

The Effect of Outcome Uncertainty on Treatment Choices Among ART-Naïve HIV-Positive African Americans (AAs)

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Abstract

OBJECTIVE: To quantify preferences for well-defined short-term adverse event (AE) risks and relatively uncertain long-term risks among treatment-naïve HIV-positive African Americans (AAs).

METHODS: Self-identified antiretroviral treatment (ART)-naïve HIV-positive AAs were recruited through clinics. Respondents completed a series of choice-format conjoint trade-off tasks that required them to select between hypothetical treatment alternatives with varying levels of efficacy and AE risks. Treatment attributes included virologic failure (VF), hypersensitivity reaction (HSR), bone damage, kidney damage, and outcomes of bone or kidney damage (degree to which the problem could be treated successfully). All attributes were expressed as probabilities of occurrence. Relative importance weights were estimated using multivariate, random-parameters, or mixed-logit estimation.

RESULTS: A total of 153 patients completed the survey. Without considering the different outcomes associated with the long-term AEs, bone and kidney damage were the most important (most undesirable) attributes and short-term HSR and VF were the least important (least undesirable) attributes. Specifically, bone damage was approximately twice as important as HSR in influencing treatment preferences ($P<0.1$). When considering the outcome of a long-term AE, patients were not concerned about bone or kidney damage if these could be treated successfully. Nor were patients concerned with kidney damage when the outcome was uncertain. Patients were strongly averse to the risk of bone damage when the problem could not be treated successfully or when the outcome was uncertain ($P<0.01$) and to the risk of kidney damage when the problem could not be treated successfully ($P<0.01$).

CONCLUSIONS: Patients have preferences over both the risks of different AEs and the uncertainty surrounding their outcomes. ART-naïve HIV-positive AA patients indicated that short-term AEs with relatively certain outcomes are less problematic than long-term AEs with uncertain outcomes. Clinicians should consider such preferences when talking with their patients about alternative treatment options.

Introduction

- An estimated 1 million Americans, 0.33% of the United States (US) population, have been diagnosed with HIV.¹
- In the US, African-American (AA) individuals are disproportionately affected.
- Antiretroviral treatments have improved with the introduction of new drug combinations.
- Some new ARTs offer added dosing convenience but may be associated with short- and long-term adverse events (AEs).
- AEs have been reported with virtually all ARTs.
- AE risk factors may vary according to race.

Objective

- To quantify preferences for well-defined short-term AE risks and relatively uncertain long-term risks among ART-naïve HIV-positive AAs.

Methods

Subjects

- Inclusion criteria:
 - Aged 18 years or older
 - US resident
 - Self-reported African American or black
 - HIV-positive but ART-naïve
 - Able to read and understand English at the sixth-grade level (about age 12)
- Recruitment:
 - Participants were recruited through clinical sites.
 - All subjects provided online informed consent.
 - The final sample was 153.

Survey Instrument

- The survey instrument was developed using focus groups, face-to-face interviews, and consultation with clinical experts.
- Participants completed the Web-enabled survey instrument at study clinics.
- A stated-choice (SC) survey method was used, as follows:
 - The survey consisted of a series of choices between pairs of hypothetical treatment profiles.
 - Each treatment profile was defined as a set of attributes.
 - Survey choices elicited subject tradeoffs among varying levels of different attributes.
 - This method is the most valid and reliable technique available for quantifying preferences.^{2,3,4,5}
- Participants chose between 10 pairs of treatment options (Figure 1).
 - Choices were characterized by varying levels of benefit, short-term and long-term AE risks, and the outcome associated with the long-term AE risks (Table 1).
 - Attribute levels were chosen to encompass the range over which events might plausibly occur (based on published studies) and over which subjects likely will have preferences, even if the level is clinically implausible.
 - The benefit outcome constituted changes/reductions in the chance that the medicine does not work (virologic failure) within 1 year of starting treatment.⁶
 - AE risks were described using a risk-grid approach.⁷
 - AE risks included the following:
 - Chance of a serious allergic reaction (HSR) within 6 weeks of starting treatment
 - Chance of bone damage (decreased bone mineral density or osteoporosis) within 5 years of starting treatment
 - Chance of kidney damage within 5 years of starting treatment
 - Outcomes associated with long-term serious AEs (bone and kidney damage) included the following:
 - AE (bone or kidney damage) can be treated successfully if detected
 - Do not know if AE (bone or kidney damage) can be treated successfully if detected
 - AE (bone or kidney damage) cannot be treated successfully if detected
- The experimental design included the following:
 - Combinations of attribute levels in each alternative in each choice question that were developed using rigorous statistical techniques
 - A statistically efficient experimental design with known statistical properties^{8,9,10}
 - Three survey versions with different combinations of choice questions, randomly assigned to subjects
- The survey instrument also collected demographic information (age, sex, education, and employment status) and the year in which the subject learned he or she was HIV-positive.

Figure 1. Example of Choice Question Comparing HIV Treatment Options

Medicine Feature	Medicine A	Medicine B
CHANCE THAT MEDICINE DOES NOT WORK	15 people out of 100 (15%)	7 people out of 100 (7%)
CHANCE OF ALLERGIC REACTION	12 people out of 100 (12%)	1 person out of 100 (1%)
CHANCE OF BONE DAMAGE	10 people out of 100 (10%)	5 people out of 100 (5%)
CHANCE OF KIDNEY DAMAGE	1 person out of 100 (1%)	10 people out of 100 (10%)
WHAT HAPPENS IF YOU HAVE BONE OR KIDNEY DAMAGE	Don't know if problem can be treated successfully	Problem can be treated successfully

Which medicine would you choose if these were the only options available?
 Medicine A Medicine B

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

Treatment Attribute	Levels
Chance that medicine does not work	7% 15% 21%
Chance of having an allergic reaction	None 1% 8% 12%
Chance of bone damage	None 1% 5% 10%
Chance of kidney damage	None 1% 5% 10%
What happens if you have bone damage or kidney damage	<ul style="list-style-type: none"> • You don't know if the problem can be treated successfully. • The problem can be treated successfully. • The problem cannot be treated successfully.

Analysis

Relative Importance

- Random utility modeling techniques¹¹ were used to estimate the treatment preference function.
- Relative importance weights were estimated using multivariate, random-parameters (mixed-logit) estimation.

Maximum Acceptable Risk

- Measure of risk tolerance—maximum additional probability of AE that subjects are, on average, willing to accept for a given decrease in the risk of virologic failure.

Results

Demographic Characteristics (Table 2)

Table 2. Demographic Information for Survey Subjects

Variable	n	Percentage
Age	146	
Years, mean (SD)	41.8 (8.6)	n/a
Sex	151	
Male	88	58.3%
Female	63	41.7%
Highest Education Level	151	
Less than high school	17	9.9%
High school	65	44.4%
Some college	55	36.4%
Bachelor's degree or higher	14	9.3%
Employment Status	149	
Full-time	23	15.5%
Part-time	15	10.1%
Self-employed	14	9.4%
Homemaker	10	6.7%
Student	3	2.0%
Retired	2	1.3%
Disabled/unable to work	48	32.2%
Unemployed but looking for work	28	18.8%
Unemployed and not looking for work	6	4.0%
Years of HIV-Positive Status	139	
Years, mean (SD)	7.6 (6.8)	n/a

n = number; SD = standard deviation; n/a = not applicable.

Relative Importance

- Without considering the different outcomes associated with the long-term AEs (Figure 2):
 - Bone and kidney damage were the most important (most undesirable) attributes.
 - Short-term HSR and VF were the least important (least undesirable) attributes.
 - Specifically, bone damage was approximately twice as important as HSR in influencing treatment preferences ($P<0.1$).
- When the outcome of long-term AEs was considered (Figure 3):
 - Bone damage that could be treated successfully was not important.
 - Kidney damage that could be treated successfully or if the outcome was uncertain was only marginally important.
 - Bone damage that could not be treated successfully or when the outcome was uncertain ($P<0.01$ for each) and kidney damage that could not be treated successfully ($P<0.01$) were very important.

Maximum Acceptable Risk

- Without considering the outcomes of long-term AEs, maximum acceptable risk (MAR) associated with the short-term HSR was higher than the MAR for either bone or kidney damage indicating that these subjects are more averse to the risks of bone damage and kidney damage than to the risk of HSR.¹²

Figure 2. Relative Importance of Attributes (Not Considering Outcomes of Long-Term Adverse Events)

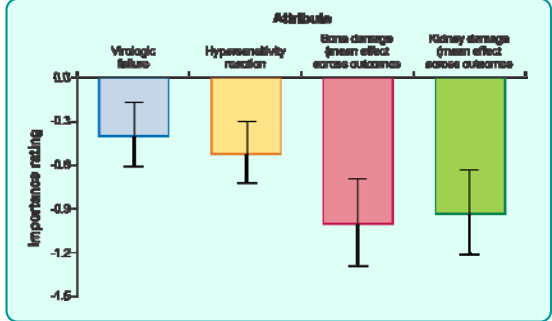
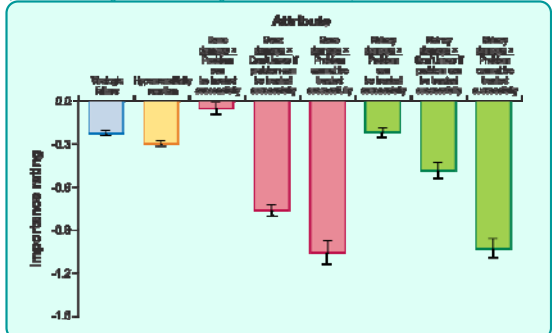


Figure 3. Relative Importance of Attributes (When Considering Outcomes of Long-Term Adverse Events)



Discussion

- These data suggest that patients understand the goal of HIV therapy and recognize that to achieve this goal they may have to accept some tradeoffs.
- Results also suggest that patients would prefer a well-defined AE with a short-term risk instead of the potential for AEs in the long term, especially if these long-term AEs have an uncertain outcome.
- Efficacy was defined by virologic response and not CD4 cell count or occurrence of opportunistic infections, although these outcomes are usually related.
- Participants in this study were ART-naïve and African American; results may not be generalizable to other populations.
- Finally, the result of this analysis suggests that well-informed patients have clear and measurable preferences for treatment attributes. Thus, physicians should provide full counseling to patients before prescribing any regimen.

Conclusions

- Patients have preferences over both the risks of different AEs and the uncertainty surrounding their outcomes.
- ART-naïve HIV-positive AA patients indicated that short-term AEs with relatively certain outcomes are less problematic than long-term AEs with uncertain outcomes.
- Clinicians should consider such preferences when talking with their patients about alternative treatment options.

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