}(A|L)\}.$$

On the contrary, decomposition (S7.2) cannot be made for a continuous exposure. It is then necessary to have an additional model for $E\{Q_\tau(Y|A,L)|L\}$.

Since the retargeting of $\hat{Q}_\tau(Y|A,L)$ is done on the full data set, it is no longer possible to do proper cross-fitting for $E\{Q_\tau(Y|A,L)|L\}$. In that case, a model to estimate the conditional expectation of $\widetilde{Q}_\tau(Y|A,L)$ given L should be trained using only 80% of the data, but $\widetilde{Q}_\tau(Y|A,L)$ would already have been targeted using all data. This makes it no longer possible to train a model for $E\{\widetilde{Q}_\tau(Y|A,L)|L\}$ without involving the remaining 20% of the data. One way to resolve this problem is to do the

targeting in each fold separately. However, forcing equation (3.6) to hold in every fold does not guarantee that it holds for the entire data set, especially in smaller samples. Alternatively, one could choose not to target the quantile estimator in $E\{Q_\tau(Y|A,L)|L\}$. However, instead of repeating the targeting algorithm in Section 3.3 until convergence, we propose to do step 2 only once, which is justified by the sketched proof in S6. Thus, the resulting retargeted estimator for $Q_\tau(Y|A,L)$ will be

$$\widetilde{Q}_\tau(Y|A,L) = \hat{Q}_\tau(Y|A,L) + \hat{\epsilon} w(\hat{Q}_{\tau,i}),$$

with

$$\hat{\epsilon} = \arg\min_{\epsilon} \left| \frac{1}{n} \sum_{i=1}^{n} w\big(\hat{Q}_{\tau,i}\big) \left[\tau - I\left\{ Y_i \leq \hat{Q}_{\tau,i} + \epsilon w\big(\hat{Q}_{\tau,i}\big) \right\} \right] \right|. \tag{S7.3}$$

The nuisance parameter $E\{Q_\tau(Y|A,L)|L\}$ can then be estimated based on the following identity:

$$\begin{aligned} E\{\widetilde{Q}_\tau(Y|A,L)|L\} &= E\{\hat{Q}_\tau(Y|A,L) + \hat{\epsilon} w(\hat{Q}_{\tau,i})|L\} \\ &= E\{\hat{Q}_\tau(Y|A,L)|L\} + \hat{\epsilon} E\left[\frac{A - \hat{E}(A|L)}{\hat{f}\{\hat{Q}_\tau(Y|A,L)|A,L\}} |L \right]. \end{aligned} \tag{S7.4}$$

Therefore, an estimator can be constructed by estimating $E\{\hat{Q}_\tau(Y|A,L)|L\}$ and $E[\{A - \hat{E}(A|L)\}/\hat{f}\{Q_\tau(Y|A,L)|A,L\}|L]$ separately, possibly via cross-fitting. In this way, the value of ϵ can be learned via (S7.3) after estimating the 2 models in (S7.4) that determine $E\{Q_\tau(Y|A,L)|L\}$, which allows us to do the retargeting on the entire data set.

S8 More details about the construction of estimator (3.11)

Assume that a (stepwise) variable selection estimator for $Q_\tau(Y|A,L)$ has the following form:

$$\hat{Q}_\tau(Y|A,L) = \hat{\beta}_\tau A + \hat{\alpha}^T L^*,$$

with L^* consisting of a subset of variables of L. Retargeting

$$\widetilde{Q}_\tau(Y|A,L) = \hat{Q}_\tau(Y|A,L) + \hat{\epsilon} w(\hat{Q}_{\tau,i}),$$

then leads to:

$$\widetilde{Q}_\tau(Y|A,L) = \hat{\beta} A + \hat{\alpha}^T L^* + \epsilon \frac{A - \hat{E}(A|L)}{\hat{f}(\hat{Q}_\tau(Y|A,L)|A,L)}.$$

Then, one can obtain

$$\begin{aligned}
&\widetilde{Q}_\tau(Y|A,L) - E\Big(\widetilde{Q}_\tau(Y|A,L)\big|L\Big) \\
&= \hat{\beta} A + \hat{\alpha}^T L^* + \epsilon \frac{A - \hat{E}(A|L)}{\hat{f}(\hat{Q}_\tau(Y|A,L)|A,L)} - E\left(\hat{\beta} A + \hat{\alpha}^T L^* + \epsilon \frac{A - \hat{E}(A|L)}{\hat{f}(\hat{Q}_\tau(Y|A,L)|A,L)}\big|L\right) \\
&= \hat{\beta}(A - \hat{E}(A|L)) + \epsilon \left\{ \frac{A - \hat{E}(A|L)}{\hat{f}(\widetilde{Q}_\tau(Y|A,L)|A,L)} - E\left(\frac{A - \hat{E}(A|L)}{\hat{f}(\widetilde{Q}_\tau(Y|A,L)|A,L)}\right)\right\}
\end{aligned}$$

which allows us to construct a TMLE estimator as follows:

$$\begin{aligned}
\hat{\Psi}_\tau^{TMLE} &= \frac{1}{n}\sum_{i=1}^n \frac{A_i - \hat{E}(A_i|L_i)}{\frac{1}{n}\sum_{i=1}^n (A_i - \hat{E}(A_i|L_i))^2} \Bigg[\widetilde{Q}_\tau(Y_i|A_i,L_i) \\
&\qquad - \hat{E}\Big(\widetilde{Q}_\tau(Y_i|A_i,L_i)\big|L_i\Big) + \frac{\tau - I\{Y_i \le \widetilde{Q}_\tau(Y_i|A_i,L_i)\}}{\hat{f}(\widetilde{Q}_\tau(Y_i|A_i,L_i)|A_i,L_i)}\Bigg] \\
&= \hat{\beta} + \frac{1}{n}\sum_{i=1}^n \frac{A_i - \hat{E}(A_i|L_i)}{\frac{1}{n}\sum_{i=1}^n (A_i - \hat{E}(A_i|L_i))^2} \Bigg[\epsilon \Bigg\{ \frac{A_i - \hat{E}(A_i|L_i)}{\hat{f}(\widetilde{Q}_\tau(Y_i|A_i,L_i)|A_i,L_i)}
\end{aligned}$$

$$- \hat{E}\left(\frac{A_i - \hat{E}(A_i|L_i)}{\hat{f}(\widetilde{Q}_\tau(Y_i|A_i,L_i)|A_i,L_i)}\Big|L_i\right)\Bigg\} + \frac{\tau - I\{Y_i \leq \widetilde{Q}_\tau(Y_i|A_i,L_i)\}}{\hat{f}(\widetilde{Q}_\tau(Y_i|A_i,L_i)|A_i,L_i)}\Bigg].$$

Similarly to (3.8), the last term will be approximately zero.

S9 Simulations

S9.1 Data-generating mechanisms for the simulation experiments

Experiment 1 and 2

In the first setting of experiment 1, the data was generated as follows, inspired by a setting used in Sun et al. (2021). Some minor adjustments were made to prevent the coefficient of determination (R^2) from exceeding 0.8, as this is often unrealistic. Four confounding variables were generated according to

$$\begin{pmatrix} L_1 \\ L_2 \\ L_3 \\ L_4 \end{pmatrix} \sim \mathcal{N} \left\{ \begin{pmatrix} 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}, \begin{pmatrix} 1 & 0.5 & 0.2 & 0.3 \\ 0.5 & 1 & 0.7 & 0 \\ 0.2 & 0.7 & 1 & 0 \\ 0.3 & 0 & 0 & 1 \end{pmatrix} \right\}. \tag{D.1.1.1}$$

The dichotomous exposure A follows a Bernoulli distribution conditional on $L = (L_1, L_2, L_3, L_4)$, with true propensity score given by $P(A = 1|L) = \text{expit}(-0.5 + 0.2L_1 - 0.4L_2 - 0.4L_3 + 0.2L_4)$.

In the homoscedastic setting, the outcome Y was generated as

$$Y = 1 + A + \sin(L_1) + L_2^2 + L_3 + L_4 + L_3L_4 + \epsilon, \tag{D.1.1.2}$$

where ϵ follows a Gamma(k, θ) distribution with shape parameter $k = 1$ and scale parameter $\theta = 2$ and is independent from A and L. Under heteroscedasticity, we chose $\epsilon \sim \text{Gamma}(1, 2 + A)$.

In the third setting of experiment 1, we studied the proposed estimators' finite sample behaviour for a continuous exposure. Here, A was generated according to a normal distribution $\mathcal{N}(\mu, 2^2)$, with $\mu = -0.5 + L_1 - 2L_2 - 2L_3 + L_4$. The outcome Y was generated from (D.1.1.2), where $\epsilon \sim \text{Gamma}(1, 4)$ is independent from A and L.

In experiment 2, we generated a setting where the propensity scores could take extreme values (i.e., values close to 0 or 1), leading to little overlap between exposed and unexposed individuals. Therefore, we generated a dichotomous exposure A, with $P(A = 1|L) = \text{expit}(-0.5 + 0.2L_1 - 0.4L_2 - 0.4L_3 + 0.2L_4 + 0.5L_1^2 - 0.5L_2^2 + 0.5L_3L_4)$, where L follows the same multivariate normal distribution (D.1.1.1) as in experiment 1. The outcome was generated according to (D.1.1.2), with $\epsilon \sim \text{Gamma}(1, 3)$. To gain insight into these propensity scores, histograms are provided below. The left histogram shows a histogram of the propensity scores used in experiment 1 (with binary A). On the right, a histogram of the propensity scores from experiment 2 is shown. Each time, a sample of size 100,000 was generated according to the two data-generating mechanisms. Then a histogram of the propensity scores was constructed. It is clear that more extreme propensity scores occur in experiment 2.

Experiment 3

In this experiment, we first chose the exposure to be randomized with $P(A = 1) = 0.5$, independently from all other variables. Baseline covariates follow the same multi-

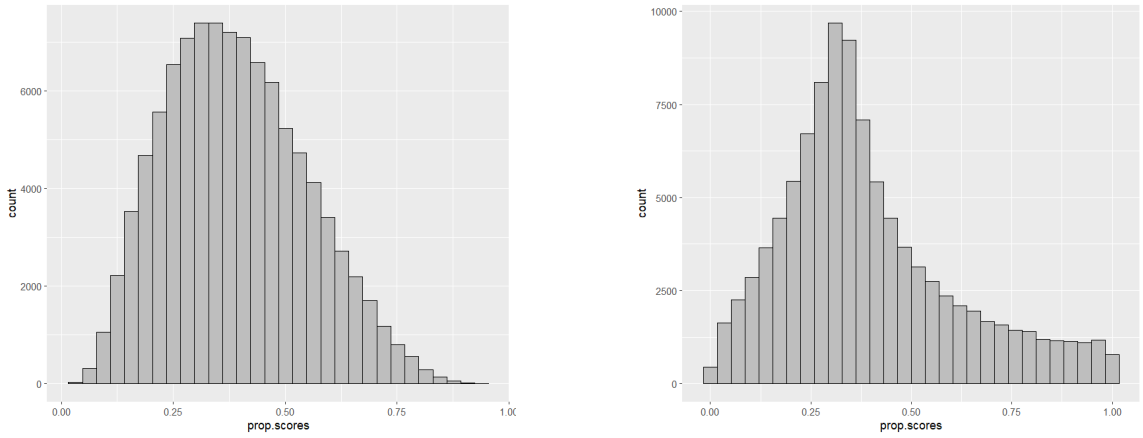

Figure 1: Propensity score histograms corresponding to the binary exposure settings of experiment 1 (left) and experiment 2 (right).

variate normal distribution (D.1.1.1) as in experiment 1. The outcome was generated from (D.1.1.2), again with $\epsilon \sim \text{Gamma}(1, 2)$.

Experiment 4

In this simulation experiment, we considered a covariate vector of dimension 50, based on the data-generating mechanism in Belloni et al. (2013). In particular, we generated a 50-dimensional covariate vector $L \sim \mathcal{N}(0, \Sigma)$, where Σ was an autoregressive correlation matrix with correlation parameter 0.5. A continuous exposure was generated according to a normal distribution with mean $\sum_{k=1}^{10} L_k/k$ and unit residual variance. The outcome Y was generated from $Y = A + \sum_{k=1}^{5} L_k/k + \sum_{k=11}^{15} L_k/(k-10) + \epsilon$, with $\epsilon \sim \mathcal{N}(0, 2^2)$ independent from A and L.

S9.2 Additional simulation results for experiment 1

This experiment consisted of three simulation settings, where the data generating mechanism was each time slightly changed. In setting 1, we studied the proposed estimators' behaviour for a binary exposure and a homoscedastic outcome where the exposure effect had the same magnitude for all quantiles. In setting 2, we adjusted the setting slightly so that the outcome variability differed for both exposure groups. This implies that the exposure effect is different for different values of τ. In setting 3, the exposure was continuous. The results are shown in Table 1.

For all estimators except CSQR, quantile random forests (via the 'grf' package described in Athey et al. (2019)) were used to learn $Q_\tau(Y|A, L)$. To learn $E(A|L)$, SuperLearner was used; this is an ensemble learner described in van der Laan et al. (2007). The SuperLearner library included generalized linear models with and without elastic net regularization, generalized additive models, and random forests. These estimators were also used to estimate $E\{Q_\tau(Y|A, L)|L\}$ based on the decomposition (S7.2). To obtain the nuisance parameter $f\{Q_\tau(Y|A, L)|A, L\}$, we estimated the conditional density of Y given A and L via the 'fk_density' function from the R package 'FKSUM' (Hofmeyr, 2021, 2022). This function gives a fast approximation of a univariate density based on recursive computations in evaluation points of choice. Since our interest lies in estimating a conditional density function, we estimated the density of $Y - Q_\tau(Y|A, L)$ and evaluated it at 0. This estimation procedure assumes

that the distribution of $Y - Q_\tau(Y|A, L)$ is independent of A and L. An alternative way of estimating the conditional density is explained below.

In the third setting of this experiment, we studied the proposed estimators' finite sample behaviour for a continuous exposure. The nuisance parameters were all estimated as before, except for $E\{Q_\tau(Y|A, L)|L\}$ as the decomposition (S7.2) is no longer possible for continuous A. To estimate this parameter, we again used SuperLearner with the same library as before, using the random forest estimate of $Q_\tau(Y|A, L)$ as outcome. For the TMLE-CF estimator, the nuisance parameters described at the end of Section 3.4 are also estimated using SuperLearner.

Setting	**estimator**	$\tau = 0.5$				$\tau = 0.75$				$\tau = 0.9$			
		bias	**SD**	**SE**	**Cov**	**bias**	**SD**	**SE**	**Cov**	**bias**	**SD**	**SE**	**Cov**
1	CSQR	-0.17	19	20	96.6	-0.51	33	35	96.3	-1.1	56	60	96.0
	Plug-in	-70	12	1.5	0.1	-72	14	1.8	0.5	-64	22	3.6	1.6
	DML	-15	19	19	85.9	-35	29	25	63.7	-56	32	22	33.0
	DML-CF	-16	18	18	84.2	-24	28	25	79.2	-31	43	35	77.4
	TMLE	-41	21	19	45.2	-71	32	26	27.0	-110	28	45	12.6
	TMLE-CF	1.2	22	25	97.2	2.8	39	37	93.5	14	68	63	91.4
2	CSQR	-0.59	26	26	93.7	-2.7	45	46	93.6	-6.8	75	78	94.4
	Plug-in	-89	26	2.7	0.6	-120	42	4.1	1.1	-160	60	6.8	1.5
	DML	-15	27	22	83.0	-45	46	30	57.8	-120	66	28	16.5
	DML-CF	-20	26	20	75.6	-43	43	30	61.7	-78	69	42	49.6
	TMLE	-45	27	23	49.4	-76	49	32	38.0	-195	67	34	4.0
	TMLE-CF	5.0	29	28	93.9	10	50	42	88.7	13	88	70	87.6
3	CSQR	-0.13	3.5	3.6	95.6	-0.29	5.8	6.3	95.8	0.10	10	11	94.6
	Plug-in	-17	6.4	1.6	0.5	-25	7.9	1.9	0.2	-39	11	2.1	0.0
	DML	-7.9	6.8	3.6	45.1	-16	8.5	4.6	21.6	-34	11	4.3	1.7
	DML-CF	-6.2	3.9	3.1	48.5	-10	6.0	4.4	40.0	-19	9.1	6.2	23.0
	TMLE	-11	7.1	3.6	29.3	-18	9.3	4.9	18.9	-41	12	5.2	1.6
	TMLE-CF	-1.1	4.4	4.2	92.9	0.016	7.7	6.3	90.0	1.2	14	10	85.3

Table 1: Simulation results for experiment 1: sample size $n = 500$, quantile τ, Monte Carlo bias, Monte Carlo standard deviation (SD), average of the influence function based standard errors (SE) and coverage of 95% Wald confidence intervals (Cov). All values have been multiplied by 10^2.

Experiment 1 was partially carried out with the computationally more expensive 'haldensify' estimator for the conditional density of Y given A and L. This could be done via the 'haldensify' package (Hejazi et al., 2022), which uses the highly adaptive lasso (HAL) (Benkeser and Van Der Laan, 2016; van der Laan, 2017). This conditional density could then be evaluated in the estimated quantile without making any additional assumptions. In setting 3 we did not consider a TMLE estimator because this was computationally too heavy. The results are shown in Table 2.

In general, the DML(-CF) estimator performs better when using this conditional density estimator. However, the TMLE-CF estimator performs better when using the simpler 'FKSUM' density estimator, especially for more extreme quantiles. TMLE shows much larger bias than TMLE-CF because the TMLE targeting step depends heavily on estimated nuisance functions (in particular the conditional density evaluated at the estimated quantile). When nuisances are estimated on the same data used for targeting, overfitting bias can be amplified through the TMLE update. Cross-fitting eliminates the dependence between nuisance estimation and the target update, greatly reducing this bias.

Table 3 shows a summary of the term we tried to make zero with targeted learning (3.6). When using cross-fitting, we observe that this term is very close to zero, averaging over all simulation runs.

The TMLE(-CF) estimator for continuous exposure was adjusted such that only

Setting	estimator	$\tau = 0.5$				$\tau = 0.75$				$\tau = 0.9$			
		bias	**SD**	**SE**	**Cov**	**bias**	**SD**	**SE**	**Cov**	**bias**	**SD**	**SE**	**Cov**
1	CSQR	0.21	19	20	97.4	-1.2	33	35	95.3	-2.9	57	60	95.7
	Plug-in	-70	13	1.5	0.1	-73	14	1.8	0.1	-63	23	3.5	0.2
	DML	-3.6	25	22	91.0	-6.6	42	32	83.6	-32	40	35	79.5
	DML-CF	-5.9	22	21	91.9	-17	33	30	86.8	-40	36	25	59.2
	TMLE	-39	25	23	58.8	-69	41	33	44.7	-140	66	45	15.1
	TMLE-CF	-1.4	24	24	95.3	-1.4	39	30	85.6	15	76	24	47.8
2	CSQR	0.044	25	26	94.6	-0.025	44	45	94.6	-4.0	74	79	95.3
	Plug-in	-87	27	2.8	0.5	-120	40	4.1	1.0	-150	59	6.8	1.3
	DML	3	32	27	90.7	-11	55	39	78.5	-97	64	42	39.3
	DML-CF	-5.0	28	24	88.0	-34	43	33	74.0	-110	60	26	15.2
	TMLE	-39	30	29	70.0	-92	57	43	44.1	-210	72	51	6.3
	TMLE-CF	7.0	31	28	91.6	6.5	49	33	82.3	32	89	25	40.9
3	CSQR	0.19	3.4	3.6	94.6	-0.11	6.2	6.3	94.0	-0.30	10	11	94.9
	Plug-in	-17	6.4	1.6	1.5	-25	8.2	1.9	0.5	-39	11	2.1	0.3
	DML	-5.2	7.1	4.2	63.4	-8.1	9.3	5.8	60.8	-33	11	4.5	2.6
	DML-CF	-4.8	4.0	3.4	66.7	-13	5.7	3.4	13.4	-2.8	8.1	3.1	0.5

Table 2: Simulation results for experiment 1 with density estimated via the 'haldensify' R package: sample size 500, Monte Carlo bias, Monte Carlo standard deviation (SD), average of the influence function based standard errors (SE) and coverage of 95% Wald confidence intervals (Cov). All values have been multiplied by 10^2.

	TMLE	TMLE-CF
Minimum	-0.22	-0.059
1st Quartile	-0.087	-0.0029
Median	-0.0028	0.00013
Mean	-0.036	0.00023
3rd Quartile	0.00013	0.0033
Maximum	0.20	0.064

Table 3: Summary of the term we wish to make zero with targeted learning (3.6) for the homoscedastic setting in experiment 1.

1 targeting step was carried out. For binary exposure, this step was repeated until convergence. In Table 4, we show the results of the 1-step TMLE estimator for binary exposure (experiment 1, setting 1). Comparing these results with the results in Table 1, it can be observed that 1-step targeting does not achieve the same performance as targeting until convergence.

Quantile	estimator	bias	SD	SE	Cov
0.5	TMLE.1	-0.38	0.25	0.19	44.6
	TMLE.1-CF	0.082	0.27	0.18	83.0
0.75	TMLE.1	-0.71	0.34	0.25	25.2
	TMLE.1-CF	0.10	0.44	0.25	73.7
0.9	TMLE.1	-1.1	0.47	0.27	14.0
	TMLE.1-CF	0.16	0.75	0.34	62.2

Table 4: Simulation results for the homoscedasticity setting in experiment 1 with the 1-step TMLE estimator: sample size $n = 500$, quantile τ, Monte Carlo bias, Monte Carlo standard deviation (SD), average of the influence function based standard errors (SE) and coverage of 95% Wald confidence intervals (Cov).

S9.3 Additional simulation results for experiment 2

In this experiment, we generated a setting where the propensity scores could take extreme values (i.e. values close to 0 or 1), leading to little overlap between exposed and unexposed individuals. We evaluated the same estimators as in experiment 1 and included a naive (misspecified) quantile regression model (QR) that only included main effects. The results are shown in Table 5.

S9.4 Additional simulation information for experiment 3

Athey et al. (2023) estimate so-called weighted average quantile treatment effects

$$\int_0^1 \left\{ Q_\tau(Y^1) - Q_\tau(Y^0) \right\} \, \mathrm{d}W(\tau), \tag{S9.5}$$

for certain weights $W(\tau)$ that integrate to one, and $W(0) = 0$, $W(1) = 1$. The first estimator (IFB) is an influence function based estimator, derived from the efficient influence function of (S9.5) under a location shift model. It is a semiparametric efficient estimator for (S9.5). The second estimator (WAQ) is a weighted average

Sample size	estimator	$\tau = 0.5$				$\tau = 0.75$				$\tau = 0.9$			
		bias	**SD**	**SE**	**Cov**	**bias**	**SD**	**SE**	**Cov**	**bias**	**SD**	**SE**	**Cov**
500	CSQR	-0.30	29	30	94.6	0.68	51	52	94.8	-3.0	92	91	94.2
	QR	16	36	36	92.3	33	55	58	92.7	44	91	95	94.1
	Plug-in	-72	14	1.5	0.0	-74	17	2.0	0.4	-62	36	4.7	5.8
	DML	-12	32	33	93.1	-37	44	41	82.0	-56	54	35	54.0
	DML-CF	-21	27	25	85.3	-35	40	36	80.5	-39	63	46	74.7
	TMLE	-59	33	33	55.0	-97	45	43	35.1	-110	97	45	31.8
	TMLE-CF	-6.5	32	34	95.4	-13	55	52	92.9	-14	100	87	91.2
1000	CSQR	-0.089	20	21	95.6	0.37	36	37	95.0	-3.0	61	63	95.3
	QR	17	25	26	91.1	33	40	40	86.4	43	64	65	90.8
	Plug-in	-66	12	1.1	0.0	-69	16	1.5	0.2	-60	27	3.2	2.1
	DML	-14	21	22	90.5	-34	32	29	74.3	-57	36	23	34.0
	DML-CF	-22	19	17	73.6	-32	29	24	68.1	-41	43	29	59.7
	TMLE	-59	22	22	24.1	-100	33	30	9.7	-130	86	29	17.2
	TMLE-CF	-6.8	22	23	94.3	-9.5	39	37	93.0	-14	69	62	90.7

Table 5: Simulation results for experiment 2: sample size n, quantile τ, Monte Carlo bias, Monte Carlo standard deviation (SD), average of the influence function based standard errors (SE) and coverage of 95% Wald confidence intervals (Cov). All values have been multiplied by 10^2.

quantile estimator. It is a plug-in estimator for (S9.5):

$$\int_0^1 \left\{ \hat{Q}_\tau(Y^1) - \hat{Q}_\tau(Y^0) \right\} w_f(\tau) \, \mathrm{d}\tau,$$

where the weights $w_f(\tau)$ are such that they provide an efficient L-estimator under the location shift assumption and the assumption that the density f of the counterfactual outcome is known (see Athey et al. (2023) for details). Since these estimators assume a location shift, they are only implemented for estimating the median.

S9.5 Additional simulation results for experiment 4

Table 6 contains the results for the following estimators for the data generating mechanism described in experiment 4: the correctly specified quantile regression estimator (CSQR), the naive plug-in (Plug-in) estimator, the debiased machine learning esti-

mator (3.4) based on quantile random forests without cross-fitting (DML) and with 5-fold cross-fitting (DML-CF), the targeted learning estimator (3.8) without cross-fitting (TMLE) and with 5-fold cross-fitting (TMLE-CF). We furthermore included some adjusted estimators. One is obtained by performing quantile regression with AIC-based backward stepwise variable selection (QRvs). Another one is the debiased machine learning estimator defined in (3.10) where quantile random forests are replaced by quantile regression with AIC-based backward stepwise variable selection, once without cross-fitting (DMLvs) and once with 5-fold cross-fitting (DMLvs-CF). The third one is the TMLE estimator defined in (3.11), once without cross-fitting (TMLEvs) and once with 5-fold cross-fitting (TMLEvs-CF).

Quantile	estimator	n = 250				n = 500			
		bias	**SD**	**SE**	**Cov**	**bias**	**SD**	**SE**	**Cov**
	CSQR	0.66	15	16	96.0	0.25	10	11	95.7
	QRvs	2.4	17	16	91.9	0.36	12	11	92.8
	Plug-in	-36	11	3.6	0.9	-23	8.6	2.6	2.7
	DML	-12	20	20	90.1	-20	13	12	59.4
	DML-CF	6.6	16	15	90.9	4.0	10	10	92.1
$\tau = 0.5$	DMLvs	2.0	18	13	81.8	0.33	12	9.9	90.2
	DMLvs-CF	1.6	17	9.8	74.0	0.043	12	8.5	84.1
	TMLE	-33	18	20	61.0	-26	15	12	40.0
	TMLE-CF	19	20	22	87.7	8.5	13	15	92.8
	TMLEvs	-29	25	13	67.5	-0.49	15	10	81.7
	TMLEvs-CF	1.3	20	19	94.3	-0.32	13	12	94.8
	CSQR	-0.016	16	18	96.7	-0.54	12	12	95.0
	QRvs	-1.4	19	17	91.3	0.0095	13	12	93.2
	Plug-in	-42	12	4.1	1.1	-29	9.1	2.9	1.4
	DML	-19	20	19	77.8	-22	13	11	47.3
	DML-CF	-0.44	18	17	94.4	-2.3	12	11	92.3
$\tau = 0.75$	DMLvs	-0.78	20	12	77.2	-0.24	13	9.9	86.2
	DMLvs-CF	-0.90	18	10	72.7	-0.21	12	8.8	82.5
	TMLE	-41	21	20	45.0	-37	16	12	19.9
	TMLE-CF	16	24	24	88.5	5.7	16	16	93.7
	TMLEvs	-3.9	28	13	57.4	-1.1	17	9.9	72.5
	TMLEvs-CF	0.52	21	21	94.0	-0.28	14	13	93.5
	CSQR	-0.88	21	22	95.7	0.39	14	15	95.8
	QRvs	0.065	23	20	89.7	0.094	16	14	90.8
	Plug-in	-64	8.4	037	0.0	-50	7.5	3.1	0.0
	DML	-50	16	19	27.3	-46	9.1	9.1	0.8
	DML-CF	-9.0	25	26	93.0	-14	16	16	84.8
$\tau = 0.9$	DMLvs	-0.52	25	11	60.9	-0.23	17	9.3	73.8
	DMLvs-CF	0.41	20	11	73.0	0.021	14	9.5	80.7
	TMLE	-67	23	23	18.1	-67	16	13	3.1
	TMLE-CF	21	38	33	83.1	4.2	27	22	88.1
	TMLEvs	-6.1	41	11	30.4	-1.2	26	9.5	42.8
	TMLEvs-CF	0.21	24	24	94.4	-0.18	16	16	93.7

Table 6: Simulation results for variable selection: sample size n, quantile τ, Monte Carlo bias, Monte Carlo standard deviation (SD), average of the influence function based standard errors (SE) and coverage of 95% Wald confidence intervals (Cov). All values have been multiplied by 10^2.

S10 Data analysis

S10.1 Summary statistics of the data

We reanalysed an observational study to estimate annual health care and lost productivity costs associated with excess weight among the adult population in Belgium, using national health data. Gorasso et al. (2022) estimated the average difference in health care costs between individuals with underweight (BMI < 18.5) and normal weight ($18.5 \leq$ BMI < 25) versus overweight ($25 \leq$ BMI < 30) and obesity (BMI ≥ 30) using a linear main effect model. We used the proposed TMLE estimator (3.10) with 5-fold cross-fitting to assess the conditional association between health care cost and body weight (dichotomized as underweight and normal weight vs. overweight and obesity), considering the same set of candidate baseline variables as Gorasso et al. (2022).

From the 3818 individuals included in the analysis, 1878 belonged to the group with overweight or obesity and 1940 had normal weight or were underweight. Potential confounders were sex (hc04), being at risk due to a lack of leisure time physical activity (PA08_2), drinking sugared soft drinks daily (NH07_2), alcohol overconsumption (F $>$ 14 drinks/week; M $>$ 21 drinks/week) (AL05_4B), being a heavy daily smokers (20+ cigarettes/day), age (age3c), household educational level (ET_1) and household level of income (IN_1). Classic mean and propensity overlap weighted

mean with 95% confidence intervals are given in Table 7. We observe that the populations are very similar.

Variable	**Propsensity Overlap Population**	**Original Population**
hc04 (Woman)	0.513 (0.487, 0.539)	0.509 (0.493, 0.524)
PA08_2 (Yes)	0.753 (0.730, 0.775)	0.748 (0.735, 0.762)
NH07_2 (No)	0.775 (0.754, 0.796)	0.778 (0.765, 0.791)
AL05_4B (No)	0.938 (0.927, 0.950)	0.936 (0.928, 0.944)
TA07_3 (No)	0.930 (0.918, 0.942)	0.936 (0.928, 0.944)
age3c: 18–34 years	0.247 (0.222, 0.271)	0.250 (0.236, 0.264)
age3c: 35–65 years	0.544 (0.518, 0.570)	0.552 (0.537, 0.568)
age3c: ≥66 years	0.209 (0.188, 0.231)	0.198 (0.185, 0.210)
ET_1: No diploma or primary	0.059 (0.047, 0.072)	0.069 (0.061, 0.077)
ET_1: Lower secondary	0.121 (0.104, 0.139)	0.117 (0.106, 0.127)
ET_1: Higher secondary	0.339 (0.315, 0.364)	0.325 (0.310, 0.340)
ET_1: Higher education	0.480 (0.454, 0.506)	0.489 (0.473, 0.505)
IN_1: Quintile 1	0.109 (0.094, 0.124)	0.111 (0.101, 0.121)
IN_1: Quintile 2	0.141 (0.124, 0.158)	0.142 (0.131, 0.153)
IN_1: Quintile 3	0.208 (0.186, 0.229)	0.207 (0.194, 0.220)
IN_1: Quintile 4	0.254 (0.231, 0.278)	0.252 (0.239, 0.266)
IN_1: Quintile 5	0.288 (0.265, 0.312)	0.288 (0.274, 0.302)

Table 7: Comparison of means with 95% Confidence Intervals of the baseline covariates in the propensity overlap population and in the original population

These propensity overlap weighted mean estimates are obtained as follows. For each baseline covariate $X \subseteq L$ (with L the full set of baseline covariates), define

$$\theta = \frac{E\{P(A=1|L)P(A=0|L)X\}}{E\{P(A=1|L)P(A=0|L)\}}.$$

This is the corresponding weighted average of X. We can estimate θ based on its efficient influence function (under the nonparametric model), which is

$$\frac{\{A - P(A=1|L)\}^2(X-\theta)}{E\{P(A=1|L)P(A=0|L)\}} = \frac{\{A - E(A|L)\}^2(X-\theta)}{E[\{A-E(A|L)\}^2]}.$$

Similarly to the estimation strategy in the main paper, we obtain a debiased machine

learning estimator as

$$\hat{\theta} = \sum_{i=1}^{n} \frac{\{A_i - \hat{E}(A_i|L_i)\}^2 X_i}{\sum_{j=1}^{n} \{A_j - \hat{E}(A_j|L_j)\}^2}.$$

Confidence intervals are easily constructed based on its asymptotic normality (under sufficient rate conditions for the propensity score estimator) and the fact that its variance can be well-approximated by the sample variance of the influence functions.

S10.2 Sensitivity analysis for the data analysis

As shown by the simulation studies, the uncertainty of the proposed TMLE estimator is sometimes underestimated for extreme quantiles. Depending on how the folds in the cross-fitting procedure are chosen, the results may differ. We repeated the analysis for the 90th percentile 10 times with different seeds, once with 5-fold cross-fitting and once with 10-fold cross-fitting. The results are shown in Fig. 2

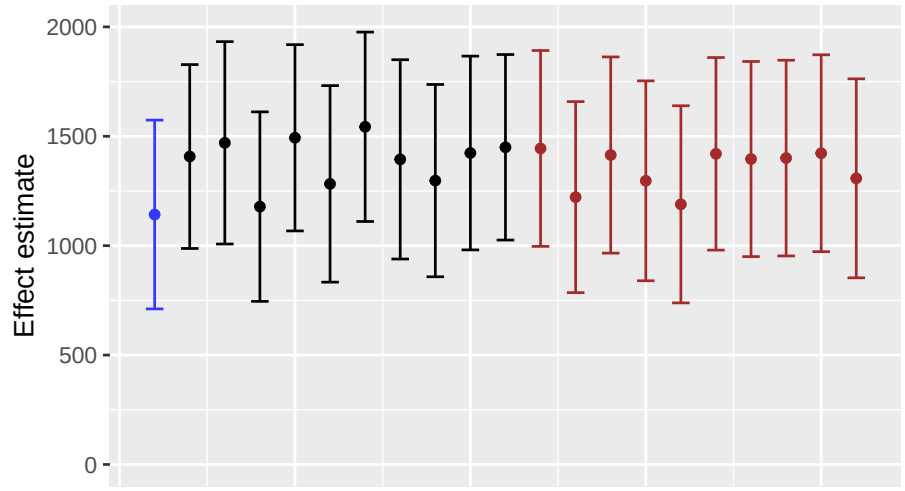

Figure 2: Repeating the analysis 10 times for the 90th percentile, once with 5 folds (shown in black), once with 10 folds (shown in brown). The blue interval corresponds to the one reported in Section 5.

S11 Debiased estimators for $E\{Q_\tau(Y|A=1,L)-Q_\tau(Y|A=0,L)\}$ and $\mathrm{Var}\{Q_\tau(Y|A=1,L)-Q_\tau(Y|A=0,L)\}$ for binary A

The efficient influence function of $E\{Q_\tau(Y|A=1,L)-Q_\tau(Y|A=0,L)\}$ equals

$$Q_\tau(Y|A=1,L)-Q_\tau(Y|A=0,L)-E\{Q_\tau(Y|A=1,L)-Q_\tau(Y|A=0,L)\}$$
$$+\frac{A}{\pi(L)}\frac{\tau-I\{Y\le Q_\tau(Y|A=1,L)\}}{f(Q_\tau(Y|A=1,L)|A=1,L)}-\frac{1-A}{1-\pi(L)}\frac{\tau-I\{Y\le Q_\tau(Y|A=0,L)\}}{f(Q_\tau(Y|A=0,L)|A=0,L)}.$$

A one-step estimator is then

$$\frac{1}{n}\sum_{i=1}^{n}\hat{Q}_\tau(Y_i|A_i=1,L_i)-\hat{Q}_\tau(Y_i|A_i=0,L_i)$$
$$+\frac{A_i}{\hat{\pi}(L_i)}\frac{\tau-I\{Y_i\le\hat{Q}_\tau(Y_i|A_i=1,L_i)\}}{\hat{f}(\hat{Q}_\tau(Y_i|A_i=1,L_i)|A_i=1,L_i)}-\frac{1-A_i}{1-\hat{\pi}(L_i)}\frac{\tau-I\{Y_i\le\hat{Q}_\tau(Y_i|A_i=0,L_i)\}}{\hat{f}(\hat{Q}_\tau(Y_i|A_i=0,L_i)|A_i=0,L_i)}.$$

In comparison, the debiased estimator (3.4) for dichotomous A for the weighted estimand reduces to

$$\frac{1}{n}\sum_{i=1}^{n}\frac{\{A_i-\hat{\pi}(L_i)\}^2}{\frac{1}{n}\sum_{i=1}^{n}\{A_i-\hat{\pi}(L_i)\}^2}\left\{\hat{Q}_\tau(Y_i|A_i=1,L_i)-\hat{Q}_\tau(Y_i|A_i=0,L_i)\right\}$$
$$+\frac{1}{n}\sum_{i=1}^{n}\frac{\hat{\pi}(L_i)\{1-\hat{\pi}(L_i)\}}{\frac{1}{n}\sum_{i=1}^{n}\{A_i-\hat{\pi}(L_i)\}^2}\left[\frac{A_i}{\hat{\pi}(L_i)}\frac{\tau-I\{Y_i\le\hat{Q}_\tau(Y_i|A_i=1,L_i)\}}{f(\hat{Q}_\tau(Y_i|A_i=1,L_i)|A_i=1,L_i)}\right.$$
$$\left.-\frac{1-A_i}{1-\hat{\pi}(L_i)}\frac{\tau-I\{Y_i\le\hat{Q}_\tau(Y_i|A_i=0,L_i)\}}{f(\hat{Q}_\tau(Y_i|A_i=0,L_i)|A_i=0,L_i)}\right].$$

The efficient influence function of $\mathrm{Var}\{Q_\tau(Y|A=1,L)-Q_\tau(Y|A=0,L)\}$ equals

$$[Q_\tau(Y|A=1,L)-Q_\tau(Y|A=0,L)-E\{Q_\tau(Y|A=1,L)-Q_\tau(Y|A=0,L)\}]^2$$
$$-\mathrm{Var}\{Q_\tau(Y|A=1,L)-Q_\tau(Y|A=0,L)\}$$
$$+2\left[Q_\tau(Y|A=1,L)-Q_\tau(Y|A=0,L)-E\{Q_\tau(Y|A=1,L)-Q_\tau(Y|A=0,L)\}\right]$$
$$\times\left\{\frac{A}{\pi(L)}\frac{\tau-I\{Y\le Q_\tau(Y|A=1,L)\}}{f(Q_\tau(Y|A=1,L)|A=1,L)}-\frac{1-A}{1-\pi(L)}\frac{\tau-I\{Y\le Q_\tau(Y|A=0,L)\}}{f(Q_\tau(Y|A=0,L)|A=0,L)}\right\}.$$

A one-step estimator is then

$$\frac{1}{n}\sum_{i=1}^{n}\left[\hat{Q}_\tau(Y_i|A_i=1,L_i)-\hat{Q}_\tau(Y_i|A_i=0,L_i)-\hat{E}\left\{\hat{Q}_\tau(Y_i|A_i=1,L_i)-\hat{Q}_\tau(Y_i|A_i=0,L_i)\right\}\right]^2$$
$$+2\frac{1}{n}\sum_{i=1}^{n}\left[\hat{Q}_\tau(Y_i|A_i=1,L_i)-\hat{Q}_\tau(Y_i|A_i=0,L_i)-\hat{E}\left\{\hat{Q}_\tau(Y_i|A_i=1,L_i)-\hat{Q}_\tau(Y_i|A_i=0,L_i)\right\}\right]$$

$$\times \left\{ \frac{A_i}{\pi(L_i)} \frac{\tau - I\{Y_i \leq \hat{Q}_\tau(Y_i|A_i=1,L_i)\}}{\hat{f}(\hat{Q}_\tau(Y_i|A_i=1,L_i)|A_i=1,L_i)} - \frac{1-A_i}{1-\pi(L_i)} \frac{\tau - I\{Y_i \leq \hat{Q}_\tau(Y_i|A_i=0,L_i)\}}{\hat{f}(\hat{Q}_\tau(Y_i|A_i=0,L_i)|A_i=0,L_i)} \right\}.$$

S12 Debiased estimator for Φ_τ

First note that

$$\begin{aligned}
\Phi_\tau &= E\left[w(L)\left\{\Psi_\tau(L) - \Psi_\tau(w)\right\}^2\right] \\
&= E\left\{w(L)\Psi_\tau(L)^2\right\} - \Psi_\tau^2 \\
&= \frac{1}{E\{\mathrm{Var}(A|L)\}} E\left[\frac{\mathrm{Cov}\{A, Q_\tau(Y|A,L)|L\}^2}{\mathrm{Var}(A|L)}\right] - \Psi^2.
\end{aligned}$$

The efficient influence function equals

$$\begin{aligned}
&2\frac{\mathrm{Cov}\{A, Q_\tau(Y|A,L)|L\}}{\mathrm{Var}(A|L)} \frac{\{A - E(A|L)\}}{E\{\mathrm{Var}(A|L)\}} \\
&\quad \times \left(Q_\tau(Y|A,L) - E\{Q_\tau(Y|A,L)|L\} + \frac{\tau - I\{Y \leq Q_\tau(Y|A,L)\}}{f\{Q_\tau(Y|A,L)|A,L\}} \right) \\
&\quad - 2\Psi EIF_\Psi - (\Phi + \Psi^2)\frac{\{A - E(A|L)\}^2}{E\{\mathrm{Var}(A|L)\}} - \frac{\mathrm{Cov}\{A, Q_\tau(Y|A,L)|L\}^2}{\mathrm{Var}(A|L)^2} \frac{\{A - E(A|L)\}^2}{E\{\mathrm{Var}(A|L)\}},
\end{aligned}$$

where EIF_Ψ is the efficient influence function of Ψ. A debiased estimator for Φ is obtained as the value that makes the sample average of the efficient influence functions zero;

$$\begin{aligned}
&\frac{2}{n}\sum_{i=1}^n \frac{\widehat{\mathrm{Cov}}\{A_i, \hat{Q}_\tau(Y_i|A_i,L_i)|L_i\}}{\widehat{\mathrm{Var}}(A_i|L_i)\frac{1}{n}\sum_{i=1}^n\{A_i - \hat{E}(L_i)\}^2} \{A_i - \hat{E}(A_i|L_i)\} \left[\hat{Q}_\tau(Y_i|A_i,L_i) - \hat{E}\{\hat{Q}_\tau(Y_i|A_i,L_i)|L_i\}\right. \\
&\left. + \frac{\tau - I\{Y_i \leq \hat{Q}_\tau(Y_i|A_i,L_i)\}}{\hat{f}\{\hat{Q}_\tau(Y_i|A_i,L_i)|A_i,L_i\}}\right] - \hat{\Psi}_\tau^2 - \frac{1}{n}\sum_{i=1}^n \frac{\widehat{\mathrm{Cov}}\{A_i, \hat{Q}_\tau(Y_i|A_i,L_i)|L_i\}^2}{\widehat{\mathrm{Var}}(A_i|L_i)^2\frac{1}{n}\sum_{i=1}^n\{A_i - \hat{E}(L_i)\}^2} \{A_i - \hat{E}(A_i|L_i)\}^2.
\end{aligned}$$

S13 Generalization to link function

There are settings in which it could be useful to generalize the estimand (2.2) so that it includes a link function. A realistic example is a survival analysis where the outcome can only take positive values (e.g., when it is assumed to be exponentially distributed with exponential hazard). The quantile in our estimand could take negative values, which makes no sense in this setting. It would be reasonable here to use a link function and replace model (2.3) by

$$g\{Q_\tau(Y|A,L)\} = \beta_\tau A + g\{Q_\tau(Y|A=0,L)\}, \tag{S13.6}$$

with link function g equal to the natural logarithm. This straightforwardly leads to the following estimand for β_τ:

$$\Theta_\tau = \frac{E[\{A-E(A|L)\}(g\{Q_\tau(Y|A,L)\} - E[g\{Q_\tau(Y|A,L)\}|L])]}{E[\{A-E(A|L)\}^2]}. \tag{S13.7}$$

For this estimand, the efficient influence function can be calculated in the same way as in the proof of Theorem 1. The main difference occurs in Lemma 2. With link function, by making use of the chain rule one would obtain

$$\begin{aligned}
&\frac{d}{dt}(A-E_t(A|L))g\{Q_{\tau,t}(Y|A,L)\}\Big|_{t=0} \\
&= \frac{d}{dt}(A-E_t(A|L))\Big|_{t=0} g\{Q_{\tau,t}(Y|A,L)\} + (A-E(A|L))\frac{d}{dt}\left(g\{Q_{\tau,t}(Y|A,L)\}\right)\Big|_{t=0} \\
&= -\frac{\mathbb{1}_{\tilde{l}}(L)}{f(L)}(\tilde{a}-E(A|L))g\{Q_{\tau,t}(Y|A,L)\} + \{A-E(A|L)\}g'\{Q_\tau(Y|A,L)\}\frac{d}{dt}Q_{\tau,t}(Y|A,L)\Big|_{t=0} \\
&= -\frac{\mathbb{1}_{\tilde{l}}(L)}{f(L)}(\tilde{a}-E(A|L))g\{Q_{\tau,t}(Y|A,L)\}
\end{aligned}$$

$$+ \{A - E(A|L)\} g'\{Q_\tau(Y|A,L)\} \mathbb{1}_{\tilde{a},\tilde{l}}(A,L) \frac{\tau - I\{\tilde{y} \leq Q_\tau(Y|A,L)\}}{f(Q_\tau(Y|A,L),A,L)}$$

such that the efficient influence function is

$$\phi(Y,A,L) = \frac{A - E(A|L)}{E[\{A - E(A|L)\}^2]} \Big[g\{Q_\tau(Y|A,L)\} - E[(g\{Q_\tau(Y|A,L)\}|L] + \frac{\tau - I\{Y \leq Q_\tau(Y|A,L)\}}{f\{Q_\tau(Y|A,L)|A,L\}} g'\{Q_\tau(Y|A,L)\} - \Theta_\tau\{A - E(A|L)\} \Big].$$

The proposed estimators can be easily adjusted for the estimation of Θ_τ.

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