

Cost-Effectiveness Analysis of Combined Phenotype and Genotype Drug Resistance Testing versus Genotyping Alone

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BACKGROUND Previously published studies concluded that genotypic testing for resistance to highly active antiretroviral therapy (HAART) is cost-effective when compared to decisions based on clinical opinion alone. We compared the cost-effectiveness of combined phenotype and genotype testing (PTGT) [“Phenosense GT” by Monogram Biosciences] vs. genotyping alone (GT) for different subgroups of treatment-experienced patients defined by CD4 count.

METHODS A Markov model was used to determine the cost per quality adjusted life year (QALY) and incremental cost-effectiveness of using PTGT vs. GT. Data were derived from prior studies which examined physician choices of HAART regimen based on GT or PTGT information. A susceptibility score (SS) was calculated for each HAART regimen, by summing the number of drugs to which the virus is susceptible. Published data provided estimates of treatment success that were greater for HAART regimens with $SS \geq 3$ compared to HAART regimens with $SS \leq 2$. Patient quality of life and survival outcomes were derived from existing datasets. Treatment costs were estimated at \$1,500 per month for HAART and \$1,211 per month for all other medical costs.

Figure 1: GUESS III Method

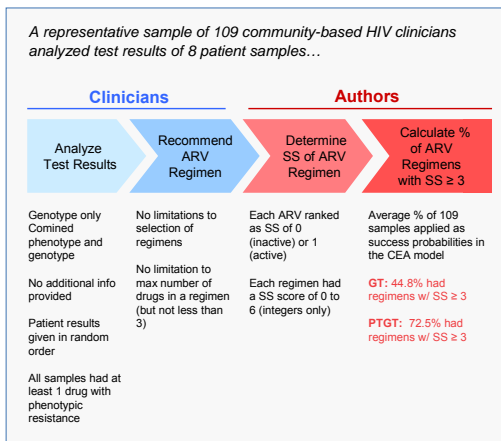
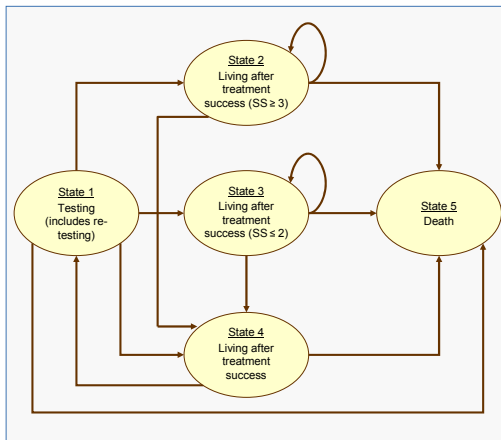
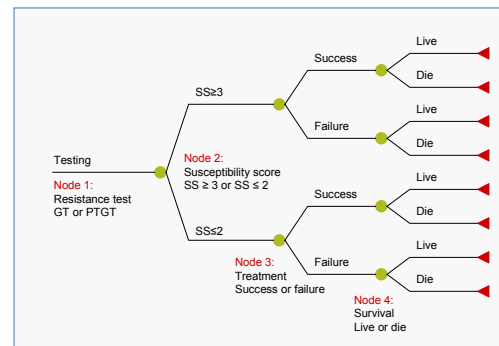


Figure 2: Model States



A Markov model comparing the cost, QALYs, and survival of patients receiving HAART after genotypic resistance testing or combined phenotypic and genotypic resistance testing. (SS = susceptibility score) A 6-month cycle was used to model clinically meaningful time frames.

Figure 3: Model Structure



The model begins with a cohort of patients receiving resistance testing (Node 1). Based on the test results, a clinician determines a HAART regimen. The HAART regimen has a probability of having a susceptibility score greater than or equal to 3 or less than or equal to 2 (Node 2). Each regimen has a chance of success or failure, with higher rates of success for regimens with higher SS (Node 3). After treatment over a six-month period, patients may live or die, with higher rates of patient survival for those experiencing treatment success (Node 4).

Table 1: Variables

Variable	Value
Probabilities	
Susceptibility score (SS)	
Probability of regimen with $SS \geq 3$ from:	
Genotyping alone	44.8%
Combined phenotyping and genotyping	72.5%
Treatment success	
Regimens with $SS \leq 2$	23.25%
Regimens with $SS \geq 3$	49.0%
Survival, 6-month	
After treatment success	99.0%
After treatment failure	97.7%
Quality of life (QOL)	
Adjustments	
Discount factor of QOL after treatment success	0.870
Discount factor of QOL after treatment failure	0.810
Economic	
Testing	
Genotypic resistance testing (GT)	\$355
Phenotypic resistance testing	\$855
Combined resistance testing (PTGT)	\$1,210
Therapy	
HAART	\$1,500 / month
Other related medical costs	\$1,211 / month
Other	
Discount factor for costs, annual basis ¹	3%
Death adjustment ²	50%
Probability of continued success	90%

¹ Model conducted using current year dollars
² Patients who die during a given 6-month cycle live an average of half the length of the period, and so incur half the costs and QALYs

Table 2: Baseline Results

Description	GT	PTGT
Costs	\$160,040	\$161,299
QALYs	4.54	4.59
Cost per QALY	\$35,326	\$35,175
ICER, PTGT to GT	\$28,812 per QALY	

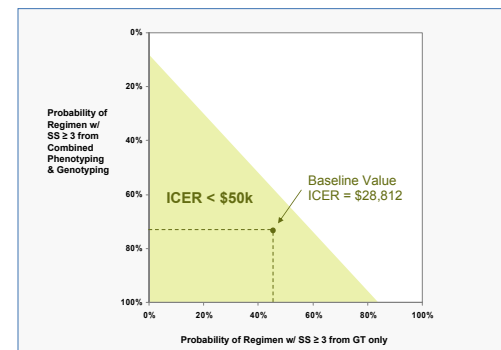
ICER = Incremental Cost-Effectiveness Ratio

Table 3: Sensitivity Analysis Results

Description	ICER, PTGT to GT
CD4 < 50	\$38,215 per QALY
CD4 50-200 (baseline value)	\$28,812 per QALY
CD4 > 200	\$35,109 per QALY
Lower SS threshold: $SS \geq 2$ vs. $SS \leq 1$	\$47,948 per QALY
Baseline SS threshold: $SS \geq 3$ vs. $SS \leq 2$	\$28,812 per QALY
Higher SS threshold: $SS \geq 4$ vs. $SS \leq 3$	\$56,455 per QALY
Other medical costs = \$0	\$30,159 per QALY
Other medical cost variability =	
0%	\$38,172 per QALY
5% (baseline value)	\$28,812 per QALY
10%	\$18,911 per QALY
20%	Cost saving/Dominant ¹
With continued treatment success or failure	Cost saving/Dominant ²

¹ PTGT had both lower cumulative costs and higher QALYs than GT. ICER would be calculated as -\$889.
² PTGT had both lower cumulative costs and higher QALYs than GT. ICER would be calculated as -\$18,061.

Figure 4: 2-way Sensitivity Analysis



RESULTS For treatment-experienced patients with CD4 50-200 at initial resistance testing, the baseline analysis showed the cost per QALY over 6 years to be nearly identical for PTGT and GT (\$35,175 vs. \$35,236, respectively), despite the higher cost of PTGT testing. Overall model results were similar to previously published reports on the cost-effectiveness ratio for GT. The incremental cost-effectiveness ratio (ICER) of PTGT to GT was \$28,812 per QALY. Sensitivity analyses conducted for other CD4 level patient subgroups, and using a wide range of values for model parameters, resulted in similar ICERs.

CONCLUSION Genotyping in combination with actual phenotyping is cost-effective compared to genotyping alone across a range of CD4 counts in treatment-experienced HIV patients. Cost-effectiveness ratios improve as the benefit of continued treatment success is incorporated into the analysis.

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- Corzillius M et al. "Cost effectiveness analysis of routine use of genotypic antiretroviral resistance testing after failure of antiretroviral treatment for HIV." *Antiviral Therapy* 2004, 9:27-36.
- Gebo KA et al. "Costs of HIV medical care in the era of highly active antiretroviral therapy." *AIDS* 1999, 13:963-9.
- Zolopa AR et al. "Clinical Selection of HRV Regimens is Influenced by the Type of Resistance Test Information Provided," poster presentation at the 12th Conference on Retroviruses and Opportunistic Infections, Feb 2005, Boston, MA.