Poster board #: 619

Improved Viral Load Monitoring Capacity With Rank-Based Algorithms for Pooled Assays

Tao Liu, PhD[1]; Joseph W. Hogan, ScD[1]; Renxia Huang, ScM[2]; Rami Kantor, MD[3]

[1]Center for Statistical Sciences, Brown University, Providence, RI; [2]Fulcrum Analytics, Norwalk, CI; [3]Division of Infectious Diseases, Brown University, Providence, RI, USA

Background

- HIV viral load (VL) monitoring is recommended globally by the World Health Organization (WHO) for patients on antiretroviral therapy (ART).
- Cost and infrastructure in resource limited settings (RLS) still limit widespread implementation of the WHO guidelines.
- **VL pooling** can reduce the number of assays needed to ascertain individuals' VL. (May et al. JAIDS 2010)
- If the pooled sample is positive (i.e. has detectable VL), a deconvolution process is performed to determine the virological status of individual samples that derived it.
- However, existing VL pooling methods ignore information from routinely-collected clinical markers (RCMs), such as CD4 count/percent and treatment adherence.
- RCMs are correlated with VL and can provide valuable information about the likelihood of virological failure .

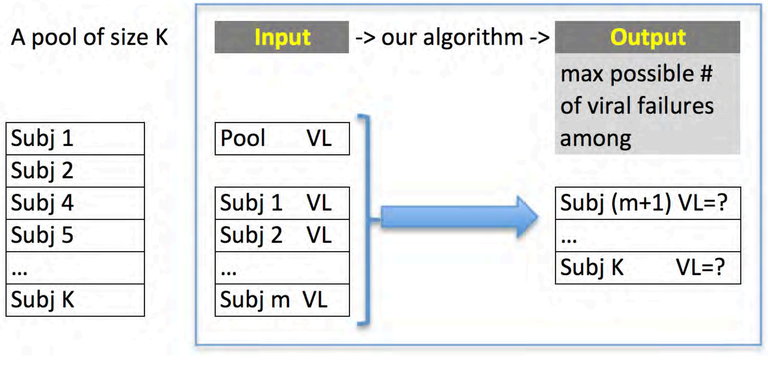
Objective

Improve the test efficiency by ***utilizing RCMs in VL pooling assay deconvolution***, to reduce the number of assays needed.

Methods

We developed a pooling deconvolution algorithm that uses RCMs to determine an optimal individual sample testing sequence for resolving a positive pool:

Step 1: Combine blood samples from *K* individuals to form a pool, and obtain VL of the pool;
Step 2: If the pool is "positive", use RCMs in a prediction model to estimate risk ***S*** of viral failure for each sample in the pool;
Step 3: Assay individual samples ***sequentially*** in a descending ***rank order*** of their risk scores ***S***;
Step 4: Apply the proposed algorithm to determines the max possible number of virological failures in the remaining pool; see Figure.



Iterate through Steps 3-4 and stop when the max possible number of virological failure among the remaining samples is 0, i.e. no viral failures.

Methods

Using simulations, we examine the potential advantages of our approach by comparing to
(1) Individual VL testing;
(2) Standard pooling without algorithm;
(3) Algorithm-based pooling without rank-ordering

Simulations were based on data from 597 women at the Miriam Hospital HIV Clinic (Providence, USA).

- The cohort had a median VL 75 copies/mL (IQR 75~400), CD4 count 407 cells/μL (IQR 254-576), and CD4% 23 (IQR 17-30).
- RCMs: CD4, CD4%, and their 6-month changes.
- Viral failure was defined using three VL thresholds: 150, 400, and 1000 copies/mL.

Results

ART Failure Threshold (copies/mL)	ART Failure Prevalence	Expected Number of VL Assays Required to Determine Individual-Level Viral Failure (% of Reduction Compared with Individual Testing)			
		Individual Testing	Standard Deconvolution*	Algorithm-Based Deconvolution*	**Rank-based Deconvolution***
VL > 150	30%	597 (REF)	698 (-17)	489 (18)	**444 (26)**
VL > 400	25%		598 (-0.2)	426 (29)	**373 (38)**
VL > 1000	20%		548 (8.2)	387 (35)	**331 (45)**

- VL testing is fundamental for HIV treatment monitoring but is expensive to implement in RLS.
- Standard pooling algorithms may not yield significant improvements.
- Existing algorithm-based pooling deconvolution without rank ordering reduces the number of VL assays by 18-35%.
- Our pooling rank-based algorithm further reduces VL assays by 26-45%.

Conclusion

Rank-based deconvolution based on RCMs can substantially increase the capacity of comprehensive VL monitoring, suggesting its potential utility in RLS.