

American International Health Alliance

Project Closeout Report

Evaluation of Integration of Medication-assisted Treatment for Injection Drug Users into HIV Medical Care in Leningrad Oblast, Russia

Agreement #AID-118-A-12-00010

December 21, 2012



Preface

This closeout report provides a comprehensive overview of the activities carried out through a Public Health Evaluation titled, "Evaluation of Integration of Medication-assisted Treatment for Injection Drug Users into HIV Medical Care in Leningrad Oblast, Russia," which was awarded to AIHA on July 16, 2012 through USAID cooperative agreement AID-118-A-12-00010. The three-year award followed a preparation period that that was initiated through a USAID purchase order in December 2010 and included a lengthy protocol development, review, and approval process to ensure the integrity and feasibility of the study.

Due to the decision of the Russian Government to terminate all USAID-supported activities in country as of October 1, 2012, AIHA was unable to move this public health evaluation beyond the development of the year-one work plan.

AIHA is a 501(c)(3) nonprofit corporation created by the US Agency for International Development (USAID) and leading representatives of the US healthcare sector in 1992 to serve as the primary vehicle for mobilizing the volunteer spirit of American healthcare professionals to make significant contributions to the reform of healthcare overseas through partnerships. AIHA's mission is to advance global health through volunteer-driven partnerships and initiatives that mobilize communities to better address healthcare priorities while improving productivity and quality of care. Founded in 1992 by a consortium of American associations of healthcare providers and of health professions education, AIHA facilitates and manages twinning partnerships between institutions in the United States and their counterparts overseas. To date, AIHA has supported some 170 capacity-building partnerships that link American volunteers with communities, institutions, and colleagues in 34 countries in a concerted effort to improve healthcare services and delivery.

Operating with funding from USAID; the Health Resources and Services Administration (HRSA) of the US Department of Health and Human Services; the US Library of Congress; the Global Fund to Fight AIDS, Tuberculosis and Malaria; and other donors, AIHA's partnerships and programs represent one of the US health sector's most coordinated responses to global health concerns.

AIHA wishes to express its sincerest gratitude to the countless professionals in the Russian Federation and the United States. AIHA's programs have been so successful because these individuals demonstrated the courage and commitment to change; the patience, dedication, and hard work to gain new knowledge and skills; and a generous spirit of trust and collaboration. Together they made significant contributions to improving healthcare services and delivery for people around the globe. AIHA also thanks USAID and the Russian Ministry of Health and Social Development for the opportunity and privilege of working so closely with them and for their steadfast support of our programs in Russia.

Finally, AIHA gratefully acknowledges the contributions of our dedicated staff in Washington, DC, as well as our regional office in Russia whose work assured the successful management and implementation of this project, as well as the preparation of this closeout report.

The contents are the responsibility of AIHA and do not necessarily reflect the views of USAID, the United States Government, the Russian Ministry of Health and Social Development, or the Government of the Russian Federation.

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I. Background

The HIV/AIDS pandemic made its way to Russia some 10 years after it began to emerge as a significant public health threat in most other countries spanning the globe. Following the collapse of the former Soviet Union in 1991, however, HIV started snaking into the Russian Federation along with drug trafficking that followed the ancient Silk Road from the East through Central Asia. Today, Russia's HIV epidemic is one of the most volatile in the world, with rising rates of new infections at a time when the rates in many other countries are leveling off or even declining.

From its outset, Russia's HIV epidemic has been driven primarily by injecting drug use, heroin in particular. People who use injection drugs (PWID) are still a major driver of the epidemic. Chronic opioid use often results in increasingly risky behaviors, such as the sharing of needles, use of drugs during sex, sex trading, and group sexual encounters — all of which increase HIV transmission.

For people who are already living with HIV or AIDS and in need of antiretroviral therapy (ART), this continued drug use markedly impairs both access and adherence to treatment. Delayed initiation of ART — and interruptions to treatment once it has been initiated — can result in significant morbidity and mortality. HIV-infected patients who use or are dependent on opioids often are either lost to care or unable to adhere to complex treatment regimens, which results in the development of resistance to antiretroviral medications (ARVs), including transmission of resistant virus strains to other people.

Because of this, evidence-based treatment of opioid dependence in the form of medication-assisted treatment (MAT) represents an important method for improving health outcomes in this population. MAT also represents one of the most effective secondary HIV prevention strategy among the PWID population.

II. Project Overview & Description

In response to the demonstrated need in country, USAID initiated in December 2010 a purchase order for AIHA to lead collaborative efforts to design, develop, facilitate the approval process for a public health evaluation protocol for the “Evaluation of Integration of Medication-assisted Treatment for Injection Drug Users into HIV Medical Care.”

Working closely with the USAID, the Russian Ministry of Health and Social Development, and the Principle Investigator at Yale University School of Medicine, AIHA engaged four leading Russian healthcare institutions to participate in the project, forming the design and implementation team (see Table 1 on page 5).

AIHA managed the protocol development and approval process, which included establishing said protocol development team and selecting participation sites; drafting English and Russian-language versions of the study protocol for submission to USAID and OGAC; and incorporating US Government input into revised documents, which were then approved by both US

agencies. The study protocol was then sent to each partner institution for review and subsequently approved by Institutional Review Boards (IRBs) in Russia on March 15, 2012 and in the United States on March 12, 2012.

During this lengthy approval process, AIHA facilitated multiple meetings with representatives of Janssen Pharmaceuticals to secure preferential discounts for the procurement of the medication Vivitrol for the study.

In July 2012, USAID awarded AIHA a three-year cooperative agreement to carry out the “Evaluation of Integration of Medication-assisted Treatment for Injection Drug Users into HIV Medical Care in Leningrad Oblast, Russia.”

Working closely with all stakeholders, AIHA developed a detailed year-one work plan, which was submitted to USAID on September 14, 2012.

The overall objective of this public health evaluation was to examine Russian models of integrating drug treatment — including MAT for opioid dependence — and HIV care that can be sustained and scaled up nationally as part of the Russian HIV/AIDS continuum of care response.

People living with HIV (PLHIV) who met the criteria for both opioid dependence and treatment with highly active antiretroviral therapy (HAART) were to participate in this healthcare delivery strategy.

Specifically, over a 12-month period of time, the study would have sought to:

- Determine the efficacy of long-term, extended-release Vivitrol (d-NTX) on retention in HIV care, HIV disease progression, substance abuse habits, and social outcomes among opioid-dependent PLHIV and receiving HAART as compared to individuals not receiving the medication; and
- Compare and evaluate whether a model of integrated care that includes treatment for HIV and opioid dependence within the same setting is effective in achieving outcomes in comparison to a non-integrated care model in which patients receive treatment for each condition separately at an AIDS Center and a Narcology Center.

A randomized study was to be used to assess the relative differences in outcomes during both the treatment phase (the first six months) and the follow-up phase (subsequent six months).

A total of 135 participants were to be enrolled in the study and were to be block randomized into one of the three study arms with stratification based on the presence of co-morbid alcohol use disorders (see Table 2 on page 6).

Table 1: Project Design & Implementation Team

Partner Institutions & Key Stakeholders

- **Saint Petersburg State Medical University**
- **Leningrad Oblast Narcological Dispensary**
- **Leningrad Oblast AIDS Center**
- **Gatchina Regional Hospital**
- **Yale University School of Medicine**
- **US Agency for International Development**
- **American International Health Alliance**

Table 2: Randomized Block Distribution of Study Participants

Description of Study Pathways	
Arm 1	Integrated HIV care and Vivitrol treatment arm (n=45)
Arm 2	Non-integrated HIV care and Vivitrol treatment arm (n=45)
Arm 3	Standard of care arm; no Vivitrol (n=45)

As described in Table 2 above, a total of 45 participants were to be enrolled in each of the treatment pathways or “arms” of the study. Participants in the integrated (Arm 1) and non-integrated (Arm 2) pathways would have received Vivitrol every 28 days (-7 or +14 days) for the first six months of the protocol, while participants in the control pathway (Arm 3) would have received the current standard of care comprised of relapse prevention counseling and referral to an AIDS Center for HIV care.

All recruitment and enrollment activities were to take place at Leningrad Oblast Narcological Dispensary (LOND). After detoxification at LOND, eligible Arm 1 patients would have received both HIV and narcological care and treatment at the Leningrad Oblast AIDS Center or at the Gatchina Regional Hospital. Arm 2 patients would have received HIV care and treatment at the Leningrad Oblast AIDS Center or at Gatchina Regional Hospital and narcological care at LOND.

Data Analysis and Evaluation Plan

The analytic plan for this public health evaluation project was based on established procedures for randomized controlled trials, specifically those that are conducted to determine an effect size for a larger trial. The following section outlines the primary research questions as well as the proposed analytic plan.

HIV Treatment Outcomes

I. Retention in HIV Care

The primary hypothesis of the evaluation was that the provision of Vivitrol (d-NTX) would result in greater retention in HIV care. Specifically, participants in the integrated care arm were expected to have greater retention compared to participants in the non-integrated and control arms. Participants in the non-integrated care arm were expected to have greater retention than those in the control arm, but results were expected to remain inferior to the integrated arm. The definition of linkage to HIV care was to be based on making at least one visit to the AIDS Center to meet with an infectious disease specialist. Retention was defined as having one visit to see the said specialist each quarter. Thus, a binary variable for each quarter would be created to confirm whether the subject was involved in care. A chart review of the visit was to be conducted to ensure that the content of the visit was associated with health maintenance.

II. Initiation of HAART

AIHA believes the proposed public health evaluation was strengthened by including only indi-

viduals who were eligible for initiation of HAART (i.e. their CD4<350 in accordance with Russian Federation and WHO criteria for initiating HAART). In this way, we could have examined two aspects of HAART initiation: 1) time to first HAART prescription; and 2) retention on HAART over the 12-month observation period. Our hypothesis was that the integrated arm would have a higher percentage of subjects who initiate HAART compared to other groups.

III. Viral Load (VL) and CD4 Outcomes

In the United States, studies have shown that patients receiving substance abuse treatment for opioid dependence are “healthier” over time in care with higher CD4 counts and lower VL than compared to IDUs not in treatment for drug abuse. For VL, we would have measured the percentage of subjects whose VL is <50 copies/mL (undetectable) as well as the mean reduction in VL. Our hypothesis was that subjects in the integrated arm (who would have been more likely to initiate HAART) would have a higher proportion of viral suppression.

IV. Sexual HIV Risk Behaviors

We would have use standardized measures of change in HIV risk behaviors compared to the 30 days before enrolling in the detoxification program. We hypothesized that injection-related risk behaviors would be reduced most in both d-NTX arms, but not influence sexual risk behaviors.

Substance Abuse Treatment Outcomes

I. Retention in Narcological Care

Retention in narcological treatment, namely monthly visits for substitution therapy, would have been measured to control for other outcome variables in the final analysis.

II. Time to Relapse to Opioid Use

Using Kaplan Meier curves and Cox Linear regression, we would have measured the mean time to relapse to heroin use through self-reporting and urine toxicology screening, comparing the three groups. Our hypothesis was that both of the Vivitrol groups would have longer times to relapse than the control group.

III. Opioid-free Urine Testing

The percentage of opioid-free urine tests over the entire project would have been measured with both the Integrated and Non-Integrated Arms expected to yield superior results than the Control Arm.

IV. Addiction Severity

Mean scores on the ASI were to be measured for drug use from baseline and at 3, 6, 9, and 12-month time points.

V. Overdose

Both the Integrated and Non-Integrated Arms were expected to be superior to the Control Arm.

VI. Injection-related HIV Risk Behaviors

Standard measures of injection risk will be measured. Both the Integrated and Non-Integrated Arms would be expected to have less injection-related risk than the Control Arm.

Social and Criminal Justice Outcomes

I. Quality of Life

Using the SF-36, both the mean scores on the Physical and Mental Health Subscales were to be compared.

II. Reintegration with Family

This was to be measured using both the social support scale and family integration surveys.

III. Employment

Both time to employment as well as mean days of working will be compared between the three groups.

IV. Days of Criminal Activity

Time of criminal involvement would have been measured using the ASI.

AIHA, the Principle Investigator, and our implementing partners posited that the findings from this evaluation would have suggested optimal treatment and care models for the effective use of medication-assisted treatment for injection drug users who are opioid dependent had it been completed as planned.

III. Overview of Start-up Activities Completed

Immediately after receiving notification of the public health evaluation award from USAID, AIHA initiated start-up activities to chart the course of all future work on the project.

During the first quarter of the project, from August 1 to September 30, 2012, AIHA conducted the following preparatory activities:

- Developed a list of personnel responsibilities;
- Signed individual contracts with key Russian partners in St. Petersburg; and
- Prepared a contract with US partners at Yale University.

AIHA also convened a working meeting with the Russian principles in St. Petersburg. This event was held August 21-22 and attended by 17 Russian team members. Two AIHA representatives facilitated the planning and project overview meeting, leading the development process. Key results from this event are detailed in Table 3 on page 9 of this report.

During this timeframe, AIHA and other stakeholders completed development of 22 study forms and tools and conducted a number of meetings and discussions on ACASI development, defining contractors and procedures for this aspect of the public health evaluation. AIHA also conducted a meeting with the representatives of Janssen Pharmaceuticals on August 15, 2012 to reach an agreement of the number of the Vivitrol injections for needed for the project and other logistical matters such as costs, shipping and transfer orders, and distribution procedures.

Following up on these discussions, AIHA conducted a number of meetings with «ФАРМ-ЛЕКС,» the Vivitrol distributor in the Russian Federation, as well as other Russian parties in preparation for a contract to purchase the medication and distribute it to the study sites. Other discussions were conducted with representatives of EUROCOM-MED Ltd., which is the only official distributor of the HIV-rapid test “Ora Quick” in Russia. Subsequently, AIHA prepared a contract for the procurement of “Ora Quick.”

AIHA conducted a series of discussions with the NGO Global Health Institute, which is situated at Pavlov State Medical Institute in St. Petersburg; AIHA reached an agreement with the organization for the purchase of lab supplies and tests that would have been used for the public health evaluation. Other start-up activities included a number of discussions with Russian partners on supplies provision and the preparation for the training of public health evaluation personnel, as well as for a meeting of key stakeholders, both of which were scheduled to take place in early December 2012.

For an outline of AIHA’s year one work plan proposed for this public health evaluation in Russia, please refer to Table 4 on page 10.

Table 3: Key Results from August Planning Meeting in St. Petersburg

Start-up Activities: Russia Team Meeting, August 21-22, 2012

- **Memorandum of Understanding signed to formalize AIHA’s partnership with all Russian institutions participating in the public health evaluation**
- **Collaboration Agreement with Pavlov State Medical University signed to establish their participation in the study**
- **Study flow, personnel roles and responsibilities, protocol and forms, development of the ACASI system, and the evaluation timeline were all discussed**
- **Amendments to the study protocol and suggestions for improving patient enrollment were submitted by the Russian partners**
- **Next steps of evaluation implementation were discussed and approved**

Table 4: Planned Year 1 Activities for the Public Health Evaluation Project in Russia

Proposed Public Health Evaluation Activity Outline: 2012-2013

Three Month Preparatory Period

- 1.1 Confirm the participation of all institutions and personnel
- 1.2 Finalize study protocol and forms
- 1.3 Develop list of personnel responsibilities
- 1.4 Translate necessary documents (including forms) from English to Russian and vice versa
- 1.5 Hire and contract project personnel
- 1.6 Complete procurement of lab supplies and tests (including contracts with distributors)
- 1.7 Complete procurement of d-NTX from Janssen (50% of total amount)
- 1.8 Purchase of computers, cell phones, and office supplies
- 1.9 Develop program ACASI system
- 1.10 Design and finalize study database
- 1.11 Training of project staff; meeting of PHE principals
- 1.12 Procure additional medical insurance for study participants
- 1.13 Begin active recruitment of study participants

Study Implementation Period

- 1.14 Enrollment of participants (December 1, 2012)
- 1.15 Follow-up of study participants
- 1.16 Enter, clean, and aggregate study data
- 1.17 Monthly St. Petersburg study working group meeting with interim report to AIHA coordinator
- 1.18 Survey for providers about Vivitrol experience

IV. Conclusion

The proposed public health evaluation titled “Evaluation of Integration of Medication-assisted Treatment for Injection Drug Users into HIV Medical Care in Leningrad Oblast, Russia,” funded by USAID and to be implemented by AIHA and key Russian and US stakeholders would have helped to determine the efficacy of long-term, extended-release Vivitrol (d-NTX) on retention in HIV care. It also would have made valuable contributions to the care and treatment of PLHIV who are opioid dependent by examining outcomes related to HIV disease progression, social outcomes, and ongoing issues with substance abuse within the target population in Leningrad Oblast.

The resulting data and analysis of the evaluation could then have served as an evidence base for improving treatment, care, and support for this high-risk population in Leningrad Oblast and elsewhere in Russia. The study also could have had an impact on care for opioid dependant PLHIV in other countries throughout the region and in settings outside Eurasia where similar problems with providing care to this challenging cohort of PLHIV-PWID patients exists.

Unfortunately, the public health evaluation had to be terminated abruptly due to the closure of USAID-supported operations in the Russian Federation. AIHA remains hopeful, however, that other sources of funding may be found, so that this important study may continue in the future.

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