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ORIGINAL PAPER

Adherence to Antiretroviral Therapy Among Incarcerated Persons with HIV: Associations with Methadone and Perceived Safety

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Abstract
With adequate support, people with HIV (PWH) may achieve high levels of adherence to antiretroviral therapy (ART) during incarceration. We examined factors associated with ART utilization and adherence among incarcerated PWH (N = 150) in Indonesia. ART utilization was positively associated with HIV status disclosure (adjusted odds ratio [aOR] = 5.5, 95% CI 1.2–24.1, p = 0.023), drug dependency (aOR = 3.9, 95% CI 1.2–12.6, p = 0.022), health service satisfaction (aOR = 3.2, 95% CI 1.7–6.2, p < 0.001), and perceived need for medical treatment (aOR = 1.6, 95% CI 1.1–2.5, p = 0.011), and negatively associated with chance locus of control (aOR = 0.3, 95% CI 0.1–0.7, p = 0.013). Most participants utilizing ART (74.5%) reported less than "perfect" ART adherence. ART adherence was independently associated with perceived personal safety (β = 0.21, 95% CI 0.01–0.40, p = 0.032) and methadone utilization (β = 0.84, 95% CI 0.10–1.67, p = 0.047). PWH receiving methadone had a sixfold higher adjusted odds of being highly-adherent to ART (aOR = 6.3, 95% CI 1.1–35.7, p = 0.036). Interventions that increase methadone utilization and personal safety may improve ART adherence among incarcerated PWH.

Keywords Adherence · Antiretroviral therapy · HIV · Methadone · Prisons · Substance use

Introduction

An estimated 389,000 persons with HIV (PWH) are incarcerated worldwide [1]. For some PWH, incarceration provides an opportunity to initiate and sustain adherence to antiretroviral therapy (ART) [2]. The provision of simple, well-tolerated antiretroviral therapy (ART) regimens in combination with directly observed therapy [3] and innovations such as telemedicine [4] have expanded the use of ART in criminal justice settings and allowed many incarcerated PWH to achieve viral suppression [3, 5]. Yet even in high-income prison settings ART adherence may be suboptimal [6], necessitating further investigation of risk factors for non-adherence among prisoners and development of appropriate interventions.

Prisons also play an important role in HIV management in low- to middle-income countries (LMICs), especially those where drug use is criminalized and people who inject drugs (PWID) are overrepresented in criminal justice populations [1]. Yet, less is known about ART adherence among PWH incarcerated in LMICs. Recent work suggests that ART coverage in LMIC prisons is lower [7–9], and HIV-related mortality considerably higher [10]. Given the high prevalence of HIV and substance use disorders in LMIC prisons [1], failure to provide recommended HIV and addiction treatment services to persons during incarceration could be an important obstacle to achieving targets for HIV prevention and treatment in the community [1, 11].

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Challenges to ART utilization and adherence in prisons are multi-level. Incarcerated PWH may have low levels of social support and healthcare access before incarceration and higher prevalence of substance use, mental illness, and co-infections that can delay ART initiation or interfere with adherence [2, 6, 12]. Prison health services may be unequipped to effectively manage the multiple health needs of incarcerated PWH [13]. Also limiting uptake of ART are prejudicial attitudes toward HIV among prisoners and prison staff [14, 15]. Some incarcerated PWH may hide their HIV status, skip doses, or forgo ART entirely in order to maintain privacy in an environment perceived as hostile [16, 17]. Prison overcrowding introduces other stressors and competing priorities such as food scarcity and substance use that may interfere with effective treatment [17–19]. Finally, these institutional effects may endure and adversely influence ART adherence long after prison release [20, 21].

The HIV epidemic in Indonesia is one of the largest and least well-controlled HIV epidemics worldwide [22]. Criminalization of drug use has resulted in high rates of incarceration among PWID, many of whom are HIV-infected [23]. HIV prevalence is highest in specialized narcotic prisons (7.2%) that house persons sentenced for drug-related offenses [24, 25]. HIV testing is routinely offered to persons during processing into correctional facilities and to individuals who report risk behaviors in prison [26]. A national policy has expanded ART coverage in prisons and multi-component interventions have shown some success in reducing HIV transmission risk behaviors [27]. Yet mortality among HIV-infected prisoners remains extremely high [10]. The purpose of this study was to examine correlates of ART utilization and adherence among HIV-infected male prisoners in Indonesia. Understanding factors associated with lower ART adherence may help target those at risk for non-adherence and identify gaps in recommended HIV treatment services.

Conceptual Framework

In this analysis, we draw on two complementary frameworks, the Behavioral Model for Vulnerable Populations [28] and the "risk environment" model [29], which previously have been described for prisoners [30, 31]. In the Behavioral Model, *predisposing factors* are characteristics of the individual or community that influence health service utilization and may include substance use, health beliefs, and cultural norms. *Enabling/disabling factors* are those that facilitate or impede the use of recommended health services and may include the cost, distribution, and quality of health services. *Need factors* encompass both self-perceived and objective health needs including evaluation of disease stage or comorbid conditions.

More recent theoretical work suggests that aspects of the physical, social, and economic environments, including drug policies and law enforcement approaches, may increase health risks to people living with HIV and substance use disorders [30, 32–34]. Our analysis is also guided, therefore, by the risk environment framework [35], which considers social and environmental change essential preconditions for individual behavior change. Figure 1 shows an integrated health behavior model for the prison risk environment.

Methods

Study Design

This cross-sectional analysis uses baseline data collected from participants enrolled in a randomized controlled trial of Project ATHENA (Adherence Through Home Education and Nursing Assessment), an evidence-based medication adherence intervention that was culturally adapted for the Indonesian prison setting [36]. This trial is registered with ClinicalTrials.gov (NCT03397576). Incarcerated HIV-positive men were recruited and randomized equally to receive the adapted ATHENA intervention (ATHENA-I) or standard care as a control. Subjects randomized to ATHENA-I participated in monthly group medication adherence coaching sessions within prison based on a Freirian educational model [37], followed by monthly home visits by a nurse and peer educator for up to six months following prison release. Here, we analyze variables collected from participants on their enrollment date, including measures of ART utilization and adherence, the main study outcomes.

Study Setting

This study was conducted in two large male prison facilities located in Jakarta, Indonesia, including one narcotic prison. Under national guidelines, ART was prioritized for those with advanced HIV (WHO clinical stages 3 and 4). Most commonly prescribed ART regimens included zidovudine plus lamivudine with nevirapine or efavirenz, and were dispensed weekly as self-administered therapy. As part of standard care in these settings, patients utilizing ART were monitored by nurses and physicians and offered peer support and directly observed therapy if suboptimal adherence was suspected. Methadone was available to patients meeting criteria for opioid dependence.

Recruitment

From February 2017 to March 2018, researchers used sequential sampling to recruit incarcerated persons who were Indonesian citizens ≥ 18 years of age, HIV diagnosed and aware of their status, and fluent in Bahasa Indonesia. To ensure equitable selection and minimize privacy risks,

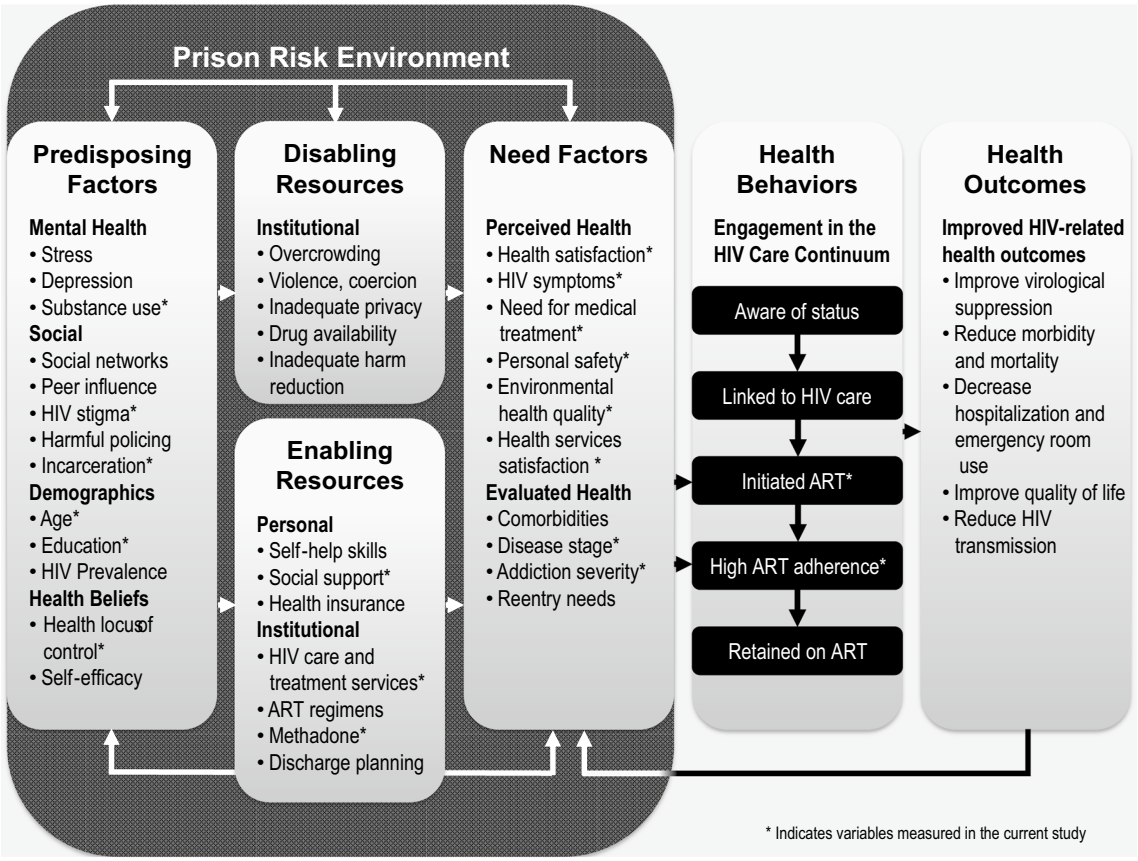

Fig. 1 Integrated health behavior model for the prison risk environment

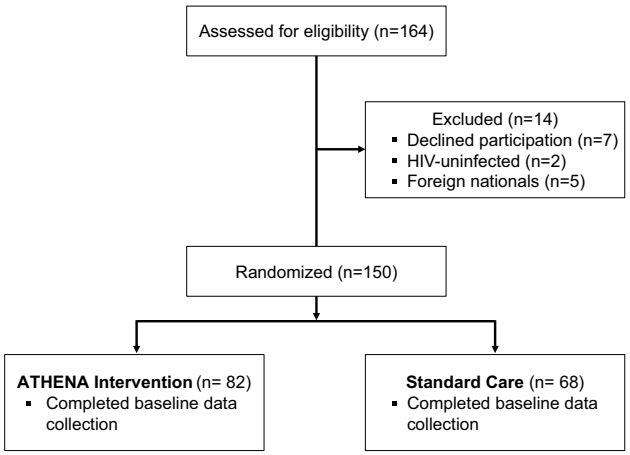

Fig. 2 Study flow diagram

prison medical staff introduced the study to patients during their regularly scheduled clinic appointments and arranged a meeting with researchers for patients wanting to learn more about the study. Figure 2 shows a study flow diagram for participants included in the study.

Data Collection

Immediately after study enrollment, all subjects completed confirmatory HIV testing, $CD4^+$ T-lymphocyte quantification using Alere PIMA™ Analyzer, and a computer-assisted questionnaire. The questionnaire and study measures underwent a rigorous forward–backward translation process [38] and were administered on handheld Android computer tablets via a secure web-based application [39, 40].

Measures

Dependent Variables

ART utilization was defined as any consumption of ART regardless of adherence and assessed with a single question asking participants whether they had consumed ART within the past 30 days (*yes* or *no*). *ART adherence* in the past 30 days was measured using the single item self-rating scale (SRSI), a 6-point Likert-type scale that asks participants to rate their overall adherence from *very poor to excellent*[41]. To anchor response choices, participants were told

that "excellent" adherence meant taking all prescribed medicine on time within the last 30 days. ART adherence was analyzed in two ways: (1) as a continuous outcome using the full range of response choices; and (2) as a dichotomous outcome categorizing participants who rated their ART adherence as "excellent" as having "perfect ART adherence."

Independent Variables

Pre-disposing factors included a participant's age, education, HIV diagnosis date and location (prison or community), length of incarceration (time spent in jail/prison for the current sentencing period), and type of correctional facility (e.g. narcotic prison) where the participant was currently incarcerated. A multidimensional measure of HIV stigma previously adapted for the Indonesian prison setting [42] was used to assess the frequency with which participants experienced HIV-related stigma on a 5-point Likert-type scale from *never* to *always*. Total scores were calculated from 15 items distributed onto subscales measuring *anticipated stigma*, *internalized stigma,* and *addiction stigma.* Scores were transformed linearly on a 1 to 5 scale with higher scores indicating higher perceived stigma. Reliability was high (15 items; $\alpha = 0.91$).

The multidimensional health locus of control scale was used to assesses the degree to which participants attributed health outcomes to their own actions (internal subscale), fate or supernatural influences (chance subscale), or the actions of family members and physicians (powerful others subscale) [43, 44]. Orthogonal subscales consisted of 6 Likert-type items to which respondents rated their level of agreement from *strongly agree* to *strongly disagree*. Items were reworded to focus specifically on HIV-related health problems. Cronbach's alphas for the internal, chance, and powerful others subscales were 0.59, 0.80, and 0.55, respectively.

Substance use was assessed using the Texas Christian University Drug Screen [45], which was previously adapted for use in prisons in Indonesia [18]. Participants were asked which drugs they used in the three months before incarceration and during the current prison term with probes about the frequency and route of administration for each drug.

Enabling/disabling resources included a participant's history of ART utilization and hospitalization, and whether they were seen by an HIV care provider or consumed ART in the three months before incarceration. Information about participants' current ART regimens was obtained from medical records. Participants were assessed as *currently utilizing methadone* if they reported consuming methadone within the past two weeks, regardless of adherence.

Drawing on existing social support instruments for PWH [46], and previous qualitative work [42], we developed an 8-item scale to measure anticipated social support after prison release. Examples of items included, "When I get out of prison, if I have problems, my friend or partner will help me" and "I worry when I get out of prison my family will not accept me." Participants indicated their level of agreement on a 5-point scale from *strongly agree* to *strongly disagree* with higher scores indicating higher anticipated social support. We conducted principal components analysis (PCA) of the 8 items and assessed sampling adequacy. The Kaiser–Meyer–Olkin (KMO) statistic (0.77) indicated that all items usefully contributed to PCA and scores were calculated as the average of all 8 items. Reliability was acceptable (8 items; $\alpha = 0.74$). Participants also were asked whether they had been visited by friends or family members during incarceration (*yes* or *no*) or disclosed their HIV diagnosis to a close friend or family member (*yes* or *no*).

Need factors important to our conceptual framework included six Likert-type items to assess participants' satisfaction with their health and access to prison health services, perceived need for medical treatment, environmental health quality, and personal safety. Examples of questions included, "How satisfied are you with your access to health services?" and "How safe do you feel in your daily life?" Response choices ranged from (1) *not at all* to (5) *always*.

HIV symptoms were assessed using the Revised Sign and Symptom Checklist for HIV [47] that was shortened to 15 items based on pilot testing. Participants were asked to rate the frequency and severity of symptoms during the past two weeks (*none, mild* = noticed the symptom, *moderate* = bothered by the symptom, *severe* = symptom interfered with usual activity). Total scores were calculated by summing individual items and dividing by 15. Reliability was good (15 items; $\alpha = 0.83$).

Drug dependence was assessed using the Rapid Opioid Dependence Screen (RODS), which measures health and social consequences of opioid use and corresponds well to DSM-IV criteria [48]. Based on pre-testing, we substituted for "opioids" the Indonesian word, *"narkoba"* (lit. narcotics), which participants interpreted more reliably, resulting in a broader measure of drug dependency. Consistent with the original measure, participants who responded "yes" to three or more items were classified as "drug dependent." Reliability of the seven items was acceptable ($\alpha = 0.72$). To estimate opioid dependence in our sample, we created an interaction variable to classify as "opioid dependent" participants who were both "drug dependent" and using heroin or other opioids immediately before incarceration.

Statistical Analysis

Statistical analyses were conducted using SPSS Version 21 (IBM Corp. Armonk, NY, 2012). Routine data cleaning and preparation procedures were employed to check data consistency and score instruments. Due to low missing data

(< 0.1%), neither listwise deletion nor imputation was used. We estimated bivariate associations (simple linear regression and unadjusted odds ratios) for each of the 37 independent variables shown in Table I. Guided by these bivariate analyses and the study's conceptual framework, we selected for inclusion in candidate multivariate models variables with a significant bivariate association ($p < 0.05$) and/or theorized to influence ART adherence. Our sample sizes for modeling ART utilization and adherence allowed us to estimate parameters for 15 and 11 variables, respectively, without over-fitting. Variables in the final multivariate models were adjusted for all other variables in the final model. VIF for variables in the final model indicated few problems with collinearity.

Ethics Statement

Study procedures followed international guidelines for HIV-related research in prisons [49]. The protocol was approved by institutional review boards at the University of Illinois at Chicago and the University of Indonesia. Participants were selected equitably and without the involvement of prison staff and provided written informed consent to participate.

Results

Participant Characteristics

Table 1 shows characteristics of participants in the final sample (N = 150). Participants were 34 years of age on average and over half (56.7%) had completed high school. Most (74.7%) were incarcerated in a narcotic prison. Participants had been HIV diagnosed for 4.6 years on average and most (70%) were diagnosed in prison, including 42.7% who were diagnosed during the current prison term. Few participants were engaged in HIV care (24.7%) or receiving ART (27.3%) before incarceration. Two-thirds of participants (68.7%) had $CD4^+$ T cell counts below 350 cells/μL and more than one-third (38.0%) had $CD4^+$ T-cell counts indicating severely compromised immunity (≤ 200 cells/μL). Most participants used opioids (53.3%) and/or methamphetamine (78%) in the three months before incarceration. Most participants (62%) also reported drug use during the current prison term. Most participants (81.3%) met criteria for drug dependence (RODS score ≥ 3). Nearly half (49.3%) were both drug dependent and using opioids before incarceration, yet very few (6.7%) were currently utilizing methadone.

Most participants (74%) had someone who they counted on for care and support before incarceration, yet participants anticipated only moderate social support (Mean = 3.7, SD = 0.5) after prison release. Most participants had disclosed their HIV status to a friend or family member (88%)

Table 1 Participant characteristics (N = 150)

Variable	N (%)
Demographic	
Age in years (Mean ± SD)	34.3 ± 7.5
Finished high school	85 (56.7)
Married/in a relationship	84 (56.0)
Incarcerated in a narcotic prison	112 (74.7)
Years incarcerated (Mean ± SD)	2.0 ± 1.3
HIV Treatment	
Years since HIV diagnosis (Mean ± SD)	4.6 ± 4.1
HIV diagnosed during current prison term	64 (42.7)
Engaged in HIV care before incarceration	37 (24.7)
Receiving ART before incarceration	41 (27.3)
Previous HIV-related hospitalization	33 (22.1)
$CD4^+$ T-lymphocyte cells/μL (Mean ± SD)	289 ± 179
≤ 200 cells/μL	57 (38.0)
201–350 cells/μL	46 (30.7)
351–500 cells/μL	26 (17.3)
> 500 cells/μL	21 (14.0)
HIV-related symptoms score (Mean ± SD)	50.2 ± 45.4
Currently utilizing ART	110 (73.3)
Efavirenz-based regimen	94 (62.7)
Fixed-dose ART regimen	93 (62.0)
Substance use	
Drug dependent	122 (81.3)
Opioid dependent	74 (49.3)
Pre-incarceration opioid use	80 (53.3)
Pre-incarceration methamphetamine use	117 (78.0)
Within-prison drug use	93 (62.0)
Within-prison drug injection	14 (9.3)
Current methadone utilization	10 (6.7)
Social support	
Anticipated social support score (Mean ± SD)	3.7 ± 0.5
Had support person before incarceration	111 (74.0)
Family/friends have visited during incarceration	126 (84.0)
Disclosed HIV status to friend/family member	132 (88.0)
HIV stigma	
Anticipated stigma score (Mean ± SD)	2.7 ± 1.1
Internalized stigma score (Mean ± SD)	2.6 ± 1.3
Overlapping stigma score (Mean ± SD)	2.8 ± 1.1
HIV-related stigma score (Mean ± SD)	2.7 ± 1.0
Health satisfaction	
Health satisfaction (Mean ± SD)	3.6 ± 0.9
Health services satisfaction (Mean ± SD)	3.6 ± 0.8
Need for medical treatment (Mean ± SD)	3.6 ± 1.2
Perceived personal safety (Mean ± SD)	3.5 ± 1.3
Environmental health quality (Mean ± SD)	3.1 ± 1.4
Health locus of control	
Internal subscale score (Mean ± SD)	3.9 ± 0.4
Chance subscale score (Mean ± SD)	3.3 ± 0.6
Powerful others subscale score (Mean ± SD)	3.7 ± 0.4

HIV-related symptoms are scored 0–266. All other scales are scored 1–5

ART antiretroviral therapy, *SD* standard deviation

and/or been visited by friends/family members (84%) in prison. HIV-related stigma scores (*Mean* = 2.6, *SD* = 1.0) indicated that, on average, participants endorsed perceptions or experiences of HIV stigma less often than *sometimes* (mean score = 3). About one-third of participants (38%) had HIV stigma scores higher than 3, indicating perceptions or experiences of HIV stigma between *sometimes* and *always*.

On average, participants were only moderately satisfied with their current health (*Mean* = 3.6, *SD* = 0.9) and access to health services (Mean = 3.6, SD = 0.8). Likewise, mean scores for self-perceived need for medical treatment (Mean = 3.6, SD = 1.2), personal safety (Mean = 3.5, SD = 1.3), and environmental health quality (Mean = 3.1, SD = 1.4) indicated that participants on average endorsed these items less than *often*. Almost one quarter of participants (23%) responded that they *seldom* or *never* felt safe in their daily life.

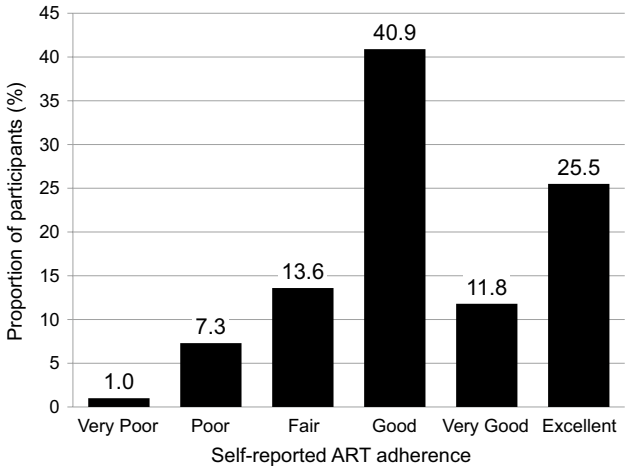

Fig. 3 Self-reported antiretroviral therapy (ART) adherence

ART Utilization Rates and Adherence Levels

Nearly three quarters of participants (73.3%) utilized ART, all of whom were receiving highly-active combination therapy with three drugs. Among those currently utilizing ART (N = 110), most were on a fixed-dose ART regimen containing efavirenz (62.0%). Participants had been utilizing ART for 3.2 years on average, and most participants currently utilizing ART had initiated ART during the current (53%) or previous (21%) prison term. Figure 3 shows self-reported ART adherence in the sample. Most participants utilizing ART reported their adherence within the past 4 weeks as good or very good (Mean = 4.3, SD = 1.2), while one quarter (25.5%) reported *perfect* ART adherence.

Multivariate Associations with ART Utilization

Table 2 shows unadjusted and adjusted associations (odds ratios) with ART utilization within prison. In the final model, ART utilization was positively associated with HIV status disclosure (adjusted odds ratio [aOR] = 5.5, 95% CI 1.2–24.1, $p = 0.023$), drug dependency (aOR = 3.9, 95% CI 1.2–12.6, $p = 0.022$), satisfaction with access to prison health services (aOR = 3.2, 95% CI 1.7–6.2, $p < 0.001$), and

Table 2 Unadjusted and adjusted associations with current ART utilization using logistic regression (N = 150)

Variable	uOR	95% CI	p value	aOR	95% CI	p value
Incarcerated in a narcotic prison	0.8	0.3, 1.9	0.713	0.3	0.09, 1.0	0.070
Years incarcerated	0.9	0.7, 1.2	0.752	0.9	0.6, 1.3	0.755
Years since HIV diagnosis	**1.2**	**1.0, 1.3**	**0.002**	1.1	0.9, 1.4	0.052
HIV-related symptoms	0.8	0.3, 1.7	0.594	0.9	0.9, 1.0	0.137
Anticipated social support	0.6	0.2, 1.6	0.401	0.4	0.1, 1.3	0.131
Disclosed HIV status to friend/family	**4.2**	**1.5, 11.7**	**0.005**	**5.5**	**1.2, 24.1**	**0.023**
HIV-related stigma	1.4	0.9, 2.1	0.065	1.4	0.8, 2.6	0.152
Chance locus of control	**0.4**	**0.2, 0.7**	**0.005**	**0.3**	**0.1, 0.7**	**0.013**
Drug dependent	**3.6**	**1.5, 8.7**	**0.003**	**3.9**	**1.2, 12.6**	**0.022**
Within-prison drug use	5.2	0.6, 41.3	0.117	0.6	0.2, 1.7	0.378
Health satisfaction	1.1	0.7, 1.6	0.572	0.7	0.4, 1.5	0.481
Health services satisfaction	**1.6**	**1.1, 2.5**	**0.012**	**3.2**	**1.7, 6.2**	**<0.001**
Need for medical treatment	**1.8**	**1.3, 2.4**	**<0.001**	**1.6**	**1.1, 2.5**	**0.011**
Perceived personal safety	1.1	0.8, 1.4	0.451	1.4	0.9, 2.2	0.106
Environmental health quality	1.0	0.7, 1.3	0.918	0.8	0.5, 1.2	0.321

Unadjusted odds ratios are shown only for variables included in the final model. Variables in the final multivariate model are adjusted for all other variables in the final model

Bold values are significant at $p < 0.05$

uOR unadjusted odds ratio; *aOR* adjusted odds ratio; *CI* confidence interval

perceived need for medical treatment (aOR = 1.6, 95% CI 1.1–2.5, $p = 0.011$), and negatively associated with chance locus of control (aOR = 0.3, 95% CI 0.1–0.7, $p = 0.013$). The association between methadone and ART utilization could not be computed in logistic regression because all ten participants utilizing methadone were also utilizing ART (X^2 [1, N = 150] = 3.89, $p < 0.05$).

Multivariate Associations with ART Adherence

Table 3 shows simple and multiple linear regression coefficients for independent variables associated with ART adherence. In simple linear regression, ART adherence was positively associated with anticipated social support and perceived personal safety, and negatively associated with HIV-related symptoms. In multiple linear regression, a significant positive association was observed between ART adherence and perceived personal safety (β=0.21, 95% CI 0.01–0.40, p = 0.032) and current methadone utilization (β= 0.84, 95% CI 0.10–1.67, p = 0.047). In a logistic regression model that adjusted for these same factors (Table 4), a significant positive relationship was observed between current methadone utilization and perfect ART adherence (aOR = 6.3, 95% CI 1.1–35.7, p = 0.036).

Table 3 Simple and multiple linear regression coefficients for variables associated with ART adherence (N = 110)

Variable	Unadjusted			Adjusted		
	β	95% CI	p value	β	95% CI	p value
Incarcerated in a narcotic prison	0.21	−0.33, 0.76	0.436	0.37	−0.22, 0.98	0.216
Years incarcerated	0.09	−0.07, 0.25	0.259	0.09	−0.08, 0.26	0.307
Years receiving ART	0.05	−0.01, 0.12	0.122	0.01	−0.05, 0.08	0.684
Fixed-dose ART regimen	−0.34	−0.88, 0.20	0.215	−0.18	−0.75, 0.38	0.518
HIV-related symptoms	**−0.007**	**−0.01, −0.00**	**0.015**	−0.004	−0.01, 0.00	0.190
Anticipated social support	**0.51**	**0.04, 0.98**	**0.033**	0.24	−0.26, 0.76	0.343
HIV-related stigma	−0.19	−0.44, 0.04	0.116	−0.08	−0.34, 0.18	0.545
Internal health locus of control	0.32	−0.20, 0.85	0.226	0.37	−0.16, 0.90	0.169
Perceived personal safety	**0.25**	**0.07, 0.42**	**0.007**	**0.21**	**0.01, 0.40**	**0.032**
Opioid dependent	−0.03	−0.47, 0.49	0.961	−0.22	−0.70, 0.24	0.342
Current methadone utilization	0.75	−0.06, 1.56	0.070	**0.84**	**0.10, 1.67**	**0.047**

Regression coefficients are shown only for variables included in the final model. Variables in the final multivariate model are adjusted for all other variables in the final model

Bold values are significant at $p < 0.05$

β unstandardized beta coefficient, *CI* confidence interval, *ART* antiretroviral therapy

Table 4 Unadjusted and adjusted associations with perfect ART adherence using logistic regression (N = 110)

Variable	uOR	95% CI	p value	aOR	95% CI	p value
Incarcerated in a narcotic prison	1.0	0.3, 2.7	0.948	2.2	0.5, 8.8	0.267
Years incarcerated	1.2	0.9, 1.6	0.175	1.3	0.9, 2.0	0.110
Years receiving ART	**1.1**	**1.0, 1.3**	**0.020**	1.0	0.9, 1.2	0.209
Fixed-dose ART regimen	**0.3**	**0.1, 0.8**	**0.017**	0.4	0.1, 1.5	0.208
HIV-related symptoms	0.9	0.9, 1.0	0.090	0.9	0.9, 1.0	0.338
Anticipated social support	**3.0**	**1.0, 8.7**	**0.036**	1.8	0.4, 7.3	0.392
HIV-related stigma	0.6	0.3, 1.0	0.067	0.7	0.4, 1.2	0.264
Internal health locus of control	2.2	0.7, 6.4	0.125	2.8	0.8, 9.9	0.100
Perceived personal safety	1.3	0.9, 1.9	0.139	1.3	0.8, 2.1	0.206
Opioid dependent	0.5	0.1, 1.8	0.350	0.3	0.1, 1.1	0.076
Current methadone utilization	**5.3**	**1.3, 20.5**	**0.015**	**6.3**	**1.1, 35.7**	**0.036**

Unadjusted odds ratios are shown only for variables included in the final model. Variables in the final multivariate model are adjusted for all other variables in the final model. Bold values are significant at $p < 0.05$

uOR unadjusted odds ratio, *aOR* adjusted odds ratio, *CI* confidence interval, *ART* antiretroviral therapy

Discussion

Findings here suggest that prisons in Indonesia continue to play an important role in HIV diagnosis and treatment, especially for PWH with advanced HIV and substance use disorders. Not only were the majority of PWH (67%) diagnosed in prison, many were diagnosed recently (42.7%), and most PWH (68.7%) were entering care at low $CD4^+$ T-cell thresholds (< 350 cells/μL). Most PWH utilizing ART in this sample (73.6%) first initiated ART in prison and ART coverage (73.3%) was substantially higher compared to PWH in community settings in Indonesia and globally [50, 51]. These findings show that prisons may serve as gateways to the national healthcare system and are important sites for expanding ART coverage in Indonesia, a country where only 14% of PWH in the community receives ART [52].

Despite relatively high ART coverage in these prisons, ART adherence levels were low and concerning, especially given that most ART regimens included efavirenz, which has a low genetic barrier to resistance in the setting of suboptimal ART adherence levels [53]. Our finding that only one quarter (25.5%) of PWH utilizing ART reported perfect adherence is much lower than the pooled proportion of ART adherent prisoners (54.6%) in a recent systematic review and meta-analysis [6], and suggests that most PWH receiving ART may not achieve viral suppression [41]. Although participants were not asked about their reasons for non-adherence, previous research at these sites suggests that HIV stigma and negative perceptions of ART are widespread and may limit ART acceptance [42, 54]. Also, our finding that perceived personal safety was independently correlated with ART adherence supports previous qualitative work [16, 17, 55], and suggests that measures to address prison overcrowding, bullying, and other threats to safety may improve ART adherence.

An estimated 49.3% of incarcerated PWH in this sample were opioid dependent, which is higher than global estimates in prisoners [12], and draws attention to the need to expand medication-assisted therapies such as methadone treatment, which not only increases ART utilization, but also may lead to higher ART adherence and viral suppression levels [56]. Indonesia is one of a few countries worldwide where methadone is available in prisons for the treatment of opioid dependence [57], yet this study suggests that not enough PWH are receiving methadone, which appears to be an important facilitator for ART utilization. In this study, PWH receiving methadone treatment, although few in number, had a sixfold increase in the adjusted odds of being highly adherent to ART. Expansion of methadone treatment to opioid-dependent PWH in these settings could increase ART adherence, decrease development of ART resistance mutations that would accelerate HIV progression, and may substantially reduce HIV transmission among PWID after prison release [30].

Findings here have important implications for ART delivery in prison settings. Currently, many clinic tasks, including ART distribution, are performed by prisoner volunteers. While this sort of "task-shifting" has potential to increase ART adherence, interventions such as directly observed therapy (DOT), routine viral load testing, and adherence coaching also are needed. Although studies in U.S. prisons have concluded that DOT offers no advantage over self-administered ART [3, 5, 58], supervised consumption of ART, nevertheless, may be an effective approach to increase adherence in LMIC prison settings where stigma and substance use coexist, and could be practically implemented by training prisoner volunteers, many of whom already take ART. Routine viral load testing is now recommended for all PWH regardless of whether they are receiving therapy. Yet cost is an important barrier in many LMICs [59], including Indonesia where prevention resources may be misallocated [60]. Although peer support is available in these prisons, there is an urgent need for evidence-informed behavioral interventions to improve ART adherence, which are presently unavailable due to limited human resources in prisons as well as gaps in the scientific evidence for medication adherence interventions with this population [61].

Finally, although this study provides important insights into factors associated with ART adherence in a prison setting, there are some notable limitations. Absent other adherence measures or cognitive interviews, uncertainty exists about the reliability of our adherence measure. Responses other than "perfect", which was defined for participants by the researchers in very concrete terms, may not have been interpreted consistently by all participants. Although we measured many important variables within our theoretical framework, other variables including ART beliefs and physician trust, which may influence ART adherence in this population [54, 55, 62], were not assessed. Our approach to estimate opioid dependence could misclassify participants who, although drug-dependent and using opioids before incarceration, were mainly dependent on substances other than opioids. Our sample size allowed us to detect some important associations, yet absence of an association may be due to insufficient power and this study provides no evidence of the directionality of the observed associations. Finally, participants were drawn from just two all-male prisons in Jakarta and not randomly selected, which limits generalizability, including to female prisoners in Indonesia who have lower rates of drug injection but higher HIV prevalence [24]. Nevertheless, this study is one of the first and largest studies to examine factors associated with ART adherence among prisoners in a LMIC and provides important new evidence

about the role of methadone and perceived safety in HIV treatment.

Conclusion

Although ART utilization in these Indonesian prisons has expanded, a substantial number of incarcerated PWH, including those with advanced HIV, may not achieve optimal adherence. Closer monitoring and adherence coaching may be required to improve ART adherence within prison and after prison release. Pharmacological treatment with methadone may be one of the most important factors leading to ART utilization and adherence but benefits few PWH within these settings where many PWH are opioid dependent. Patient concerns about the lack of personal safety in prison also may interfere with adherence, necessitating organizational changes that reduce overcrowding and improve privacy for ART administration.

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Compliance with Ethical Standards

Conflict of interest The authors declare no conflicts of interest.

Ethical Approval All procedures involving human participants were conducted in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all individual participants included in the study.

References

1. Dolan K, Wirtz AL, Moazen B, Ndeffo-mbah M, Galvani A, Kinner SA, et al. Global burden of HIV, viral hepatitis, and tuberculosis in prisoners and detainees. Lancet. 2016;388(10049):1089–102.
2. Rich JD, Beckwith CG, Macmadu A, Marshall BDL, Brinkley-Rubinstein L, Amon JJ, et al. Clinical care of incarcerated people with HIV, viral hepatitis, or tuberculosis. Lancet. 2016;388(10049):1103–14.
3. Wohl DA, Stephenson BL, Golin CE, Kiziah CN, Rosen D, Ngo B, et al. Adherence to directly observed antiretroviral therapy among human immunodeficiency virus—infected prison inmates. Clin Infect Dis. 2003;36(12):1572–6.
4. Young JD, Patel M, Badowski M, Mackesy-Amiti ME, Vaughn P, Shicker L, et al. Improved virologic suppression with HIV subspecialty care in a large prison system using telemedicine: an observational study with historical controls. Clin Infect Dis. 2014;59(1):123–6.
5. Meyer JP, Cepeda J, Wu J, Trestman RL, Altice FL, Springer SA. Optimization of human immunodeficiency virus treatment during incarceration: viral suppression at the prison gate. JAMA Intern Med. 2014;174(5):721–9.
6. Uthman OA, Oladimeji O, Nduka C. Adherence to antiretroviral therapy among HIV-infected prisoners: a systematic review and meta-analysis. AIDS Care. 2017;29(4):489–97.
7. Fu JJ, Bazazi AR, Altice FL, Mohamed MN, Kamarulzaman A. Absence of antiretroviral therapy and other risk factors for morbidity and mortality in Malaysian compulsory drug detention and rehabilitation centers. PLoS ONE. 2012;7(9):e44249.
8. Azbel L, Wickersham JA, Grishaev Y, Dvoryak S, Altice FL. Burden of infectious diseases, substance use disorders, and mental illness among Ukrainian prisoners transitioning to the community. PLoS ONE. 2013;8(3):e59643.
9. Telisinghe L, Charalambous S, Topp SM, Herce ME, Hoffmann CJ, Barron P, et al. HIV and tuberculosis in prisons in sub-Saharan Africa. Lancet. 2016;388(10050):1215–27.
10. Culbert GJ, Crawford FW, Murni A, Waluyo A, Bazazi AR, Sahar J, et al. Predictors of mortality within prison and after release among persons living with HIV in Indonesia. Res Rep Trop Med. 2017;8:25–35.
11. Nachega JB, Sam-Agudu NA, Mofenson LM, Schechter M, Mellors JW. Achieving viral suppression in 90% of people living with human immunodeficiency virus on antiretroviral therapy in low- and middle-income countries: progress, challenges, and opportunities. Clin Infect Dis. 2018;66(10):1487–91.
12. Fazel S, Bains P, Doll H. Substance abuse and dependence in prisoners: a systematic review. Addiction. 2006;101(2):181–91.
13. Bick J, Culbert G, Al-Darraji HA, Koh C, Pillai V, Kamarulzaman A, et al. Healthcare resources are inadequate to address the burden of illness among HIV-infected male prisoners in Malaysia. Int J Prison Health. 2016;12(4):253–69.
14. Muessig KE, Rosen DL, Farel CE, White BL, Filene EJ, Wohl DA. "Inside these fences is our own little world": prison-based hiv testing and hiv-related stigma among incarcerated men and women. AIDS Educ Prev. 2016;28(2):103–16.
15. Hinduan ZR, Suherman H, Pinxten WJ, Alisjahbana B, Hospers HJ. HIV-related knowledge and attitudes among Indonesian prison officers. Int J Prison Health. 2013;9(2):92–102.
16. Culbert GJ. Violence and the perceived risks of taking antiretroviral therapy in US jails and prisons. Int J Prison Health. 2014;10(2):94–110.
17. Shalihu N, Pretorius L, van Dyk A, Vander Stoep A, Hagopian A. Namibian prisoners describe barriers to HIV antiretroviral therapy adherence. AIDS Care. 2014;26(8):968–75.
18. Culbert GJ, Waluyo A, Iriyanti M, Muchransyah AP, Kamarulzaman A, Altice FL. Within-prison drug injection among HIV-infected male prisoners in Indonesia: a highly constrained choice. Drug Alcohol Depend. 2015;149:71–9.
19. Izenberg JM, Bachireddy C, Wickersham JA, Soule M, Kiriazova T, Dvoriak S, et al. Within-prison drug injection among HIV-infected Ukrainian prisoners: prevalence and correlates of an extremely high-risk behaviour. Int J Drug Policy. 2014;25(5):845–52.
20. Milloy MJ, Kerr T, Buxton J, Rhodes T, Guillemi S, Hogg R, et al. Dose-response effect of incarceration events on nonadherence to HIV antiretroviral therapy among injection drug users. J Infect Dis. 2011;203(9):1215–21.
21. Loeliger KB, Altice FL, Desai MM, Ciarleglio MM, Gallagher C, Meyer JP. Predictors of linkage to HIV care and viral suppression

after release from jails and prisons: a retrospective cohort study. Lancet HIV. 2018;5(2):e96–106.
22. Joint United Nations Programme on HIV/AIDS. The Gap Report. Geneva: UNAIDS, 2014.
23. Morineau G, Bollen LJ, Syafitri RI, Nurjannah N, Mustikawati DE, Magnani R. HIV prevalence and risk behaviours among injecting drug users in six indonesian cities implications for future HIV prevention programs. Harm Reduct J. 2012;9(1):37.
24. Blogg S, Utomo B, Silitonga N, Ayu N, Hidayati D, Sattler G. Indonesian national inmate bio-behavioral survey for HIV and syphilis prevalence and risk behaviors in prisons and detention centers, 2010. SAGE Open. 2014. https://doi.org/10.1177/2158244013518924.
25. Nelwan EJ, Van Crevel R, Alisjahbana B, Indrati AK, Dwiyana RF, Nuralam N, et al. Human immunodeficiency virus, hepatitis B and hepatitis C in an Indonesian prison: prevalence, risk factors and implications of HIV screening. Trop Med Int Health. 2010;15(12):1491–8.
26. Nelwan EJ, Isa A, Alisjahbana B, Triani N, Djamaris I, Djaja I, et al. Routine or targeted HIV screening of Indonesian prisoners. Int J Prison Health. 2016;12(1):17–26.
27. Nelwan EJ, Indrati AK, Isa A, Triani N, Alam NN, Herlan MS, et al. Effect of HIV prevention and treatment program on HIV and HCV transmission and HIV mortality at an Indonesian narcotic prison. Southeast Asian J Trop Med Public Health. 2015;46(5):880–91.
28. Gelberg L, Andersen RM, Leake BD. The behavioral model for vulnerable populations: application to medical care use and outcomes for homeless people. Health Serv Res. 2000;34(6):1273–302.
29. Rhodes T. The 'risk environment': a framework for understanding and reducing drug-related harm. Int J Drug Policy. 2002;13(2):85–94.
30. Altice FL, Azbel L, Stone J, Brooks-Pollock E, Smyrnov P, Dvoriak S, et al. The perfect storm: incarceration and the high-risk environment perpetuating transmission of HIV, hepatitis C virus, and tuberculosis in Eastern Europe and Central Asia. Lancet. 2016;388(10050):1228–48.
31. Althoff AL, Zelenev A, Meyer JP, Fu J, Brown SE, Vagenas P, et al. Correlates of retention in HIV care after release from jail: results from a multi-site study. AIDS Behav. 2013;17(Suppl 2):S156–70.
32. Strathdee SA, Beletsky L, Kerr T. HIV, drugs and the legal environment. Int J Drug Policy. 2015;26:S27–32.
33. Booth RE, Dvoryak S, Sung-Joon M, Brewster JT, Wendt WW, Corsi KF, et al. Law enforcement practices associated with HIV infection among injection drug users in Odessa, Ukraine. AIDS Behav. 2013;17(8):2604–14.
34. Strathdee SA, Hallett TB, Bobrova N, Rhodes T, Booth R, Abdool R, et al. HIV and risk environment for injecting drug users: the past, present, and future. Lancet. 2010;376(9737):268–84.
35. Rhodes T. Risk environments and drug harms: a social science for harm reduction approach. Int J Drug Policy. 2009;20(3):193–201.
36. Culbert GJ, Williams AB. Cultural adaptation of a medication adherence intervention with prisoners living with HIV in Indonesia: a pragmatic approach to intervention development. J Assoc Nurses AIDS Care. 2018;29(3):454–65.
37. Williams AB, Burgess JD, Danvers K, Malone J, Winfield SD, Saunders L. Kitchen table wisdom: a Freirian approach to medication adherence. J Assoc Nurses AIDS Care. 2005;16(1):3–12.
38. Degroot AM, Dannenburg L, Vanhell JG. Forward and backward word translation by bilinguals. J Mem Lang. 1994;33(5):600–29.
39. Chatfield A, Javetski G, Lesh N. CommCare Evidence Base. Dimagi; 2013.
40. Flaming A, Canty M, Javetski G, Lesh N. The CommCare evidence base for frontline workers. 2015.
41. Feldman BJ, Fredericksen RJ, Crane PK, Safren SA, Mugavero MJ, Willig JH, et al. Evaluation of the single-item self-rating adherence scale for use in routine clinical care of people living with HIV. AIDS Behav. 2013;17(1):307–18.
42. Culbert GJ, Earnshaw VA, Swasti Wulanyani NM, Wegman MP, Waluyo A, Altice FL. Correlates and experiences of HIV stigma in prisoners living with HIV in Indonesia: a mixed-method analysis. J Assoc Nurses AIDS Care. 2015;26(6):743–57.
43. Wallston KA, Strudler Wallston B, DeVellis R. Development of the multidimensional health locus of control (MHLC) scales. Health Educ Monogr. 1978;6(1):160–70.
44. Wallston KA. The validity of the multidimensional health locus of control scales. J Health Psychol. 2005;10(5):623–31.
45. Institute of Behavioral Research. Texas Christian University Drug Screen V. Fort Worth: Texas Christian University, Institute of Behavioral Research; 2014.
46. Cortes A, Hunt N, McHale S. Development of the scale of perceived social support in HIV (PSS-HIV). AIDS Behav. 2014;18(12):2274–84.
47. Holzemer WL, Henry SB, Nokes KM, Corless IB, Brown MA, Powell-Cope GM, et al. Validation of the sign and symptom check-list for persons with HIV disease (SSC-HIV). J Adv Nurs. 1999;30(5):1041–9.
48. Wickersham JA, Azar MM, Cannon CM, Altice FL, Springer SA. Validation of a brief measure of opioid dependence: the rapid opioid dependence screen (RODS). J Correct Health Care. 2015;21(1):12–26.
49. Lazzarini Z, Altice FL. A review of the legal and ethical issues for the conduct of HIV-related research in prisons. AIDS Public Policy J. 2000;15(3–4):105–35.
50. Degenhardt L, Mathers BM, Wirtz AL, Wolfe D, Kamarulzaman A, Carrieri MP, et al. What has been achieved in HIV prevention, treatment and care for people who inject drugs, 2010–2012? A review of the six highest burden countries. Int J Drug Policy. 2014;25(1):53–60.
51. Levi J, Raymond A, Pozniak A, Vernazza P, Kohler P, Hill A. Can the UNAIDS 90-90-90 target be achieved? A systematic analysis of national HIV treatment cascades. BMJ Glob Health. 2016;1(2):e000010.
52. Joint United Nations Programme on HIV/AIDS. Country Snapshot 2018: Indonesia. UNAIDS Regional Support Team for Asia and the Pacific and AIDS Data Hub: 2018.
53. Gardner EM, Burman WJ, Steiner JF, Anderson PL, Bangsberg DR. Antiretroviral medication adherence and the development of class-specific antiretroviral resistance. AIDS (Lond, Engl). 2009;23(9):1035.
54. Culbert GJ, Bazazi AR, Waluyo A, Murni A, Muchransyah AP, Iriyanti M, et al. The influence of medication attitudes on utilization of antiretroviral therapy (ART) in Indonesian prisons. AIDS Behav. 2016;20(5):1026–38.
55. Altice FL, Mostashari F, Friedland GH. Trust and the acceptance of and adherence to antiretroviral therapy. J Acquir Immune Defic Syndr. 2001;28(1):47–58.
56. Low AJ, Mburu G, Welton NJ, May MT, Davies CF, French C, et al. Impact of opioid substitution therapy on antiretroviral therapy outcomes: a systematic review and meta-analysis. Clin Infect Dis. 2016;26:1094.
57. Larney S, Dolan K. A literature review of international implementation of opioid substitution treatment in prisons: equivalence of care? Eur Addict Res. 2009;15(2):107–12.
58. White BL, Golin CE, Grodensky CA, Kiziah CN, Richardson A, Hudgens MG, et al. Effect of directly observed antiretroviral therapy compared to self-administered antiretroviral therapy on adherence and virological outcomes among HIV-infected prisoners: a randomized controlled pilot study. AIDS Behav. 2015;19(1):128–36.

59. Roberts T, Cohn J, Bonner K, Hargreaves S. Scale-up of routine viral load testing in resource-poor settings: current and future implementation challenges. Clin Infect Dis. 2016;62(8):1043–8.
60. Gray RT, Reyes J, Nadjib M, Harimurti P, Wilson DP. Assessment of the allocation of HIV funding in Indonesia. World Bank; 2012.
61. Kouyoumdjian FG, McIsaac KE, Liauw J, Green S, Karachiwalla F, Siu W, et al. A systematic review of randomized controlled trials of interventions to improve the health of persons during imprisonment and in the year after release. Am J Public Health. 2015;105(4):e13–33.
62. Farhoudi B, Alipour A, Ghodrati S, Seyedalinaghi S, Zanganeh M, Mohraz M. Barriers to adherence to antiretroviral treatment among inmates of a prison in Tehran, Iran: a qualitative study. Arch Clin Infect Dis. 2018;13(2):e57911. https://doi.org/10.5812/archcid.57911.