Methods: From November 2005 to November 2007, consecutive treatment naïve patients initiating ART at the clinic were enrolled. Clinical information is collected every month and CD4+ count measured every 6 months. This analysis includes patients who had completed at least 10 months of follow up. Response to therapy was assessed by changes in CD4 cell counts, weight, and occurrence of opportunistic infections. WHO staging, adherence levels and patient retention were also assessed.

Results: During the study period, 694 of 2686 in care, started ART; the mean age was 34 years, 76% were female, 40% were in WHO stage 3&4, mean body weight was 54.5 kg (SD = 9.5) and median CD4 cell count 118/mm².

Outcomes could not be assessed in 19% of 694 (43 died, 50 were lost to follow up, 36 were transferred out to other health centers).

The mean increase in CD4+ count at 6 months was 135/mm³ and median body weight increase was 5.0 kg. 68% of 565 active gained weight. ART initiation reduced incidence of opportunistic infections(OR:3.35, P = 0.003). Over 98% of patients had >95% adherence. Patients with WHO stage 182 were twice more likely to be active compared to those with WHO stage 384.(OR:1.84, P = 0.002).

Conclusion: HAART programs can be feasibly implemented at lower health facilities providing general outpatient care with satisfactory clinical and immunological outcomes and patient retention rates.

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25.012

An Advanced ARV Drug Resistance Expert Rule System in BioNumerics®

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Automated drug resistance predictions, based on mutation analysis, is increasingly important in virology. Unfortunately most mutation analysis systems are closed systems, leaving the user unaware on which mutation rules are fired and what part of data caused them to fire. Based on curves obtained after direct sequencing, mutants can easily be spotted, identified and inventoried.

We present an integrated open Expert Rule System (ERS) build into the BioNumerics® software that allows researchers to create, adapt and (re)evaluate e.g. drug resistance rules (double loop learning). The ERS consists of 5 major steps:

- data input directly from the BioNumerics® database or from external sources (e.g. RT-sequences)
- data conversion for the data processing (e.g. AA-conversion and mutation detection against a consensus)
- decision rules application, yielding a statistics report on some or all rules (e.g. rules for all NRTI drugs)
- ERS interpretation, yielding resistance predictions for each drug with anticipation scores based on fuzzy logic
- reporting in a written format, a database format, or publication on a website

The tool can be shown as an interactive GUI or run for background HT batch analysis. The ERS was tested with publicly available HIV data and drug resistance algorithms, but is ‘open’ for custom rule development. Discordances between different algorithms can be easily monitored and examined. This framework is not restricted to HIV, but can be used for e.g. HBV as well.

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Identifying Trends in Viral Replication and Immune Status Markers Among Patients Living with HIV: Impact of the Initial Antiretroviral Therapeutic Regimen on Response to Treatment

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In HIV infection, a long asymptomatic period precedes disease development. However, viral-host interaction is dynamic. Mathematical models have been crucial to rule out the concept of viral latency. The present study aims at evaluating viral-host interactions in HIV infection, investigating the impact of initial antiretroviral therapy (ART) (mono therapy vs. double therapy vs. highly active therapy) in the course of disease. Using a database with at least six sequential CD4+ cell counts and HIV viral load assessments of 1391 patients under follow-up in São Paulo, Brazil, we classified patients according to a linear approximation model of plasma viral loads and CD4+ cell counts into favourable and unfavourable outcomes. We validated the linear approach according to two criteria, based on $\chi^2$ and $Q^2$ ($\chi^2$/degrees of freedom). Association between outcomes and the initial therapy was sought after analyzing the viral load and CD4+ cell counts slopes. No particular initial regimen was shown associated with plasma viral undetectability during follow-up. Only 20% of patients with persistent vireamia presented a beneficial effect of ART. Unfavourable outcomes were associated with most patients who resumed vireamia transiently or at the end of follow-up. For most patients with intermittent vireamia ending with undetectable or detectable viral loads, results indicated favourable and unfavourable outcomes, respectively, regardless of the initial ART regimen. Distinct outcomes occurred among patients with oscillatory viral loads: most of those who started therapy with two or three drugs had a favourable outcome, in contrast to those started on monotherapy. We conclude that mathematical tools have demonstrated that the initially prescribed ART was not associated with the long-term response to therapy for most analysed patients. Favourable outcomes can be associated to reinforcement of adherence or changes in ART regimens during follow-up. Emergence and positive selection of drug-resistant viral strains might be hypothesized as implicated in unfavourable outcomes.

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