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**Reasons for and virological consequences of treatment interruption in patients resuming antiretroviral therapy**
A mixed methods study of patients in the "Back-to-Care" program at the Lighthouse Clinic Lilongwe/Malawi

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Scaling up of antiretroviral therapy (ART) in resource-limited settings moved impressively towards universal access, particularly in Malawi. Along with increasing numbers of people on ART, public health HIV programmes are facing a number of challenges including the support of patients on lifelong therapy and the prevention of temporary or permanent loss of patients in care. Retention in care and drug adherence are considered preventive in terms of treatment failure, whereas interruption of treatment is associated with an increased risk of developing drug resistance. This study evaluated reasons for and virological consequences of treatment interruption in patients receiving ART at the Lighthouse in Lilongwe, Malawi.
A mixed methods design was used to evaluate patients resuming ART after treatment interruption between January 2008 and November 2009. Among all patients who missed their scheduled appointments for ≥21 days, the *Back-to-Care* (B2C) programme identified those patients who stopped or had an irregular intake of ART, which is defined as treatment interruption. Key characteristics were analysed to describe the cohort of patients with treatment interruption and to identify risk factors. Reasons for treatment interruption were quantified in patients prior to their return to the clinic using a standardized questionnaire (B2C form; n=147) with pre-defined categories. In addition, in-depth interviews were performed upon the return of patients for resumption of ART and free-text comments of B2C forms were used to identify additional reasons for treatment interruption and gain a better understanding of the individual circumstances leading to treatment interruption. In-depth interviews (n=26) also addressed known factors supporting drug adherence and retention in care. Finally, virological consequences of treatment interruption including the prevalence of virological failure and patterns of drug resistance were investigated to evaluate the practise of resuming first-line ART after treatment interruption. Qualitative data analysis was based on a thematic framework approach. Viral load (VL) was analysed at least two months after resumption of ART. For samples with a VL ≥1000 copies/ml, drug resistance related mutations were determined.
Between January 2008 and December 2009, 14 121 patients aged 15 years and above received ART at the Lighthouse. Within this period, the B2C team identified 581 (4,1%) patients with complete stop or irregular intake of prescribed antiretroviral drugs. Out of these, 347 returned to the Lighthouse for resumption of therapy. Two thirds of patients interrupted ART within the first year after initiation of ART.
Despite the presence of social support and sufficient knowledge regarding possible consequences of treatment interruption, all patients experienced situations that resulted in a period of interruption of treatment. These causes reflect both economic and strong personal factors, which apparently outweighed patients' knowledge and awareness of the possible consequences of treatment interruption and were given priority over keeping an appointment for a drug re-fill. The most common reason was travel, which further differentiated into work- or family-related travel. Patients further stated transport costs and health care provider related reasons, which included perceived or enacted discrimination by health care workers. Other drivers of treatment interruption were treatment fatigue/forgetfulness, the patients' health

status, adverse drug effects, pregnancy/delivery, religious belief or perceived/enacted stigma.
The evaluation of virological outcomes following resumption of the 1st line regimen revealed that the majority of patients with treatment interruption had viral suppression and showed no signs of treatment failure. However, almost one third of patients had previously unnoticed virological failure, which was associated with drug resistance to 1st line regimen, consisting of stavudine, lamivudine and nevirapine. The identified drug resistance patterns led to a loss of the available NNRTI and limited NRTI treatment options at the time of the study, but left all patients the possibility to switch to Malawi's 2nd line treatment. Analysis of key characteristics of patients did not reveal any risk factors for virological failure.
Addressing the challenges patients face on lifelong therapy, strategies must be developed that prevent or reduce discontinuation of ART. Therefore, a profound understanding of the reasons for treatment interruption is the basis for interventions such as need-adjusted counselling, which specifically target common adherence challenges such as travel or health system related barriers. Patients with treatment interruption are at an increased risk of developing and spreading drug resistance. The unsatisfactory prediction of treatment failure using non-laboratory algorithms underscores the importance of VL testing for the management of patients resuming ART, which must be addressed to assure further progress in the global fight against HIV/AIDS.