Effectiveness of Antiretroviral Therapy among HIV-Infected Prisoners: Reincarceration and the Lack of Sustained Benefit after Release to the Community

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(See the editorial commentary by Boutwell and Rich on pages 1761–3)

Responses to highly active antiretroviral therapy (HAART) in correctional settings and their sustained benefit in prisoners after release are currently not known. To examine the human immunodeficiency virus type 1 (HIV-1) RNA level (VL) and CD4 lymphocyte response to HAART during incarceration and upon reentry to the correctional system, we conducted a retrospective cohort study of longitudinally linked demographic, pharmacy, and laboratory data from the Connecticut prison system. During incarceration, the mean CD4 lymphocyte count increased by 74 lymphocytes/μL, and the mean VL decreased by 0.93 log10 copies/mL (P<.0001). Fifty-nine percent of the subjects achieved a VL of <400 copies/mL at the end of each incarceration period. For the 27% of subjects who were reincarcerated, the mean CD4 lymphocyte count decreased by 80 lymphocytes/μL, and the mean VL increased by 1.14 log10 (P<.0001). Although HAART use resulted in impressive VL and CD4 lymphocyte outcomes during the period of incarceration, recidivism to prison was high and was associated with a poor outcome. More effective community-release programs are needed for incarcerated patients with HIV disease.

In the United States, the incidence of HIV infection is 5 times greater [1, 2] and the incidence of AIDS is 4 times greater [3] among incarcerated persons than among the general population. The high prevalence of injection drug users, homeless persons, persons of lower education and socioeconomic status, and persons with mental illness have resulted in the markedly high rates of HIV infection in the US correctional system. In community settings, these individuals have derived less benefit from HAART than have others [4–6]. Correctional facilities provide an important public health opportunity to prevent and treat HIV infection [7, 8]. Two-thirds of HIV-infected correctional inmates have HIV infection diagnosed and initiate treatment for the first time during their incarceration [9, 10]. This suggests that they are not interfacing with HIV testing sites in community settings. Moreover, nearly three-quarters of these individuals first initiate antiretroviral therapy while incarcerated [9, 10], emphasizing the importance of access to appropriate antiretroviral therapy and provision of adequate HIV specialists who treat HIV infection in accordance with federal guidelines within the correctional system.

Since the introduction of HAART, there have been no systematic evaluations of HAART in correctional settings. Moreover, there have been no assessments of the virological and immunological impact of HAART among this population, whose members often do not receive care for HIV infection in community settings.
Furthermore, the long-term benefits of introducing HAART to individuals in the correctional setting have not been assessed.

METHODS

Study site. The Connecticut Department of Correction (CTDOC) is an integrated correctional system with 18 facilities (17 for men and 1 for women) that includes both pretrial detainees and sentenced inmates. The average daily census of the CTDOC in July 2003 was 19,171 persons. Of these, 92.4% are men and 79.5% have been sentenced. The demographic characteristics of prisoners in the CTDOC are similar to that for correctional inmates in the northeast United States, with 44% being black and 27% being Hispanic [11]. Previous anonymous surveillance data suggest that the prevalence of HIV infection among Connecticut prisoners is 6.1% among men [12] and 9.2% among women [13]. In the midyear of 2000, there were 928 prisoners (5.5% of the total custody population) who were known to be HIV infected in Connecticut [3].

HIV testing is completely voluntary and is available by inmate self-request or by referral from a clinician. In 2000, a total of 5584 inmates in Connecticut agreed to be tested for HIV infection [14]. The University of Connecticut Correctional Managed Care (Farmington, CT) provides all medical care at each of the facilities. The Yale University AIDS Program (New Haven, CT) and other individual HIV infection specialists sub-contract to provide the HIV care. An HIV nurse specialist is available at each of the facilities to coordinate HIV care. All antiretroviral medications approved by the US Food and Drug Administration are available at the formulaire for treatment of HIV infection. Since 1997, recommended HIV care in Connecticut is in accordance with federal guidelines issued by the US Department of Health and Human Services (DHHS). The majority of correctional inmates self-administer their HIV medications. In select cases, the HIV specialist may order that medications be administered as directly observed therapy.

All HIV-infected prisoners who are scheduled for release to the community are referred for transitional case management services by a community-based organization. The case managers begin the transition process 3 months before the end of incarceration and work with the client for a minimum of 30 days after release or until a community case manager can accept the client. At a minimum, each prisoner is provided with a 2-week supply of medications, a medical appointment with an HIV care provider, emergency housing and food, and assistance with other identified unmet needs.

Data sources. Data were obtained retrospectively on all HIV-infected inmates who had received antiretroviral therapy within the CTDOC during the period of 1 January 1997 through 31 December 2002. Three primary sources of data were linked to establish the longitudinal cohort. First, all pharmacy data that included any antiretroviral therapy were linked to all laboratory data that included HIV-1 RNA levels and CD4 lymphocyte counts. Once assimilated, these data were linked to the statewide correctional database system that included demographic information and admission and release dates. Once linked, all unique identifiers were stripped from the data and provided on a password-protected disk for analysis. The institutional review boards at the Yale School of Medicine (New Haven, CT), the University of Connecticut Health Center (Farmington, CT), and the CTDOC (Wethersfield, CT) independently approved the research.

Study population. In the final analysis, only prisoners who met the following criteria were included: (1) the prisoner was HIV seropositive, (2) the prisoner was an inmate at the CTDOC, (3) the prisoner had been prescribed HAART for ≥6 consecutive months during the prison sentence, (4) the prisoner had available baseline and follow-up HIV RNA levels and CD4 lymphocyte counts, and (5) pharmacy prescriptions for HAART were available. The denominator of interest included incarceration periods of ≥6 months. Individuals with ≥1 incarceration were included, and each incarceration was evaluated as a separate occurrence. Individuals who were reincarcerated during the study period and who had been released from the CTDOC for ≥3 months were analyzed for their first HIV-1 RNA level and CD4 lymphocyte count upon reincarceration to establish the durability or sustainability of therapeutic benefit after release from prison.

Data scheme. A total of 1866 HIV-infected inmates in the CTDOC who received ≥6 consecutive months of HAART were identified from the database during the study period. The demographic characteristics of this group are shown in table 1. To fully characterize this population, there were 1099 prisoners with continuous incarceration periods of ≥6 months who were not missing demographic data, laboratory data, or admission and discharge dates. The mean duration and number of incarcerations in table 1 are identified from the 1099 continuous incarceration periods used in the final analysis. The characteristics of the individuals who were excluded because of missing information did not differ from those of the final cohort, for whom only incarceration periods are analyzed (data not shown).

Statistical analysis. HIV-1 RNA levels were measured using the Amplicor 1.0 assay (Roche), and CD4 lymphocyte counts were measured with flow cytometry using FACscaliber (Becton Dickinson) at the University of Connecticut’s Health Science Center Laboratory. All data analyses were conducted at the Yale University School of Medicine using SAS software, version 8.2 (SAS Institute). Initial univariate analyses were conducted on all demographic indicators and outcome variables using Student’s t test and χ² analyses. F-tests were utilized when controlling for baseline CD4 lymphocyte count and baseline
Table 1. Demographic characteristics of 1866 prisoners in a study of antiretroviral therapy efficacy.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean years</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>39</td>
</tr>
<tr>
<td>Women</td>
<td>36</td>
</tr>
<tr>
<td>Sex, %</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>81</td>
</tr>
<tr>
<td>Women</td>
<td>19</td>
</tr>
<tr>
<td>Race, %</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>17</td>
</tr>
<tr>
<td>Black</td>
<td>50</td>
</tr>
<tr>
<td>Hispanic</td>
<td>33</td>
</tr>
<tr>
<td>Duration of incarceration, mean days$^a$</td>
<td>478</td>
</tr>
<tr>
<td>No. of incarceration periods of $\geq$6 months$^a$</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>88</td>
</tr>
<tr>
<td>2</td>
<td>11</td>
</tr>
</tbody>
</table>

NOTE. Data are percentage of persons, unless otherwise indicated.

$^a$ Data are for 1099 persons.

VL. Student’s t test was used to compare HIV-1 levels and CD4 lymphocyte counts during incarceration and after release to the community.

RESULTS

Effectiveness of HAART within the correctional setting. Demographic characteristics of the 1866 HIV-infected prisoners who had $\geq$6 consecutive months of incarceration are provided in table 1. HIV-infected prisoners in Connecticut were more likely to be older, female, of racial/ethnic minorities, and substance abusers, compared with the overall correctional inmate population (data not shown). The mean time in prison was 478 days, and only 12% of inmates had $\geq$2 incarceration periods of $>6$ months each.

Overall, 59% of subjects achieved an HIV-1 RNA level that was less than the level of detection (i.e., $<400$ copies/mL) by the end of their incarceration. Table 2 depicts the HIV-1 RNA and CD4 lymphocyte responses to HAART in the correctional system. Compared with baseline levels, there was a significant mean reduction in the HIV-1 RNA level of $0.93 \log_{10}$ copies/mL and a mean CD4 lymphocyte increase of 74 lymphocytes/μL ($P<.0001$). Age and race did not correlate with achievement of an HIV-1 RNA level that was less than the level of detection. However, women had significantly greater reductions in the HIV-1 RNA level than did men ($1.26$ vs. $0.86 \log_{10}$ copies/mL; $P<.0001$).

Effect of community release on HIV-1 RNA level and CD4 lymphocyte count. Additional analyses were conducted to evaluate the effect of discharge to the community on mean HIV-1 RNA level and CD4 lymphocyte count. Of the 292 prisoners (27%) who were treated with HAART in prison and reincarcerated after having spent $\geq$3 months outside the correctional setting (median duration, 127 days), a change in the HIV-1 RNA level and CD4 lymphocyte count was calculated from the last value before community release to the first value at the time of reincarceration. Overall, this subset of subjects experienced a mean increase in the CD4 lymphocyte count of 67 lymphocytes/μL during their incarcerations. Conversely, they had a mean decrease in the CD4 lymphocyte count of 80 lymphocytes/μL during the period of release into the community ($P<.0001$). Similarly, this same group had a reduction in the HIV-1 RNA level of $1.04 \log_{10}$ copies/mL during incarceration. After release to the community, however, the HIV-1 RNA level increased by $1.14 \log_{10}$ copies/mL by the time of reincarceration ($P<.0001$). Only 2 subjects had an HIV-1 RNA level that was less than the level of detection at the time of reincarceration.

DISCUSSION

To our knowledge, this is the first cohort study that directly examines the effectiveness of antiretroviral therapy in the HAART era within the correctional setting, as well as the reversal of these benefits after release to the community. Three important outcomes from this study have important public health and policy implications.

First, it is impressive that as many as 59% of patients achieved an undetectable HIV-1 RNA level ($<400$ copies/mL) by the end of their incarceration period. These results are comparable to or better than those found in most community clinic settings [15, 16]. Although the rate of mortality due to HIV infection/AIDS markedly decreased among prisoners in New York during the early HAART era, the direct association between HAART use and this outcome was suggestive but not definitive [17]. In the present cohort study, we were able to examine the direct benefit of HAART on the individual and prison-system level. For instance, we found that $>99$% of prisoners in Connecticut...
during the time period of 1997–2002 were prescribed HAART, in accordance with DHHS guidelines [18]. Such prescription patterns of HAART surpass previously published accounts of prescribing patterns for HIV-infected persons in other prisons [19–22] and in community settings [23, 24]. Moreover, in a large national study of access to antiretroviral therapy, individuals with demographic characteristics similar to those of this prison population were unlikely to receive HAART [25], and, for those who did [26], the clinical outcomes were less impressive compared with those of other populations [27]. More importantly, these results demonstrate that, when correctional facilities are able to provide appropriate clinical HIV care, inmates have clinical improvements that are as good as those found in community settings. These findings also support the view that incarcerated populations that are disproportionately affected by higher rates of HIV infection, mental illness, and injection drug use achieve impressive outcomes in the correctional setting, although these persons have otherwise done poorly in community settings [28–31].

Second, female prisoners had a more significant decrease in HIV-1 RNA levels than did male prisoners. One previous study of factors associated with improved survival among incarcerated persons found that female prisoners have a significant survival advantage over their male counterparts [32]. This finding has not been replicated in a longitudinal study of cohorts of individuals in the community living with HIV infection when controlling for duration of infection [33–35]. There are multiple explanations for the improved clinical benefit among women in our study. Women may have been more adherent to therapy than were men. Previous studies involving this population suggest that men and women have identical rates of adherence to therapy in prison [10]. Alternatively, all women are housed in 1 facility, whereas men may be moved between 17 different sites within the CTDOC. It is therefore possible that transfer between correctional facilities may have interfered with continuity of care or adherence to regimens or have even led to loss of medications [36]. The level of care provided to women may also have differed from that for men. Although good HIV care extends beyond the adherence to guidelines, 99% of patients were prescribed antiretroviral medication in accordance with DHHS guidelines, and this did not appear to differ between men and women.

Finally, it is of great concern from a public health perspective that the benefits of HAART provided in the correctional setting were lost after release to the community for those persons who were later reincarcerated. Although this nonsustained benefit of HAART among reincarcerated inmates represents only 27% of the population studied, it does represent a serious problem for a critical minority of prisoners whose transition to the community was ineffective. Moreover, our study only examined those individuals who had been reincarcerated after remaining in the community for ≥3 months. Clearly, case management alone is not sufficient. More effective prison-release programs to reduce the high recidivism rate for this population are urgently needed. The potential outcome for these individuals, as well as for those who did not fit our criteria for recidivism, is that they may return to the community with subsequent poor adherence to therapy and resultant multidrug-resistant strains of HIV. Recent studies have also demonstrated a high prevalence of drug-resistant HIV among prisoners that is comparable to or greater than that found in the surrounding community [37, 38]. It is unclear from our study whether released subjects discontinued HAART completely or whether their outcomes resulted solely from suboptimal adherence. Data from prospective studies of complete discontinuation of HAART for 12 weeks demonstrate decreases in CD4 lymphocyte count similar to our findings, suggesting that HAART had been discontinued completely for several weeks before reincarceration [39, 40]. In either case, released HIV-infected prisoners have the potential to infect partners in the community via needle sharing or sexual contact [2]. Important factors in transmission would include the HIV-1 RNA level and the presence of antiretroviral resistance.

In studies of HIV-infected individuals who were released from prison, it was found that the overwhelming majority of persons engaged in high-risk sexual behavior and drug use after release, potentially leading to transmission of multidrug-resistant HIV [41, 42]. Another study showed that the major risk factor for heterosexually acquired HIV infection in African-American women was having sexual intercourse with an HIV-infected former prisoner [43]. These findings, taken together with our findings in which a transitional case management program is employed, suggest that more-comprehensive programs are necessary to effectively link HIV-infected inmates to adequate medical, psychiatric, and drug treatment services after release to the community. Moreover, such programs should not only address the unmet medical and social needs of this population but unsafe sexual and drug use behaviors as well. For recidivist drug users, drug treatment programs for this popu-

<table>
<thead>
<tr>
<th>Laboratory value</th>
<th>Baseline value</th>
<th>Last value</th>
<th>Change in value</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD4 lymphocyte count, mean lymphocytes/μL</td>
<td>330</td>
<td>404</td>
<td>+74</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>HIV-1 RNA level, mean copies/mL (log_{10} copies/mL)</td>
<td>59,820 (3.76)</td>
<td>14,200 (2.83)</td>
<td>−45,620 (−0.93)</td>
<td>&lt;.0001</td>
</tr>
</tbody>
</table>
Substitution therapy—highly effective in community settings—is absent from all prisons and jails in the United States, except for those in New York City. Enrollment in community-based methadone treatment programs has resulted in reductions in criminal activity, reincarceration, and HIV risk behaviors [44]. Novel approaches to either integrate substitution treatment (i.e., methadone or buprenorphine treatment) into correctional settings or arrange for them upon release are urgently needed [45].

Connecticut provides Project TLC [36, 46], a transitional case-management program that links soon-to-be released HIV-infected prisoners with community support services. This program, as well as comprehensive social support programs in Rhode Island [47, 48], Hampden County, Massachusetts [49], and California [50], has demonstrated a number of effective immediate positive outcomes. It has not, however, demonstrated a reduction in recidivism or any long-term health benefit. Our findings suggest that the positive health benefits derived while incarcerated are lost to many persons after release to the community. Therefore, interventions that focus on this population should perhaps provide a transitional form of structure, rather than only provide social support, that will allow individuals to become self-efficacious over time. Examples of structural interventions that have reduced HIV risk behavior and transmission include methadone maintenance and syringe-exchange programs. Directly administered antiretroviral therapy, another structural intervention, has also resulted in im-

Figure 1. Mean change in HIV-1 RNA levels (in log_{10} copies/mL) during incarceration and after 3 months release to the community. VL, virus load.

Figure 2. Change in mean CD4 lymphocyte count from last incarceration value to first reincarceration value after discharge to community for ≥3 months.
proved biological outcomes for drug users in community settings [51–53] and for prisoners [54, 55].

One limitation of this study is the lack of identifiable predictors of virological failure in this cohort, such as prior ART experience, genotypic resistance, comorbid conditions, toxicity from HAART and adherence to therapy. It would have been impossible to determine prior antiretroviral history in this group from the existing database. Moreover, we limited our analysis to only those who received ≥6 months of treatment, although others serving shorter sentences may also have benefited from short-term HAART. Despite these limitations, the majority of all inmates achieved an undetectable HIV-1 RNA level at the end of their incarceration period. One other limitation was the lack of a control group among those we defined as recidivists to the correctional facility. We cannot infer that all released HIV-infected prisoners do poorly. Nonetheless, it is critical to identify correlates of reincarceration and to implement effective interventions that will sustain the benefit of HAART provided to all prisoners while incarcerated.

We limited our data to only those individuals who had previously been prescribed ≥6 months of HAART within the correctional setting and who had been reincarcerated after ≥3 months of being within the community. We chose this time cutoff to define a group of persons who would have been outside of the correctional system for a time period extending beyond the 30-day period of care provided by the transitional case-management program and to remove those individuals who had not stabilized their HIV condition within the correctional system. Further evaluations of the reasons for reincarceration are needed to determine how substance abuse, mental illness, or socially destabilizing factors such as homelessness impacted the negative consequences of release to the community. Notwithstanding this limitation, the clinical and public health relevance of our findings for recently released prisoners cannot be overemphasized.

This study supports the importance of the correctional system for the provision of HIV care for individuals who often do not benefit from HAART in community settings. Moreover, when HIV care is properly provided in this setting, immunological and virological benefits are observed. However, despite existing prison-release programs that are predicated on making appointments for patients and providing for short-term needs, important biological outcomes associated with morbidity and mortality are not attained for those who are reincarcerated. Prisoners in this Connecticut population benefited therapeutically, but the favorable outcomes of HAART were lost among those who were reincarcerated. Development of alternative strategies for continuing care after release to the community is desperately needed to avoid increased morbidity and mortality among these individuals and the transmission of multidrug-resistant HIV to their sex and drug-use partners.

Acknowledgments

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References


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