PRR-??

Patient Preferences and Stated Adherence for Hepatitis C Virus Treatments

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Abstract

OBJECTIVES: To estimate patient preferences for attributes of hepatitis C virus (HCV) treatments and the effect of product attributes on stated medication adherence.

METHODS: HCV patients, 18 years and older completed an online survey instrument that included 9 conjoint choice-format trade-off tasks. Subjects chose among pairs of hypothetical medication alternatives, each defined by chance that the medication will eliminate the virus completely (Efficacy), injection frequency, duration of flu-like symptoms after each injection, injection device (Device), average number of days of work missed each week (Lost work days), probability of reversible hair thinning while on treatment (Hair thinning), and probability of developing clinical depression while on treatment (Depression). Subjects also answered 3 rating questions assessing how often people with HCV would miss or skip doses of medications with different characteristics. We used mixed-logit methods to estimate mean relative importance weights for each attribute. We used a Heckman two-stage model to estimate first the effect of subject characteristics and the effect of medication attributes on non-adherence.

RESULTS: 150 subjects completed the survey. In the model, number of flu days (Flu days) was specified as injection frequency multiplied by the duration of flu-like symptoms after every injection. Efficacy was the most important attribute. The remaining attributes were ranked in order of importance as follows: Depression, Flu days, Lost work days, Hair thinning, and Device. Subjects with prior experience were less likely to be non-adherent and increases in the number of flu days increased the likelihood of non-adherence.

CONCLUSIONS: The results of this study demonstrate that efficacy is the most important medication attribute to patients but medication side effects like the number of flu days affect stated medication adherence. Reducing the number of flu days by reducing the frequency of injections or the duration of flu-like symptoms after each injection may increase medication adherence.

Objective

To estimate patient preferences for attributes of hepatitis C virus (HCV) treatments and the effect of product attributes on stated medication adherence.

Methods

Subjects

- Inclusion criteria
  - Aged 18 years or older
  - United States (US) resident
  - Self-reported diagnosis of HCV
- Recruitment
  - Synovate Healthcare Research
    - Online chronic illness panel
  - Final sample was 150

Survey Instrument

- Web-enabled survey instrument
- Discrete-choice experiment (stated-choice [SC] survey method)
  - Elicits subject tradeoffs among alternatives with varying levels of different attributes
  - Is the most valid and reliable technique available for quantifying preferences[1,2,3,4]
- Nine choices from among constructed medication alternatives, each described by efficacy outcomes, side-effect risks, adverse-event outcomes, and mode of administration (Table 1)
  - Subjects were asked to choose the option they would prefer if these were the only options available to them (Figure 1)
- Three rating questions assess how often people with HCV would miss or skip doses of medications with different characteristics (Figure 2)
- Survey instrument also collected standard demographic information (e.g., age, gender, race, marital status, and education), and items about the subjects' experiences with HCV and HCV treatments

Methods (continued)

Table 1. Treatment Attributes and Levels Used in the Survey Instrument

Medicine Feature (Attribute)	Abbreviated Label	Levels
Chance that the medicine will eliminate the virus completely	Efficacy	• 40 out of 100 (40%) • 50 out of 100 (50%) • 70 out of 100 (70%)
How often you take injections	Frequency	• Once a week (4 times a month) • Once every 2 weeks (2 times a month) • Once every 4 weeks (once a month)
Flu-like symptoms after every injection	Flu	• For 1 day • For 3 days
Injection device	Device	• Vial and syringe • Self-injection device
Average number of days of work you will miss each week	Lost work days	• None • 1 day • 2 days
Chance of reversible hair thinning	Hair thinning	• No chance • 25 out of 100 (25%) • 40 out of 100 (40%)
Chance of developing clinical depression	Depression	• 5 out of 100 (5%) • 12 out of 100 (12%) • 25 out of 100 (25%)

Figure 1. Example of Choice-Format Trade-Off Question

Medicine Features	Medicine A	Medicine B
Chance that the medicine will eliminate the virus completely	50 people out of 100 (50%)	70 people out of 100 (70%)
How often you take injections	Once a week (4 times a month)	Once every 2 weeks (2 times a month)
Flu-like symptoms after every injection	For 1 day	For 1 day
Injection device	Vial and syringe	Self-injection device
Average number of days of work you will miss each week	1 day	2 days
Chance of reversible hair thinning	40 people out of 100 (40%)	25 people out of 100 (25%)
Chance of developing clinical depression	5 people out of 100 (5%)	12 people out of 100 (12%)
Which medicine would you choose if these were the only options available?	Medicine A ❑	Medicine B ❑

Figure 2. Example of Adherence Question

Medicine Features	Medicine A	Medicine B
Chance that the medicine will eliminate the virus completely	40 people out of 100 (40%)	50 people out of 100 (50%)
How often you take injections	Once a week (4 times a month)	Once every 2 weeks (2 times a month)
Flu-like symptoms after every injection	For 3 days	For 3 days
Average number of days of work you will miss each week	2 days	1 day
Chance of developing clinical depression	25 people out of 100 (25%)	12 people out of 100 (12%)

How likely do you think people with hepatitis C would be to miss or skip does of each medicine?	Much more likely to miss or skip doses with Medicine A	A little more likely to miss or skip doses with Medicine A	Equally likely to miss or skip doses with Medicine A and Medicine B	A little more likely to miss or skip doses with Medicine B	Much more likely to miss or skip doses with Medicine B
	❑	❑	❑	❑	❑

Methods (continued)

Analysis

- Estimated relative preference weights using multivariate, random-parameters, or mixed-logit estimation[5,6]
  - Importance weights for each medication feature
  - Effects of changes in attribute levels on predicted preference shares
- Used a Heckman two-stage participation model to estimate the effect of subject characteristics and the effect of medication attributes on non-adherence
  - In the first stage, the dependent variable indicates whether a subject chose a response other than "I would be equally likely to miss or skip doses"
  - In the second stage of the adherence model, non-adherence is modeled as a function of treatment characteristics

Results

Demographic Characteristics

- Mean age: 47.8 years (SD 9.8)
- Caucasian: 86%
- Female: 50%
- Married: 45%
- Some college education or higher: 71%

HCV Treatment Experience (N = 150)

- Currently on first course of therapy (receiving treatment for the first time): 10%
- Treatment naïve (never received treatment): 47%
- Treatment experienced (currently on treatment but not for the first time, or received treatment in the past): 43%

Experience With Medications While on Last Course of Treatment: Applicable to Treatment-Experienced Subjects Only (Table 2)

- Took injections once a week (4 times a month): 53%
- Experienced flu-like symptoms 1 or 2 days after each injection: 51%
- Worked full-time: 56%
- Experienced hair thinning: 60%
- Felt depressed: 68%

Table 2. Experience With Medications: Applicable to Treatment-Experienced Subjects Only

Question Description	Treatment Experienced (n = 57)[a]
Which best describes how often you took injections while on your last course of treatment?	
Daily (7 times a week)	8 (14.0%)
3 times a week	19 (33.3%)
Once a week (4 times a month)	30 (52.6%)
How often did you experience flu-like symptoms while on your last course of treatment?	
1 day after each injection	18 (31.6%)
2 days after each injection	11 (19.3%)
3 days after each injection	14 (24.6%)
> 3 days after each injection	6 (10.5%)
I did not have flu-like symptoms	8 (14.0%)
Did you work while receiving your last course of treatment?	
Yes, I worked full time	32 (56.1%)
Yes, I worked part time	5 (8.8%)
No	20 (35.1%)
On average, how many days of work per week did you miss while on your last course of treatment?	
None	21 (56.8%)
1 day	11 (29.7%)
2 days	5 (13.5%)
Did you experience hair thinning while on your last course of treatment?	
Yes	34 (59.6%)
No	23 (40.4%)
Did you feel depressed while you were on your last course of treatment?	
Yes	39 (68.4%)
No	18 (31.6%)

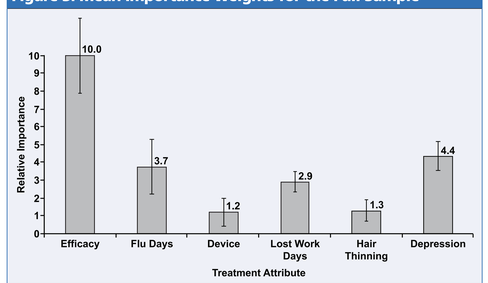
[a] Answered questions asked of the those indicating having treatment experience (total treatment experienced was 64 and 7 did not answer any of the medicine features questions)

Results (continued)

Importance Weights (Figure 3)

- In the preference model, Flu days = Flu-like symptoms after every injection × How often you take injections
  - Example
    - If flu-like symptoms after every injection = 3 days
    - How often do you take injections = Once a week (4 times a month)
    - Then Flu days = 3 × 4 = 12
- Importance weights for each attribute level are scaled between 0 and 10
  - The most important attribute was Efficacy
    - Efficacy is statistically significantly more important than the other five attributes ($P < 0.05$)
  - The least important attribute was Device
  - Depression and Flu days are statistically significantly more important than Hair thinning and Device ($P < 0.05$)
  - Importance weights for Flu days, Lost work days, and Depression are not statistically different from each other

Figure 3. Mean Importance Weights for the Full Sample[a]



[a] The vertical bars surrounding each mean importance weight denote the 95% CI about the point estimate.

Adherence

- The first stage of the model indicates that subjects with prior treatment experience are less likely to choose something other than "equally likely to miss or skip doses"
  - Subjects with prior experience were less likely to be non-adherent
- The second stage of the model indicates that increases in the number of flu days increased the likelihood of non-adherence
  - Increases in the number of injections
  - Increases in flu-like symptoms after each injection
  - For a given baseline adherence rate, independent of treatment attributes

Overall adherence rate =
Baseline adherence rate × Predicted relative adherence rate (Table 3)

- Example
  - Assume a baseline adherence rate of 80% with no flu days
  - Suppose the number of flu days per month is increased to 4
  - Then adherence will decline from 80% to 66.4% (0.80 × 0.83)

Table 3. Predicted Relative Adherence as a Function of Flu Days

Flu Days (Days)	Mean	Lower Bound	Upper Bound
0	1.00	1.00	1.00
1	0.88	0.79	0.95
2	0.85	0.75	0.93
3	0.84	0.73	0.92
4	0.83	0.71	0.91
6	0.81	0.69	0.90
12	0.77	0.64	0.87

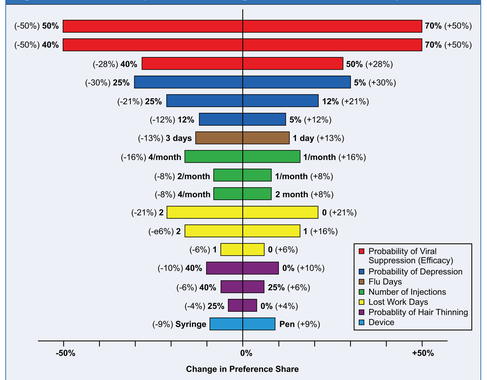
Effects of Changes in Attribute Levels on Predicted Preference Shares (Figure 4)

- If the attributes are equal between two medications, the predicted preference share is 50% for each medication
  - Assumes that all other attributes are held constant

Results (continued)

- An increase in preference share (from 50%) for the better alternative is exactly offset by a decrease in preference share for the worse alternative
  - Example
    - Medicine A has a chance of developing clinical depression of 5%
    - Medicine B has a chance of developing clinical depression of 25%
    - All other attributes are the same between Medicine A and Medicine B
    - Then, predicted preference share for Medicine A is 80% and the change in the preference share is +30% (50% + 30%)
    - And predicted preference share for Medicine B is 20% and the change in the preference share is -30% (50% - 30%)
- Increasing the efficacy from 40% to 70% or 50% to 70% has the highest impact on predicted preference share

Figure 4. Mean Importance Weights for the Full Sample[a]



Note: If the attributes are equal between two medications, the predicted preference share is 50% for each medication. Assumes that all other attributes are held constant.

[a] An increase in preference share (from 50%) for the better alternative is exactly offset by a decrease in preference share for the worse alternative.

Conclusions

- **Efficacy is the most important treatment attribute to patients; but side effects, like the number of flu days, affect stated and predicted adherence**
- **Reducing the number of flu days by reducing the frequency of injections or the duration of flu-like symptoms after each injection may increase medication adherence**
- **Sensitivity analyses demonstrate that preference shares are most sensitive to an increase in efficacy. Increases in efficacy equal to or greater than 20 percentage points will cause 100% of patients to choose the more efficacious option, regardless of the other treatment attributes**

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