SUPPLEMENT TO "UNDERSTANDING DOCTOR DECISION MAKING: THE CASE OF DEPRESSION TREATMENT"

JANET M. CURRIE
Woodrow Wilson School, Princeton University and NBER

W. BENTLEY MACLEOD
Department of Economics, Columbia University and NBER

APPENDIX: ON LINE APPENDIX

Proof of Proposition 2

PROPOSITION: *A Bayesian rational doctor chooses drug A over drug B in period* 1 *if and only if*

$$\mu_{j1A} + \zeta_j V_{j1A} \geq \mu_{j1B} + \zeta_j V_{j1B},$$

an equality that is satisfied to the first order if and only if

$$\mu_{j1A} + \tau_j \hat{\sigma}_{j2A} \geq \mu_{j1B} + \tau_j \hat{\sigma}_{j2B}, \tag{A.1}$$

where

$$\tau_j = \frac{\zeta_j}{1 - \zeta_i} L(0) \simeq 0.4 \frac{\zeta_j}{1 - \zeta_i}.$$

PROOF: The first inequality follows immediately from the definition of the payoffs. For the second inequality, take a Taylor series expansion of $V(x)$ around $x = 0$:

$$V(x) = \int_x^{-\infty} t f(t) dt + \big(1 - F(x)\big)x,$$

$$V'(x) = x f(x) - f(x)x + \big(1 - F(x)\big)$$

$$= \big(1 - F(x)\big).$$

Hence,

$$V(x) \simeq L(0) + \frac{x}{2}.$$

Thus, we have

$$U\big(d_1 = A, d_{2A}^*\big) \simeq \mu_{j1A} + \zeta_j \hat{\sigma}_{j2A} \left(L(0) + \left(\frac{\mu_{j1B} - \mu_{j1A}}{2\hat{\sigma}_{j2A}} \right) \right)$$

$$= \mu_{j1A} + \zeta_j \hat{\sigma}_{j2A} L(0) + \zeta_j \frac{\mu_{j1B} - \mu_{j1A}}{2}.$$

Janet M. Currie: jcurrie@princeton.edu
W. Bentley MacLeod: wbmacleod@wbmacleod.net

We have a similar expression for drug B:

$$U\left(d_1 = B, d_{2B}^*\right) = \mu_{j1B} + \zeta_j \hat{\sigma}_{j2B} L(0) + \zeta_j \frac{\mu_{j1A} - \mu_{j1B}}{2}.$$

Rearranging the mean terms, we get that to the first order, $U(d_1 = A, d_{2A}^*) \geq U(d_1 = B, d_{2B}^*)$ if and only if

$$\mu_{j1A} + \frac{\zeta_j}{(1 - \zeta_j)} L(0) \hat{\sigma}_{j2A} \geq \mu_{j1B} + \frac{\zeta_j}{(1 - \zeta_j)} L(0) \hat{\sigma}_{j2B},$$

from which we get (A.1). The numerical approximation to $L(0) \simeq 0.4$ is to be found in the appendix to Raiffa and Schlaifer (2000).   *Q.E.D.*

A.1. *Drug Effects and Dropouts: How Data for Table V is Constructed*

This document will go drug-by-drug and show how the data used to model doctor tastes in the simulations were constructed. All cited papers are listed in the bibliography at the end. Each drug is listed by its pharmaceutical name, with its primary trade name included in parentheses. All effect means and standard deviations use the Hamilton-17 (HAMD-17) scale as their metric of improvement. Market shares were computed by the authors using the 2014 IQVIA data.

1. *Sertraline (Zoloft)*: All effect data were drawn from Hieronymus, Emilsson, Nilsson, and Eriksson (2015) Table 2, which includes multiple sertraline studies. First, the average was taken over all sertraline studies to get average means and standard deviations of the HDRS-17 score both at baseline and endpoint. Mean effects were computed as the difference between average baseline score and average endpoint score. To compute standard deviations, we take advantage of the assumption that baseline scores and drug effects are independent. Under this assumption,

$$\sigma_{\text{endpoint}}^2 = \sigma_{\text{baseline}}^2 + \sigma_{\text{effect}}^2.$$

Solving for σ_{effect}, we have

$$\sigma_{\text{effect}} = \sqrt{\sigma_{\text{endpoint}}^2 - \sigma_{\text{baseline}}^2}.$$

2. *Citalopram HBR (Celexa)*: All effect data were drawn from Hieronymus et al. (2015) Table 2, which includes multiple citalopram studies. Means and standard deviations were computed using an identical procedure as used for sertraline.

3. *Fluoxetine HCl (Prozac)*: All effect data were drawn from Hieronymus et al. (2015) Table 2, which includes multiple fluoxetine studies. Means and standard deviations were computed using an identical procedure as used for sertraline.

4. *Escitalopram Oxal (Lexapro)*: All effect data were drawn from Llorca, Azorin, Despiegel, and Verpillat (2005), Table 3. The mean effect was taken to be the difference in Hamilton-17 score between baseline and LOCF (Last Observation Carried Forward). Like for sertraline, we take advantage of the assumed independence between the baseline score and effect, and compute the standard deviation of the effect

as

$$\sigma_{\text{effect}} = \sqrt{\sigma_{\text{LOCF}}^2 - \sigma_{\text{baseline}}^2}.$$

5. *Trazodone HCl (Oleptro)*: The mean effect was drawn from Kasper (1995) Table 3, line 3 (Belgium). The effect is expressed as the mean change in HAMD-17 score for a single study. No data were found on the standard deviation of the effect for trazodone. However, Van Moffaert et al. (1995) claimed that the standard deviation of mirtazapine's effect is about 20% lower than that for trazodone. Thus, we let $\sigma_{\text{effect}}^{\text{traz}} = \sigma_{\text{effect}}^{\text{mirt}}$, where $\sigma_{\text{effect}}^{\text{mirt}}$ is defined below.

6. *Duloxetine HCl (Cymbalta)*: The mean effect was drawn fom Detke, Lu, Goldstein, Hayes, and Demitrack (2002, Table 2). The effect is expressed as the mean change in HAMD-17 for a single study. The standard deviation of the effect was drawn from page 227 of Goldstein, Mallinckrodt, Lu, and Demitrack (2002) which does not provide the standard deviation derived from their data but rather an "assumed" standard deviation of 7. We can hope that this standard deviation was informed by their data, but are not sure of this.

7. *Wellbutrin XL*: No papers were found measuring the direct effect and standard deviation for bupropion. However, Maneeton, Maneeton, Eurviriyanukul, and Srisurapanont (2013) claimed that these would be approximately the same as those for venlafaxine. For this reason, the effect and standard deviation of the effect of bupropion was made identical to that for venlafaxine (see below).

8. *Amitriptyline HCl (Elavil)*: All effect data were drawn from Kasper (1995) page 30 (within the text). These data came from a single study of both amitriptyline and mirtazapine. You will notice they provided data for both "mean change from baseline" and "reductions at the endpoint". The data pulled are those corresponding to reductions at the endpoint.

9. *Venlafaxine (Effexor)*: All effect data were drawn from Table 1 of Kirsch, Deacon, Huedo-Medina, Scoboria, Moore, and Johnson (2008), which includes several different formulations of venlafaxine. In order to obtain a single figure for the mean and standard deviation of change, the average was taken over the relevant studies presented in the table. Note that the *d* denotes the standard deviation.

10. *Mirtazapine (Remeron)*: All effect data were drawn from Kasper (1995), page 27 (within the text). These data came from an analysis of pooled data of mirtazapine trials.

11. *Paroxetine (Paxil)*: All effect data were drawn from Hieronymus et al. (2015) Table 2, which includes multiple paroxetine studies. Means and standard deviations were computed using the same procedure as for sertraline. Note that these paroxetine studies include a variety of different dosages.

12. *Placebo*: Most of the studies we have come across provide data on the effect of placebos on patients with major depressive disorder. We have defined our "placebo" effects and standard deviations by taking the average over the data provided in Hieronymus et al., which provides data on 18 different placebo-controlled trials. To compute the mean and standard deviation of the effect, we employ the same procedure used for sertraline, for example (please see above).

A.2. *Market Shares of Drugs*

TABLE A-I

MARKET SHARES OF ALL ANTI-DEPRESSANT PRESCRIPTIONS, 2006 AND 2014 (BRANDED PRODUCTS IN ITALICS UNDER THE EQUIVALENT GENERIC PRODUCT)[a]

	Drug Class		Molecule		Specific Product	
	2006	2014	2006	2014	2006	2014
SSRI	54.40	54.03				
Sertraline			14.02	14.63	4.69	14.56
(Zoloft)					*9.33*	*0.07*
Citalopram			6.17	12.83	5.98	12.81
(Celexa)					*0.19*	*0.02*
Fluoxetine			11.08	10.57	10.69	10.53
(Prozac)					*0.39*	*0.04*
Escitalopram			13.05	9.68	. . .	9.50
(Lexapro)					*13.05*	*0.18*
Paroxetine			9.71	5.33	7.86	5.28
(Paxil)					*1.85*	*0.05*
Other			0.37	0.99	0.37	0.99
SNRI	13.50	15.04				
Venlafaxine			9.14	7.09	0.18	6.99
(Effexor)					*8.96*	*0.10*
Duloxetine			4.33	6.84	. . .	6.36
(Cymbalta)					*4.33*	*0.48*
Other			0.03	1.11	0.03	1.11
NDRI	11.45	10.46				
Bupropion			11.45	10.46	2.88	10.29
(Wellbutrin)					*8.57*	*0.17*
SARI	7.37	9.42				
Trazadone			7.12	9.35	7.12	9.35
Other			0.25	0.07	0.25	0.07
Tricyclic	10.77	8.16				
Amitriptyline			6.62	5.15	6.62	5.15
Other			4.15	3.01	4.15	3.01
Tetracyclic	2.44	2.84				
Mirtazapine			2.36	2.82	2.36	2.82
(Remeron)			*0.08*	*0.02*	*0.08*	*0.02*
MAOI	0.07	0.05	0.07	0.05	0.07	0.05
Total	100.00	100.00	100.00	100.00	100.00	100.00

[a]Authors' calculations from the IQVIA data. Different drug classes correspond to different hypothesized methods of action. Only the most commonly prescribed drugs in each class are listed. In most cases, there is a generic and a branded drug. For example, Zoloft is the brand name and the equivalent generic is sertraline. We give the molecule the generic name. The table shows that 11 drugs account for most of the market, though 33 drugs were sold. "Wellbutrin" includes the branded drugs Wellbutrin, Budeprion, Forfivo, and Aplenzin; "Paxil" includes both Paxil and Pexeva.

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