

Development and Validation of a Model to Predict Virologic Failure Using Administrative Claims

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Background

- Combination antiretroviral treatment (cART) regimens:
 - typically include at least three drugs from two different drug classes
 - are effective in suppressing viral load (amount of HIV RNA in the blood)
 - have dramatically reduced HIV-related morbidity and mortality
- Clinicians follow treatment effectiveness by measuring HIV viral load on a regular basis
- Ability of payers to assess real-world effectiveness of cART regimens using claims databases is limited, as these databases usually do not contain lab values, including HIV viral load
 - *Thus, when patients switch regimens, payers cannot determine if cause is virologic failure or some other reason*

Objectives

- Primary Objective
 - To develop and validate a claims signature model that can use administrative claims data to estimate the likelihood of virologic failure among HIV patients who switch cART regimens
- Secondary Objective
 - To apply the validated claims signature model to a claims dataset as a worked example

Methods: Data

- Created three datasets of adult HIV patients who switched from one cART regimen (“pre-switch” regimen) to another cART regimen (“post-switch” regimen)
 - development dataset – data from *HIV Insight*, an HIV clinical registry with detailed clinical data including lab data (n=1,691)
 - validation dataset – administrative claims data from *i3/Ingenix LabRx* **with** integrated lab data (n=1,073)
 - application dataset -- administrative claims data from *i3/Ingenix LabRx* **without** integrated lab data (n=3,954)

Methods: Population

Patient selection criteria:

- HIV-infected adult
 - development dataset: any patient enrolled in registry
 - validation & application datasets: any patient that has a claim with an ICD-9 code^a for HIV (042, V08)
- Evidence of treatment with cART
- Had ≥ 1 regimen switch between Jan 2003 and March 2008
 - cART regimens (all with NRTI backbone): PI-based, NNRTI-based, or PI- and NNRTI-based^b
 - Switch defined as first change of at least 1 drug in regimen during study interval^c

e.g., AZT/3TC+EFV \rightarrow TDF/FTC/EFV^d

^a ICD-9, International Classification of Diseases, Ninth Revision

^b NRTI, nucleoside/nucleotide reverse transcriptase inhibitor; PI, protease inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor

^c excluded changes between lamivudine and emtricitabine, which were considered therapeutically interchangeable

^d AZT, zidovudine; 3TC, lamivudine; EFV, efavirenz; TDF, tenofovir; FTC, emtricitabine

Methods: Analysis

- Calculated observed rates of virologic failure in development and validation datasets
- Developed generalized linear models for binomial outcome to predict odds of virologic failure (using development dataset)
 - Base model: main effects for all independent variables
 - Final model: stepwise addition of significant interaction terms
- Validated models for use with claims data (using validation dataset)
 - Goodness-of-fit: Hosmer-Lemeshow test
 - Predictive abilities: C statistics
- Applied the validated claims signature model to a claims dataset as a worked example (using administrative dataset)

Methods: Dependent Variable

- The dependent variable was **virologic failure of cART regimen**, defined as:
 - HIV RNA level >400 copies/mL after 24 weeks of therapy
 - or*
 - detectable^a HIV RNA level after 48 weeks of therapy
 - or*
 - detectable HIV RNA level after prior suppression^b

^a Detectable level defined by threshold of lab test used

^b Prior suppression = undetectable HIV RNA level within 30 days prior to pre-switch regimen start

Methods: Independent Variables

- Clinical experts identified the independent variables
 - Demographics
 - Payer type
 - Treatment history (naïve vs experienced)
 - Healthcare utilization^a
 - Drug-related adverse events^b
 - Regimen types (PI vs NNRTI vs PI&NNRTI)
 - Pill burden
 - Time on pre-switch regimen
 - Switch year
 - Change in regimen type
 - Change in regimen intensity^c

^a number of physician visits or any emergency department or hospital care 90 days before switch and HIV mRNA, CD4, and resistance tests 180 days before switch; ^b new diagnosis of abacavir sensitivity, anemia, hyperlipidemia, lipoatrophy or lipodystrophy, or new treatment with erythropoietin, loperamide, or neurontin; ^c change in total number of medications within a regimen class (e.g., NRTI, NNRTI, or PI) and/or a change in class

Results: Model Development (1)

Base model:

- Included all main effect variables
- Demographic variables not significant predictors of virologic failure as cause of switch
- Odds ratios (ORs) for significant predictors:

Independent variable	OR (95% CI)
Treatment-naïve	0.60 (0.41-0.89)
Longer time on first regimen	
181-360 vs. <180 days	45.15 (26.11-78.08)
>360 vs. <180 days	48.50 (26.84-87.64)
Greater than 2 vs. no physician visits during the 90 days prior to switch	2.25 (1.09-4.61)
More than one HIV RNA or CD4 count test within 30 days of switch	2.12 (1.36-3.33)
Any resistance test in the 180 days before switch	4.60 (3.01-7.03)

Results: Model Development (2)

Final model:

- Included all main effect variables from base model
- Added 3 significant interaction terms:
 - Treatment history and post-switch regimen type
 - Time on pre-switch regimen and age
 - Time on pre-switch regimen and any resistance testing
- Improved model fit:

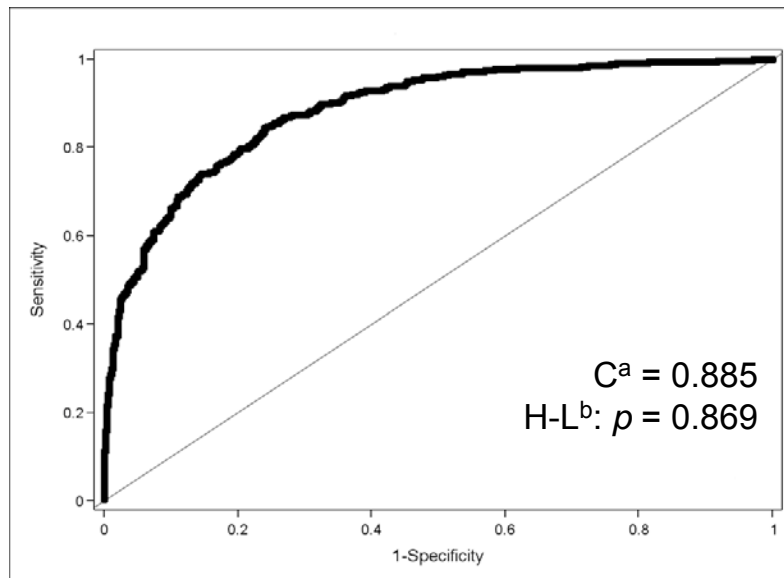
	Area Under ROC Curve (C statistic)	Hosmer-Lemeshow Goodness-of-Fit (<i>P</i> value)
Base Model	0.875	<0.001
Final Model	0.885	0.869

Results: Model Validation

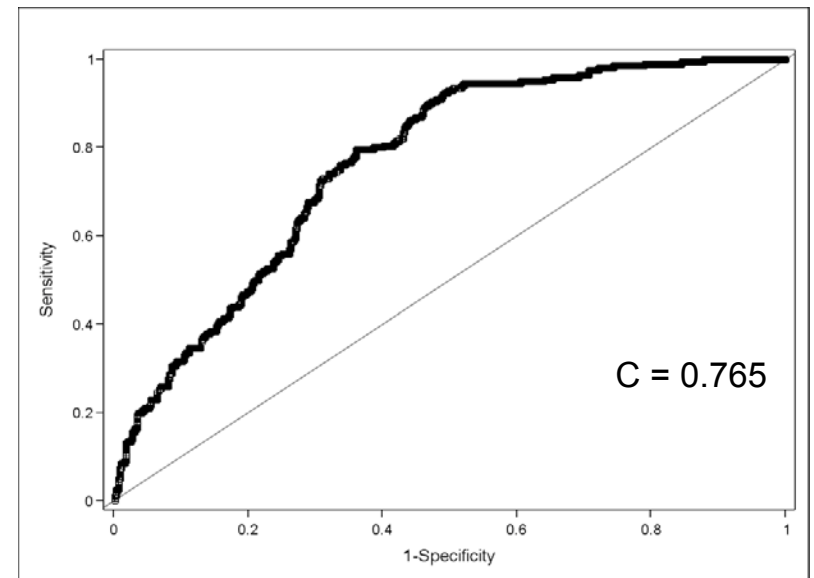
Applied final model to validation dataset

- Estimated probability of virologic failure:
 - Observed: 18.6%
 - Predicted: 18.9%
- Evaluated model's predictive ability:

Development dataset



Validation dataset



^a C statistic for ROC curves

^bHosmer-Lemeshow goodness-of-fit test

Results: Model Application

Applied validated claims signature model to a claims dataset

- Predicted overall virologic failure rate: 13.8%
- Selected variable-specific predictions of virologic failure:

	% Predicted to Have Virologic Failure
Treatment naïve before first regimen	
Yes	10
No	15
No. of days on first regimen	
1-180	3
181-360	35
≥361	28
Any resistance test in 180 days before switch	
Yes	24
No	13

Conclusions & Implications

- A model was developed using registry data to estimate likelihood of virologic failure among patients who switched cART regimens
- The model's goodness-of fit-and predictive abilities for use with claims data were validated using claims data with lab values
 - As a worked example, the validated claims signature model was applied to a claims dataset without lab values
- The model can assist payers in improving healthcare quality and reducing costs by allowing them:
 - To estimate costs of virologic failure to their plan
 - To identify treatments with rising rates of virologic failure
 - To monitor the level of virologic failure in their patient population
 - To develop strategies to reduce the level of virologic failure