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HIV-1 viral load monitoring: an opportunity to reinforce treatment adherence in a resource-limited setting in Thailand

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Summary This paper describes a program to increase patients' treatment literacy regarding viral load (VL) monitoring through patient education materials and a counseling protocol, implemented by peer counselors, in order to reinforce adherence to first-line treatment. VL monitoring and second-line antiretroviral treatment were introduced into an established first-line treatment program in a rural district hospital in Thailand. All patients (171 adults and 14 children) taking antiretroviral treatment for more than 6 months participated and those with detectable VL were targeted for additional adherence support. The main outcome measure recorded was the number of detectable results becoming undetectable after counseling. Four adults and one child had a persistently high VL and switched to second-line treatment. Of 51 adults (30%) with an initial low detectable VL, 47/51 identified likely explanations, usually linked with poor adherence. Following counseling, VL became undetectable in 45/51 cases and some patients could resolve long-standing psychosocial problems. We conclude that HIV-1 VL monitoring together with targeted counseling for patients with detectable VL can promote adherence to treatment, providing an opportunity to delay onset of HIV-1 resistance. When implemented with a patient-centered approach, it can be a very useful tool for psychosocial support.

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1. Introduction

As highly active antiretroviral treatment (HAART) becomes increasingly available in resource-limited settings,¹ the

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emergence of HIV-1 resistance is becoming a significant challenge.^{2,3} Ensuring treatment adherence is essential, and HIV-1 viral load (VL) testing has been recommended to highlight poor adherence.⁴

WHO guidelines recommend VL monitoring primarily to guide decisions to switch regimens.⁵ Its additional use to reinforce adherence has been documented in South Africa^{6,7} and other resource-limited settings.⁸ If VL is to be used optimally to reinforce adherence, however, some issues need to be resolved regarding patients' understanding and involvement. How should they be prepared to take the test? How do they interpret the results? To our knowledge there has been no literature discussing these aspects.

In this article we describe our experience in introducing VL monitoring in a resource-limited setting in Thailand, and the tools we developed, focusing on treatment literacy and patient involvement.

2. Project description

2.1. Setting

Kuchinarai (population 103 000) is a typical rural district in northeastern Thailand. The population are mostly subsistence rice farm laborers. Antenatal HIV prevalence in 2006 was 2.6%, compared with a national rate of 1.0%. First-line HAART has been available since February 2002. Adherence is monitored by pill count and self-report, methods that tend to overestimate adherence.⁹ In August 2006, following new Ministry of Public Health guidelines, VL testing and second-line HAART were introduced.

2.2. HIV-1 VL monitoring

We offered VL counseling and testing to adults and children taking HAART for a minimum of 6 months (see below). HIV-1 RNA assays were performed in the reference laboratory of the Thai Red Cross HIV Clinical Research Centre using a b-DNA method with a lower limit of detection of <50 copies/ml. If VL was >1000 copies/ml, genotype resistance testing was performed.

We divided patients into three categories depending on the result. Those with undetectable VL proceeded to 6 monthly monitoring thereafter. Those with low detectable VL (>50 to <1000 copies/ml) were offered additional adherence support and follow-up VL after 3 months: intuitively a reasonable time for solving adherence problems. Patients with a high detectable VL (>1000 copies/ml) and confirmed HIV-1 resistance were offered appropriate counseling together with second-line treatment. If genotype testing failed to show resistant mutations, they continued first-line treatment and had follow-up VL at 3 months. We recorded results of routine clinical follow-up in standardized software (FUCHIA).¹⁰

2.3. Developing education materials and a pre- and post-VL testing protocol

Our strategy was to use VL testing as an opportunity to help patients reflect on their commitment to treatment, their adherence and other behavior that possibly leads to resistance, and to make their own decisions on how to change. We developed educational materials and a counseling pro-

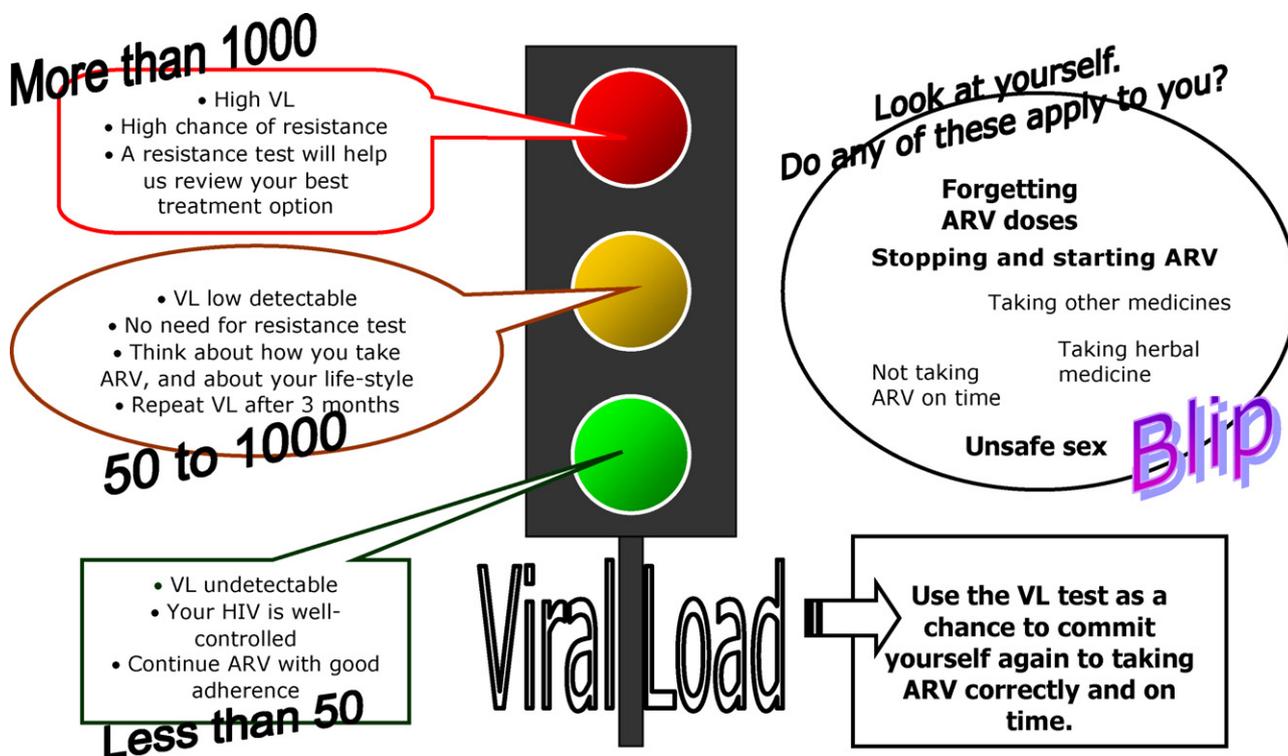


Figure 1 'Traffic lights' poster used to guide patients through the process of HIV-1 viral load testing. ARV: antiretrovirals.

to guide patients through this process and help them to link their VL result with their adherence to treatment.

Despite the low educational level of many patients, explaining the concept of resistance was straightforward (they were mostly farmers and so familiar with the concept from pesticide use). The challenges were to develop an education tool that explained the three possible results of VL testing [undetectable (<50 copies/ml), low detectable (>50 copies/ml to <1000 copies/ml) and high detectable (>1000 copies/ml)] in a non-judgmental way, and to overcome the stigmatizing label 'treatment failure'.

We tried using three faces (smiling, neutral and frowning) as a visual aid, but the frown raised some extreme negative feelings. We then tried 'traffic lights': everyday, non-threatening objects indicating three alternative courses of action, but where certain rules must be observed. Figure 1 shows a poster developed to guide the process of self-reflection and explain procedures for follow-up testing and future treatment options. This was understood both by adults and children, the youngest of whom was aged 6.

Once patients understood the purpose and implications of VL testing, they were encouraged to proceed to pre-VL test counseling. Table 1 shows our protocol for pre- and post-counseling. Peer counselors, already experienced in other

aspects of treatment support, quickly developed expertise to implement this protocol under supervision of a nurse counselor.

3. Results

We report results for all patients having their first VL test between August 2006 and December 2007, together with follow-up tests until June 2008: 171 adults and 14 children (aged 6 to 12) were eligible; all were tested on at least three occasions, and remained in clinical follow-up throughout this period (Table 2). At the time of their first VL test, median time on HAART for adults was 35 months (range 6–62 months) and for children 47 months (range 17–56 months).

Considerations of previous toxicity, pregnancy or concomitant tuberculosis (TB) treatment meant that patients were taking a variety of HAART regimens. Most were taking either a fixed-dose combination of d4T/3TC/NVP ($n=78$) or d4T + 3TC + EFV ($n=43$). No association was found between VL and drug regimen (data not shown).

Initial and all follow-up VL were undetectable in 116 adults and 13 children. High VL together with HIV-1 resistance was found in four adults and one 12-year-old child, who all switched to second-line regimens.

Table 1 Guideline for pre- and post-VL test counseling.

General points for counselors

- These points apply to counseling for both adults and children.
- The objectives are to change behavior that may lead to the development of HIV-1 resistance and to support the patient. Help patients link their behavior to the VL result, and promote confidence and skills for behavior change. Encourage patients to decide what aspects of their behavior to change based on their options and own strengths and experiences.
- Take a non-judgmental attitude. Avoid the expression 'treatment failure'.
- Encourage patients to reflect on their commitment to treatment. 'How?' questions, such as 'How did you feel when you forgot your medicine?' are better than 'Why?' questions, which can sound like accusations ('Why did you forget your medicine?').
- Counseling should be performed within the context of existing social network support and may be performed one-on-one, or in the presence of friends or family, or during a group meeting for People with HIV/AIDS.

Pre-viral load test counseling

- Give enough basic information to explain the implications of the three possible outcomes and options for treatment in each case.
- Ask the patient if he/she wants to proceed with VL testing (he/she has the right to delay or refuse).
- In case he/she decides to proceed, ask what result he/she expects, based on adherence or other factors. Ask how he/she will feel, and how he/she will make necessary adjustments in case of detectable VL.
- Give time for the patient to think through any psychosocial or other issues that may emerge. Arrange the test or make an appointment for further counselling as appropriate.

Post-viral load test counseling

- Ask what the patient remembers about VL and what he/she expected the result to be.
- Give the VL result clearly and ensure it is understood.
- Ask again the reasons for the result. Allow time for reflection. Answer any questions honestly. Always aim to improve the patient's self-esteem.
- In case of detectable VL, patients may need to release emotions, before they can consider their different options and change behaviour.
- Encourage realistic plans to improve adherence. For example those who forget medication during or after a heavy drinking session can be advised to take their medication an hour or so early, before going out to get drunk, rather than be told not to get drunk.

Make a further appointment if necessary.

VL: viral load.

Table 2 Summary of HIV-1 viral load test results.

	n (%)
Adults	171 (100)
VL consistently undetectable (<50 copies/ml)	116 (68)
VL high (>1000 copies/ml) on initial test and HIV-1 resistance detected; switched to second-line regimen	4 (2)
VL low detectable (>50 copies/ml) on one or more occasion ^a	51 (30)
First VL low detectable ^a	40 (23)
Follow-up VL after 3 months undetectable (<50 copies/ml)	36 (21)
Follow-up VL after 3 months low detectable (>50 to <1000 copies/ml) but subsequent VL after 6 months or more undetectable (<50 copies/ml)	1 (0.5)
Further follow-up VL after another 3 months remains low detectable (>50 to <1000 copies/ml)	3 (1.5)
First VL undetectable (<50 copies/ml) and 6 months later second VL low detectable (>50 to <1000 copies/ml)	9 (5)
Further follow up VL after another 3 months undetectable (<50 copies/ml)	8 (4)
Further follow up VL after another 3 months remains low detectable (>50 to <1000 copies/ml)	1 (1)
First and second VL undetectable (<50 copies/ml); third VL low detectable (>50 to <1000 copies/ml)	2 (1)
Further follow-up VL undetectable (<50 copies/ml)	1 (0.5)
Further follow-up VL remains low detectable (>50 to <1000 copies/ml)	1 (0.5)
Children	14
VL consistently undetectable (<50 copies/ml)	13
VL high (>1000 copies/ml) on initial test and HIV-1 resistance detected; switched to second-line regimen	1

VL: viral load.

^a Among the 51 adults whose first VL was low detectable, 49 were in the range >50 to <1000 copies/ml, and two were in the range >1000 to <2000 copies/ml but no HIV-1 resistance was detected.

Among the remaining adults (51/171), 40 (23%) had low detectable VL on their first test and 11 (6%) had undetectable VL initially but developed low detectable VL later: 9 (5%) on their second test and 2 (1%) on their third test. All patients with detectable VL received 3 month and 6 month follow-up tests. In 47/51 cases, the result became undetectable following the intervention. No patients progressed to high VL with resistance.

3.1. Patients' explanations of detectable VL

The following explanations emerged during counseling sessions. Of 51 adults with low detectable VL, 39 (18 men, 21 women) linked their result with poor adherence: insufficient time to organize taking their medicines (8 men, 3 women); getting drunk with friends (9 men, 1 woman); fear of disclosure (3 men, 5 women); and stopping or stopping/starting treatment (2 men, 2 women).

A further eight (6 men, 2 women) had always adhered well and identified regular unsafe sex as the explanation. Four men were very surprised by their detectable VL, or did not believe it, and could not put forward any explanation.

The counseling process uncovered unresolved psychosocial issues for some patients (see below). Some patients found they had the strength to address these issues. However, VL testing created negative feelings for some patients, emphasizing the need for careful assessment during pre-VL test counseling.

3.2. Case histories

3.2.1. Toey and Lek

Toey and her husband Lek have been married for 10 years. Lek does not like to use condoms during sex; Toey com-

plained about this from time to time, but the couple had never worked through this issue. Since they started HAART, Toey's adherence has always been good, but Lek occasionally missed some doses. They had their first VL tests in August 2006 after 3 years on HAART. Both had detectable VL: Toey 69 copies/ml and Lek 922 copies/ml. Toey became more assertive with Lek about her worry that unprotected sex was increasing their HIV levels. After trying different kinds of safer sex, the couple found *coitus interruptus* the most suitable for them. Three months later, Toey's VL was undetectable although Lek's remained detectable (59 copies/ml). After 6 months Lek's VL became undetectable. The couple are more relaxed with each other now and feel that talking openly with each other about safer sex has improved their relationship in general.

3.2.2. Ott

Ott started HAART in September 2003. In early 2006, his wife left him, taking their daughter with her. He began to drink heavily and stopped taking his treatment correctly. He attempted to hang himself but was found by his family. Peer counselors visited him and told how they had learned to cope in similar situations. No longer feeling alone, Ott realised he wanted to live and decided to take better care of himself. He expected to have a very high VL, but the result, although detectable, was low (172 copies/ml) and motivated him further to adhere to treatment. Three months later his VL was undetectable. He now feels he can put the past behind him and look to the future.

3.2.3. Leu

Leu, his wife and his son are all HIV-positive. Leu developed cryptococcal meningitis in 2003, and felt desperate until he heard about HAART. All three family members started HAART, were highly motivated, and had good adherence. In

October 2006 they had VL testing; Leu's VL was detectable (298 copies/ml), although his wife's and son's were undetectable. Old feelings of despair returned when he heard this result and he wanted to give up treatment. His peer counselor persuaded him to continue, and 3 months later a follow-up VL was undetectable.

4. Discussion

In 45/51 patients, low detectable VL became undetectable following counseling and behavior change. How should these data be interpreted? The causation and significance of VL in the range >50 to <1000 copies/ml are debated⁹ and the concept of 'blips' (transient low-level viremia without clinical consequences) complicates the picture.^{11,12} Similar numbers of blips could plausibly be expected to occur at the time of the first, second and third VL, but among our patients 23% had low detectable VL on their first test and only 6% developed detectable VL later. Opportunistic infections can result in transient increases in VL,^{8,13} but at the time of VL testing, only two patients had ongoing opportunistic infections (CMV retinitis and extra-pulmonary TB). VL was undetectable, and remained so, in both these patients, so this is an unlikely explanation for the trends. The explanations identified by patients themselves, mostly linked with poor adherence, remain a likely cause. More importantly, these proved to be an entry point for discussion on patients' commitment to treatment.

Poor treatment adherence, the commonest cause of treatment failure, can be improved: in one program in South Africa, where patients with detectable VL receive targeted adherence support by peer counselors, only 2% patients developed persistent virological failure.⁷ Treatment literacy is a factor contributing to improved adherence and is associated with improved outcomes on HAART.^{14,15} The adherence support provided by patient groups adds significantly to life years saved in Thailand's treatment program,¹⁶ and the 100% follow-up rate in our program may be related to the patient-centered approach taken.

A recent modeling study concluded that VL monitoring provides only a modest benefit in resource-limited settings when a single VL is used solely for deciding when to switch to second-line treatment.¹⁷ However, the model did not consider the potential of VL as an adherence reinforcement tool.¹⁸ In Thailand the cost of VL (\$US59 per test) and genotyping (\$US47 per test) is not unaffordable, at least for program-surveillance purposes. The role of patient education and meaningful participation by patients in the process of VL monitoring also merits wider attention.

In conclusion, VL monitoring and targeted counseling for patients with detectable results can provide an opportunity for promoting adherence to first-line treatment. VL can be as much a tool for psychosocial support as a biomedical tool to detect treatment failure. Educating patients and taking psychosocial aspects into consideration provides opportunities to delay the onset of HIV-1 resistance and to support patients.

Authors' contributions: DW, AKK and NF conceived and designed the study; AKK, SK, NS, PT and NT coordinated the study; SK, PT and NT collected the data; DW, AKK, TR and

MK analyzed and interpreted the data; DW, TR, NS and NF drafted the manuscript; DW and NF revised the manuscript for final submission. All authors read and approved the final manuscript. DW is guarantor of the paper.

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Ethical approval: This paper presents routinely collected data and includes Ministry of Public Health authors. Approval to publish the results was received from the local Office of Disease Prevention and Control and the MSF Ethics Review Board. Informed written consent was obtained to publish the case studies.

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