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Developing an adherence support intervention for patients on antiretroviral therapy in the context of the recent IDU-driven HIV/AIDS epidemic in Estonia

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Abstract

There is limited data on and experience with interventions for antiretroviral therapy (ART) adherence support for patients on ART in Eastern Europe. We sought to identify a feasible adherence support intervention for delivery amongst HIV-positive adults receiving care in Estonia, where the HIV/AIDS epidemic has been mainly concentrated among injection drug users. Our application of intervention mapping strategies used existing literature, formative research and multidisciplinary team input to produce a brief clinic-based intervention entitled the Situated Optimal Adherence Intervention Estonia (sOAI Estonia) which uses both Next-Step Counseling and Information-Motivation-Behavioral Skills Model approach to facilitate integration of ART into the context and demands of daily life. We present the intervention development process, the resulting sOAI Estonia approach, and describe a randomized controlled trial which is underway to evaluate the intervention (results due in spring 2013).

Keywords

ART; HAART; adherence; intervention

Introduction

Potent combined antiretroviral therapy (ART) has transformed HIV infection from an acute to a chronic disease, and recent evidence suggests that ART can prevent HIV transmission to HIV-uninfected partners (Cohen et al., 2011). While availability of, and access to, ART are necessary conditions for rapid and sustained viral suppression, adequate long-term adherence is essential to realize the individual, and potential public, health benefits ART can provide (Altice, Mostashari, & Friedland, 2001; Mannheimer et al., 2005; World Health Organisation [WHO], 2003). However, even the current more “forgiving” regimens present challenges for long-term, sustained adherence (Amico, Harman, & Johnson, 2006; Bae et al., 2011; Simoni et al., 2003). ART adherence is now widely recognized as a critical health promotion behavior for HIV-positive individuals on therapy and a public health priority (WHO, 2003).

Optimising ART adherence is attracting considerable activity, and several meta-analyses suggest interventions can improve adherence (Amico et al., 2006; de Bruin et al., 2010; Simoni et al., 2006), but there is less consistent evidence of an effect on viral load (Simoni et al., 2006). The United States Centers for Disease Control (CDC) recently unveiled evidence-based interventions for ART adherence, with only 8 interventions categorised as having good evidence and none in their best evidence category (CDC, 2011). However, adherence intervention approaches have not been evaluated within a general adult clinic population in Eastern Europe. Thus while available intervention approaches may provide guidance for how to best intervene with this population, the application and adaptation of both an adherence intervention and the behavioral model underlying it to a new population requires targeted attention.

We sought to identify a feasible adherence support intervention amongst HIV-positive adults receiving care in Estonia, where the HIV/AIDS epidemic has mainly involved injection drug users (IDUs) (Malta et al., 2010; Mathers et al., 2008). Here, we describe the development of a targeted intervention program where patient-level adherence factors, adult learning, tailored support, and patient-centered principles were leveraged to create a brief clinic-based intervention to promote patient-knowledge, motivation, and skills in integrating ART adherence into the context and demands of daily life. To our knowledge, this is the first systematic intervention development program specifically targeting the needs of people living with HIV (PLWH) in Estonia.

Background

In 2009, Estonia had the highest rate of new HIV cases (30.7 per 100 000) in Europe (European Centre for Disease Prevention and Control [ECDC], 2010), and an estimated HIV prevalence of 1.2% in the adult population (Joint United Nations Programme on HIV/AIDS [UNAIDS]). The region most affected by HIV is Ida-Viru County, close to the Russian border, where the epidemic erupted in 2001. In 2010 this area accounted for 45% of newly registered HIV cases, with a rate per 100 000 inhabitants more than 3.5 times that of all Estonia (Estonian Health Board, 2011; Statistics Estonia, 2011). As in other Eastern European countries, IDUs are disproportionately represented in the HIV positive population (ECDC, 2010; Laisaar et al., 2011, UNAIDS/WHO, 2009). Local studies in Estonia have documented a 40–90% HIV prevalence among IDUs (National Institute for Health Development, 2009; Uusküla et al., 2006; Uusküla et al., 2007; Wilson et al., 2007).

In Estonia, ART is available free of charge to anybody requiring it through infectious diseases departments in five major hospitals, primarily on an out-patient basis. There are estimated to be about 11,000 PLWH in Estonia and almost 3,000 of them require ART (Lai et al., 2009). It has been suggested that poor health outcomes (e.g. virologic failure) of patients on ART and the recent rapid increase in drug-resistance (Avi et al., 2011) stem predominantly from poor adherence. However, until recently, there was little evidence about factors specific to Estonia (Uusküla et al., 2012).

Methods

The current project was initiated in response to heightened awareness of potential problems with adherence amongst patients in care because of high rates of viral failure at one of the 2 clinics providing HIV care in Ida-Viru county–Ida-Viru Central Hospital, serving 651 HIV-infected individuals in 2010 (372 on ART at year end) (Estonian Health Insurance Fund, 2011). It was also realized that the kinds of ART adherence support presently offered—mainly treatment regimen information giving, did not appear to meet the needs of the target population or share common features with interventions demonstrated in other countries

(Amico et al., 2006; Simoni et al., 2008). A detailed mapping for intervention or adherence support needs was necessary to identify in-clinic strategies that could leverage patient-centered practices to best support the specific needs of adult PLWH in care in Eastern Estonia. This systematic process was based on Intervention Mapping (IM)—a theory- and evidence-based health promotion intervention development and evaluation framework (Bartholomew et al., 2006; Kok et al., 2004). Each step in IM drew from and built upon several main sources of data—a detailed literature review, discussion amongst a multidisciplinary international research team, and formative research (Table 1). Previously published methods were followed or adapted (Bartholomew et al., 2006; Kok et al., 2004; Wolfers et al., 2007; Wolfers et al., 2007; Cote et al., 2008; Kok et al., 2006; Perez-Rodrigo et al., 2005).

Results

Needs Assessment

Data on ART adherence determinants were obtained from focus-group sessions involving 14 individuals (5 female, age range 18–50). The main barriers to ART adherence identified by these groups were: lack of time (e.g. busy with a baby), drug/alcohol abuse, concerns regarding potential or experienced side-effects from antiretrovirals (ARVs) (dizziness/vertigo, psychological effects, feeling sick/malaise), and considering ART unnecessary (e.g., feeling healthy and thus no need for “the chemicals”). The main facilitators identified were: support from a family member/partner, desire to be healthy to raise a child, linking ART medication taking to already established medication taking routines, and use of tools or methods for organizing pill-taking (reminders from a family member/partner, using a pill-box, setting an alarm on a mobile phone, keeping medication in a visible place at home, always carrying a pill for “just in case”).

We identified gaps in ART adherence knowledge among PLWH on ART, low beliefs in medication efficacy, challenges to sustained motivation and in skills needed to achieve and maintain optimal adherence. Misconceptions related to ART included defining non-adherence as not taking medication for a long period—a month or two, as well as uncertainty about the actual function and effects of ARVs. Beliefs that ART caused multiple physical and social burdens were expressed. Skills to manage side-effects, social burden, and sustaining high rates of adherence were also noted.

From providers, we identified inconsistencies in how ART adherence was discussed with patients as well as how frequently—no standard protocol was followed and most discussions appeared to occur early in the course of prescribing ART. Later in the treatment, non-adherence appeared to be infrequently reported by patients, and doctors tended to “discover” problems with adherence only from poorly controlled viremia, drops in CD4, or failure to pick up medication refills.

These potential gaps in patient information, motivation, social support, and skills, combined with an understanding that current standard of care for adherence did not presently involve a strong patient-education component or open discussions concerning challenges (or successes) with adherence, guided our identification of program objectives and intervention development.

Proximal program objectives identification

We developed a heuristic guide informed by all data sources (elicitation groups, research team, and literature) depicted in Figure 1. We sought to promote two core sets of behaviors—“integrating the treatment plan into one’s daily routine” and “handling situations in which ART is difficult to take”. Thus, while the objective was to increase or sustain high rates of

adherence, the proximal determinants that guided our intervention development were areas that all patients could discuss without having to disclose whether doses were actually missed.

Theory and strategy selection

We adapted the Information-Motivation-Behavioral Skills (IMB) theory of ART adherence (Fisher et al., 2008; Fisher et al., 2006; Munro et al., 2007).

Based on this model and our initial work, we identified knowledge, motivation, and skills as critical change objectives (Figure 1).

For our intervention approach, we adapted Next-Step Counseling (NSC) to ART adherence. NSC has previously been used in a number of HIV pre-exposure chemoprophylaxis (PrEP) trials (Amico et al., 2010; Grant et al., 2010). NSC involves brief guided discussions targeting identification of adherence-related needs and strategizing on them using motivational interviewing techniques. We also included a brief education session using a flip-chart with images and metaphors of HIV infection, and explaining the actions of ARVs, and resistance.

Program development

The intervention comprised 3 one-on-one sessions with a trained study nurse approximately 3 months apart (Figure 2). The frequency was chosen to distribute the intervention over an optimal time period and to minimise extra visits by linking the counseling sessions to patients' regular medication refill visits.

Intervention Session 1 included three main components: an explanation of the study and the role of the nurse as a collaborator with the participant; going through the educational flip chart and eliciting reactions to this; and a NSC discussion. A standardized flip-chart was created specifically for sOAI Estonia. It uses heuristics and metaphors to promote understanding and personalized knowledge of HIV in the body and how ARVs can protect the immune system. This material was made available for review, as needed, at subsequent sessions. A metaphor—an "Immune Factory" concept—showing the human immune system as a CD4 cell factory, attacked by HIV and protected by ARVs (Figure 3), was created to increase patients' understanding of HIV, promote agency and empowerment of the patients in control of their HIV, and foster the development of a common language between the nurse-counselor and the patient. While the same flip-chart was used for all participants, the nurse aimed to provide information in a manner that adopted the participant's language, was responsive to his/her interests, and adjusted content for each participant's level of understanding and knowledge.

After eliciting participant reactions to the flip chart, the nurse initiated a NSC discussion (Figure 4). A Neutral Assessment (NA) approach (Amico et al., 2010) was adopted to promote participants' sense of candor and comfort in having open discussions about ART adherence. As part of the evaluation of the sOAI Estonia intervention self-reported adherence data was also collected via interviews, conducted by a different nurse from the one who had administered the NSC, who was trained in NA strategies to optimize self-report.

Intervention Sessions 2 and 3 involved a brief check on any questions arising from the first session, and implementation of the NSC discussion. Each NSC discussion concluded with identifying something the participant would try to help with adherence between visits. At the following session, the nurse asked the participant how this had gone and then discussed current experiences with ART and what the participant now felt would be most helpful to

integrate daily ART into his/her life. The final visit also included a discussion of how the participant would continue to work on meeting his/her adherence-related needs as the intervention formally discontinued. Participants, however, did continue to see the nurse during their routine clinical visits as she was part of the clinical team.

Program implementation

The intervention nurse and interviewer received 2 half-day training sessions in July 2010 and 3 subsequent 2-hour boosters over the next 3 months. Study material was all in English, Estonian and Russian, staff training was conducted in English with Estonian and Russian translation, and on-site booster sessions were conducted in Estonian and Russian. A study manual on NSC and NA, a one-page NSC counseling record form, and a standard questionnaire for patient interviews (including adherence assessment) were employed to standardize and monitor the implementation. Further support included regular discussions with the project manager who visited the study-nurses at least once a month, providing methodological and practical intervention implementation support.

Program evaluation

The sOAI Estonia intervention is being evaluated in a randomized controlled trial (RCT) at Ida-Viru Central Hospital. A convenience sample of 150 consecutive patients attending the infectious diseases department, eligible when HIV infected, 18 years of age, speaking/reading either Estonian or Russian, receiving or starting ART, without known triple class antiretroviral drug resistance, were recruited during July–November 2010. Study participants were centrally randomized to the intervention (sOAI Estonia) or the control (standard care) arm, and followed for 12 months.

The study aims to evaluate ART adherence and the impact of the sOAI Estonia program compared to regular counseling. The primary outcome is the level of ART adherence measured by patient 3-day recall self-report (Chesney et al., 2000) and hospital medication dispensing records at baseline, and after 6 and 12 months. In addition, data on HIV-1 RNA level and CD4+ immune cell count is collected at same time points. Information on participants' socio-demographics, HIV infection and ART history and attitudes, alcohol and drug abuse, incarceration and sexual risk behavior are also being collected. Results will be available in 2013, baseline characteristics of study participants are described elsewhere (Uusküla et al., 2012). Amongst the 75 patients assigned to the intervention condition (2/3 male, median age of 32, predominantly unemployed, 65% reporting IDU-related HIV acquisition, median of 6 years living with HIV, and 2 years on ART), first sOAI Estonia intervention data collected identified several facilitators and barriers (Table 2), consistent with the needs assessment conducted while developing the intervention.

Discussion

The importance of building an intervention on both theory and empirical evidence has been well recognized (Bartholomew et al., 2006; Craig et al., 2008). We applied Intervention Mapping (IM) as a valuable check-list to ensure covering all the appropriate intervention objectives; keep the objectives and activities grounded on both theory and evidence, and the intervention compatible with the target population; anticipate potential diffusion issues and respond them immediately throughout the process (Kok et al., 2004).

While interveners in previous ART adherence intervention studies have included pharmacists, psychologists, nurses, physicians, physician assistants, peer advocates and even computer-based virtual counselors (Simoni et al., 2006; Simoni et al., 2008), multidisciplinary teams have often been involved in intervention development (WHO, 2003;

Bartholomew et al., 2006; Rueda et al., 2006). We recognized the importance of having a multidisciplinary team, as no single specialist would have possessed expertise to cover all the methodological and practical issues of the complex topic of ART adherence within the local environment and service-system.

One prerequisite for any intervention development is assessing the need(s) of the target population—in our case, PLWH receiving ART. In Estonia the issue of suboptimal ART utilization i.e. low treatment adherence was first recognized by service providers and not patients. Our focus group interviews revealed another facet of treatment adherence—patients' lack of knowledge about ART adherence. Patients had been told that not taking their pills as prescribed would lead to resistance, but did not fully understand how resistance developed and how missing one pill or a few every once in a while could contribute to this. The importance of daily pill-taking was especially hard to recognize by patients who did not feel ill, but experienced medication side-effects. We observed, that adherence in some patients deteriorated over time (before the intervention) as HIV-related symptoms diminished, yet medication side-effects increased. This has also been reported by other researchers (Simoni et al., 2008).

During the focus group interviews we learnt that some patients preferred to miss a pill rather than potentially reveal their HIV status to other people. Based on this finding, we felt that the IMB model of adherence, also applied in other ART adherence interventions (Sabin et al., 2010), provided a good reflection of the issues reported in our elicitation work. In developing the intervention, we considered strategies noted in multiple sources e.g. recommendations by professional organizations—the American Psychology Association (APA) (APA, 1997) and the American Public Health Association (Jani AA, 2004), and several authors (Simoni et al., 2003; Rueda et al., 2006; Chesney, 1997).

The selection of Next-Step Counseling as a flexible approach, focused on facilitators and experiences with adherence, versus a barriers-based approach, appeared well-matched to what our patient population was willing to explore with clinic staff. It is important to note that other intervention approaches were reviewed and several could have been modified and applied in our setting. Our program of research began, however, with what we identified as a minimum intensity intervention that had high generalizability due to low use of resources, as we were most interested in identifying promising interventions with immediate application to our clinical care environments. Feasibility, acceptability, and fidelity will be reviewed as part of the evaluation alongside the RCT.

As our aim was to develop a feasible intervention transferable to all medical institutions providing HIV/AIDS care in Estonia and potentially abroad, we had to ensure that the intervention would fit into the daily routine of the clinic, would not (in most part) require extra staff; could be performed in a relatively short amount of time and thus added to other routine interactions with patients in the clinic; would reach the patients when they attend the clinic and not require additional visits. In our study we provided extra training for two nurses, and adherence counseling (in the intervention arm) was added to patients' routine monthly clinic visits. Hospital personnel have not complained about excessive work load during the study, but report better understanding of their patients through enhanced communication. The nurse-counselors have also reported feeling rewarded by the “Aha! “ effect their explanations about HIV and ARVs generated in many counseled patients.

Conclusions

With limited published data on interventions for ART adherence support for patients receiving ART in Eastern Europe, our research contributes one possible intervention

development approach and resulting intervention, currently under evaluation. Intervention mapping strategies provided an excellent framework for applying formative research / elicitation work, existing literature, and multidisciplinary input into the development of an intervention program for PLWH in Estonia, which if effective, has possible applications in further development of HIV/AIDS treatment services in Estonia, and potentially in neighbouring countries with similar socioeconomic and HIV epidemic evolution.

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FIGURE 1.
Matrix of the Situated Optimal Adherence Intervention Estonia (sOAI Estonia) Objectives

FIGURE 2.
Antiretroviral Treatment Adherence Promotion Session Flow in Situated Optimal Adherence Intervention Estonia (sOAI Estonia)

FIGURE 3.
Selected Slides from the Situated Optimal Adherence Intervention Estonia (sOAI Estonia)
“Immune Factory” Information Flipchart

STEP 1:	INTRODUCE [Frame] . . . the counseling session
STEP 2:	REVIEW . . . patient's experiences in the clinic concerning adherence and ARVs to date (first session) OR progress made on strategy selected at previous session (follow-up sessions)
STEP 3:	EXPLORE . . . the context in which one negotiates and experiences adherence (ease and difficulty of managing, experiencing, and approaching medication-taking)
STEP 4:	TAILOR . . . the discussion to focus on increasing ease with which the patient approaches medication-taking [may include working medication-taking into daily life, sustaining successful strategies, or promoting less difficulty in specific situations] based on context and engagement in the counseling session
STEP 5:	IDENTIFY . . . the NEXT STEP towards increasing ease/decreasing difficulty of adherence by working on WHAT would need to happen for the patient to make progress or maintain effective approaches
STEP 6:	STRATEGIZE . . . with the patient on HOW progress could be made towards achieving that next step
STEP 7:	AGREE ON. . . WHICH of the strategies discussed the patient would be willing to try between now and the next time you meet and determine if an ACTION PLAN for that strategy is needed and what that would entail
STEP 8:	RECORD [Close and Document]

FIGURE 4.
Next-Step Counseling in Situated Optimal Adherence Intervention Estonia (sOAI Estonia)

TABLE 1
Development Framework and Data Sources of the Situated Optimal Adherence Intervention Estonia (sOAI Estonia)

INTERVENTION MAPPING			Research Team	Literature review	Formative research
<i>Description</i>	<u>Protocol steps:</u>	<u>International multidisciplinary team:</u>		<u>Electronic databases:</u>	<u>Qualitative research to obtain data on local ART adherence determinants in Ida-Viru County:</u>
	1 needs assessment	a.	2 public health researchers, experienced in HIV/IDU, medical doctors (University of Tartu, Estonia)	a. MEDLINE,	a. interviews with 4 medical service providers;
	2 proximal program objectives identification			b. Cochrane CENTRAL	
	3 theory and strategy selection	b.	researcher/instructor in health behavior change, experienced in ART adherence, a psychologist (University of Connecticut, USA)	c. ISI-Web of Science	b. 2 focus-group discussions with PLWH receiving ART in
	4 program development			Period of interest: January 2000 through December 2009	
	5 program implementation	c.	2 nurse counselors (Ida-Viru Central Hospital, Estonia), supporting the researchers in adapting the intervention to local conditions	<u>Key domains:</u>	<ul style="list-style-type: none"> a peer-to-peer HIV counseling center in Ida-Viru Central Hospital a nearby opioid substitution treatment center run by an NGO
	6 program evaluation			1 Highly Active Antiretroviral Therapy (HAART)	
				2 medication adherence / patient compliance	Interviews conducted by a sociologist (University of Tartu, Estonia)
				3 behavior theory/ methods	
				4 intervention	
				5 program development	Search conducted by one of the public health researchers (University of Tartu, Estonia)
<i>Activities</i>	Activities (by step) described in manuscript 'Results'	a.	Individual data evaluation	Electronic information space search	About 120 min discussions in participants' native language, tape-recorded after informed consent, transcribed verbatim for analysis. Interviews initially coded for major themes, further refined in an iterative process of data coding, charting, and interpretation.
		b.	Team discussions <ul style="list-style-type: none"> meetings teleconferences 		
<i>Period</i>	January — June 2010	January — June 2010		January — February 2010	April 2010

* Miles, & Huberman, 1994

ART Adherence Characteristics of the Situated Optimal Adherence Intervention Estonia (sOAI Estonia) Pilot Study Participants in the Intervention (sOAI Estonia) Arm

TABLE 2

Characteristic	Male		Female		Total		
	n	%	n	%	n	%	
Adherence failure (at least 1 pill missed in last 3 days, self-reported [*])	yes	3	6%	2	7%	5	7%
	no	44	94%	26	93%	70	93%
Adherence facilitators	social support (<i>inc/</i> having a child)	28	60%	16	57%	44	59%
	future perspectives (desire to stay alive/healthy)	27	57%	14	50%	41	55%
	routinization of pill-taking (a well-established method)	16	34%	6	21%	22	29%
	good health / feeling	3	6%	8	29%	11	15%
	other (<i>inc/</i> difficult to answer)	12	26%	9	32%	21	28%
Adherence barriers	medication side-effects	18	38%	15	54%	33	44%
	irregular, intensive personal or working-life	11	23%	9	32%	20	27%
	alcohol / illicit drug abuse	8	17%	2	7%	10	13%
	other (<i>inc/</i> difficult to answer and respondents at ART initiation)	20	43%	7	25%	27	36%
	no problems with / barriers to pill-taking	2	4%	0	0%	2	3%

^{*} The AACTG Adherence Instrument (Chesney et al., 2000)