The Impact of Patient, Disease, and Treatment-Related Factors on Quality of Life for HIV Patients on HAART

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Introduction

- As differences in highly-active antiretroviral therapy (HAART) regimen potency diminish, other aspects of therapy, such as quality of life (QOL), may impact regimen choice.
- However, little information exists about the impact of dosing, adverse events (AEs), and other factors on QOL in HIV.
- We pooled data from 5 open-label clinical trials of HAART to assess the impact of these factors on utilities derived from SF-36 data.

Methods

- Data were pooled from 5 open-label clinical trials (APV30003, ESS30008, ESS40001, ESS40002, ESS40013) sponsored by GSK.
- Trial participants (n=1,327) completed the SF-36 at multiple time periods (4,707 total records).
- SF-36 data were converted to SF-6D and EQ-5D social preference weighted utilities as per Brazier et al (2002) and McEwan et al (2004), respectively.
- Utility was modeled as a function of patient and disease characteristics, regimen attributes, and frequent and/or clinically relevant AEs using a maximum likelihood mixed model.
- The estimated equation was then used to predict mean utility scores by CD4+ cell count range based on the observed value of the predictors.

Results

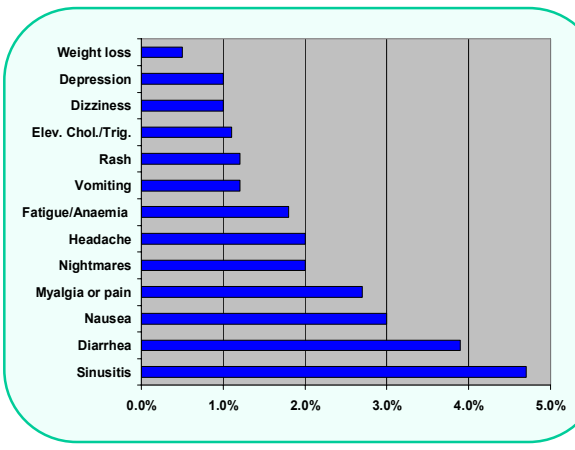
- Approximately two-thirds of the population was male, and nearly 90% of the population was aged between 25 and 54 (Table 1).
- Most subjects were White, but Hispanics and Blacks were well represented.
- 70% resided in the US.

Table 1. Analysis Population Demographics

Variable		Frequency (%)
Overall		1327 (100%)
Gender:	Female	290 (21.9%)
	Male	1037 (78.1%)
Age:	18-24	76 (5.7%)
	25-34	432 (32.6%)
	35-44	530 (39.9%)
	45-54	215 (16.2%)
	≥55	68 (5.1%)
	Missing	6 (0.5%)
Race:	Hispanic	344 (25.9%)
	Black	401 (30.2%)
	White	559 (42.1%)
	Asian/Other	23 (1.7%)
Region:	Europe	95 (7.2%)
	US	943 (71.1%)
	Rest of World	289 (21.8%)

- Of the 4707 utility scores for analysis, 1600 (34%) were associated with ≥1 AE.
- There were 760 (16%) utility scores associated with ≥1 Grade 2 (moderate) or higher event.
- Sinusitis was the most frequently reported AE (Figure 1).

Figure 1. Adverse Event Frequencies (%)



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References

- **Brazier** et al. The estimation of a preference-based measure of health from the SF-36. J Health Econ. 2002;21(2):271-292.
- Kind P, **McEwan P**, et al. Advances in mapping health-related quality of life: An EQ-5D index based on SF-36 data. Presented at ISPOR's 9th Annual International Meeting, Arlington, Virginia. May 2004.
- **Walters** SJ, Brazier JE. What is the relationship between the minimally important difference and health state utility values? The case of the SF-6D. Health Qual Life Outcomes. 2003;1:4.
- **Revicki** et al. Change in clinical status, health status, and health utility outcomes in HIV-infected patients. Med Care. 1995;33(4 Suppl):AS173–AS182.
- **Tsevat** et al. The will to live among HIV-infected patients. Ann Intern Med. 1999;131(3):194–198.
- **Mrus** et al. Utilities derived from visual analog scale scores in patients with HIV/AIDS. Med Decis Making. 2003;23(5):414-421.
- **Schackman** et al. Comparison of health state utilities using community and patient preference weights derived from a survey of patients with HIV/AIDS. Med Decis Making. 2002;22(1):27-38.
- **Simpson** et al. Cost-effectiveness of lopinavir/ritonavir versus nelfinavir as the first-line highly active antiretroviral therapy regimen for HIV infection. HIV Clin Trials. 2004;5(5):294-304.

Results (cont.)

- The predicted utility model parameter estimates are shown in Table 2.

Table 2. Utility Model Parameter Estimates

Utility Model Parameter	Estimate (SE)	
	Brazier Algorithm	McEwan Algorithm
Intercept	0.827 (0.022) **	0.942 (0.024) **
Age	-0.001 (0.000) **	-0.003 (0.000) **
Female	-0.037 (0.009) **	-0.061 (0.010) **
Hispanic (vs. White)	0.019 (0.010)	0.018 (0.011)
Black (vs. White)	0.029 (0.009) **	0.012 (0.010)
Asian or Other Race (vs. White)	-0.034 (0.028)	0.003 (0.031)
Europe (vs. US)	-0.010 (0.016)	0.014 (0.017)
Rest of the World (vs. US)	0.012 (0.009)	0.017 (0.010)
Injection Drug Use	-0.056 (0.016) **	-0.077 (0.018) **
AIDS at Baseline	-0.002 (0.012)	0.004 (0.013)
Undetectable Viral Load	0.005 (0.004)	0.009 (0.004) *
CD4 >200 (vs. ≤200)	0.025 (0.006) **	0.029 (0.007) **
Transition to AIDS During Trial	-0.002 (0.029)	-0.017 (0.031)
Any Prior HIV Conditions	-0.036 (0.011) **	-0.042 (0.012) **
ART Naïve at Trial Entry	0.004 (0.009)	0.005 (0.010)
Total # of Pills Prescribed/ Day	0.001 (0.001)	0.000 (0.001)
QID Dosing vs BID	0.120 (0.132)	0.080 (0.146)
TID Dosing vs BID	-0.131 (0.058) *	-0.061 (0.064)
QD Dosing vs BID	0.022 (0.015)	0.014 (0.016)
Treatment Symmetry	-0.016 (0.009)	-0.015 (0.010)
Take WITH Food/Drink	-0.028 (0.011) **	-0.025 (0.011) *
Take WITHOUT Food/Drink	-0.002 (0.009)	0.009 (0.010)
AE Grade ≥2	-0.012 (0.005) *	-0.024 (0.006) **
Sinusitis	-0.006 (0.007)	0.001 (0.007)
Diarrhea	-0.009 (0.008)	-0.010 (0.008)
Nausea	-0.008 (0.009)	-0.009 (0.010)
Myalgia or Pain	-0.028 (0.009) **	-0.030 (0.010) **
Headache	-0.010 (0.011)	-0.005 (0.012)
Nightmares	-0.020 (0.010)	-0.008 (0.011)
Fatigue or Anemia	-0.013 (0.011)	-0.006 (0.012)
Vomiting	-0.005 (0.014)	-0.009 (0.015)
Rash	-0.010 (0.013)	-0.034 (0.014) *
Elev. Cholesterol or Triglycerides	0.006 (0.015)	0.036 (0.016) *
Depression	-0.054 (0.015) **	-0.077 (0.015) **
Dizziness	-0.033 (0.015) *	-0.043 (0.016) **
Weight Loss	-0.015 (0.020)	-0.021 (0.022)
Other AE	-0.012 (0.004) **	-0.008 (0.005)

* indicates the parameter estimate is significant at p<0.05. ** indicates the parameter estimate is significant at p<0.01. ART = antiretroviral; AE = adverse event.

- Positive (negative) coefficients indicate that utility for individuals with that parameter is higher (lower) than individuals without (0 to 1.0 scale where 1.0 = full health).
- Age, female gender, injectable drug use, prior HIV-associated conditions, low CD4+ count and food/drink requirements were associated with reduced utility in both models, although parameter estimates tended to be smaller under the Brazier algorithm.
- Myalgia or pain, depression and AE severity consistently reduced utility. Elevated cholesterol or triglycerides increased utility in both models, but was statistically significant only with the McEwan algorithm.
- Walters (2003) suggests a SF-6D minimally important difference of 0.03, indicating that AEs substantially impact patients' QOL.
- Table 3 compares predicted utilities from the Brazier and McEwan based models to published, directly-derived standard gamble (SG) utilities or SG-based estimates.

Table 3. Predicted Utility by CD4+ Range

CD4+ Range	Brazier Model	McEwan Model	Directly-Derived SG*		SG-Based Estimates	
			Revicki (1995)**	Tsevat (1999)***	Schackman (2002)**	Simpson (2004)***
>500	0.80	0.86	0.80	0.88	0.97	0.95
350-499	0.78	0.85	0.80	0.78	0.97	0.93
200-349	0.78	0.84	0.82	0.78	0.91	0.93
100-199	0.75	0.81	0.80	0.83	0.85	0.85
<100	0.74	0.80	0.80	0.70	0.85	0.78

*As reported in Mrus et al. (2003). **Estimates for AIDS were classified as ≤200, symptomatic HIV as 200-349, and asymptomatic HIV as ≥350. *** Average value across CD4+ groups. SG = standard gamble.

Discussion

- Even in this relatively healthy and highly adherent clinical trial population, quality of life was affected by treatment regimen attributes and adverse events in addition to demographic and disease-related factors.
- These methods produce plausible estimates of utility, particularly compared to directly-derived SG utilities.
- The ability of the models to detect reductions in utility associated with some adverse events may have been limited due to the infrequent administration of the SF-36 at time points early in the course of therapy initiation (4 – 8 weeks), when short-term events are likely to occur. Also, most patients received BID regimens and many received fixed-dose combinations.

Conclusions

- HAART regimen characteristics and adverse events affect quality of life, and should be considered alongside efficacy when making treatment choices.
- Similar models studying the full range of HIV progression and treatment options would add to this work.