



Adherence to Methadone Maintenance Treatment and Antiretroviral Therapy



Questions

1. What factors promote and/or limit adherence to opiate substitution treatment among HIV-positive intravenous drug users?
2. What factors promote and/or limit adherence to highly active antiretroviral therapy among HIV-positive intravenous drug users on opiate substitution treatment?
3. Can targeted models of service delivery improve retention, adherence to treatment and health outcomes for HIV-positive intravenous drug users?

Key Take-Home Messages

- HIV-positive intravenous drug users (IDUs) are at greater risk of non-adherence to highly active antiretroviral therapy (HAART) compared to the general HIV population.(1-3)
- Psychological problems, active drug use and incarceration are the main barriers to HAART adherence among HIV-positive IDUs.(3-5)
- When engaged in stable care with adequate support and experienced staff, IDUs can have HAART adherence and clinical outcomes comparable to non-IDU patients.(1;6)
- Reduction in substance use and enrollment in an opiate substitution treatment plan, such as methadone maintenance treatment, are associated with improved HAART adherence.(3;7-10) Oral substitution treatment for IDUs reduces drug-related behaviours with a high risk of HIV transmission, but has less effect on sex-related risk behaviours.(11)
- Several factors/strategies have been shown to be effective in engaging and retaining people in opioid substitution treatment and in encouraging adherence to HAART:
 - Contingency management – a system of incentives and disincentives designed to make continued drug use less attractive

EVIDENCE INTO ACTION

The OHTN Rapid Response Service offers HIV/AIDS programs and services in Ontario quick access to research evidence to help inform decision making, service delivery and advocacy. In response to a question from the field, the Rapid Response Team reviews the scientific and grey literature, consults with experts, and prepares a brief fact sheet summarizing the current evidence and its implications for policy and practice.

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and abstinence more attractive – is effective in reducing supplemental drug use in patients enrolled in methadone maintenance treatment. (12)

- Vouchers for free methadone maintenance treatment are more effective in linking active drug users to drug treatment than case management services.(13)
 - Administration of higher doses during methadone treatment (60mg/day or more) is associated with increased adherence to drug treatment programs and effective treatment for opioid dependence. (11;14)
 - Patients receiving methadone and HAART from their primary care provider may have increased adherence to both and feel a greater sense of trust and security.(1)
 - DOT (Directly Observed Therapy)-HAART may be an effective adherence intervention when delivered to individuals at risk for non-adherence and focused on maximizing participant convenience and providing additional adherence support.(2)
- Future research needs to evaluate the effectiveness of delivering maintenance treatment focused on patient engagement with HAART in primary care settings.(1)

The Issue and Why It's Important

Substance users often face co-morbidities and co-occurring conditions; however, those with HIV tend to be hardest hit and experience the poorest outcomes. Integrating opiate addiction and HIV care has the potential to improve health outcomes for this vulnerable population. However, people with HIV who use substances face considerable challenges adhering to both methadone maintenance treatment and HAART. A better understanding of the barriers and/or supports to treatment adherence is required to support the implementation of effective interventions.

What We Found

We identified systematic reviews and a few primary studies that were relevant to the questions posed for this rapid response. These studies looked at a range of interventions to address various aspects of adherence to methadone maintenance treatment and HAART, such as circumstances, barriers and facilitators that promote (or limit) adherence to methadone maintenance treatment and HAART, health care service delivery models designed to improve retention, adherence to treatment, and health outcomes for recovering substance users living with HIV.

Interventions to improve adherence to methadone maintenance therapy

Contingency management

Contingency management is based on the principles of operant conditioning, which suggest that all behaviours, including drug use, are maintained by environmental influences and therefore can be changed by altering the consequences. Contingency management provides a system of incentives and disincentives designed to make continued drug use less attractive and abstinence more attractive.(12) Interventions in outpatient methadone maintenance treatment settings that used a contingency management approach were found to be effective in reducing supplemental drug use by people undergoing treatment.(12) A statistical analysis of 30 quantitative studies included in one systematic review revealed that several parameters were effective in promoting drug-abstinence while patients were in treatment, including: using methadone dose increases or take-homes as incentives, using immediate reinforcement, targeting a single drug and testing urine three times a week. The review concluded that, to change behaviours and maintain adherence, reinforcements should be immediate, targeted toward changing a single behaviour, and be closely monitored.(12)

Treatment vouchers

A randomized-controlled trial conducted in San Francisco outlined the first six months of offering treatment vouchers and case management for opioid-dependent patients in emergency departments, wound clinics, in-patient units and methadone clinics in urban public hospitals.(13) Participants were randomized to one of four groups (voucher alone, case management alone, both interventions or usual care) to test two interventions: one provided participants with a voucher for six months of standard methadone treatment at no charge and the second provided six months of case management services. Although the study's primary aim was to provide an economic evaluation of the cost of treatment, it concluded that vouchers were more effective in linking opioid-dependent hospital patients to drug treatment: 90% of participants randomized to receive vouchers alone enrolled in methadone maintenance treatment whereas only 44% of those randomized to receive case management without vouchers enrolled. Furthermore, when the voucher program ended, many participants arranged to be in another treatment program.(13)

Optimal methadone dosing

The optimal dose of methadone should be determined on an individual basis, however research evidence indicates that methadone doses ranging from 60 to 100mg/day are more effective than lower dosages in retaining patients and in reducing use of heroin and cocaine during treatment.(11;14)

Factors that influence HAART adherence

Active drug use has been found consistently to be associated with non-adherence.(3) In a study of African American active crack cocaine users, 53% self-reported full compliance with their physicians' recommendations while one-third (31%) reported they were compliant more than half the time.(15) Another study conducted with active IDUs in the Baltimore area found similar rates of self-reported non-adherence (44%) in the previous two weeks,(16) while a study from Italy found statistically significant lower compliance rates among active IDUs (32%) compared to non-drug users (42%).(17)

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A literature review of various targeted service delivery models provided comprehensive descriptions and comparisons of several studies on adherence to HAART in HIV-infected individuals, IDUs and IDUs currently receiving opiate substitution treatment.(1). Factors strongly associated with HAART adherence in the general HIV population included: overall high social status, education, history of drug dependence and housing as well as trusting open relationships with care providers. Social supports and a positive state of mind were also associated with increased adherence in the general HIV-positive population.(1) Factors associated with non-HAART adherence in the HIV-positive IDU population included ongoing drug injection (which was also associated with increased addictive behaviours, such as alcohol consumption), the lack of stable relationships and depression.(1;3)

Two Vancouver-based studies evaluated the underlying reasons why people who inject drugs discontinue HAART and found the main factor was recent incarceration.(5)

Several studies found that psychological problems, including negative outcome expectations, high rates of anxiety and high rates of depression, were associated with poor adherence.(3;18-21) Patients who begin with positive expectations of HAART treatment but develop negative perceptions after months of treatment are just as likely to be non-adherent as patients who have negative perceptions about HAART throughout treatment.(3)

Interventions to improve adherence to antiretroviral therapy

HAART dosing regimens

Dosing, specifically HAART regimens administered three or more times a day, are associated with lower levels of adherence in people who use substances; however, a recent study did not provide evidence that a once-a-day regimen was associated with better adherence than twice-a-day regimens.(1)

Consistent engagement in methadone maintenance/substitution therapy

In the United States, HIV-positive IDUs with access to Medicaid who consistently participated in a methadone program had better uptake of and more consistent use of HAART than people who either did not participate or participated inconsistently in methadone maintenance treatment.(1) Consistent engagement in methadone programs also increased HAART adherence among HIV/Hepatitis C co-infected IDUs.(1;10)

Another systematic review, citing studies from Canada and France, noted that methadone maintenance treatment and buprenorphine maintenance therapy were positively associated with optimal HAART adherence.(3;10;21)

Sites dispensing opiate substitution treatment are a point of access to HAART for people who inject drugs, as HAART could be combined with drug treatment dispensed and taken under surveillance of the service provider. Opioid substitution treatment may also strengthen patients' social support networks, thereby increasing chances of adherence to both methadone maintenance therapy and HAART.(1)

Directly Observed Therapy (DOT)-HAART

One systematic review analyzed 17 studies involving a total of 3,169 outpatients receiving DOT-HAART treatment to assess its impact on virologic suppression, immunologic response (mean change in CD4 cell count from baseline) and adherence (proportion of individuals achieving at least 95%

adherence to prescribed doses). This review found that DOT-HAART had a significant effect on HAART adherence (as well as on virologic and immunologic outcomes), although its efficacy was not supported when analyses were restricted to randomized controlled trials. DOT-HAART showed greatest treatment effect when it was targeted to individuals at greater risk of non-adherence and focused on maximizing participant convenience and providing enhanced adherence support.(2)

Although critics feel DOT-HAART cannot be sustained over the course of life-long treatment, it does improve HAART adherence. Qualitative data suggest that other mechanisms may also contribute to DOT-HAART effectiveness, such as positive effects on patients' trust and communication with providers, increased patient motivation to engage in daily activities and become involved in the community, improved adherence to other aspects of medical care, and greater utilization of other forms of social and adherence support.(2)

Choosing a convenient site for DOT-HAART interventions, such as a methadone clinic or the patient's residence, could increase their effectiveness. Interventions delivered in patient homes, community-based vans, prisons and methadone clinics may impose minimal additional burden on patients. Time and expenses of daily travel to a site that is not part of a patient's daily routine (such as an HIV clinic or hospital) may create barriers to DOT-HAART adherence, particularly in resource-poor settings where the relative cost of traveling to health facilities is even greater.(2)

Optimal service models for methadone maintenance therapy

Integrating methadone maintenance therapy with primary care

Prescribing opioid substitution treatment in primary care settings may facilitate regular access to general care. Physicians involved in opiate substitution treatments who also work with social workers, pharmacists and other health care workers can provide more comprehensive care. The positive effects of these integrated programs may be due to the fact that patients who have become accustomed to taking medication chronically for opiate substitution treatment may be less reluctant to accept other drugs, such as antiretroviral regimens.(1)

Comprehensive care for patients should consist of better coordination between health-care providers, improved patient-provider relationships, overcoming stereotypes about drug use, and providing adherence support to IDUs beginning HAART. When engaged in stable care with adequate support and experienced staff, IDUs can have HAART adherence and clinical outcomes comparable to non-IDU patients.(1;6)

Factors That May Impact Local Applicability

All the studies included in the summary were conducted in high income countries (i.e. US, Canada, UK, Spain, Italy, and France). Nevertheless, the findings may not reflect the cultural and social realities of Atlantic Canada (the region that requested this rapid response) nor the care delivery models provided there and may not be generalizable.

What We Did

We used "methadone" as a search term in the Cochrane Library and www.healthevidence.org and similarly searched the Database of Abstracts of Reviews of Effects (DARE) by searching for methadone AND HIV. We also

searched Medline using a similar search strategy (Methadone [MeSH term] AND HIV [text term]), which was limited to articles published since 1996 and a search filter for systematic reviews. We also searched for relevant references in identified reviews.