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# Treatment Effect Bounds under Monotonicity Assumptions: An Application to Swan-Ganz Catheterization

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We consider different bounds on the average effect of a treatment that follow from access to an instrument combined with alternative monotonicity restrictions. We consider three alternative sets of nonnested, structural restrictions:

- The "monotone treatment response" (MTR) assumption proposed by Charles F. Manski and John Pepper (2000), hereafter MP, that imposes a priori the restriction that the outcome is increasing in the treatment;

- The MTR assumption that imposes a priori the restriction that the outcome is decreasing in the treatment; and

- The restrictions of Shaikh and Vytlacil (2005), hereafter SV, that impose monotonicity of the outcome in the treatment and of the treatment in the instrument, but do not impose the direction of the monotonicity in either case. We use these different approaches to study the effects of Swan-Ganz catheterization on patient mortality.

In Section I, we describe each of the resulting bounds when there are no other exogenous covariates that directly affect the outcome. We show that if the effect of the treatment is positive and the assumptions of SV hold, then the bounds of SV coincide with those of MP that assume a priori that the effect of the treatment is positive. If the effect of the treatment is instead negative and the assumptions of SV hold, then the bounds of SV coincide with those of MP that assume a priori that the effect of the treatment is negative. Hence, the trade-off between the analyses of SV and MP in the case of no exogenous covariates besides the instrument is that the latter requires one to know a priori whether the effect of the treatment is positive or negative, while the former requires one to impose monotonicity of the treatment in the instrument in order to be able to determine the sign of the treatment effect from the distribution of the observed data. If there are exogenous regressors that vary conditional on the fitted value of the treatment, then the SV bounds become much narrower than the MP bounds.

We show further that it is not possible to determine the sign of the treatment effect in the same way as SV under the assumptions of MP. Current work by Cecilia Machado, Shaikh, and Vytlacil (2008) develops the sharp bounds for the average treatment effect under the restriction that the outcome is monotone in the treatment, but without assuming the direction of the monotonicity a priori or that the treatment is monotone in the instrument.

In Section II, we construct bounds on the average effect of Swan-Ganz catheterization on patient mortality under each of these three sets of assumptions. The data used are the same as in the influential observational study on the effect of Swan-Ganz catheterization on patient mortality by A. Connors et al. (1996). This study assumes that there are no unobserved differences between patients who are catheterized and patients who are not catheterized, and finds that catheterization increases patient mortality 180 days after admission to the intensive care unit (ICU). The three approaches described above permit such differences, but require an instrument. We propose and justify the use of an indicator for weekend admission to the ICU as an instrument for catheterization in this context. Under the assumptions of SV, Bhattacharya, Shaikh, and Vytlacil (2005) find that catheterization increases patient mortality at all time horizons beyond seven days after admission to the ICU. We expand this analysis here to consider the assumptions of MP.

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## I. Model and Bounds

Let $Y$ denote the outcome of interest and $D$ the treatment. In our application, $Y$ is an indicator for patient death within the given number of days after admission into the ICU unit, and $D$ is an indicator for catheterization within 24 hours of admission to the ICU. Let $Z$ be a binary instrument for treatment. To simplify the notation, suppose that $Z$ is ordered so that $\Pr\{Y = 1|Z = 1\} > \Pr\{Y = 1|Z = 0\}$. In our application, we will use an indicator variable for whether the patient was admitted into the ICU on a weekday as our instrument. Note that all results easily extend to the case where $Z$ is nonbinary and there are exogeneous covariates $X$ that directly determine $Y$; see Remark 1 below and SV for further discussion.

Consider the following triangular system of equations:

$$Y = r(D, \varepsilon), \tag{1}$$

$$D = s(Z, v).$$

Let $Y_1$ denote the outcome that would be observed if the individual receives treatment and let $Y_0$ denote the outcome that would be observed if the individual does not receive treatment. In our framework, these potential outcomes are given by $Y_1 = r(1, \varepsilon)$ and $Y_0 = r(0, \varepsilon)$. In this notation, the effect of catheterization on mortality is $Y_1 - Y_0$. The average effect of the catheterization on mortality is therefore $E[Y_1 - Y_0] = \Pr\{Y_1 = 1\} - \Pr\{Y_0 = 1\}$.

We maintain the assumption that $(Y, D)$ is determined by (1). We will assume further that $Z \perp\!\!\!\perp (\varepsilon, \nu)$ and that $(\varepsilon, \nu)$ has a strictly positive density with respect to Lebesgue measure on $\mathbb{R}^2$. Consider the following three sets of structural assumptions:

ASSUMPTION MP-I: $r(1, \varepsilon) \geq r(0, \varepsilon)$ *for almost every value of* $\varepsilon$.

ASSUMPTION MP-D: $r(1, \varepsilon) \leq r(0, \varepsilon)$ *for almost every value of* $\varepsilon$.

ASSUMPTION SV: *Either (MP-I) or (MP-D) holds and, in addition,* $s(1, \nu) \geq s(0, \nu)$ *for almost every* $\nu$ *or* $s(1, \nu) \leq s(0, \nu)$ *for almost every* $\nu$.

Assumption MP-I is the structural monotonicity restriction that treatment weakly increases the outcome. Assumption MP-D is the structural monotonicity assumption that treatment weakly decreases the outcome. Assumption SV is the structural assumption that the outcome is monotone in treatment and that the treatment is monotone in the instrument, but does not impose the direction of the monotonicity in either case. Assumptions MP-I and MP-D are the MTR assumptions considered in MP, while assumption SV is considered in SV. Note that these assumptions are nonnested.

REMARK 1: Note that the monotonicity of $D$ in $Z$ in assumption SV is different from the "monotone instrumental variables" (MIV) or "monotone treatment selection" (MTS) assumptions considered in MP. The MIV assumption is a weakening of the standard restriction that the $Y_0$ and $Y_1$ are mean independent of $Z$: under the MIV restriction, $Z$ may be endogenous though with the endogeneity in a known direction. The MTS assumption is a restriction on the selection bias into treatment —that the direction of endogeneity of selection into treatment is known a priori. Neither the MTS nor MIV assumptions is related to $D$ as a structural function of $Z$.

Let $\mathbf{1}\{\cdot\}$ denote the logical indicator function. Following Vytlacil (2002), we have that assumption SV is equivalent to

$$Y = \mathbf{1}\{\tilde{r}(D) + \varepsilon \geq 0\}, \tag{2}$$

$$D = \mathbf{1}\{\tilde{s}(Z) + \nu \geq 0\}. \tag{3}$$

We, thus, have that assumption SV nests as a special case the bivariate probit model with structural shift of Heckman (1978). Assumption MP-I is equivalent to (2) with $\tilde{r}(1) \geq \tilde{r}(0)$ and assumption MP-D is equivalent to (2) with $\tilde{r}(1) \leq \tilde{r}(0)$.

Each assumption, MP-I, MP-D, and SV, implies bounds of the form $B^L \leq E[Y_1 - Y_0] \leq B^U$ for the average treatment effect, but with different values of $B^L$ and $B^U$. It follows from the analysis of Proposition 2 of MP that the assumption MP-I implies bounds with endpoints given by

$$B^L_{MPI} = |\Pr\{Y = 1|Z = 1\} - \Pr\{Y = 1|Z = 0\}|,$$

$$B^U_{MPI} = \min_z \{\Pr\{D=1, Y=1|Z=z\} + \Pr\{D=0|Z=z\}\} - \max_z \{\Pr\{D=0, Y=1|Z=z\}\},$$

whereas assumption MP-D implies bounds with endpoints given by

$$B^L_{MPD} = \max_z \{\Pr\{D=1, Y=1|Z=z\}\} - \min_z \{\Pr\{D=0, Y=1|Z=z\} + \Pr\{D=1|Z=z\}\},$$

$$B^U_{MPD} = -|\Pr\{Y=1|Z=1\} - \Pr\{Y=1|Z=0\}|.$$

The SV bounds under assumption SV have a form that depends on the sign of $\Pr\{Y=1|Z=1\} - \Pr\{Y=1|Z=0\}$. Recall that we have ordered $Z$ such that $\Pr\{D=1|Z=1\} > \Pr\{D=1|Z=0\}$. Under this assumption, the sign of $\Pr\{Y=1|Z=1\} - \Pr\{Y=1|Z=0\}$ is the same sign as the 2SLS estimand. If $\Pr\{Y=1|Z=1\} - \Pr\{Y=1|Z=0\} > 0$, then assumption SV implies bounds with endpoints given by

$$B^L_{SV} = \Pr\{Y=1|Z=1\} - \Pr\{Y=1|Z=0\},$$

$$B^U_{SV} = \Pr\{D=1, Y=1|Z=1\} + \Pr\{D=0|Z=1\} - \Pr\{D=0, Y=1|Z=0\}.$$

If, on the other hand, $\Pr\{Y=1|Z=1\} - \Pr\{Y=1|Z=0\} < 0$, then assumption SV implies bounds with endpoints given by

$$B^L_{SV} = \Pr\{D=1, Y=1|Z=1\} - \Pr\{D=0, Y=1|Z=0\} - \Pr\{D=1|Z=0\},$$

$$B^U_{SV} = \Pr\{Y=1|Z=1\} - \Pr\{Y=1|Z=0\};$$

finally, if $\Pr\{Y=1|Z=1\} - \Pr\{Y=1|Z=0\} = 0$, then $\mathrm{E}[Y_1 - Y_0] = 0$. Thus, without imposing that the direction of the effect is known a priori, but instead by using the assumption of monotonicity of $D$ in $Z$, SV are always able to identify the direction of the effect of $D$ on $Y$.

The following lemma makes the relationship between these different bounds precise.

LEMMA 1: *If assumptions MP-I and SV hold, then $B^L_{MPI} = B^L_{SV}$ and $B^U_{MPI} = B^U_{SV}$; if assumptions MP-D and SV hold, then $B^L_{MPD} = B^L_{SV}$ and $B^U_{MPD} = B^U_{SV}$.*

PROOF:

We prove only the first assertion; the proof of the second assertion is symmetric. Suppose assumptions MP-I and SV hold. Then $\Pr\{Y=1|Z=1\} - \Pr\{Y=1|Z=0\} > 0$, so we have immediately that $B^L_{MPI} = B^L_{SV}$. Consider $B^U_{MPI}$. Using the representation (2) and (3), we have that $[\Pr\{D=1, Y=1|Z=1\} + \Pr\{D=0|Z=1\}] - [\Pr\{D=1, Y=1|Z=0\} + \Pr\{D=0|Z=0\}] = \Pr\{\tilde{s}(0) < -\nu \leq \tilde{s}(1), -\varepsilon \leq \tilde{r}(1)\} - \Pr\{\tilde{s}(0) < -\nu \leq \tilde{s}(1)\} \leq 0$. Similarly, we have that $\Pr\{D=0, Y=1|Z=1\} - \Pr\{D=0, Y=1|Z=0\} = -\Pr\{\tilde{s}(0) < -\nu \leq \tilde{s}(1), -\varepsilon \leq \tilde{r}(0)\} \leq 0$. Hence, $B^U_{MPI} = B^U_{SV}$.

REMARK 2: It might seem natural that one could follow the MP analysis without imposing a priori that one knew the sign of the treatment response but instead inferring it from the data from the sign of $\Pr\{Y=1|Z=1\} - \Pr\{Y=1|Z=0\}$ in the same manner as is done by the SV. Under their conditions, however, there is no necessary connection between the sign of the treatment response and the sign of $\Pr\{Y=1|Z=1\} - \Pr\{Y=1|Z=0\}$. To see this, consider imposing only their assumptions without imposing the additional structure of SV. Let $D_1$ denote the counterfactual choice variable corresponding to $Z=1$, and let $D_0$ denote the counterfactual choice variable corresponding to $Z=0$, i.e., $D_j = s(j, \nu)$. Suppose $Z \perp\!\!\!\perp (Y_0, Y_1, D_0, D_1)$ and that $Y_1 \geq Y_0$. It is possible to show that

$$\Pr\{Y=1|Z=1\} - \Pr\{Y=1|Z=0\} = \Pr\{Y_1 > Y_0\}(\Pr\{D_1=1, D_0=0|Y_1 > Y_0\} - \Pr\{D_1=0, D_0=1|Y_1 > Y_0\}),$$

while

$$\begin{aligned}
&\Pr\{D = 1 \mid Z = 1\} \\
&\qquad - \Pr\{D = 1 \mid Z = 0\} \\
&= \Pr\{Y_1 > Y_0\}(\Pr\{D_1 = 1, D_0 = 0 \mid Y_1 > Y_0\} \\
&\qquad\qquad - \Pr\{D_1 = 0, D_0 = 1 \mid Y_1 > Y_0\}) \\
&+ \Pr\{Y_1 = Y_0\}(\Pr\{D_1 = 1, D_0 = 0 \mid Y_1 = Y_0\} \\
&\qquad\qquad - \Pr\{D_1 = 0, D_0 = 1 \mid Y_1 = Y_0\}).
\end{aligned}$$

Thus, if it is the case that

$$\begin{aligned}
&\Pr\{D_1 = 1, D_0 = 0 \mid Y_1 > Y_0\} \\
&\qquad < \Pr\{D_1 = 0, D_0 = 1 \mid Y_1 > Y_0\}, \\
&\Pr\{D_1 = 1, D_0 = 0 \mid Y_1 = Y_0\} \\
&\qquad > \Pr\{D_1 = 0, D_0 = 1 \mid Y_1 = Y_0\},
\end{aligned}$$

then it is possible to have $\Pr\{D = 1 \mid Z = 1\} - \Pr\{D = 1 \mid Z = 0\} > 0$ while $\Pr\{Y = 1 \mid Z = 1\} - \Pr\{Y = 1 \mid Z = 0\} < 0$, even though $Y_1 \geq Y_0$ for all individuals. Parallel reasoning shows that it is possible to have $\Pr\{D = 1 \mid Z = 1\} - \Pr\{D = 1 \mid Z = 0\} > 0$, while $\Pr\{Y = 1 \mid Z = 1\} - \Pr\{Y = 1 \mid Z = 0\} > 0$, even though $Y_1 \leq Y_0$ for all individuals. Hence, under the assumptions of MP, the sign of the treatment effect cannot be inferred from the sign of $\Pr\{Y = 1 \mid Z = 1\} - \Pr\{Y = 1 \mid Z = 0\}$ as in SV. See also Guido Imbens and Joshua Angrist (1994), who show that it is possible to have $Y_1 \geq Y_0$ for all individuals and yet have a negative probability limit for the instrumental variables estimand.

REMARK 3: Throughout Section I, we have assumed that there are no exogenous $X$ covariates that directly determine $Y$, and that $Z$ is binary. Relaxing these assumptions is straightforward. If $X$ is contained in $Z$, then all of the analysis can simply be carried out conditional on $X$. If, on the other hand, there exists a component of $X$ that is not contained in $Z$, or, more generally, if at least one component of $X$ varies conditional on $\Pr\{D = 1 \mid Z\}$, then it is possible to further narrow the bounds on the average treatment effect under the SV assumptions. In the presence of such regressors, the SV bounds shrink and thus the connection between their bounds and the MP bounds breaks down. If there is a continuous component of $X$ that is not contained in $Z$, or more generally if at least one component of $X$ is continuous conditional on $\Pr\{D = 1 \mid Z\}$, then it is possible to obtain point identification. If $Z$ is not binary, then all of the analysis can be carried out with $z_1$ in place of 1 and $z_0$ in place of 0, where $z_1$ maximizes $\Pr\{D = 1 \mid Z = z\}$ and $z_0$ minimizes $\Pr\{D = 1 \mid Z = z\}$. For further details, see SV and Vytlacil and Nese Yildiz (2007).

## II. Empirical Results

We reanalyze data from a well-known observational study by Connors et al. (1996) on the impact of Swan-Ganz catheterization on mortality outcomes. A Swan-Ganz catheter is a slender tube with sensors that measures hemodynamic pressures in the right side of the heart and in the pulmonary artery. Once in place, the catheter is often left in place for days, so it can continuously provide information to ICU doctors. This information is often used to make decisions about treatment, such as whether to give the patient medications that affect the functioning of the heart. While there are some risks associated with the placement of the catheter itself, such complications are rare. Rather, the greater risk may come after successful catheter placement. Information from Swan-Ganz catheterization may, for example, lead to false diagnoses of heart failure, which in turn may lead doctors to administer inappropriate treatments.

Connors et al. (1996) analyze data on mortality outcomes for 5,735 patients from ICUs at five prominent hospitals. For a detailed description of the data, see Bhattacharya, Shaikh, and Vytlacil (2005). Connors et al. (1996) reach the controversial conclusion that patients who are catheterized within 24 hours of admission to the ICU are 1.27 times more likely to die within 180 days of their admission. Even at seven days after ICU admission, Connors et al. (1996) find that catheterization increases mortality. This conclusion was very surprising to ICU doctors, many of whom continue to use the Swan-Ganz catheter to guide therapy in the ICU. Max Harry Weil (1998), among others, argue that this conclusion was invalid because the method used by Connors et al. (1996)—propensity score matching—assumes that there are no unobserved differences between

patients who are catheterized and patients who are not catheterized. In Bhattacharya, Shaikh, and Vytlacil (2005), we show that catheterized and noncatheterized patients in these data differ in many clinically and statistically significant ways. It is therefore unlikely that they do not differ on *unobserved* dimensions as well.

To allow for such differences between patients, we instead use the methods described in Section I to bound the average effect of catheterization on mortality. We use an indicator for whether the patient was admitted to ICU on a weekday—defined to be Tuesday to Friday—as an instrument for Swan-Ganz catheterization. This same variable has been used as an instrument for treatment by Barton Hamilton, Vivian Ho, and Dana P. Goldman (2000) in their study of the effect of queuing time on mortality in a Canadian population undergoing hip-fracture surgery. We argue in Bhattacharya, Shaikh, and Vytlacil (2005) that this variable meets the two crucial requirements for an instrument's validity for four important clinical groups, defined according to primary diagnosis upon ICU admission: acute respiratory failure, congestive heart failure, massive organ system failure (MOSF) with malignancy, and MOSF with sepsis. First, we argue that this variable is strongly correlated with the application of the treatment: on weekends, patients are less likely to be catheterized because of staffing differences. Second, within observable risk classes, it is uncorrelated with outcomes; that is, mortality rates have little to do with the particular day of the week that a patient is admitted to the ICU and more to do with the arc of the patient's medical condition. We therefore restrict our analysis to these four groups.

Using this instrument, we calculate bounds on the treatment effect of catheterization where our outcome is mortality at after 7, 30, 60, 90, and 180 days after admission to the ICU. Figure 1 plots the 95 percent confidence intervals implied by the MP-I, MP-D, and SV assumptions. The estimates of the MP-I and SV bounds are identical because

$$(4)\quad P\{\text{death at } x \text{ days} \mid \text{weekday admission}\} - P\{\text{death at } x \text{ days} \mid \text{weekend admission}\}$$

is greater than zero for all horizons $x$ that we examine. However, at seven days after ICU admission, the 95 percent confidence interval around these bounds includes zero. At 30 days after admission to the ICU and beyond, the 95 percent confidence interval around these bounds suggests that catheterization increases mortality.

By contrast, the MP-D bounds all suggest that catheterization reduces mortality. The 95 percent confidence interval around the MP-D bounds implies that catheterization either reduces mortality or has no effect. As we discuss in Remark 2, under the assumptions of MP, it is impossible to distinguish between the MP-I and MP-D bounds based on the sign of (4) alone.

REMARK 4: Confidence regions displayed in Figure 1 are computed following the methodology developed in Joseph P. Romano and Shaikh (2006). Note that while the estimates of the MP-I bounds and SV bounds are the same, the confidence regions are different because of the fact that the SV bounds allow for the possibility that catheterization decreases mortality, whereas the MP-I bounds do not. Please see Bhattacharya, Shaikh, and Vytlacil (2005) for further details regarding the calculation of confidence bounds.

## III. Conclusion

In this paper, we consider the relationship between the bounds of SV and the bounds of MP. We have two main theoretical results. First, in the special case in which there are no exogenous covariates other than the instrument, we show that if the assumptions of SV and MP both hold, then the two sets of bounds agree. Second, we show further that it is not possible to extend the MP analysis so as to infer the sign of the treatment effect from the data in the same way as SV. Hence, the trade-off between the analyses of SV and MP in the case of exogenous regressors is that the latter requires one to know a priori whether the effect of the treatment is positive or negative, whereas the former requires one to impose additional structure in order to determine the sign of the treatment effect from the distribution of the observed data.

In our empirical work, we apply these methods to analyze the effect of Swan-Ganz catheterization on patient mortality. We reanalyze observational data collected by Connors et al. (1996). To account for the possibility of unobserved differences between catheterized and noncatheterized patients, we use day-of-week of admission as an instrument. Based on the

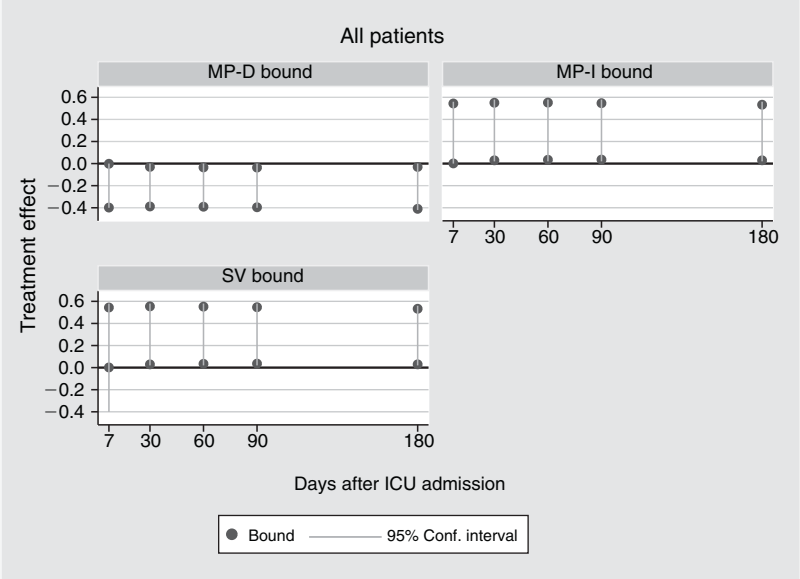


FIGURE 1. PERCENT MANSKI-PEPPER AND SHAIKH-VYTLACIL BOUNDS

assumptions of SV, we find that catheterization increases mortality 30 days and after the procedure is performed. Based on the assumptions of MP, we cannot conclude whether catheterization increases or decreases mortality.

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