Preferences for Oral Antidiabetic Agents Among People With Type 2 Diabetes

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BACKGROUND

- Currently many of the available oral antidiabetic agents (OADs) for type 2 diabetes mellitus (T2DM) are associated with side effects such as weight gain and increased cardiovascular risk.[1, 2, 3]
- Understanding patient preferences for medications with different features is important for predicting likely adherence to OAD treatments with different side effects.

OBJECTIVE

To quantify the strength of preferences and likely adherence to therapy of people with T2DM for outcomes of OADs.

METHODS

Subjects

- Inclusion criteria
  - Aged 18 years or older
  - United States or United Kingdom resident
  - Not currently using insulin or exenatide (injections)
  - Currently taking OADs to treat T2DM
- Recruitment
  - Harris Interactive recruited subjects from their online Chronic Illness Panel
  - All subjects provided online informed consent
  - The final sample was 407

Survey Instrument

- Web-enabled survey instrument
- Stated-choice survey method
  - Elicits subject tradeoffs among alternatives with varying levels of different features
  - Is the most valid and reliable technique available for quantifying preferences[4, 5, 6, 7]
- Ten choices between pairs of constructed treatment options (Figure 1)
  - Choices characterized by varying levels of glucose control (Table 1) and side effects (Table 2)
  - Benefit outcome constituted changes in HbA1c levels
    - Three baseline HbA1c levels—8.5%, 9.5%, and 10.5%
    - Each baseline HbA1c level was randomly assigned to subjects
    - Changes in HbA1c levels varied by assigned baseline HbA1c level
  - Side effects included
    - Number of mild-to-moderate hypoglycemic events per month
    - Water retention
    - Weight gain in the first 6 months of treatment
    - Mild stomach upset
    - Chance of a heart attack
  - Subjects were asked to choose the option they would prefer if these were the only two options available to them (forced-choice format)
  - Once subjects chose an option, they answered a follow-up adherence question that asked them how likely they would be to miss or skip doses of the medication
- Survey instrument also collected standard demographic information, as well as a number of items about the subjects' experiences with T2DM
  - Age, gender, marital status, race, and education
  - How long they have been diagnosed with T2DM
  - How they manage their T2DM
  - Prescription medications they currently take
  - Current weight
  - How often they currently miss or skip a dose of their medication

Figure 1. Example of Choice Question Comparing T2DM Treatment Options

Medication Feature	Medication A	Medication B
HbA1c change	6.0 6.5 7.0 7.5 8.0 8.5 9.0 9.5 10.0 10.5 — Optimal | Less than optimal | Poor	6.0 6.5 7.0 7.5 8.0 8.5 9.0 9.5 10.0 10.5 — Optimal | Less than optimal | Poor
Number of hypoglycemic events per month	1 to 2	More than 2
Water retention	Yes	No
Weight gain in first 6 months	None	10 pounds
Mild stomach upset	Mild nausea and vomiting or diarrhea that continues as long as you take the medicine	No stomach problems
Chance of a heart attack	**No additional person (0%)** will have a heart attack	**10 additional people out of 1,000 (1.0%)** will have a heart attack
Which medication would you choose?	I would choose Medication A ☐	I would choose Medication B ☐

How likely would you be to miss or skip doses of each medication?	Much more likely to miss or skip doses with Medication A ☐	A little more likely to miss or skip doses with Medication A ☐	Equally likely to miss or skip doses with Medication A and Medication B ☐	A little more likely to miss or skip doses with Medication B ☐	Much more likely to miss or skip doses with Medication B ☐

Table 1. Levels for Glucose-Control Feature

HbA1c Level	Blood Sugar Control	What Does It Mean?
Less than 7%	Optimal control	Your blood sugar is well controlled
7% to 8%	Suboptimal control	Your blood sugar is not perfect, so your doctor will want to continue to monitor it closely
More than 8%	Poor control	Your blood sugar levels are too high and need to be lowered

Table 2. Levels for Side Effect Features Used in the Survey Instrument

Side Effect Feature	Levels
Number of hypoglycemic events per month	None Less than 1 1 to 2 More than 2
Water retention	No Yes
Weight gain in first 6 months	None 5 pounds 10 pounds 20 pounds
Mild stomach upset	No stomach problems Mild nausea and vomiting or diarrhea that goes away after about a week or two Mild nausea and vomiting or diarrhea that continues as long as you take the medicine
Chance of a heart attack	No additional person will have a heart attack 1 additional person out of 1,000 (0.1%) will have a heart attack 5 additional people out of 1,000 (0.5%) will have a heart attack 10 additional people out of 1,000 (1.0%) will have a heart attack

Analysis

- Estimate satisfaction scores using multivariate, random-parameters, or mixed-logit estimation
- Estimate Heckman two-stage ordered probit model to predict likely adherence

RESULTS

Table 3. Demographic Information for Subjects (N = 407)

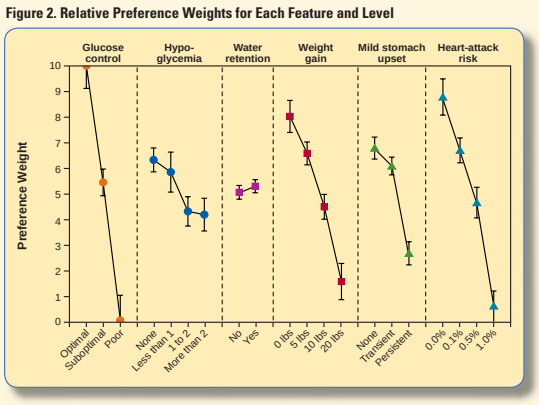
Category	Mean (SD)	
Age (years)	57 (11.8)	
Income (US$)[a]	57,948 (42,667)	
Category	**n**	**Percent**
Gender		
Male	251	62%
Female	156	38%
Marital Status		
Single, never married	39	10%
Married	253	62%
Divorced	53	13%
Widowed	8	2%
Separated	21	5%
Living with partner	33	8%
Current Employment Status[b]		
Employed full time	112	28%
Employed part time	37	9%
Self-employed	23	6%
Not employed but looking for work	10	2%
Not employed and not looking for work	32	8%
Retired	178	44%
Student	10	2%
Homemaker	31	8%
Race/Ethnicity		
White	381	94%
Black	7	2%
Native American or Alaska native	2	< 1%
Mixed racial background	6	1%
Other race	2	< 1%
Hispanic	4	1%
Asian	3	1%
Missing	2	< 1%
Highest Education		
Less than high school	21	5%
High school diploma or GED	83	20%
Some college, no degree	47	12%
Technical school	98	24%
Associate degree	18	4%
Bachelor's degree	51	13%
Some graduate school but no degree	36	9%
Graduate or professional degree (e.g., MBA, MS, MD, PhD)	53	13%

[a] The exchange rate used to convert British pounds to US dollars is US$1.00 = £0.54017.
[b] Total sums to more than the sample size (100%) for this multiple response question.

Relative Preference Weights (Figure 2)

- Relative preference weights for each medication feature and level are scaled between 0 and 10.
  - For the most important feature (glucose control), the best level (optimal control) is assigned a relative preference weight of 10, and the worst level (poor control) is assigned a relative preference weight of 0.
  - All other feature levels are scaled relative to the most important feature.
- The distance between the relative preference weight for the best level and worst level of a feature can be interpreted as the relative importance of the feature.
  - Glucose control (change in HbA1c levels) was the most important feature.
  - Medication-related heart-attack risk and weight gain were the second and third most important features, respectively.
  - Transient stomach problems that resolve after 1 or 2 weeks were not important to subjects' treatment choices, but persistent stomach problems were.
  - Mild-to-moderate hypoglycemia was only a predictor of treatment choice when it occurred more than once a month.
  - Water retention was the least important feature.

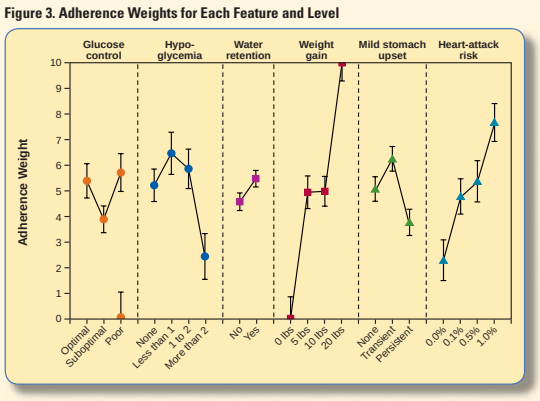
Figure 2. Relative Preference Weights for Each Feature and Level



Adherence (Figure 3)

- Subject-specific characteristics that increased the likelihood that a given subject would be nonadherent to future OADs include nonadherence with current medication and previous medication-related weight gain.
- Weight gain and heart attack risk have the greatest impact on the likelihood that a subject will miss or skip doses of his or her diabetes medication.
  - As the size of the weight gain or the magnitude of the heart-attack risk increases, so does the likelihood that a subject will miss or skip doses.
- Weight gain results were as follows:
  - Weight gain of 5 or 10 pounds has a statistically significant effect on nonadherence.
  - Weight gain of 20 pounds yields a statistically significant increase in the likelihood of nonadherence relative to a 5- to 10-pound increase in weight.
- Treatment-related heart-attack risk results were as follows:
  - Treatment-related heart-attack risk between 0.1% and 0.5% results in a statistically significant increase in the likelihood of nonadherence.
  - Treatment-related heart-attack risk of 1.0% yields a statistically significant increase in the likelihood of nonadherence relative to a risk of 0.5%.
- Subjects are likely to be less adherent to OADs that cause weight gain or are associated with treatment-related heart-attack risk.

Figure 3. Adherence Weights for Each Feature and Level



CONCLUSIONS

- While people with T2DM believe glucose control is important, medication side effects influence patients' treatment choices.
- Efficacy as measured under controlled, clinical-trial conditions may overstate actual treatment effectiveness as a result of patient concerns over OAD side effects.
- OADs that are associated with weight gain and increased cardiovascular risk may result in poor medication adherence and thus limit their effectiveness in controlling blood glucose levels.

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