

# Increasing Prevalence of NNRTI-Associated Drug Resistance Mutations in Patients with Acute/Early HIV in San Francisco

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## Abstract

**Background.** In prior data, the prevalence of transmitted drug resistance (TDR) in recently HIV-infected patients in the Options Project cohort in San Francisco declined from an annual peak of 19-27% of patients in 2000-2002 to 10-11% in 2003-2004. We sought to assess changes in the prevalence of TDR in San Francisco since 2003.

**Methods.** All patients enrolled in the Options Project, a longitudinal cohort study in San Francisco of acute/early HIV (< 12 months) underwent genotyping analysis at or soon after entry into the cohort. Patients were assessed for the presence of an initial genotype of at least one drug resistance mutation, using published guidelines which exclude common polymorphisms (Shafer, 2007). Genotypes were excluded if performed >10 days after initiation of antiretroviral (ARV) therapy. The prevalence of transmitted drug resistance mutations, as well as the prevalence of these mutations by class (NNRTI, NNRTI, PI) was assessed in each year from 2003-2007. A chi-square test for linear trend was used to assess whether prevalence changed significantly over time.

**Results.** Of a total of 7224 patients who entered the cohort from 2003-2007 and underwent initial genotyping, 36 (16%) had evidence of transmitted drug resistance mutations. There was a statistically significant increase in the prevalence of transmitted drug resistance mutations over the study period ( $p = 0.01$ ). There was a statistically significant increase in the prevalence of NNRTI mutations ( $p = 0.04$ ). Changes over time in the prevalence in NNRTI mutations were not significant ( $p = 0.2$ ), nor were changes in PI mutations ( $p = 0.9$ ).

	2003	2004	2005	2006	2007
Total pts.	58	54	43	29	40
Any resistance	10%	11%	19%	17%	28%
NNRTI	7%	6%	12%	7%	15%
NNRTI	2%	6%	9%	10%	8%
PI	9%	4%	0%	7%	8%

**Conclusions.** We observed a fairly steady and statistically significant increase in the prevalence of TDR in San Francisco from a nadir in 2003. This was driven most strongly by increases in NNRTI resistance, while PI resistance was steady or declined. This increase may be related to the increasing use of NNRTIs and subsequent development of resistance in persons receiving treatment.



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## Results

- Of the 266 patients who entered the cohort from 2003-2008 and underwent initial genotyping, 40 (15%) had evidence of transmitted drug resistance.
- From 2003-2007, both overall transmitted drug resistance ( $p = 0.01$ ) as well as NNRTI resistance ( $p = 0.04$ ) increased.
- There was a significant drop in transmitted drug resistance from 28% in 2007 to 10% in 2008 (chi-square;  $p = 0.04$ ).
- Changes over time in the prevalence of NNRTI mutations were not significant.
- Changes over time in the prevalence of PI mutations were likewise not significant.

Figure 1. Prevalence of transmitted drug resistance by drug class, 2003-2008

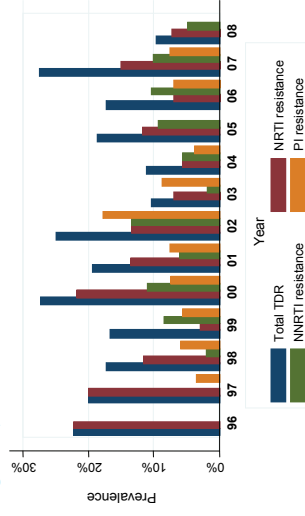


Table 1. Prevalence of transmitted drug resistance by drug class, 2003-2008

	2003	2004	2005	2006	2007	2008
Patients (n)	58	54	43	29	40	42
Any resistance	10%	11%	19%	17%	28%	10%
NNRTI	7%	6%	12%	7%	15%	7%
NNRTI	2%	6%	9%	10%	8%	5%
PI	9%	4%	0%	7%	8%	0%

## Conclusions

- From a nadir in 2003, we observed an increase in the prevalence of transmitted drug resistance through 2007.
- This rise was driven most strongly by increases in NNRTI resistance, perhaps reflective of increasing use of NNRTIs.
- There was a significant drop in transmitted drug resistance from 28% in 2007 to 10% in 2008. This may reflect increasing virologic suppression of drug-resistant patients using new recently-licensed ARVs including maraviroc (approved 8/07), raltegravir (10/07), and etravirine (1/08).
- PI resistance did not change significantly during the study period.

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