The utility of resistance testing in the clinical management of HIV-1 infection

…….Should HIV clinicians investigate resistance or resist investigations?

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BACKGROUND: The aim of this study was to review the utility of genotypic resistance testing. The prevalence of antiretroviral drug resistance in the UK is approximately 8% among antiretroviral therapy (ART)-naïve patients and 50% among ART-experienced patients. Current guidelines recommend early testing in all newly diagnosed patients and prior to starting ART in selected persons at risk of re-infection. Suboptimal suppression of viral load (VL) by ART should prompt further resistance testing (BHIVA guideline, 2011).

METHODOLOGY: HIV-1 genotypes, VL measurements and ART prescriptions were retrospectively collated for all patients who received one or more resistance test from May 2009-2010 at Chelsea and Westminster Hospital. Resistance to ART was determined using the Stanford algorithm.

RESULTS: A total of 1086 resistance tests were conducted on 998 patients (Figure 1). There were 137 test failures. A low VL was predictive of test failure (50% of failed tests vs. 16% of successful tests had a VL <200 copies/ml) (Figure 2). Seventy percent of all successful tests were conducted on ART naïve patients, of whom 47 (8%) had resistance to at least one class of ART classed as 'low-level' or greater at the first test (23 NRTI, 18 NNRTI and 12 PI). In contrast, 22/122 (18%) of ART-experienced patients, who had not had a previous test, had baseline resistance (15 NRTI, 10 NNRTI and 6 PI) (Figure 3). Excluding test failures, tests were repeated on 54 ART-naive patients and 143 ART-experienced patients. Up to 15 repeat tests were ordered per patient since 2001. Only 6/64 of the repeat tests conducted on naive patients showed increased resistance (Figure 4). In comparison, 35/166 tests repeated on ART-experienced patients showed increased resistance, yet only 8/166 (5%) informed a change in ART within three months. There were 33/166 repeat tests that resulted in a change in ART despite no change in resistance. There was no significant difference in log-fold VL decrease between those switching ART because of newly detected resistance or those switching despite no change in resistance (1.22 ± 1.16 vs. 0.83 ± 1.31, respectively; student-t test; not significant) (Figure 5).

CONCLUSIONS: The majority of repeat resistance tests provide no new information, particularly amongst treatment-naive patients. Repeating resistance tests among treatment-experienced patients rarely informs ART-regime change and changing therapy on an empirical basis may be equally effective in suppressing VL.

Figure 1: ART-resistance tests conducted at Chelsea and Westminster Hospital May 2009-2010

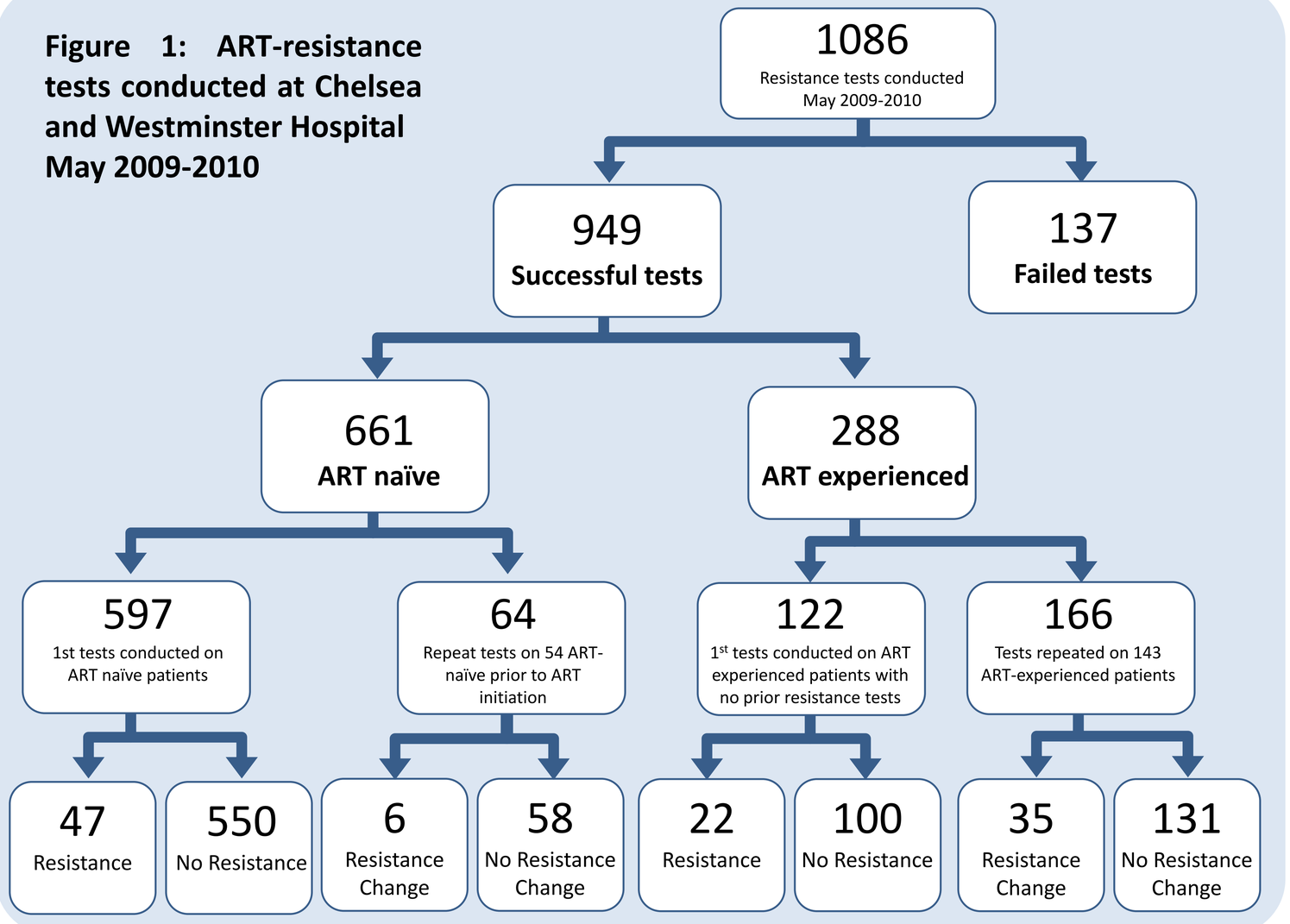
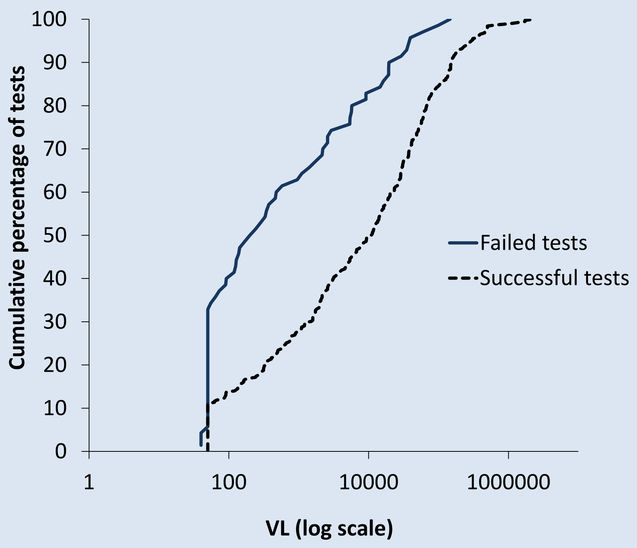


Figure 2: Samples with low viral loads resulted in test failure



Samples resulting in test failure were collected from patients with low viral loads, in accordance with the technical difficulties in amplifying material from few copies of template RNA

Figure 3: Resistance detected in ART-naïve and ART-experienced patients at the first test

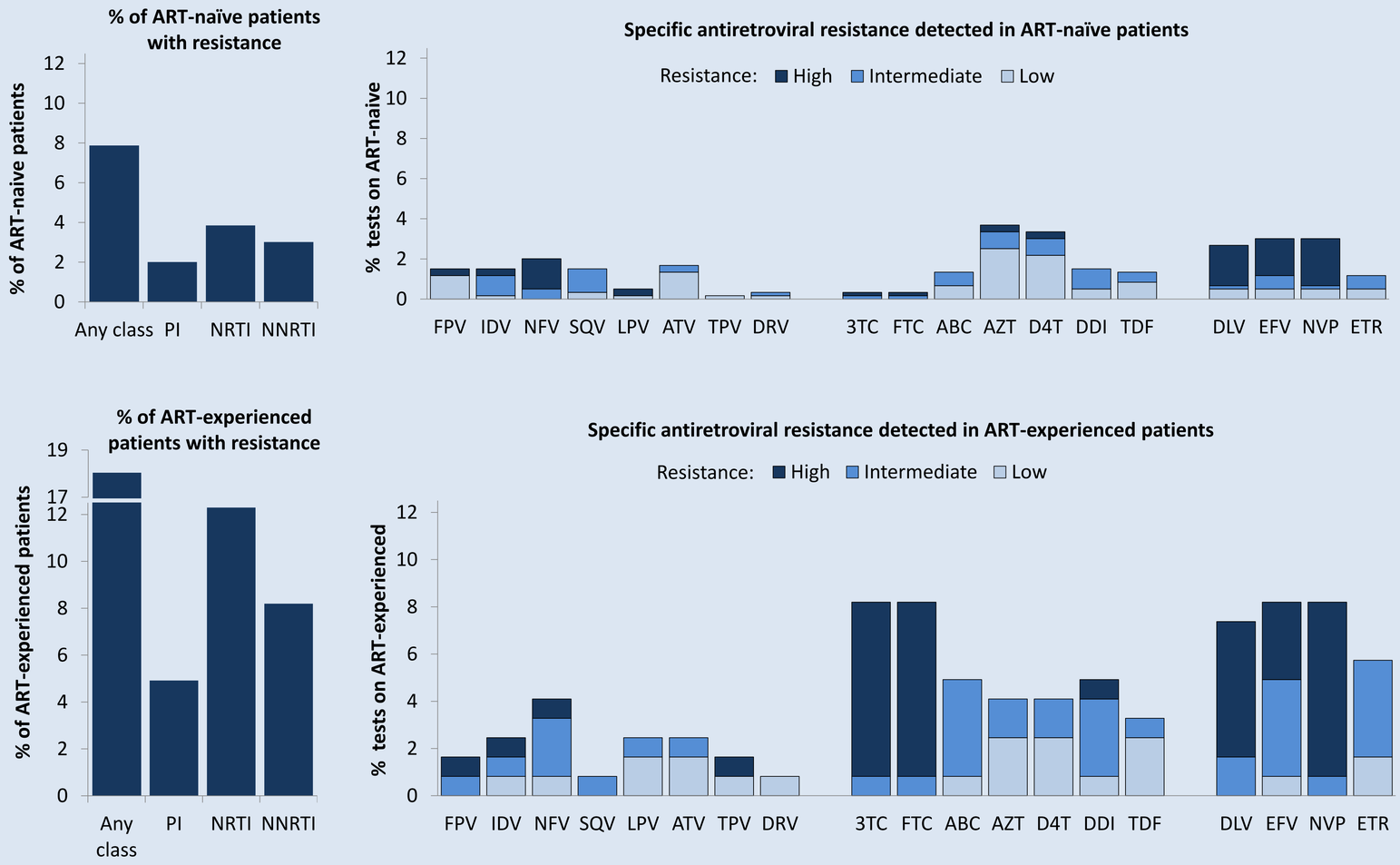
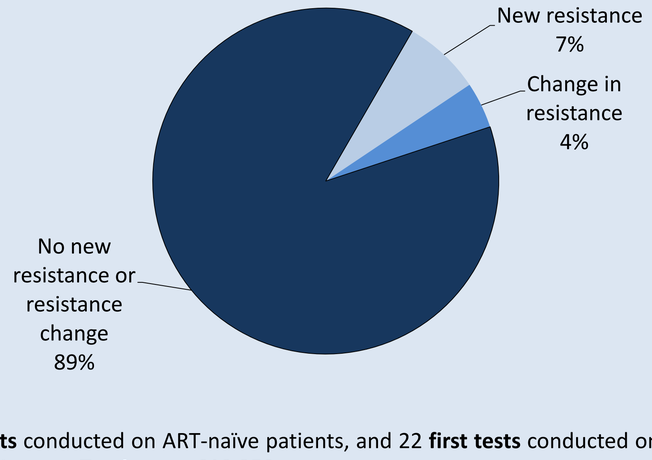


Figure 4: The majority of tests reported no change in resistance

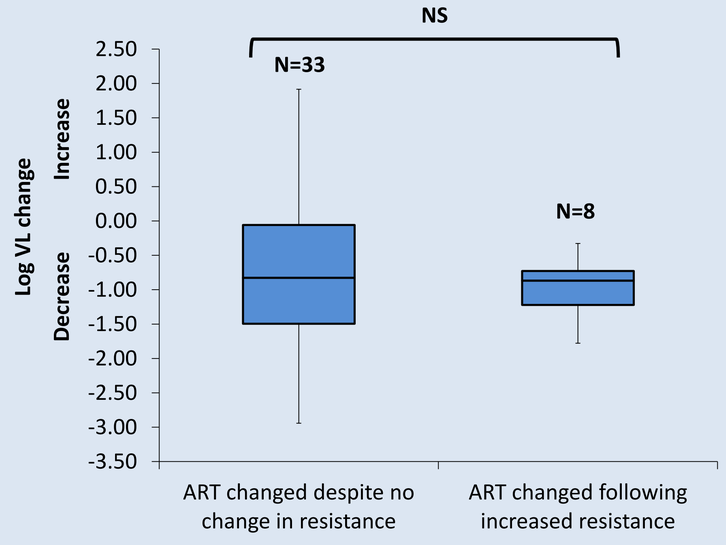


A total of 47 **first tests** conducted on ART-naïve patients, and 22 **first tests** conducted on ART-experienced patients reported resistance. **Total cost = £10,350**

A total of 6 tests **repeated** on ART-naïve patients prior to ART initiation and 35 **repeated** on ART-experienced patients reported a change in resistance. **Total cost = £6,150**

A total of 749 tests provided no new resistance information. **Total cost = £112,350**

Figure 5: Resistance testing did not significantly impact clinical outcome



Of the 35 tests repeated on ART experienced patients only 8 informed a change in ART.

A total of 33 ART-experienced patients had ART changed despite a recent resistance test showing no change in ART sensitivity.

Changes to ART regime informed by resistance testing did not result in better viral load control than patients who had ART changed on an empirical basis.

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