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Imputing Clinical Records from Routine Laboratory Data: Date of ART Initiation in South Africa

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ABSTRACT

Background: Lack of nationally representative data hinders assessment of national HIV treatment programs in many low-resource settings. Where laboratory data are collected on a national scale, such data could be used to create a national monitoring cohort but only if information on treatment initiation can be determined. We developed a novel method to impute dates of antiretroviral treatment (ART) initiation from routine laboratory data in South Africa's public sector HIV program that could be applied to a national labs database such as South Africa's National Health Laboratory Service (NHLS) database and assessed validity of this approach.

Methods: We analyzed data from two large clinical HIV cohorts: Hlabisa (rural primary care clinics and one sub-district hospital in KwaZulu-Natal) and Right to Care (network of urban clinics in Gauteng). Both cohorts contain known ART initiation dates and lab test results are imported directly from NHLS. While the ART initiation date for patients was known (gold standard), we imputed ART start dates using only lab data that would be available in a laboratory database. To do this, we identified the date of "ART workup"; the lab tests used to determine treatment readiness in national HIV treatment guidelines (first documented hemoglobin or alanine transaminase test among patients with a CD4 count in the 12 months prior to these tests). We then calculated the median time from the ART workup to ART initiation and imputed ART start date as the date of ART workup plus that median time. We calculated sensitivity (SE), specificity (SP), positive predictive value (PPV), and negative predictive value (NPV) of our imputed start date to be within 6 months of the actual ART start date.

Results: We analyzed data from over 80,000 HIV-positive adults of whom >90% had a documented workup. Among patients who had a workup and initiated ART, the median time to initiation was 16 days (IQR 7, 31) in Hlabisa and 21 (IQR 8, 43) in RTC cohort. Among patients with known ART start dates, SE of the imputed start date was 83% in Hlabisa and 88% in RTC, indicating this method will correctly estimate the ART start date for about 85% of those with a recorded ART workup. In Hlabisa, PPV was 95%. SP (100%) and NPV (92%) were also very high.

Conclusions: Routine lab data can be used to infer ART initiation dates in South Africa's public sector with high rates of classification. Lab data can be used to monitor and evaluate health systems performance and improve the accuracy and completeness of clinical records.

BACKGROUND

- Where data from routine laboratory tests are systematically available, such information may be used to impute missing data in clinical records.
- In South Africa, HIV patients who are eligible to initiate antiretroviral therapy (ART) should have certain laboratory tests conducted prior to treatment initiation - the ART workup which includes hemoglobin (Hb) and the liver function test alanine transaminase (ALT).
- We sought to impute ART start dates by identifying ART workup dates using laboratory data and assessed its' validity with respect to sensitivity, specificity, positive predictive value, and negative predictive value.

METHODS

Study Population and Data Sources

The South African National Health Laboratory Service (NHLS) provides laboratory services to all public-sector facilities including all laboratory testing required for ART monitoring

We analyze data from two large clinical research cohorts with known dates of ART initiation and lab data directly integrated with the NHLS:

- Hlabisa HIV Treatment and Care Programme including all HIV patients initiating ART at 17 primary health care clinics and one sub-district hospital in rural Hlabisa sub-district of KwaZulu-Natal province since mid-2004
- The Right to Care (RTC) Clinical Cohort includes all HIV patients initiating ART at 7 RTC-supported primary health care clinics and one provincial hospital in urban and peri-urban settings in Gauteng province

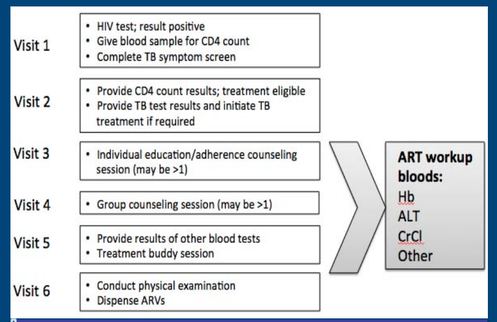


Figure 1: Visit schedule prior to ART initiation

Analytic Variables

1. ART workup = date of first documented Hb or ALT among patients with a CD4 count in the previous 12 months prior to, or in the month following, the ART workup date
2. Known date of initiation = earliest date when a triple-drug ART regimen was dispensed
3. Based on three once-weekly counseling sessions between ART workup and ART initiation (depicted in Figure 1), we assumed an interval of 21 days between ART workup and ART initiation
4. Imputed ART start = 21 days after date of ART work-up

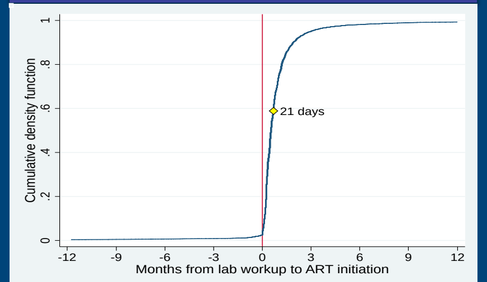
Validation of Imputed Start Dates

1. To test 21 day assumption: describe the distribution of times from ART workup to known ART initiation in the clinical cohorts
2. Evaluated the performance of imputed ART start dates using known dates of ART initiation as the gold standard, and calculated the sensitivity (Se), specificity (Sp), positive predictive value (PPV), and negative predictive value (NPV) of our imputed ART start dates.
3. Imputed start date considered a "match" to known ART start date if imputed start date is within a six-month window period of known ART start date.

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RESULTS

Figure 2: Time from ART workup to ART initiation



- In the Hlabisa cohort, 21,766 patients had a documented ART initiation date and 18,836 (87%) had a documented ART workup.
- In the RTC cohort, 69,283 had a documented ART initiation date, of whom 63,914 (92%) had a documented ART workup.
- Median interval ART workup to initiation = 16 days (IQR 7–31) in Hlabisa cohort and 21 days (IQR 8-43) in RTC cohort (Figure 2).
- High estimates of Se, Sp, PPV and NPV were noted regardless of including CD4 count in the workup definition (Table 1)
- In addition, Se of the imputation method remained high even when the definition of a matching window period was altered between 3 and 9 months after ART workup date (Table 3).

Table 1 – Sensitivity, specificity, positive and negative predictive values of imputation method

		HB/ALT + CD4	HB/ALT only
Sensitivity (RTC cohort)		**Truly initiated ART = yes**	
ART workup in 6mo prior to known ART start date?	Yes	61,105	61,632
	No	8,178	7,651
	Sensitivity	**88.2%**	**89.0%**
Sensitivity (Hlabisa cohort)		**Truly initiated ART = yes**	
ART workup in 6mo prior to known ART start date?	Yes	17,970	18,393
	No	3,796	3,373
	Sensitivity	**82.6%**	**84.5%**
Specificity		**Truly initiated ART = no**	
Ever had an ART workup?	Yes	79	84
	No	35,556	35,551
	Specificity	**99.8%**	**99.8%**
Positive Predictive Value (PPV)		**Had ART workup = yes**	
Known ART start date in 6mo after ART workup date?	Yes	17,970	18,393
	No	866	963
	PPV	**95.4%**	**95.2%**
Negative Predictive Value (NPV)		**Had ART workup = no**	
Ever initiated ART?	Yes	3009	2,521
	No	35,556	35,551
	NPV	**92.2%**	**93.4%**

Table 2 – Effect of changing "matching" interval between ART workup and known ART start date on sensitivity

	Sensitivity	
Interval prior to known ART start	**Hlabisa cohort**	**RTC cohort**
1 month	62.7%	54.2%
3 months	80.1%	82.2%
6 months	**82.6%**	**88.2%**
9 months	83.3%	88.2%

CONCLUSIONS

- Chronic disease management in low-resource settings is informed by routine laboratory testing and guided by standardized clinical protocols
- Routine laboratory testing data can be used to impute information about clinical decision-making that may not be complete in patient charts or aggregate statistics
- The ability to impute ART start dates using lab workups has concrete implications for program monitoring and patient care in the South African national HIV CCMT program