Double-hurdle and Heckman models for assessing patient preferences with zero responses: an example using HIV treatment adherence ratings

Orme M.E.[1], Perard R.[2]

[1] ICERA Consulting Ltd, [2] Gilead Sciences, Europe

#594

BACKGROUND

- Patient preference data often contain responses indicating no preference.
- Different interpretations of this 'zero' observation require different estimation approaches [1].
- Objectives: To compare the two-stage Heckman and double-hurdle model.

METHODS

- A prospective, multi-country, web-based survey was set up to collect data from European HIV patients currently treated with anti-retroviral therapy (ART). Data for this analysis is from the UK survey and discrete choice experiment (DCE) [2-3] which took place from June to October 2014.
- The survey methodology, a summary of patient characteristics and key results have been presented elsewhere [4].
- Before starting the DCE, respondents rated their current level of adherence on a 5-point Likert scale (How often do you skip doses of your current treatment? Never/very rarely/sometimes/often/frequently)
- The DCE consisted of 12 scenarios of two hypothetical drugs with five treatment attributes. For each of the 12 scenarios, patients used a sliding scale (0 (no preference) to 100 (strongest preference)) to rate the treatment option that they thought would maximise their adherence to treatment.
- The adherence model takes the general form:

Participation equation: $w = \gamma z_i + v_i$ (1) *Observed response*: $y_i = d.y_i^{**}$

Adherence behaviour equation: $y_i^{**} = max[0, y_i^*]$

$y_i^* = \beta x_i + u_i$ (2)

$d = \begin{cases} 1, & if\ w > 0 \\ 0, & otherwise \end{cases}$ (3)

- A zero response (y_i=*0*) can be due to:
  - Non-participation (*d=0*): Non-participation may be because the respondent always adheres to treatment regardless of the treatment attributes or the particular treatment attributes presented in the DCE do not influence adherence.
  - A utility maximising solution (*yi**=0*): The treatment attributes presented in the DCE may influence adherence but the combination of attribute levels presented in the choice set are such that the respondent's preference is neutral.
- The adherence ratings were analysed in STATA v13.1 using a Heckman and a double-hurdle model [5].
- For the Heckman 'two-stage' model:
  - Stage 1: participation model (Equation 1) estimates the probability of a non-zero observation is from a probit model fitted to the whole sample.
  - Stage 2: adherence behaviour model (Equation 2) estimates the preference weightings from the non-zero observations using the inverse Mills ratio (non-selection hazard) as an explanatory variable (calculated in stage 1).
  - This approach assumes that the decision to participate dominates.
- For the double-hurdle model:
  - Equation 1 and 2 are estimated simultaneously by assessing the impact of the treatment attributes on adherence behaviour conditional on participation.
  - It is assumed that the decision to participate and the ranking of the treatment attributes are done simultaneously
- For the Heckman and double hurdle model, the factors that affect participation can be different from the factors that affect adherence rankings based on treatment attributes.
- Note:
  - A Tobit model is a special case of the double-hurdle model where the factors affecting participation and adherence are assumed to be the same (*d=1*).
  - Another potential model is one that assumes participation is independent of the adherence rankings (a two-part model, not considered in this presentation).

RESULTS

- Responses were analysed for 278 HIV patients who are currently receiving ART.
- Overall this population were representative of the UK HIV population:
  - 72.7% of the respondents are men who have sex with men and 14.7% are female.
  - The (median) duration of treatment is 5 (range 0-27) years, age is 44 (range 21-66) years, and time since diagnosis is 8 years (range 0-30).
  - 56.8% (n=158; Table 1) of the patients reported that they occasionally miss one or more doses of their ART treatment; 36% were on a single tablet regimen (STR), 9% were taking five tablets or more per day.
- 63% (n=4183) of the observations from the UK HIV DCE were rated 'zero' .

Double-hurdle and Heckman models for assessing patient preferences with zero responses: an example using HIV treatment adherence ratings

Orme M.E.[1], Perard R.[2]

[1] ICERA Consulting Ltd, [2] Gilead Sciences, Europe

#594

RESULTS CONTINUED

Table 1: Preference weightings from Heckman Two-stage and double-hurdle model

	Heckman: Adherence model		Double-hurdle model	
Treatment Attribute x_i	**β_i (95% CI)**	**p-value**	**β_i (95% CI)**	**p-value**
Increased risk of MI	-3.55 (-4.45, -2.65)	0.00	-2.28 (-4.59, 0.04)	0.05
Sleep problems	-9.64 (-10.51, -8.76)	0.00	-7.54 (-11.56, -3.52)	0.00
One tablet	6.99 (5.48, 8.51)	0.00	6.06 (2.55, 9.57)	0.00
Two tablets	-1.33 (-2.82, 0.16)	0.08	-1.52 (-3.32, 0.27)	0.10
Three tablets	-1.72 (-3.2, -0.25)	0.02	-0.50 (-2.53, 1.53)	0.63
Avoid mealtime dosing	5.97 (5.13, 6.8)	0.00	3.95 (1.44, 6.47)	0.00
Constant	25.98 (23.62, 28.34)	0.00	93.8 (73.4, 114.3)	0.00
	Heckman: Participation model		**Double-hurdle model: Participation**	
Patient Attribute z_i	**γ_i (95% CI)**	**p-value**	**γ_i (95% CI)**	**p-value**
Age	-0.01 (-0.01, -0.00)	0.00	0.00 (0.00, 0.01)	0.56
Male	0.08 (-0.03, 0.19)	0.15	NA†	-
On a single tablet regimen	0.59 (0.50, 0.68)	0.00	0.00 (-0.02, 0.02)	0.81
Max adherence	-0.08 (-0.16, -0.00)	0.04	-0.03 (-0.10, 0.04)	0.38
Constant	1.21 (0.99, 1.43)	0.00	-0.25 (-0.59, 0.08)	0.14
Mills λ	-1.62 (-11.07, 7.84)	0.74	NA	-

MI, myocardial infarction; CI, confidence interval; Max adherence, self-reported adherence status = never miss any dose of treatment; NA, not applicable; ; † non-significant covariate (Male) dropped

- Both models provide similar treatment attribute rankings and the preference weightings (ratings) are similar (Table 1 and Figure 1):
  - Treatments associated with sleep problems have the largest negative impact on treatment adherence rankings (Figure 1).
  - One tablet daily and avoiding being tied to dosing at mealtimes were viewed to be positively correlated with adherence (Figure 1)
- Age, single tablet regimen and maximum self-reported adherence were found to be significant predictors of non-zero responses in the Heckman participation model.
- This was not the case for the double-hurdle model: this model was less effective in explaining differences across responders in this dataset.

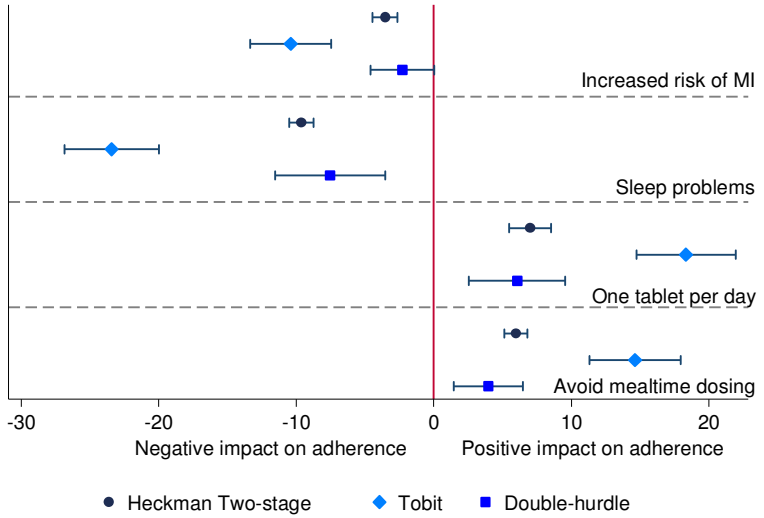

Figure 1: Comparison of treatment attribute weightings from Heckman two-stage, Tobit and double-hurdle models

CONCLUSIONS

- For this dataset the Heckman two-stage model provides the most robust estimates of likely adherence weightings.
- We infer that in our dataset a zero response represents non-participation rather than a utility maximising solution.

REFERENCES

[1] Humphreys BR. (2013) Dealing with zeros in economic data. http://www.ualberta.ca/

[2] Ryan M, et al. (2010). Using Discrete Choice Experiments to Value Health and Health Care: *Springer.*

[3] ISPOR Conjoint Analysis Experimental Design Good Research Practices Task Force (2013) Value Health 16: 3-13.

[4] Orme M, Miners A et al. (2015) 21st Annual conference of the BHIVA, 21-24 April 2015, Brighton UK.

[5] Garcia B. (2013). Stata Journal. 13 (4): 776-794