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TITLE: Side effects, dosing schedules, pill burden and perceived stress: Interaction and influence on medication adherence.

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HIV Cohort research in Royal Perth Hospital (RPH) between the years 2002-2005 found that adherence to ART predicted viral suppression and CD4 T-cell recovery and diminishing adherence was associated with indicators of perceived stress, depression and the impact of side effects, particularly fatigue and skin itching. Whether these variables were associated with a particular regimen or dosing schedule was not studied.

Patients attending the Immunology Outpatient Clinic at RPH over a 3 month period in 2008 completed a questionnaire on ART (N=156), concomitant medications, pill burden, dosing schedule, side effects and perceived stress. Doctors verified the regimen and assigned a medication score indicating ART adherence.

The majority of regimens included a nucleoside backbone of abacavir/lamivudine (50%), tenofovir/emtricitabine (23%) tenofovir/lamivudine (8%) or zidovudine/lamivudine (7%) combined with either a ritonavir-boosted PI (35%; atazanavir 22%), efavirenz (28%) or nevirapine (25%). 108 vs 48 patients were on OD vs BD regimens respectively. Adherence improved since 2005 with 75% vs 55% of patients surveyed reporting 100% adherence over the previous month. Neither dosing schedule nor pill burden was associated with poorer adherence. Non-adherent patients reported more coping difficulties ($p=0.02$) than adherent, and the number of side effects experienced correlated with higher total perceived stress score ($p=0.004$). 130 patients experienced at least one side effect, 36% taking medication for relief. Compared with five years ago reported diarrhoea was reduced (34% vs 51% of patients), but reported fatigue (59%) muscle pain (36%), headache (36%), nausea (32%) and skin itch (39%) were comparable. Although boosted PI regimens were associated with more frequent side effects than NNRTI regimens, including headache (54%), diarrhoea (54%) and fever (atazanavir: 41%), they did not strongly correlate with reduced adherence ($p=0.3$).

In our cohort adherence has improved in the last two years: simpler dosing schedules and the decreased frequency of certain side effects such as diarrhoea may have contributed. In those patients with a higher frequency of reported symptoms and perceived stress, reduced adherence may be associated with health related quality of life (HRQL) issues not measured in this study. Further research is needed to understand the interaction between HRQL and medication adherence.