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Preventing HIV transmission – a new argument for tracing patients lost to follow-up?

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Treating HIV infected patients with antiretroviral therapy (ART) lowers the risk of transmission, and helps to control the epidemic (1). Successful ART suppresses a patient's HIV viral load (the concentration of virus in blood), reducing it to level at which the probability of onward transmission drops to almost zero. Intensive testing and immediate initiation of ART could dramatically reduce HIV incidence and help eradicate the epidemic (2). Treatment failures, poor adherence and treatment interruptions may allow viral load to rise once again to a detectable level. In an earlier study, we demonstrated that introducing viral load monitoring to accurately detect treatment failure could prevent 30% of infections from patients who are taking ART (3). In the present analysis we focus on HIV transmission due to patients lost to follow-up (LTFU).

Tracing and bringing patients lost to follow-up back to care

Loss to follow-up is a serious problem in most sub-Saharan African ART programmes. Patients who do not return to the clinic may have died, transferred to another ART facility, or decided to stop, interrupt or reduce ART intake. If ART is interrupted or reduced, HIV again progresses, and this increases the risk of opportunistic infections and, ultimately, AIDS and death. When patients are LTFU, it is impossible to determine their outcomes, which makes it harder to evaluate programme success and conduct epidemiological research.

Some ART programmes now actively trace lost patients to determine the reasons for and true outcomes of LTFU, and to encourage lapsed patients to return to care. "Back-to-Care" (B2C) is an example of such a tracing programme. It was introduced in Lighthouse and Martin Preuss Centre, two large public ART clinics in Lilongwe, Malawi, in 2006 (4). Patients are declared LTFU if they do not return to the clinic within three weeks after the scheduled appointment. The tracing team tries to contact patients who are LTFU, either by calling them on the phone or making a personal visit. If they find the patient is alive, but is not receiving ART from an official provider, the tracing clerk supports the patient's return to the clinic and schedules a new appointment if the patient consents. The viral load of a patient who interrupts ART will rebound, and the probability of onward transmission increases with viral load. If tracing programmes can accelerate the return of lost patients, these patients may not be as likely to transmit the virus, since the period of lapsed treatment is shortened. In this study, we created a mathematical model to determine whether tracing patients LTFU from ART programs would lower the rate of HIV transmission.

Mathematical model to evaluate potential transmission

We analysed data from the B2C programme and constructed a mathematical model to simulate a cohort of patients who start ART but may interrupt it later. We modelled the viral load trajectories of the simulated patients and used a mathematical relationship to calculate the expected number of transmissions from each patient. We simulated 1000 patients for 5 years from ART start in four different scenarios. First, we assumed that all patients remain in care during the follow-up. Second, we included the different reasons for LTFU, such as ART interruptions, unregistered deaths and unregistered transfers, but assumed that patients were not traced. Third, we added tracing of patients 6 months after they were declared LTFU. Fourth, we changed the time of tracing so that it began immediately after patients were declared LTFU.

Introducing LTFU increased the number of expected infection transmissions from 1000 patients during 5 years from 33 to 54. Tracing patients after a 6-month delay reduced the number of infections to 51, and immediate tracing to 50. On average, preventing one new infection required 116 immediate tracing efforts, or 142 delayed tracing efforts.

Tracing can be efficient in preventing new infections

Tracing patients LTFU can be an efficient intervention which could save costs in the long term. One tracing clerk can trace approximately 5 patients a day. If about 120 tracing efforts can prevent one new infection, the price of preventing

one infection is equivalent to the costs of 1.5 months of work by a tracing clerk. The newly infected patient, on the other hand, would lose several life-years and need life-long ART care, which would cost thousands of dollars. If this can be prevented by expending a smaller amount on tracing, it would be an efficient investment. Preventing new infections is also not the primary aim of tracing. If patients whose ART is interrupted can be brought back to care, they will benefit most from tracing, since they will again receive the life-saving therapy. Tracing also provides valuable information about the true outcomes of lost patients.

Most of the transmission from lost patients cannot be prevented by tracing alone

Despite its likely long-term efficiency, tracing prevents a relatively low number of new infections. Tracing prevented less than 10% of all transmissions from patients who had started ART (4). In contrast, viral load monitoring prevents about 30% of infections from patients on treatment (and therefore approximately 20% of transmission from patients who have once started treatment) (3). This suggests that accurately monitoring patients in care may be more important than bringing patients LTFU back to care. The utility of tracing is diminished by its relative ineffectiveness: not all patients LTFU are found; patients may refuse to return to the clinic; and they do not usually return immediately. Some lost patients might also return spontaneously without tracing. High rates of LTFU do not indicate equally high rates of interrupted ART. In a recent analysis of the B2C programme by Tweya and colleagues, a considerable proportion of the patients LTFU had only transferred to other ART facilities without informing their original ART providers (4). It may thus be more efficient to focus on avoiding interruptions in the first place, than to trace patients LTFU. Tweya and colleagues identified reasons patients had interrupted ART (4), and addressing these issues could reduce drop-outs.

Treatment as prevention: a new argument for ART management interventions

Coverage of ART in low-income settings is increasing, and the guidelines have been recently updated to extend eligibility to new groups of patients (5). ART prevents transmission, and scaling up its provision is a priority. Enrolling an HIV-infected person on ART does however not guarantee that he or she will never be infectious again. Maximum preventive effect can only be achieved with constant support, including frequent laboratory monitoring and retention efforts. Laboratory monitoring and retention interventions have usually been studied from the patient's point of view, and criticized for providing minimal benefit at high cost (6-9). The calculation could change if the population-level effect is considered (7). Every prevented infection saves both life-time and money in the long term. We do not yet have direct evidence that tracing patients LTFU or viral load monitoring could reduce the epidemic, nor can these interventions be quantified to measure long-term cost-effective or cost-saving. However, we do demonstrate that tracing and viral load monitoring can to some extent prevent transmission. We risk severely underestimating the real impact of these interventions if we ignore those benefits.

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