Annals of Internal Medicine
www.annals.org

First published March 5, 2012 on annals.org.

Clinical Guidelines

Guidelines for Improving Entry Into and Retention in Care and Antiretroviral Adherence for Persons With HIV: Evidence-Based Recommendations From an International Association of Physicians in AIDS Care Panel

Melanie A. Thompson, MD; Michael J. Mugavero, MD, MHSc; K. Rivet Amico, PhD; Victoria A. Cargill, MD, MSCE; Larry W. Chang, MD, MPH; Robert Gross, MD, MSCE; Catherine Orrell, MBChB, MSc, MMed; Frederick L. Altice, MD; David R. Bangsberg, MD, MPH; John G. Bartlett, MD; Curt G. Beckwith, MD; Nadia Dowshen, MD; Christopher M. Gordon, PhD; Tim Horn, MS; Princy Kumar, MD; James D. Scott, PharmD, MEd; Michael J. Stirratt, PhD; Robert H. Remien, PhD; Jane M. Simoni, PhD; and Jean B. Nachega, MD, PhD, MPH

+ Author Affiliations

Abstract

Description: After HIV diagnosis, timely entry into HIV medical care and retention in that care are essential to the provision of effective antiretroviral therapy (ART). ART adherence is among the key determinants of successful HIV treatment outcome and is essential to minimize the emergence of drug resistance. The International Association of Physicians in AIDS Care convened a panel to develop evidence-based recommendations to optimize entry into and retention in care and ART adherence for people with HIV.

Methods: A systematic literature search was conducted to produce an evidence base restricted to randomized, controlled trials and observational studies with comparators that had at least 1 measured biological or behavioral end point. A total of 325 studies met the criteria. Two reviewers independently extracted and coded data from each study using a standardized data extraction form. Panel members drafted recommendations based on the body of evidence for each method or intervention and then graded the overall quality of the body of evidence and the strength for each recommendation.

Recommendations: Recommendations are provided for monitoring of entry into and retention in care, interventions to improve entry and retention, and monitoring of and interventions to improve ART adherence. Recommendations cover ART strategies, adherence tools, education and counseling, and health system and service delivery interventions. In addition, they cover specific issues pertaining to pregnant women, incarcerated individuals, homeless and marginally housed individuals, and children and adolescents, as well as substance use and mental health disorders. Recommendations for future research in all areas are also provided.

The availability of potent antiretroviral therapy (ART) has resulted in remarkable decreases in HIV-related morbidity and mortality in the past 15 years (1, 2). Entry into and retention in HIV medical care is critical to the provision of ART, and adherence to ART is among the key determinants of HIV treatment success (3–6). More than 2 decades of targeted research in these areas has produced a varied and complex evidence base that, to date, has not been fully evaluated or distilled into concrete recommendations for how to best monitor or support HIV care and ART adherence.

Recent data from the U.S. Centers for Disease Control and Prevention reveal that only 28% of persons with HIV in the United States have achieved viral suppression while receiving ART (7). Of those who knew they had HIV, only 69% were linked to care, and only 59% were retained in care (8). These figures and comparable global data (9, 10) challenge us to explore best practices for improving entry into and retention in care on a global scale. Only with successful care linkage and retention can ART be accessed. Once patients are in care and are receiving treatment, high levels of adherence are required to prevent the selection of resistance mutations and subsequent virologic failure (11). In a global pooled sample of 33 199 adults taking ART in over 84 observational studies, only 62% of persons achieved adherence of at least 90% of doses (12). These data underscore the need for concise and clear evidence-based recommendations to help care providers monitor and support ART adherence.

In this context, the International Association of Physicians in AIDS Care (IAPAC) convened an expert panel to develop evidence-based recommendations to optimize entry into and retention in care and ART adherence and to monitor these processes. Members of the panel are listed in Appendix 1. These guidelines aim to define best practices that can be used by practitioners and health systems to improve adherence and, in turn, health outcomes. Our recommendations are based on the best published science; however, the evidence base remains insufficient in many areas. For that reason, we also highlight areas in which additional research is needed to inform future recommendations. We realize that implementation of these recommendations may, in some cases, require that new resources be identified to bring the benefit of best practices to our clinic populations. We believe that presenting recommendations based on rigorous science is the best avenue to achieve that end.

Guidelines Focus and Target Population

These guidelines focus on interventions to improve entry into and retention in care and ART adherence for people living with HIV, as well as methods to monitor these critical processes. The target audience includes care providers, patients, policymakers, and organizations and health systems involved with implementing HIV care and treatment.

Guidelines Development Process

For these guidelines, a systematic literature search was conducted to produce an evidence base restricted to randomized, controlled trials (RCTs) and observational studies with comparators that had at least 1 measured biological or behavioral end point. For monitoring, correlation between a method and an outcome was required. A total of 325 studies met our criteria. Two reviewers independently extracted and coded data from each study using a standardized data extraction form. Panel members drafted recommendations based on the body of evidence for each method or intervention and then graded the overall quality of the body of evidence and the strength for each recommendation. Table 1 summarizes the quality and strength scales used. Details on the methods used are available in Appendix 2.

View this table:
In this window In a new window

Table 1. Grading Scales for Quality of the Body of Evidence and Strength of Recommendations

Guidelines

Appendix Table 1 summarizes all recommendations and associated quality and strength scores.

View this table:
In this window In a new window

Appendix Table 1. Summary of Recommendations With Scores for Quality of the Body of Evidence and Strength of Recommendation

Web-Only

Entry Into and Retention in HIV Medical Care

The associations between entry into and retention in HIV medical care and both individual health outcomes and HIV transmission dynamics mediated by ART have been well established in retrospective, prospective, and mathematical modeling studies (13–19). Accordingly, individual-level monitoring of entry and retention is essential to the development and evaluation of cost-effective interventions required to improve these critical components of clinical care.

Recommendation 1: Systematic monitoring of successful entry into HIV care is recommended for all individuals diagnosed with HIV (II A).

Entry into care after HIV diagnosis, defined as a visit with an HIV care provider authorized to prescribe ART, has been associated with improved survival (20). Within a given jurisdiction or service area, providers of testing services, local public health institutions, and medical clinics have a shared responsibility to monitor entry into HIV care. Roles and accountability should be clearly established on a local level. Integration of multiple data sources, including surveillance data, administrative databases, and medical clinic records, may enhance monitoring of initial entry into HIV care (21).

Recommendation 2: Systematic monitoring of retention in HIV care is recommended for all patients (II A).

Retention in care is associated with improved individual health outcomes, including HIV biomarker and clinical variables, and may reduce community-level viral burden, with implications for secondary prevention (13, 22). Although monitoring retention is routinely recommended, specific details, such as retention measures to be used and desired visit frequency, vary among jurisdictions and programs and should be in harmony with national and international guidelines. Many retention measures (for example, visit adherence, gaps in care, and visits per interval of time) and data sources (for example, surveillance, medical records, and administrative databases) have been used (23) and may be applied in accordance with local resources and standards of care. As with monitoring of linkage, integration of data sources may enhance monitoring of retention.

Recommendation 3: Brief, strengths-based case management for individuals with a new HIV diagnosis is recommended (II B).

The Antiretroviral Treatment and Access Study evaluated entry into and retention in care as part of a multisite RCT in several U.S. care sites comparing strengths-based case management sessions (up to 5 in a 90-day period) with passive referrals for local care among patients with recently diagnosed HIV infection (24). Trained social workers helped clients to identify their internal strengths and assets to facilitate successful linkage to HIV medical care. A significantly higher proportion of the case-managed participants visited an HIV clinician at least once within 6 months (78% versus 60%) and at least twice within 12 months (64% versus 49%). However, availability of resources may impede implementation in a given jurisdiction or service area.

Recommendation 4: Intensive outreach for individuals not engaged in medical care within 6 months of a new HIV diagnosis may be considered (III C).

In a sample of 104 individuals in whom HIV was diagnosed within 6 months before enrolling in the U.S. Special Projects of National Significance Outreach Initiative, 92% attended medical appointments within 6 months of enrollment (25). At study baseline, 14% of individuals had undetectable HIV-1 RNA, which increased to 45% after 12 months of follow-up. This observational demonstration project used a variety of approaches, focusing on individuals considered underserved by the health care system (such as women, youth, and people with a history of substance use or mental illness).

Recommendation 5: Use of peer or paraprofessional patient navigators may be considered (III C).

Patient navigation has been described as a model of care coordination and is largely based on peer-based programs established for patients with cancer. Patient navigators are trained to help HIV-infected patients facilitate interactions with

health care. In an analysis of 4 patient-navigation interventions from the U.S. Special Projects of National Significance Outreach Initiative, involving more than 1100 patients who were inconsistently engaged in care, the proportion with at least 2 visits in the previous 6 months increased from 64% at baseline to 87% at 6 months and 79% at 12 months in the intervention group (26). In addition, the proportion of patients with undetectable HIV-1 RNA was 50% greater at 12 months than at baseline.

Monitoring ART Adherence

Monitoring adherence is necessary to assess the effect of interventions and also to inform providers of the need to implement interventions. Measurement methods include self-reports, pharmacy refill data, pill counts, electronic drug monitors (EDMs), and drug concentrations from biological samples; each has unique strengths and weaknesses (27, 28). Many of the studies reviewed combined measures to improve sensitivity and specificity, but because of the large variability in these approaches, we will not address these potential combinations here. Regardless of measurement method, adherence is a factor that varies with time and therefore must be repeatedly assessed (29).

Recommendation 6: Self-reported adherence should be obtained routinely in all patients (II A).

Self-reported ART adherence has consistently been associated with HIV-1 RNA levels. Although it commonly overestimates adherence (30), self-reported nonadherence has a high predictive value (27). Self-report is less strongly associated with treatment response than are EDM- or pharmacy-based measures, but relative ease of implementation further supports its use in clinical care. Careful attention must be paid to collecting self-report data in a manner that makes reasonable demands on memory. Therefore, questionnaires should inquire only about specific doses taken over a short time interval (for example, in the previous week or less) and about global measures of adherence over a somewhat longer time (for example, in the previous month).

Recommendation 7: Pharmacy refill data are recommended for adherence monitoring when medication refills are not automatically sent to patients (II B).

Many observational studies across the globe have demonstrated the validity of pharmacy refill data as an ART adherence measure, including medical records (30, 31), claims data (32), and ad hoc pharmacy contact (33). Pharmacy measures are useful for as long a period as the refill records are maintained. The interval over which refill records can be used depends on the days' supply (that is, the length of time the medication dispensed is intended to last).

Recommendation 8: Drug concentrations in biological samples are not routinely recommended (III C).

The concentration of HIV medications in various biological samples has been assessed as an adherence measure in many settings; relatively few analyses have been associated with clinical outcomes (34–36). Results are inconsistent (37, 38) and are limited by assay issues and the relatively short half-life of most antiretroviral medications.

Recommendation 9: Pill counts performed by staff or patients are not routinely recommended (III C).

An association between pills counts and biological outcomes has been seen in some studies (39, 40) but not in all (41). Several studies have assessed various operational methods for conducting pill counts, such as making unannounced home visits for marginally housed individuals (3, 39, 42). Clinic-based pill counts are susceptible to pill dumping. The personnel required for pill counts and the burden of bringing medication to visits are further barriers to routine use.

Recommendation 10: EDMs are not routinely recommended for clinical use (I C).

Electronic drug monitors have been used to assess adherence in many studies (43–47). Adherence measured electronically is consistently more closely associated with HIV-1 RNA than are other methods (48, 49). In research, EDMs have been the measurement method of choice (50, 51). Unfortunately, these technologies are currently impractical outside of studies because they may be burdensome to

patients and incompatible with adherence-promoting strategies, such as pill cases.

Interventions to Improve ART Adherence

Interventions to promote ART adherence are broadly defined as strategies that aim to enhance this critical determinant of successful HIV treatment outcomes.

ART Strategies

Important determinants of ART adherence and the related construct of ART persistence (52), or uninterrupted receipt of treatment, include dosing schedule, pill count, tolerability, and toxicity profiles of ART. Advances in ART now allow simplification of dosing schedules and reduction of pill burden for a majority of patients while maintaining excellent viral suppression. Additional factors to be considered in initiating or changing ART include transmitted or emergent viral resistance, individual ART treatment history, medical and psychosocial comorbid conditions, concomitant medications, and patient preference.

Recommendation 11: Among regimens of similar efficacy and tolerability, once-daily regimens are recommended for treatment-naive patients beginning ART (II B).

Many RCTs in treatment-naive patients have compared once-daily with multiply-dosed regimens containing different drugs. As such, it is impossible to ascertain whether adherence and biological benefits derive from the dosing schedule or the regimen components. Some studies, however, have used identical ART components given once or twice daily and have demonstrated improved adherence and noninferior viral suppression with once-daily dosing (53, 54). Efficacy for once-daily dosing must be confirmed by RCTs before adoption into clinical care.

Recommendation 12: Switching treatment-experienced patients receiving complex or poorly tolerated regimens to once-daily regimens is recommended, given regimens with equivalent efficacy (III B).

Several studies have demonstrated successful switching to once-daily dosing for patients with suppressed virus on a multiply-dosed regimen (55–59). Often, studies are limited by small sample size, short follow-up, or changes in ART regimens accompanying the switch to a once-daily regimen, so factors including toxicity, tolerability, and related considerations may contribute to observed findings. Treatment history and prior ART resistance are particularly important considerations when switching regimens for treatment-experienced patients.

Recommendation 13: Among regimens of equal efficacy and safety, fixed-dose combinations are recommended to decrease pill burden (III B).

Because fixed-dose combinations (FDCs) are often approved on the basis of safety and bioequivalence rather than noninferiority to the component regimens, few data comparing adherence outcomes between FDCs and individual components are available. Therefore, many of the data in this area come from surveys of patient satisfaction or extrapolation from diseases other than HIV that are, by definition, not included in our evidence base. The evidence base contains 1 RCT and 1 comparative observational study that demonstrated an adherence benefit with FDCs (60, 61). It is important to note that when components of different half-lives are combined, there is potential for a monotherapy "tail" and subsequent resistance when doses are missed or drug is discontinued. On the other hand, the use of FDCs eliminates the possibility of taking an incomplete regimen, as may occur when one drug is not refilled on time or is simply not taken, leading to viral rebound and resistance (62).

Adherence Tools for Patients

Many commonly used self-management adherence tools, including pillboxes and medication planners or calendars, have been associated with improved adherence and HIV-1 RNA suppression (63). It is common for adherence tools to be combined with behavioral and structural interventions. Given their simplicity and observational data supporting their use, they are considered the standard of care despite limited comparative research to establish efficacy. Recommendations regarding use of these tools are limited because of this lack of evidence.

Recommendation 14: Reminder devices and use of communication technologies

with an interactive component are recommended (I B)

An adherence benefit of dose-time reminder alarms has been reported (64, 65). Strategies using cellular technology (short message service communication) have demonstrated improvement in adherence and HIV-1 RNA. Methods ranged from texting dosing reminders with or without requesting a response (66–68) to texting weekly check-ins from the clinic with telephone follow-up for those requesting it (69). One study found better ART adherence was achieved with use of texting with expected reply (interactive) than simple 1-way reminders (66).

Recommendation 15: Education and counseling using specific adherence-related tools is recommended (I A).

The available literature suggests that some tools may be more beneficial to patient adherence when combined with education or counseling. Seven studies (Appendix Table 2) evaluated a particular adherence tool (pill organizer [70], dose planner [71], reminder alarm device [72, 73], or EDM [74–76]) as distinguished from general one-on-one education and counseling. All but 1 demonstrated an effect on adherence, and 3 of the 6 that investigated effects on biological markers found significant positive effects (72, 75, 76). Three studies from the Netherlands and China that used EDMs with counseling about missed doses showed improvement in adherence (74–76), and 2 showed improvement in biological markers (75, 76). A factorial-design RCT and an RCT from Kenya showed the inferiority of using a reminder device without counseling and suggested that tools may be most successful when offered as part of a comprehensive support package (72, 77).

View this table:
In this window In a new window

Appendix Table 2. Evidence Base for Education and Counseling Recommendations Web-Only

Education and Counseling Interventions

Several systematic syntheses of behavioral interventions targeting ART adherence are available and report generally positive modest effect sizes, but the effect on HIV-1 RNA is less consistent (78–81). Recommendations are limited to those appropriate for general clinic populations; interventions targeting behavioral determinants of adherence in specific subgroups are included in other sections. Because of the volume and breadth of data supporting these recommendations, individual study results are not reviewed in detail, but Appendix Table 2 describes studies and outcomes. Across recommendations, pertinent issues exist with regard to best structure, deliverer, training, duration, timing, frequency, and targets of educational and counseling interventions, as well as optimal modalities for dissemination and implementation.

Recommendation 16: Individual one-on-one ART education is recommended (II A).

Of the 14 interventions with ART education components (82–95), 10 had favorable effects on adherence outcomes, 2 had initial effects that deteriorated over time (86, 92), and 2 showed no benefit on adherence (87, 91); only 1 study demonstrated clear benefit on biological markers (94), 6 did not evaluate biomarkers (82, 87–90, 92), and 7 showed no biomarker benefit (83–86, 91, 93, 95). Among effective interventions, education was not the only component; most interventions also included counseling or skills-building, along with activities to promote adult learning. Group-delivered education is addressed in recommendation 18.

Recommendation 17: Providing one-on-one adherence support to patients through 1 or more adherence counseling approaches is recommended (II A).

Strategies to support adherence that involve one-on-one discussions targeting enhancement of facilitators and easing of barriers are recommended. Twenty-seven interventions in the evidence base used individual adherence counseling; of the 25 evaluating adherence, 16 established positive effects (82, 84, 88–90, 93–103), 3 demonstrated as-treated or post hoc effects (83, 85, 104), 3 demonstrated early effects that deteriorated over time (86, 92, 105), and 3 demonstrated no benefit (87, 106, 107). Of the 17 that included biological outcomes, 12

demonstrated no benefit (83–86, 93, 95, 102, 103, 105–108) and 5 demonstrated positive effects (94, 97, 99, 101, 109). Although most interventions are delivered in person, there are also successful examples of telephone-based counseling or mixed in-person and telephone-based models (72, 83, 102) and home visits (95). Further, expanding one-on-one counseling to include serodiscordant partners has demonstrated some benefit on adherence, although not on HIV-1 RNA (110), while inclusion of "caregivers" with ART-naive patients had mixed results (no benefit in 1 study [91] and support for effects on adherence and HIV-1 RNA overall but not over time in another [111]). The evidence base suggests the utility of providing some form of discussion-based support to individuals receiving ART and provides a wide array of potentially effective specific interventions that should be carefully matched to clinic population needs and resources.

Recommendation 18: Group education and group counseling are recommended; however, the type of group format, content, and implementation cannot be specified on the basis of the currently available evidence (II C).

The evidence base included 7 studies of group-based education and counseling programs targeting general clinic populations (Appendix Table 2). Although some studies have demonstrated significant improvements in ART adherence, HIV-1 RNA, or CD4 cell counts (112–114) and 1 study demonstrated effects in specific subsets of participants (115), other studies showed no significant improvements in adherence (116, 117). Notably, studies targeted diverse patient groups and used a wide range of interventions, so the evidence does not clearly converge to support one particular approach to offering group education and counseling. Characterizing these interventions as "group" interventions designates their main modality, but several interventions also used an individual component or support for group members.

Recommendation 19: Multidisciplinary education and counseling intervention approaches are recommended (III B).

Use of multidisciplinary teams is distinct from multiple team members duplicating efforts or content addressing adherence; multidisciplinary team members have clearly delineated roles and cover content specific to their particular area of expertise. A health-team approach in which 109 ART-naive patients met with a pharmacist, dietitian, and social worker for targeted education and counseling before ART initiation did not produce significant effects on pharmacy-refill-based adherence at 12 months but did significantly affect HIV-1 RNA outcomes (118). Another intervention using nurses and pharmacists targeted multiple factors (such as diet, work, social support, tools, and skills-building); significant effects on adherence were reported, but HIV-1 RNA and CD4 cell count did not change significantly (64).

Recommendation 20: Offering peer support may be considered (III C).

Nine studies were reviewed and showed mixed outcomes (119–127). One reported null findings from a peer-based psychoeducational group (120), and 8 studies examining interventions involving treatment partners or peers, or both, demonstrated some success. The evidence base exhibits diverse results for use of peers. Several interventions, including treatment partners to supervise or directly administer ART (121–123, 127) and peers to provide social support (119, 124–126), showed improvement in adherence or biological markers or both. Combination of use of peers and intervention in these studies limits the ability to draw conclusion on the specific effect of peers versus the interventions they delivered.

Health System and Service Delivery Interventions

We focused on interventions targeting factors believed to be related to adherence but that are associated with systems of care or service delivery (for example, transportation to clinic and food supplements, staffing and service modifications, co-location of services) or influence social determinants, such as HIV-associated stigma.

Recommendation 21: Using nurse- or community counselor-based care has adherence and biological outcomes similar to those of doctor- or clinic counselor-based care and is recommended in underresourced settings (II B).

Two RCTs showed noninferiority of nursing ART care to physician-based care. A

trial from Uganda found a nurse–peer model was not inferior to the traditional doctor–counselor model in adherence, HIV-1 RNA, and CD4 outcomes (128). Another RCT from South Africa also demonstrated noninferiority of CD4 and HIV-1 RNA outcomes with nurses rather than doctors caring for people on ART (129). A cohort analysis, also from Uganda, with a notable limitation (the exposed cohort differed from control cohort) showed that a system of providing ART through volunteers (trained and supervised by a clinical officer) in a rural community was not inferior, in the short term, to a clinic-based standard of care (130).

Recommendation 22: Interventions providing case management services and resources to address food insecurity, housing, and transportation needs are recommended (III B).

Research with US homeless populations have shown mixed results, but HIV-1 RNA levels improved in an as-treated analysis of a housing provision intervention (131). Case management is discussed in Recommendation 32. Cohort studies from Nigeria and Zambia with comparator groups evaluated outcomes of interventions for food-insecure patients and showed that ART adherence, retention in care, and clinical outcomes can be enhanced with food supplementation programs (132, 133). Addressing transportation issues in the context of case management and a home visit also may decrease missed appointments, especially among women with mental health or substance use disorders (134).

Recommendation 23: Integration of medication management services into pharmacy systems may be considered (III C).

Pilot pharmacies in California offered services to manage adverse drug effects, evaluate patient adherence in consultation with physicians and case managers, and tailor drug regimens to accommodate specific patent needs. Analysis of claims data for pilot pharmacies found that a larger percentage of pilot pharmacy patients were classified as adherent to ART on the basis of pharmacy refill data, used fewer contraindicated regimens, and had fewer excess medication fills than patients with standard pharmacy care (135).

Recommendation 24: Directly administered ART is not recommended for routine clinical care settings (I A).

Although directly administered ART (DAART) has demonstrated benefit for some vulnerable populations (see Recommendations 28, 29, 31, and 37), well-controlled RCTs from well-resourced as well as resource-limited settings (including South Africa, Mozambique, Tanzania, Kenya, and Peru) have shown no benefit for various forms of DAART (clinic- or home-based; once-daily, twice-weekly, or once-weekly) among general populations (120–123, 127, 136–139) on adherence or biological markers. Thus, strong evidence supports not recommending DAART for routine HIV clinical care settings.

Special Populations

Treatment of a stigmatized and complex medical disorder with associated poor health outcomes is challenging in the best of circumstances for individuals with adequate social support, health literacy, stable housing, and economic resources. The additional challenges of incarceration, poverty, food and housing instability, and substance use and mental health disorders can further complicate adherence and require specialized interventions.

Pregnant Women

More than 50% of the 37.2 million adults with HIV in the world are women, and most are of childbearing age (140). Optimal ART adherence during pregnancy and the postpartum period remains a challenge globally (141–143). The evidence regarding ART adherence interventions during pregnancy comes predominantly from resource-limited settings and is focused only on short-term prevention of mother-to-child transmission (PMTCT) rather than on ART adherence throughout pregnancy and afterward.

Recommendation 25: Targeted PMTCT treatment (including HIV testing and serostatus awareness) improves adherence to ART for PMTCT and is recommended compared with an untargeted approach (treatment without HIV testing) in high-HIV-prevalence settings (III B).

A Zambian RCT designed to test universal (without HIV testing) versus targeted (for those testing positive for HIV) single-dose nevirapine for PMTCT found that although nevirapine uptake was somewhat higher in the universal-treatment group, adherence was lower in women who were illiterate and unaware of their HIV status (144). Health literacy education is recommended in these settings.

Recommendation 26: Labor ward–based PMTCT adherence services are recommended for women who are not receiving ART before labor (II B).

A cluster RCT in 12 public-sector delivery centers in Zambia found that offering HIV counseling and testing and ART adherence training in the labor ward was feasible and significantly improved nevirapine coverage and adherence (145).

Substance Use Disorders

Individuals with alcohol and other substance use disorders are at increased risk for poor retention in care, poor adherence, and virologic failure (146). Several adherence strategies not recommended for general clinic populations are effective among those with substance use disorders.

Recommendation 27: Offering buprenorphine or methadone to opioid-dependent patients is recommended (II A).

Among patients with opioid dependence, both methadone and buprenorphine maintenance treatments improve medication adherence (147–150), ART uptake (149, 150), and biomarkers (147, 151, 152). Integration of buprenorphine into HIV clinical care settings increased retention in care and ART prescription in 1 RCT, but ART adherence was unchanged because most patients were already adherent to ART at baseline (153).

Recommendation 28: DAART is recommended for individuals with substance use disorders (I B).

Four RCTs (154–157) and 3 prospective cohort studies (158–160) of DAART showed significant HIV-1 RNA or CD4 cell count improvements compared with self-administered therapy. Follow-up data from 1 trial, however, failed to demonstrate persistent effects on biological outcomes after DAART was discontinued (157).

Recommendation 29: Integration of DAART into methadone maintenance treatment for opioid-dependent patients is recommended (II B).

One RCT and several longitudinal cohort studies report improved HIV-1 RNA and adherence outcomes when DAART is integrated into methadone maintenance. Among 77 stable patients receiving methadone maintenance treatment, DAART compared with self-administered therapy significantly improved ART adherence and viral suppression over 24 weeks (161). Similarly, 3 prospective observational studies of DAART confirm improved CD4 counts and viral suppression over 12 (162, 163) and 24 (164) months compared with contemporaneous controls. Long-term durability of benefit has not been confirmed.

Mental Health

Mental health disorders may predispose individuals to acquiring HIV, are common among individuals living with HIV, and present serious challenges for HIV treatment adherence. A meta-analysis of 95 studies found a significant relationship between depression and ART nonadherence that was consistent across patients in resource-rich and resource-limited settings (165). Research has linked depressive symptoms to poor HIV care engagement and health outcomes, including impaired immunologic response and mortality.

Recommendation 30: Screening, management, and treatment for depression and other mental illnesses in combination with adherence counseling are recommended (II A).

Randomized, controlled trials indicate that cognitive-behavioral therapy for depression and psychosocial stress improves ART adherence when conducted in tandem with ART adherence counseling (115, 116, 166, 167). Combined mental health and ART adherence counseling interventions have shown significant reductions in depressive symptoms, improved ART adherence, and improved

treatment outcomes in RCTs (115, 166, 167). In contrast, an RCT of a stress management intervention with no ART adherence counseling reduced psychological distress but did not improve ART adherence or treatment outcomes (116). Evidence further indicates that pharmacologic treatment of depression is beneficial for ART adherence and treatment outcomes (168–170).

Incarceration

HIV and AIDS prevalence is higher among incarcerated populations in low-, middle-, and high-income countries (171). Globally, incarceration negatively affects continuity of care; development of trust; and, ultimately, optimal adherence (172). Incarceration provides a public health opportunity to provide ART to HIV-infected persons; however, barriers to ART delivery and adherence exist (173–175), and unintended ART interruptions sometimes occur after release (176). Key challenges to ART adherence among criminal justice populations include identifying successful strategies for medication distribution that preserve confidentiality and avoid stigma (177–180) and maintaining persistent ART use during transitions from correctional facilities to the community (181–183).

Recommendation 31: DAART is recommended during incarceration (III B) and may be considered upon release to the community (II C).

In a small, comparative observational study of 84 Italian prisoners, DAART in prison was associated with a higher proportion of patients with viral suppression to levels less than 400 copies/mL than was self-administered treatment (158). A small RCT compared ART adherence for DAART with that for self-administered treatment in 43 prisoners (184). Overall adherence was high at 92%, with a higher adherence rate in the DAART group than in the self-administered treatment group. Another RCT compared DAART given daily by community outreach workers versus self-administered treatment among 154 postrelease patients (155). Six months after release, DAART was superior to self-administered treatment in achieving viral suppression to levels less than 400 copies/mL and less than 50 copies/mL.

Homeless and Marginally Housed Individuals

In communities where stable housing is a societal norm, the homeless represent a special population with respect to ART adherence because of the multiple and often interrelated adherence challenges in this population (such as unstable housing, mental illness, substance use disorders, food insecurity, mistrust of the health care system, incarceration, and inconsistent provider–patient relationships). Homelessness itself often disrupts daily routines, including medication taking, and can make medication storage difficult. In highly resourced countries, many homeless people have concomitant mental illness or substance use disorders that are associated with incomplete adherence (185). Mistrust of the health system and inconsistent provider–patient relationships can contribute to delayed entry into care (186). The homeless have competing survival needs, including food access, which have been associated with incomplete adherence and poor viral suppression (187). Excellent adherence and reliable viral suppression can, however, be achieved despite these multiple barriers (61, 188).

Recommendation 32: Case management is recommended to mitigate multiple adherence barriers in the homeless (III B).

Case management includes referral to mental health and substance use treatment and housing (or housing vouchers), as appropriate, and can facilitate continuity when individuals are transitioning into and out of incarceration. However, referrals require the availability of infrastructure and resources, which differ dramatically among communities. One observational study in the United States showed that case management was associated with improved adherence and CD4 cell counts in a marginally housed population (189).

Recommendation 33: Pillbox organizers are recommended for persons who are homeless (II A).

Pillbox organizers offer a simple visual reminder of missed doses. In an observational study, their use was associated with improved adherence and higher probability of achieving an HIV RNA level less than 400 copies/mL in homeless people with multiple adherence barriers (63).

Children and Adolescents

HIV-infected young people between birth and 24 years of age are a developmentally diverse group, including those perinatally and behaviorally infected. For perinatally infected children, adherence to medications is determined largely by their caregivers, who often have many challenges, including HIV infection (190). Unique medication-related factors associated with nonadherence for children include difficulty swallowing pills, bad taste of medications, and difficulty timing medication administration around meals (191). Perinatally infected teens often experience deterioration in medication adherence during adolescence, as do their peers with other chronic diseases. Transition from pediatric to adult care settings may create additional adherence barriers because of disruptions in comprehensive services and insurance issues (192). Adolescents and young adults are less likely than their older counterparts to be retained in care and receive prescriptions for ART, and they have worse clinical outcomes (193, 194).

Recommendation 34: Intensive youth-focused case management is recommended for adolescents and young adults living with HIV to improve entry into and retention in care (IV B).

Among 174 HIV-infected youth, appointment attendance improved significantly after introduction of individualized case management focusing on increasing self-efficacy and developing group activities to improve support networks (195). In a cohort study of 61 young gay men who were newly diagnosed or in intermittent care, intensive case management, including initially weekly and then monthly meetings, also improved attendance to medical visits, and more intervention visits were associated with increased likelihood of ART prescription (196).

Recommendation 35: Pediatric- and adolescent-focused therapeutic support interventions using problem-solving approaches and addressing psychosocial context are recommended (III B).

A cohort study of multisystemic therapy intervention (a form of cognitive-behavioral therapy that considers multiple factors in a youth's environment that contribute to behavior change) in 19 perinatally infected youth with poor adherence showed no significant effect on caregiver-reported adherence but significantly improved virologic outcomes through 3 months after the intervention (197). Two other RCTs showed promising, if mixed, results (198, 199), whereas others demonstrated promising trends but had significant methodological limitations or did not achieve statistical significance (200, 201).

Recommendation 36: Pill-swallowing training is recommended and may be particularly helpful for younger patients (IV B).

Pill-swallowing training improved adherence in a small cohort study of 23 patients with identified pill-swallowing difficulties or who needed to switch from other formulations to pills (202).

Recommendation 37: DAART improves short-term treatment outcomes and may be considered in pediatric and adolescent patients (IV C).

Three cohort studies of DAART for perinatally infected children and adolescents living with HIV showed improvement in short-term immunologic outcomes (203-205). In the 2 studies where DAART was discontinued, however, this improvement was not sustained at follow-up (203, 204). In 1 study it did help to determine the cause of treatment failure in several patients. Another study in Cambodia showed improved immunologic outcomes for orphaned children at a cost of $60 for DAART per child per year (205). In some low-resource settings DAART may be a practical, cost-effective, long-term strategy to improve adherence for younger patients, but a plan for increasing disease self-management is needed as children transition to adolescence.

Recommendations for Future Research

Cross-cutting and broadly relevant recommendations for future research are presented here, and topic-specific recommendations are included in Table 2 (206-234). Long-term studies of intervention and postintervention outcomes on adherence and, especially, HIV biomarkers are needed. Formal cost-effectiveness analyses from a range of perspectives are needed to inform institution, government, and policy-level programmatic decisions. Similarly, rigorous implementation and dissemination studies are needed to guide best practices and

procedures for replication and scale-up of effective interventions.

View this table:
In this window In a new window

Table 2. Recommendations for Future Research

Further, there are emerging issues for which insufficient evidence exists to provide recommendations at this time. In settings where ART use has been long-standing and widespread, non-AIDS diseases now account for more deaths among persons with HIV than do AIDS-defining diseases (235). Cardiovascular disease is more common in persons with HIV than those without and accounts for a substantial proportion of serious non-AIDS events (236, 237), and although stopping ART increases this risk (238), certain HIV treatments are also associated with higher risk (239–241). HIV-infected persons have high rates of type 2 diabetes, dyslipidemia, and hypertension (242, 243). High rates of hepatitis C co-infection are seen in Asia, Eastern Europe, and the United States (244). Patients with comorbid conditions often struggle with multiple medications, increased pill burden, drug interactions and side effects, and complex medication scheduling. Comparative research is needed to evaluate intervention strategies to improve adherence and outcomes in the context of multiple comorbid conditions. Finally, new successes in biomedical HIV prevention (pre-exposure prophylaxis [245–247], microbicides [248]) have been tempered by problematic adherence, and comparative research of adherence strategies in these settings will be essential to maximize their benefit.

Conclusions

ART decreases morbidity and mortality, and early therapy is increasingly recommended for its effect on individual health (249–252), as well as for control of HIV transmission (251). Entry into and retention in medical care is a prerequisite for providing lifesaving treatments to persons with HIV. Few validated strategies exist, however, for improving this aspect of care, and the need for robust research is compelling. More data are available on interventions to improve adherence to ART in both general and special populations; however, much of the existing research lacks comparative rigor and correlation to changes in HIV-1 RNA, CD4 cell count, and clinical outcomes. To assure that implementation is feasible for evidence-based recommendations, it will be necessary to strengthen resources, including multidisciplinary linkages, dedicated to ART and care adherence. As the global economy contracts, the identification and implementation of evidence-based strategies to maximize the individual and societal benefit of HIV treatment will become increasingly important. With proper research and resources, the tools are at hand for substantially decreasing—and perhaps ending—the global HIV epidemic.

Appendix 1: Guideline Panel Members Web-Only

In addition to the authors, the following are members of the Guideline Panel and participated in discussions of the content or review of the manuscript: Magda Barini-García, MD (Health Resources and Services Administration, Rockville, Maryland); Vanessa Elharrar, MD, MPH (National Institute of Allergy and Infectious Diseases, Bethesda, Maryland); Tia Morton, RN, MS (National Institute of Allergy and Infectious Diseases, Bethesda, Maryland); Charles Holmes, MD, MPH (Office of the Global AIDS Coordinator, Washington, DC); Shoshana Kahana, PhD (National Institute on Drug Abuse, Bethesda, Maryland); Peter Kilmarx, MD (Centers for Disease Control and Prevention, Harare, Zimbabwe); Cynthia Lyles, PhD (Centers for Disease Control and Prevention, Atlanta, Georgia); Henry Masur, MD (National Institutes of Health, Bethesda, Maryland); Celso Ramos, MD, MSc (Federal University of Rio de Janeiro, Rio de Janeiro, Brazil); Evelyn Tomaszewski, MSW (National Association of Social Workers, Washington, DC); Marco Antônio de Ávila Vitória, MD (World Health Organization, Geneva, Switzerland)

Appendix 2: Methods for Guidelines Development Process Web-Only

Summary

A systematic search for studies on interventions to improve entry into and

retention in care and antiretroviral adherence and monitoring was performed. A total of 325 studies were identified for inclusion in the evidence base for the guidelines. Two reviewers independently extracted and coded data from each study using a standardized data extraction form. Differences were resolved by consensus with a third reviewer. Reviewers assessed bias in RCTs by using the Cochrane Risk of Bias Tool and in observational studies by using the Newcastle–Ottawa Quality Assessment Scale. Studies were then grouped by intervention type. Adherence monitoring articles were abstracted and graded using a modified Quality Assessment for Diagnostic Accuracy Studies (QUADAS) tool. Panel members drafted a recommendation statement based on the body of evidence for each monitoring method or intervention type. They then graded the overall quality of the body of evidence for each recommendation on the basis of its risk for bias, quantity, and consistency using methods adapted from the American College of Physicians guidelines and the Grades of Recommendation Assessment, Development and Evaluation (GRADE) System for Rating Clinical Guidelines processes. Finally, panel members graded the strength of each recommendation on the basis of not only the quality and quantity of the body of evidence but also the magnitude of benefit, risk and burdens, costs, and generalizability, recording scores on standardized forms.

Guideline Focus and Target Population

These guidelines focus on interventions to improve entry into and retention in care and ART adherence for people living with HIV as well as methods to monitor these critical processes. The target audience includes care providers, patients, policymakers, organizations, and health systems involved with implementing HIV care and treatment.

Guideline Development Process

IAPAC funded development of these guidelines through a grant from the National Institutes of Health Office of AIDS Research but did not have approval authority over specific recommendations or the completed manuscript. IAPAC convened a panel of 31 members, consisting of experts in clinical care, clinical trials, behavioral science, pharmacy, and guideline methods and patient representatives. From this panel, 20 members volunteered to be on the writing team. Each member completed a written conflict-of-interest disclosure. All potential conflicts of interest were declared, discussed, and resolved by the panel. The panel determined the issues to be covered on the basis of a systematic literature review and developed these guidelines using the Appraisal of Guidelines for Research and Evaluation (AGREE) II instrument for practice guideline assessment (253). This process was conducted in accordance with Institute of Medicine Standards for Developing Trustworthy Clinical Practice Guidelines (254).

Literature Search

Interventions

The following were the interventions of interest: 1) any intervention for improving entry into and retention in care for people with HIV and 2) any intervention for improving adherence to ART. The objective of the literature search was to identify optimal interventions for improving entry into and retention in care and ART adherence to assist with developing guidelines.

To be included, the studies had to meet the following criteria: 1) evaluated an intervention intended to improve entry into and retention in care or ART adherence; 2) had an RCT or observational design that included comparators (if sufficient RCT-level evidence for an intervention was available, then observational studies were not considered in the body of evidence); and 3) reported 1 or more relevant outcomes assessed after the intervention was completed (biological or behavioral). The following were exclusion criteria: observational studies without comparators, letters, and editorials.

The study participants were children, adolescents, and adults with HIV. The included studies had the following biological and behavioral outcomes of interest: mortality, morbidity, virologic failure, immunologic response, development of HIV resistance, adherence behaviors (as measured by self-report, pill count, electronic drug monitor, pharmacy refill, and other methods), entry into and retention in care behaviors (such as clinic attendance and loss to follow-up), and adverse events.

Identification of Studies

The search largely consisted of a systematic search performed on the Centers for Disease Control and Prevention (CDC) Prevention Research Synthesis Project Database (78), with some specific adaptations for this project. Since 1996, the CDC Prevention Research Synthesis Project has been conducting ongoing systematic searches of the HIV prevention intervention literature, focusing on HIV risk reduction and medication adherence, to establish a cumulative, comprehensive research database for conducting regular systematic reviews. This database has been developed and updated by annual automated electronic database searches, quarterly hand searches of journals, and daily ad hoc searches of the published literature from 1988 to the present. The database created for these guidelines began with pertinent evidence from 1996 and included the most recent annual electronic search of the CDC database (February 2011), hand searching through March 2011, and additional ad hoc searching through November 2011. The searches were performed with no limits for language, setting, or age. The evidence base for these guidelines was restricted to RCTs and observational studies with comparators that had at least 1 measured biological or behavioral end point.

The panel searched the following journal databases: MEDLINE, EMBASE, PsycINFO, CINAHL, and AIDSLINE (before retirement in 2000). The following conference databases were searched from July 2009 to June 2011: Conference on Retroviruses and Opportunistic Infections; IAPAC Adherence Conference; International AIDS Conference; and the International AIDS Society Conference on HIV Pathogenesis, Treatment, and Prevention.

The clinical trials databases searched were CENTRAL (Cochrane Central Register of Controlled Trials), ClinicalTrials.gov (http://clinicaltrials.gov), Current Controlled Trials (www.controlled-trials.com), and Pan-African Clinical Trials Registry (www.pactr.org)

Sixteen journals that typically contribute the most relevant citations were also hand-searched for medication adherence and retention studies. We contacted individual researchers and members of relevant organizations working in the field, including panel members, to identify studies and completed or ongoing trials.

We checked the reference lists of all studies identified by the preceding methods and examined the bibliographies of any relevant systematic reviews, meta-analyses, or current guidelines we identified during the search process.

Monitoring

In addition to producing evidence-based guidelines for entry into care, retention in care, and ART adherence interventions, the panel also targeted the identification of strategies and methods for adherence monitoring or assessment, which required separate methods to search, grade, and synthesize evidence. The resulting list of articles was reviewed to include only studies that compared an adherence measurement method with a biological outcome.

Study Inclusion Criteria

The studies must have included one or more methods of adherence measurement and compared clinical or biological outcomes (as listed above).

Search Strategy

Key word searches (*monitoring*, *measure*) were performed on the original database to identify articles specific to HIV monitoring. One panel member reviewed citations found from key word searches to determine whether they met inclusion criteria. In addition, all articles initially identified as potential intervention articles were screened to see whether they were also of relevance to HIV monitoring. Supplementary searching for relevant articles was also performed as described above.

Data Abstraction and Grading

Articles identified for inclusion were abstracted (for example, study title, date, measures used, and estimates of association) and graded by using a modified Quality Assessment for Diagnostic Accuracy Studies (QUADAS) tool (255).

Evidence Synthesis Strategy

Data on measures from the studies were compiled into summary tables listing ranges of association, quality ratings, and other factors. Quality of the body of evidence and strength of recommendation were then rated according to the methods detailed below.

Overall Grading Scale for Recommendations

We used a grading scale based on the GRADE System for rating Clinical Guidelines and the American College of Physicians methods for development of clinical practice guidelines (256, 257). This pragmatic and systematic approach allowed for transparent, intuitive, and efficient production of these guidelines. Each guideline recommendation has a grade for quality of the body of evidence and a grade for strength of recommendation. Table 1 summarizes the quality and strength scales used. The following sections detail how these 2 grades were derived.

Individual Study Evaluation Methods

Data Extraction and Management

After the initial search and article screening, 2 reviewers independently coded and entered information from the included studies onto a standardized data extraction form; differences were resolved by consensus with a third reviewer. Extracted information included the following: study details: citation, start and end dates, location, study design; participant details: study population, ages, population size; interventions details: duration, nature, and intensity of the intervention; and outcome details: mortality, clinical disease progression (AIDS and non–AIDS events), treatment response (CD4 recovery and viral load response), adherence, retention, loss to follow-up, resistance, and adverse events. These data were then summarized in a table.

Assessment of Risk for Bias in Included Studies

The 2 reviewers then assessed each of the individual studies for risk for bias; differences were resolved by consensus with a third reviewer. The results were summarized in tables. The Cochrane Risk of Bias Tool was used for RCTs (258, 259). The Cochrane tool assesses risk for bias in individual studies across 6 domains with 3 potential responses for each domain: yes, no, or unclear.

Reviewers assessed observational studies for risk for bias using the Newcastle-Ottawa Quality Assessment Scale (260). This validated scale assesses quality of cohort and case-control studies in 3 main areas by using a "star rating system" ranging from 0 to 9.

Evaluating the Body of Evidence

After each individual study was evaluated, panel members proposed draft recommendation statements based on the evidence gathered and concurrently grouped individual studies together to form the body of evidence for each specific recommendation. The body of evidence for each recommendation was then evaluated according to the factors listed in Appendix Table 3.

View this table:
In this window In a new window

Appendix Table 3. Process for Evaluating the Body of Evidence
Web-Only

All of these factors were considered in decreasing or increasing the quality of the body of evidence and were framed around the standards and interpretation listed in Table 1. Panel members then decided on a grade and, using standardized forms, detailed instances if and why they increased or decreased the quality of the body of evidence, specifically referencing the factor(s) involved.

Moving From Evidence to Recommendation

After recommendation statements had been proposed and the corresponding body of evidence for each recommendation graded, the factors listed in Appendix Table

4 were considered to determine the strength of the recommendation.

View this table:
In this window In a new window

Appendix Table 4. Factors Considered in Determining the Strength of the Recommendation Web-Only

Each of the factors was explicitly considered. Panel members then decided on a strength of recommendation and, using standardized forms, detailed how they came to this decision, specifically referencing each factor as appropriate. Note that quality of the body of evidence was only 1 factor considered in the strength of recommendation.

Comments and Modification

An international group of content experts reviewed a draft of these guidelines, and relevant modifications were made to the manuscript. Guideline panel members will review these guidelines periodically and make updates as new evidence becomes available.

Article and Author Information

Acknowledgment: The authors thank the following individuals, who were instrumental to the development of these guidelines: José M. Zuniga, PhD, MPH, and Angela Knudson (IAPAC; guideline conception, administrative support); Laura Bernard, MPH, and Kathryn Muessig, PhD (systematic review and evidence grading); Jennifer Johnsen, MD (systematic review); Anne McDonough, MPH (editing); and Adele Webb, PhD, RN (Chamberlain College of Nursing, Cleveland, Ohio; contribution to discussions of children and adolescents), and Morgan Dirlam (Georgetown University; contribution to future recommendations, concomitant medical conditions). The authors also thank the external reviewers, including: Jane Anderson, PhD, and John Walsh, MBBS (British HIV Association); Carl Stein, MHS, PA-C, (Physician Assistant AIDS Network); Donna E Sweet, MD (American Academy of HIV Medicine); Ann Deschamps, RN, MSN (European HIV Nurses Network); Robert T. Carroll, PhD, MN, RN (Association of Nurses in AIDS Care); and Donna Futterman, MD, and Brian Gazzard, MD, MA (individual reviewers). The HIV Medicine Association also provided input into these guidelines.

Grant Support: Development of the guidelines was jointly sponsored by IAPAC and the U.S. National Institutes of Health's Office of AIDS Research.

Potential Conflicts of Interest: Disclosures from authors and panel members can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M12-0061.

Requests for Single Reprints: International Association of Physicians in AIDS Care, 1640 Rhode Island Avenue NW, Suite 200, Washington, DC 20036; e-mail, iapac@iapac.org.

Current Author Addresses: Dr. Thompson: AIDS Research Consortium of Atlanta, 131 Ponce de Leon Avenue, Suite 130, Atlanta, GA 30308.

Dr. Mugavero: 1530 3rd Avenue South, Community Care Building 142, Birmingham, AL 35294-2050.

Dr. Amico: 5598 Mounting Road, Brighton, MI 48116.

Dr. Cargill: Office of AIDS Research, National Institutes of Health, 5635 Fishers Lane, Bethesda, MD 20892.

Dr. Chang: Johns Hopkins Center for Global Health, 1503 East Jefferson Street, Room 116, Baltimore, MD 21205.

Dr. Gross: Perelman School of Medicine, University of Pennsylvania, 804 Blockley Hall, 423 Guardian Drive, Pennsylvania, PA 19104-6021.

Dr. Orrell: University of Cape Town, Anzio Road, Observatory 7705, Cape

Town, South Africa.

Dr. Altice: Yale University AIDS Program, 135 College Street, Suite 323, New Haven, CT, 06510.

Dr. Bangsberg: MGH Center for Global Health, 104 Mt. Auburn Street, 3rd Floor, Cambridge, MA 02138.

Dr. Bartlett: Johns Hopkins School of Medicine, 615 North Wolfe Street, 1830 Building Room 437, Baltimore, MD 21205.

Dr. Beckwith: The Warren Alpert Medical School of Brown University, The Miriam Hospital, 164 Summit Avenue, Providence, RI 02906.

Dr. Dowshen: The Children's Hospital of Philadelphia, 34th Street and Civic Center Boulevard, 11 NW, Suite 10, Room 24, Philadelphia, PA 19104.

Dr. Gordon: National Institute of Mental Health, 6001 Executive Boulevard, Room 6212, Bethesda, MD 20892-9619.

Mr. Horn: AIDSmeds.com, 462 Seventh Avenue, 19th Floor, New York, NY 10018-7424.

Dr. Kumar: Georgetown University School of Medicine, 5PHC Building, 3800 Reservoir Road NW, Washington, DC 20007.

Dr. Scott: Western University of Health Sciences, College of Pharmacy, 309 East 2nd Street, Pomona, CA.

Dr. Stirratt: National Institute of Mental Health, 6001 Executive Boulevard, MSC-9619, Room 6199, Bethesda, MD 20892.

Dr. Remien: Columbia University, 1051 Riverside Drive, Unit 15, New York, NY 10032.

Dr. Simoni: Department of Psychology, University of Washington, 3909 Stevens Way NE, Campus Box 351525, Seattle, WA 98195-1525.

Dr. Nachega: Johns Hopkins Bloomberg School of Public of Health, 615 North Wolfe Street, Room E5527, Baltimore, MD 21205.

Author Contributions: Conception and design: M.A. Thompson, M.J. Mugavero, K.R. Amico, V.A. Cargill, L.W. Chang, R. Gross, C. Orrell, F.L. Altice, D.R. Bangsberg, J.G. Bartlett, C.G. Beckwith, N. Dowshen, C.M. Gordon, T. Horn, P. Kumar, J.D. Scott, M.J. Stirratt, R.H. Remien, J.M. Simoni, J.B. Nachega.

Analysis and interpretation of the data: M.A. Thompson, M.J. Mugavero, K.R. Amico, V.A. Cargill, L.W. Chang, R. Gross, C. Orrell, F.L. Altice, D.R. Bangsberg, J.G. Bartlett, C.G. Beckwith, N. Dowshen, C.M. Gordon, T. Horn, P. Kumar, J.D. Scott, M.J. Stirratt, R.H. Remien, J.M. Simoni, J.B. Nachega.

Drafting of the article: M.A. Thompson, M.J. Mugavero, K.R. Amico, V.A. Cargill, L.W. Chang, R. Gross, C. Orrell, F.A. Altice, D.R. Bangsberg, J.G. Bartlett, C.G. Beckwith, N. Dowshen, C.M. Gordon, T. Horn, P. Kumar, J.D. Scott, M.J. Stirratt, R.H. Remien, J.M. Simoni, J.B. Nachega.

Critical revision of the article for important intellectual content: M.A. Thompson, M.J. Mugavero, K.R. Amico, V.A. Cargill, L.W. Chang, R. Gross, C. Orrell, F.L. Altice, D.R. Bangsberg, J.G. Bartlett, C.G. Beckwith, N. Dowshen, C.M. Gordon, T. Horn, P. Kumar, J.D. Scott, M.J. Stirratt, R.H. Remien, J.M. Simoni, J.B. Nachega.

Final approval of the article: M.A. Thompson, M.J. Mugavero, K.R. Amico, V.A. Cargill, L.W. Chang, R. Gross, C. Orrell, F.L. Altice, D.R. Bangsberg, J.G. Bartlett, C.G. Beckwith, N. Dowshen, C.M. Gordon, T. Horn, P. Kumar, J.D. Scott, M.J. Stirratt, R.H. Remien, J.M. Simoni, J.B. Nachega.

Statistical expertise: L.W. Chang, F.L. Altice.

Obtaining of funding: V.A. Cargill.

Administrative, technical, or logistic support: M.A. Thompson, M.J. Mugavero, V.A. Cargill.

Collection and assembly of data: M.A. Thompson, M.J. Mugavero, K.R. Amico, V.A. Cargill, L.W. Chang, R. Gross, C. Orrell, F.A. Altice, D.R. Bangsberg, J.G. Bartlett, C.G. Beckwith, N. Dowshen, C.M. Gordon, T. Horn, P. Kumar, J.D. Scott, M.J. Stirratt, R.H. Remien, J.M. Simoni, J.B. Nachega.

References

1.**Centers for Disease Control and Prevention.** HIV Surveillance Report, 2009; vol. 21. February 2011. Accessed www.cdc.gov/hiv/surveillance/resources/reports/2009report on 21 December 2011

2.**UNAIDS.** UNAIDS Data Table 2011. 2 December 2011. Geneva, Switzerland; Joint United Nations Program on HIV/AIDS. Accessed at UNAIDS at www.unaids.org/en/media/unaids/contentassets/documents/unaidspublication/2011/JC2225_UNAIDS_datatables_en.pdf on 19 December 2011

3.**Bangsberg DR, Perry S, Charlebois ED, Clark RA, Roberston M, Zolopa AR, et al.** Non-adherence to highly active antiretroviral therapy predicts progression to AIDS. AIDS. 2001;15:1181-3. [PMID: 11416722]

4.**Hogg RS, Heath K, Bangsberg D, Yip B, Press N, O'Shaughnessy MV, et al.** Intermittent use of triple-combination therapy is predictive of mortality at baseline and after 1 year of follow-up. AIDS. 2002;16:1051-8. [PMID: 11953472]

5.**Nachega JB, Hislop M, Dowdy DW, Chaisson RE, Regensberg L, Maartens G.** Adherence to nonnucleoside reverse transcriptase inhibitor-based HIV therapy and virologic outcomes. Ann Intern Med. 2007;146:564-73. [PMID: 17438315]

6.**Paterson DL, Swindells S, Mohr J, Brester M, Vergis EN, Squier C, et al.** Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. Ann Intern Med. 2000;133:21-30. [PMID: 10877736]

7.**Centers for Disease Control and Prevention (CDC).** Vital signs: HIV prevention through care and treatment—United States. MMWR Morb Mortal Wkly Rep. 2011;60:1618-23. [PMID: 22129997]

8.**Marks G, Gardner LI, Craw J, Crepaz N.** Entry and retention in medical care among HIV-diagnosed persons: a meta-analysis. AIDS. 2010;24:2665-78. [PMID: 20841990]

9.**Rosen S, Fox MP, Gill CJ.** Patient retention in antiretroviral therapy programs in sub-Saharan Africa: a systematic review. PLoS Med. 2007;4:e298. [PMID: 17941716]

10.**Rosen S, Fox MP.** Retention in HIV care between testing and treatment in sub-Saharan Africa: a systematic review. PLoS Med. 2011;8:e1001056. [PMID: 21811403]

11.**Harrigan PR, Hogg RS, Dong WW, Yip B, Wynhoven B, Woodward J, et al.** Predictors of HIV drug-resistance mutations in a large antiretroviral-naive cohort initiating triple antiretroviral therapy. J Infect Dis. 2005;191:339-47. [PMID: 15633092]

12.**Ortego C, Huedo-Medina TB, Llorca J, Sevilla L, Santos P, Rodríguez E, et al.** Adherence to highly active antiretroviral therapy (HAART): a meta-analysis. AIDS Behav. 2011;15:1381-96. [PMID: 21468660]

13.**Giordano TP, Gifford AL, White AC Jr, Suarez-Almazor ME, Rabeneck L, Hartman C, et al.** Retention in care: a challenge to survival with HIV infection. Clin Infect Dis. 2007;44:1493-9. [PMID: 17479948]

14.**Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, et al; HPTN 052 Study Team.** Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med. 2011;365:493-505. [PMID: 21767103]

15.**Giordano TP, White AC Jr, Sajja P, Graviss EA, Arduino RC, Adu-Oppong A, et al.** Factors associated with the use of highly active antiretroviral therapy in patients newly entering care in an urban clinic. J Acquir Immune Defic Syndr. 2003;32:399-405. [PMID: 12640198]

16.**Lucas GM, Chaisson RE, Moore RD.** Highly active antiretroviral therapy in a large urban clinic: risk factors for virologic failure and adverse drug reactions. Ann Intern Med. 1999;131:81-7. [PMID: 10419445]

17.**Metsch LR, Pereyra M, Messinger S, Del Rio C, Strathdee SA, Anderson-Mahoney P, et al; Antiretroviral Treatment and Access Study (ARTAS) Study Group.** HIV transmission risk behaviors among HIV-infected persons who are successfully linked to care. Clin Infect Dis. 2008;47:577-84. [PMID: 18624629]

18.**Montaner JS, Lima VD, Barrios R, Yip B, Wood E, Kerr T, et al.** Association of highly active antiretroviral therapy coverage, population viral load, and yearly new

HIV diagnoses in British Columbia, Canada: a population-based study. Lancet. 2010;376:532-9. [PMID: 20638713]

19.**Walensky RP, Paltiel AD, Losina E, Morris BL, Scott CA, Rhode ER, et al; CEPAC Investigators.** Test and treat DC: forecasting the impact of a comprehensive HIV strategy in Washington DC. Clin Infect Dis. 2010;51:392-400. [PMID: 20617921]

20.**Tripathi A, Youmans E, Gibson JJ, Duffus WA.** The impact of retention in early HIV medical care on viro-immunological parameters and survival: a statewide study. AIDS Res Hum Retroviruses. 2011;27:751-8. [PMID: 21142607]

21.**Zetola NM, Bernstein K, Ahrens K, Marcus JL, Philip S, Nieri G, et al.** Using surveillance data to monitor entry into care of newly diagnosed HIV-infected persons: San Francisco, 2006-2007. BMC Public Health. 2009;9:17. [PMID: 19144168]

22.**Mugavero MJ, Lin HY, Willig JH, Westfall AO, Ulett KB, Routman JS, et al.** Missed visits and mortality among patients establishing initial outpatient HIV treatment. Clin Infect Dis. 2009;48:248-56. [PMID: 19072715]

23.**Mugavero MJ, Davila JA, Nevin CR, Giordano TP.** From access to engagement: measuring retention in outpatient HIV clinical care. AIDS Patient Care STDS. 2010;24:607-13. [PMID: 20858055]

24.**Gardner LI, Metsch LR, Anderson-Mahoney P, Loughlin AM, del Rio C, Strathdee S, et al; Antiretroviral Treatment and Access Study Study Group.** Efficacy of a brief case management intervention to link recently diagnosed HIV-infected persons to care. AIDS. 2005;19:423-31. [PMID: 15750396]

25.**Naar-King S, Bradford J, Coleman S, Green-Jones M, Cabral H, Tobias C.** Retention in care of persons newly diagnosed with HIV: outcomes of the Outreach Initiative. AIDS Patient Care STDS. 2007;21 Suppl 1:S40-8. [PMID: 17563289]

26.**Bradford JB, Coleman S, Cunningham W.** HIV System Navigation: an emerging model to improve HIV care access. AIDS Patient Care STDS. 2007;21 Suppl 1:S49-58. [PMID: 17563290]

27.**Deschamps AE, De Geest S, Vandamme AM, Bobbaers H, Peetermans WE, Van Wijngaerden E.** Diagnostic value of different adherence measures using electronic monitoring and virologic failure as reference standards. AIDS Patient Care STDS. 2008;22:735-43. [PMID: 18754705]

28.**Miller LG, Hays RD.** Measuring adherence to antiretroviral medications in clinical trials. HIV Clin Trials. 2000;1:36-46. [PMID: 11590488]

29.**Gross R, Yip B, Lo Re V 3rd, Wood E, Alexander CS, Harrigan PR, et al.** A simple, dynamic measure of antiretroviral therapy adherence predicts failure to maintain HIV-1 suppression. J Infect Dis. 2006;194:1108-14. [PMID: 16991085]

30.**Grossberg R, Zhang Y, Gross R.** A time-to-prescription-refill measure of antiretroviral adherence predicted changes in viral load in HIV. J Clin Epidemiol. 2004;57:1107-10. [PMID: 15528063]

31.**Bisson GP, Rowh A, Weinstein R, Gaolathe T, Frank I, Gross R.** Antiretroviral failure despite high levels of adherence: discordant adherence-response relationship in Botswana. J Acquir Immune Defic Syndr. 2008;49:107-10. [PMID: 18667926]

32.**Nachega JB, Hislop M, Dowdy DW, Lo M, Omer SB, Regensberg L, et al.** Adherence to highly active antiretroviral therapy assessed by pharmacy claims predicts survival in HIV-infected South African adults. J Acquir Immune Defic Syndr. 2006;43:78-84. [PMID: 16878045]

33.**Graham J, Bennett IM, Holmes WC, Gross R.** Medication beliefs as mediators of the health literacy-antiretroviral adherence relationship in HIV-infected individuals. AIDS Behav. 2007;11:385-92. [PMID: 17053858]

34.**Duran S, Peytavin G, Carrieri P, Raffi F, Ecobichon JL, Pereira E, et al; Antiprotease Cohort (APROCO) study group.** The detection of non-adherence by self-administered questionnaires can be optimized by protease inhibitor plasma concentration determination. AIDS. 2003;17:1096-9. [PMID: 12700466]

35.**Duong M, Piroth L, Peytavin G, Forte F, Kohli E, Grappin M, et al.** Value of patient self-report and plasma human immunodeficiency virus protease inhibitor level as markers of adherence to antiretroviral therapy: relationship to virologic response. Clin Infect Dis. 2001;33:386-92. [PMID: 11438909]

36.**Yasuda JM, Miller C, Currier JS, Forthal DN, Kemper CA, Beall GN, et al; California Collaborative Treatment Group.** The correlation between plasma concentrations of protease inhibitors, medication adherence and virological outcome in HIV-infected patients. Antivir Ther. 2004;9:753-61. [PMID: 15535413]

37.**Cuevas Gonzalez MJ, Valin LO, Perez-Simon MD, Mostaza Fernandez JL, Alcoba Leza M, Sanchez VM.** A prospective study of adherence and virologic failure in HIV-infected patients: role of a single determination of plasma levels of antiretroviral medications. J Int Assoc Physicians AIDS Care (Chic). 2007;6:245-50. [PMID: 17873246]

38.**Fletcher CV, Testa MA, Brundage RC, Chesney MA, Haubrich R, Acosta EP, et al.** Four measures of antiretroviral medication adherence and virologic response in AIDS clinical trials group study 359. J Acquir Immune Defic Syndr. 2005;40:301-6. [PMID: 16249704]

39.**Bangsberg DR, Hecht FM, Charlebois ED, Zolopa AR, Holodniy M, Sheiner L, et al.** Adherence to protease inhibitors, HIV-1 viral load, and development of drug resistance in an indigent population. AIDS. 2000;14:357-66. [PMID: 10770537]

40.**Descamps D, Flandre P, Calvez V, Peytavin G, Meiffredy V, Collin G, et al.** Mechanisms of virologic failure in previously untreated HIV-infected patients from a trial of induction-maintenance therapy. Trilège (Agence Nationale de Recherches sur le SIDA 072) Study Team). JAMA. 2000;283:205-11. [PMID: 10634336]

41.**Ferradini L, Jeannin A, Pinoges L, Izopet J, Odhiambo D, Mankhambo L, et al.** Scaling up of highly active antiretroviral therapy in a rural district of Malawi: an effectiveness assessment. Lancet. 2006;367:1335-42. [PMID: 16631912]

42.**Bangsberg DR, Charlebois ED, Grant RM, Holodniy M, Deeks SG, Perry S, et al.** High levels of adherence do not prevent accumulation of HIV drug resistance mutations. AIDS. 2003;17:1925-32. [PMID: 12960825]

43.**Arnsten JH, Demas PA, Farzadegan H, Grant RW, Gourevitch MN, Chang CJ, et al.** Antiretroviral therapy adherence and viral suppression in HIV-infected drug users: comparison of self-report and electronic monitoring. Clin Infect Dis. 2001;33:1417-23. [PMID: 11550118]

44.**Bangsberg DR.** Less than 95% adherence to nonnucleoside reverse-transcriptase inhibitor therapy can lead to viral suppression. Clin Infect Dis. 2006;43:939-41. [PMID: 16941380]

45.**Gross R, Bilker WB, Friedman HM, Strom BL.** Effect of adherence to newly initiated antiretroviral therapy on plasma viral load. AIDS. 2001;15:2109-17. [PMID: 11684930]

46.**Oyugi JH, Byakika-Tusiime J, Charlebois ED, Kityo C, Mugerwa R, Mugyenyi P, et al.** Multiple validated measures of adherence indicate high levels of adherence to generic HIV antiretroviral therapy in a resource-limited setting. J Acquir Immune Defic Syndr. 2004;36:1100-2. [PMID: 15247564]

47.**Parienti JJ, Das-Douglas M, Massari V, Guzman D, Deeks SG, Verdon R, et al.** Not all missed doses are the same: sustained NNRTI treatment interruptions predict HIV rebound at low-to-moderate adherence levels. PLoS One. 2008;3:e2783. [PMID: 18665246]

48.**Farley J, Hines S, Musk A, Ferrus S, Tepper V.** Assessment of adherence to antiviral therapy in HIV-infected children using the Medication Event Monitoring System, pharmacy refill, provider assessment, caregiver self-report, and appointment keeping. J Acquir Immune Defic Syndr. 2003;33:211-8. [PMID: 12794557]

49.**Muller AD, Bode S, Myer L, Roux P, von Steinbuechel N.** Electronic measurement of adherence to pediatric antiretroviral therapy in South Africa. Pediatr Infect Dis. 2008;27(3):257-62. [PMID: 18277933]

50.**Hugen PW, Langebeek N, Burger DM, Zomer B, van Leusen R, Schuurman R, et al.** Assessment of adherence to HIV protease inhibitors: comparison and combination of various methods, including MEMS (electronic monitoring), patient and nurse report, and therapeutic drug monitoring. J Acquir Immune Defic Syndr. 2002;30:324-34. [PMID: 12131570]

51.**Walsh JC, Mandalia S, Gazzard BG.** Responses to a 1 month self-report on adherence to antiretroviral therapy are consistent with electronic data and virological treatment outcome. AIDS. 2002;16:269-77. [PMID: 11807312]

52.**Bae JW, Guyer W, Grimm K, Altice FL.** Medication persistence in the treatment of HIV infection: a review of the literature and implications for future clinical care and research [Editorial]. AIDS. 2011;25:279-90. [PMID: 21239892]

53.**Flexner C, Tierney C, Gross R, Andrade A, Lalama C, Eshleman SH, et al; ACTG A5073 Study Team.** Comparison of once-daily versus twice-daily combination antiretroviral therapy in treatment-naive patients: results of AIDS clinical trials group (ACTG) A5073, a 48-week randomized controlled trial. Clin Infect Dis. 2010;50:1041-52. [PMID: 20192725]

54.**Molina JM, Podsadecki TJ, Johnson MA, Wilkin A, Domingo P, Myers R, et al.** A lopinavir/ritonavir-based once-daily regimen results in better compliance and is

non-inferior to a twice-daily regimen through 96 weeks. AIDS Res Hum Retroviruses. 2007;23:1505-14. [PMID: 18160008]

55.**Boyle BA, Jayaweera D, Witt MD, Grimm K, Maa JF, Seekins DW.** Randomization to once-daily stavudine extended release/lamivudine/efavirenz versus a more frequent regimen improves adherence while maintaining viral suppression. HIV Clin Trials. 2008;9:164-76. [PMID: 18547903]

56.**Dejesus E, Young B, Morales-Ramirez JO, Sloan L, Ward DJ, Flaherty JF, et al; AI266073 Study Group.** Simplification of antiretroviral therapy to a single-tablet regimen consisting of efavirenz, emtricitabine, and tenofovir disoproxil fumarate versus unmodified antiretroviral therapy in virologically suppressed HIV-1-infected patients. J Acquir Immune Defic Syndr. 2009;51:163-74. [PMID: 19357529]

57.**Maitland D, Jackson A, Osorio J, Mandalia S, Gazzard BG, Moyle GJ; Epivir-Ziagen (EZ) Switch Study Team.** Switching from twice-daily abacavir and lamivudine to the once-daily fixed-dose combination tablet of abacavir and lamivudine improves patient adherence and satisfaction with therapy. HIV Med. 2008;9:667-72. [PMID: 18631255]

58.**Portsmouth SD, Osorio J, McCormick K, Gazzard BG, Moyle GJ.** Better maintained adherence on switching from twice-daily to once-daily therapy for HIV: a 24-week randomized trial of treatment simplification using stavudine prolonged-release capsules. HIV Med. 2005;6:185-90. [PMID: 15876285]

59.**Parienti JJ, Massari V, Reliquet V, Chaillot F, Le Moal G, Arvieux C, et al; POSOVIR Study Group.** Effect of twice-daily nevirapine on adherence in HIV-1-infected patients: a randomized controlled study. AIDS. 2007;21:2217-22. [PMID: 18090049]

60.**Eron JJ, Yetzer ES, Ruane PJ, Becker S, Sawyer GA, Fisher RL, et al.** Efficacy, safety, and adherence with a twice-daily combination lamivudine/zidovudine tablet formulation, plus a protease inhibitor, in HIV infection. AIDS. 2000;14:671-81. [PMID: 10807190]

61.**Bangsberg DR, Ragland K, Monk A, Deeks SG.** A single tablet regimen is associated with higher adherence and viral suppression than multiple tablet regimens in HIV+ homeless and marginally housed people. AIDS. 2010;24:2835-40. [PMID: 21045636]

62.**Gardner EM, Sharma S, Peng G, Hullsiek KH, Burman WJ, Macarthur RD, et al.** Differential adherence to combination antiretroviral therapy is associated with virological failure with resistance. AIDS. 2008;22:75-82. [PMID: 18090394]

63.**Petersen ML, Wang Y, van der Laan MJ, Guzman D, Riley E, Bangsberg DR.** Pillbox organizers are associated with improved adherence to HIV antiretroviral therapy and viral suppression: a marginal structural model analysis. Clin Infect Dis. 2007;45:908-15. [PMID: 17806060]

64.**Levy RW, Rayner CR, Fairley CK, Kong DC, Mijch A, Costello K, et al; Melbourne Adherence Group.** Multidisciplinary HIV adherence intervention: a randomized study. AIDS Patient Care STDS. 2004;18:728-35. [PMID: 15659884]

65.**Safren SA, Hendriksen ES, Desousa N, Boswell SL, Mayer KH.** Use of an on-line pager system to increase adherence to antiretroviral medications. AIDS Care. 2003;15:787-93. [PMID: 14617500]

66.**Hardy H, Farmer E, Kumar V, Myung D, Rybin D, Drainoni ML, et al.** Assess and Remind (ARemind): A personalized cell phone reminder system is superior to a beeper to enhance adherence to antiretroviral therapy. Presented at the 4th International Conference on HIV Treatment Adherence, Miami, Florida, 5-7 April 2009|. Abstract No. 289.

67.**Pop-Eleches C, Thirumurthy H, Habyarimana JP, Zivin JG, Goldstein MP, de Walque D, et al.** Mobile phone technologies improve adherence to antiretroviral treatment in a resource-limited setting: a randomized controlled trial of text message reminders. AIDS. 2011;25:825-34. [PMID: 21252632]

68.**Uzma Q, Emmanuel F, Athar U, Zaman S.** An assessment of efficacy of interventions for improving adherence to antiretroviral therapy for HIV/AIDS cases in Islamabad, Pakistan. Presented at the 4th International Conference on HIV Treatment Adherence, Miami, Florida, 5-7 April 2009, Miami. Oral Abstract no. 172.

69.**Lester RT, Ritvo P, Mills EJ, Kariri A, Karanja S, Chung MH, et al.** Effects of a mobile phone short message service on antiretroviral treatment adherence in Kenya (WelTel Kenya1): a randomised trial. Lancet. 2010;376:1838-45. [PMID: 21071074]

70.**McPherson-Baker S, Malow RM, Penedo F, Jones DL, Schneiderman N, Klimas NG.** Enhancing adherence to combination antiretroviral therapy in non-adherent HIV-positive men. AIDS Care. 2000;12:399-404. [PMID: 11091772]

71.**Milam J, Richardson JL, McCutchan A, Stoyanoff S, Weiss J, Kemper C, et al.**

Effect of a brief antiretroviral adherence intervention delivered by HIV care providers. J Acquir Immune Defic Syndr. 2005;40:356–63. [PMID: 16249712]

72.**Mannheimer SB, Morse E, Matts JP, Andrews L, Child C, Schmetter B, et al; Terry Beirn Community Programs for Clinical Research on AIDS.** Sustained benefit from a long-term antiretroviral adherence intervention. Results of a large randomized clinical trial. J Acquir Immune Defic Syndr. 2006;43 Suppl 1:S41–7. [PMID: 17091022]

73.**Simoni JM, Chen WT, Huh D, Fredriksen-Goldsen KI, Pearson C, Zhao H, et al.** A preliminary randomized controlled trial of a nurse-delivered medication adherence intervention among HIV-positive outpatients initiating antiretroviral therapy in Beijing, China. AIDS Behav. 2011;15:919–29. [PMID: 20957423]

74.**de Bruin M, Hospers HJ, van den Borne HW, Kok G, Prins JM.** Theory- and evidence-based intervention to improve adherence to antiretroviral therapy among HIV-infected patients in the Netherlands: a pilot study. AIDS Patient Care STDS. 2005;19:384–94. [PMID: 15989434]

75.**de Bruin M, Hospers HJ, van Breukelen GJ, Kok G, Koevoets WM, Prins JM.** Electronic monitoring-based counseling to enhance adherence among HIV-infected patients: a randomized controlled trial. Health Psychol. 2010;29:421–8. [PMID: 20658830]

76.**Sabin LL, DeSilva MB, Hamer DH, Xu K, Zhang J, Li T, et al.** Using electronic drug monitor feedback to improve adherence to antiretroviral therapy among HIV-positive patients in China. AIDS Behav. 2010;14:580–9. [PMID: 19771504]

77.**Chung M, Benki-Nugent S, Richardson B, Nguti R, Simoni J, Overbaugh J, et al.** Randomized controlled trial comparing educational counseling and alarm device on adherence to antiretroviral medications in Nairobi, Kenya, over 18 months follow-up. Presented at the 4th International Conference on HIV Treatment Adherence, Miami, Florida, 5–7 April 2009. Oral Abstract no. 270.

78.HIV/AIDS Prevention Research Synthesis Project Database. Atlanta, GA: Centers for Disease Control and Prevention (CDC); 2011. Updated May 15, 2011. Accessed 15 May 2011.

79.**Amico KR, Harman JJ, Johnson BT.** Efficacy of antiretroviral therapy adherence interventions: a research synthesis of trials, 1996 to 2004. J Acquir Immune Defic Syndr. 2006;41:285–97. [PMID: 16540929]

80.**de Bruin M, Viechtbauer W, Schaalma HP, Kok G, Abraham C, Hospers HJ.** Standard care impact on effects of highly active antiretroviral therapy adherence interventions: A meta-analysis of randomized controlled trials. Arch Intern Med. 2010;170:240–50. [PMID: 20142568]

81.**Simoni JM, Pearson CR, Pantalone DW, Marks G, Crepaz N.** Efficacy of interventions in improving highly active antiretroviral therapy adherence and HIV-1 RNA viral load. A meta-analytic review of randomized controlled trials. J Acquir Immune Defic Syndr. 2006;43 Suppl 1:S23–35. [PMID: 17133201]

82.**Brock TP, Smith SR.** Using digital videos displayed on personal digital assistants (PDAs) to enhance patient education in clinical settings. Int J Med Inform. 2007;76:829–35. [PMID: 17113345]

83.**Collier AC, Ribaudo H, Mukherjee AL, Feinberg J, Fischl MA, Chesney M; Adult AIDS Clinical Trials Group 746 Substudy Team.** A randomized study of serial telephone call support to increase adherence and thereby improve virologic outcome in persons initiating antiretroviral therapy. J Infect Dis. 2005;192:1398–406. [PMID: 16170757]

84.**Fairley CK, Levy R, Rayner CR, Allardice K, Costello K, Thomas C, et al; Melbourne Adherence Group.** Randomized trial of an adherence programme for clients with HIV. Int J STD AIDS. 2003;14:805–9. [PMID: 14678587]

85.**Golin CE, Earp J, Tien HC, Stewart P, Porter C, Howie L.** A 2-arm, randomized, controlled trial of a motivational interviewing-based intervention to improve adherence to antiretroviral therapy (ART) among patients failing or initiating ART. J Acquir Immune Defic Syndr. 2006;42:42–51. [PMID: 16763491]

86.**Goujard C, Bernard N, Sohier N, Peyramond D, Lançon F, Chwalow J, et al.** Impact of a patient education program on adherence to HIV medication: a randomized clinical trial. J Acquir Immune Defic Syndr. 2003;34:191–4. [PMID: 14526208]

87.**Holzemer WL, Bakken S, Portillo CJ, Grimes R, Welch J, Wantland D, et al.** Testing a nurse-tailored HIV medication adherence intervention. Nurs Res. 2006;55:189–97. [PMID: 16708043]

88.**Johnson MO, Charlebois E, Morin SF, Remien RH, Chesney MA; National Institute of Mental Health Healthy Living Project Team.** Effects of a behavioral intervention on antiretroviral medication adherence among people living with HIV: the healthy living project randomized controlled study. J Acquir Immune Defic

Syndr. 2007;46:574–80. [PMID: 18193499]

89.**Kalichman SC, Cherry J, Cain D.** Nurse-delivered antiretroviral treatment adherence intervention for people with low literacy skills and living with HIV/AIDS. J Assoc Nurses AIDS Care. 2005;16:3–15. [PMID: 16433105]

90.**Murphy DA, Marelich WD, Rappaport NB, Hoffman D, Farthing.** Results of an antiretroviral adherence intervention: STAR (Staying Healthy: Taking Antiretrovirals Regularly). J Int Assoc Physicians AIDS Care. 2007;6:113–24. [PMID: 17538003]

91.**Rawlings MK, Thompson MA, Farthing CF, Brown LS, Racine J, Scott RC, et al; NZTA4006 Helping to Enhance Adherence to Antiretroviral Therapy (HEART) Study Team.** Impact of an educational program on efficacy and adherence with a twice-daily lamivudine/zidovudine/abacavir regimen in underrepresented HIV-infected patients. J Acquir Immune Defic Syndr. 2003;34:174–83. [PMID: 14526206]

92.**Safren SA, Otto MW, Worth JL, Salomon E, Johnson W, Mayer K, et al.** Two strategies to increase adherence to HIV antiretroviral medication: life-steps and medication monitoring. Behav Res Ther. 2001;39:1151–62. [PMID: 11579986]

93.**Smith SR, Rublein JC, Marcus C, Brock TP, Chesney MA.** A medication self-management program to improve adherence to HIV therapy regimens. Patient Educ Couns. 2003;50:187–99. [PMID: 12781934]

94.**Tuldrà A, Fumaz CR, Ferrer MJ, Bayés R, Arnó A, Balagué M, et al.** Prospective randomized two-Arm controlled study to determine the efficacy of a specific intervention to improve long-term adherence to highly active antiretroviral therapy. J Acquir Immune Defic Syndr. 2000;25:221–8. [PMID: 11115952]

95.**Williams AB, Fennie KP, Bova CA, Burgess JD, Danvers KA, Dieckhaus KD.** Home visits to improve adherence to highly active antiretroviral therapy: a randomized controlled trial. J Acquir Immune Defic Syndr. 2006;42:314–21. [PMID: 16770291]

96.**Dilorio C, Resnicow K, McDonnell M, Soet J, McCarty F, Yeager K.** Using motivational interviewing to promote adherence to antiretroviral medications: a pilot study. J Assoc Nurses AIDS Care. 2003;14:52–62. [PMID: 12698766]

97.**Dilorio C, McCarty F, Resnicow K, McDonnell Holstad M, Soet J, Yeager K, et al.** Using motivational interviewing to promote adherence to antiretroviral medications: a randomized controlled study. AIDS Care. 2008;20:273–83. [PMID: 18351473]

98.**Johnson MO, Dilworth SE, Taylor JM, Neilands TB.** Improving coping skills for self-management of treatment side effects can reduce antiretroviral medication nonadherence among people living with HIV. Ann Behav Med. 2011;41:83–91. [PMID: 20922510]

99.**Knobel H, Carmona A, López JL, Gimeno JL, Saballs P, González A, et al.** [Adherence to very active antiretroviral treatment: impact of individualized assessment]. Enferm Infecc Microbiol Clin. 1999;17:78–81. [PMID: 10193067]

100.**Parsons JT, Rosof E, Punzalan JC, Di Maria L.** Integration of motivational interviewing and cognitive behavioral therapy to improve HIV medication adherence and reduce substance use among HIV-positive men and women: results of a pilot project. AIDS Patient Care STDS. 2005;19:31–9. [PMID: 15665633]

101.**Pradier C, Bentz L, Spire B, Tourette-Turgis C, Morin M, Souville M, et al.** Efficacy of an educational and counseling intervention on adherence to highly active antiretroviral therapy: French prospective controlled study. HIV Clin Trials. 2003;4:121–31. [PMID: 12671780]

102.**Reynolds NR, Testa MA, Su M, Chesney MA, Neidig JL, Frank I, et al; AIDS Clinical Trials Group 731 and 384 Teams.** Telephone support to improve antiretroviral medication adherence: a multisite, randomized controlled trial. J Acquir Immune Defic Syndr. 2008;47:62–8. [PMID: 17891043]

103.**Weber R, Christen L, Christen S, Tschopp S, Znoj H, Schneider C, et al; Swiss HIV Cohort Study.** Effect of individual cognitive behaviour intervention on adherence to antiretroviral therapy: prospective randomized trial. Antivir Ther. 2004;9:85–95. [PMID: 15040540]

104.**Mann T.** Effects of future writing and optimism on health behaviors in HIV-infected women. Ann Behav Med. 2001;23:26–33. [PMID: 11302353]

105.**Wagner GJ, Kanouse DE, Golinelli D, Miller LG, Daar ES, Witt MD, et al.** Cognitive-behavioral intervention to enhance adherence to antiretroviral therapy: a randomized controlled trial (CCTG 578). AIDS. 2006;20:1295–302. [PMID: 16816559]

106.**Webel AR.** Testing a peer-based symptom management intervention for

women living with HIV/AIDS. AIDS Care. 2010;22:1029-40. [PMID: 20146111]

107.**Wilson IB, Laws MB, Safren SA, Lee Y, Lu M, Coady W, et al.** Provider-focused intervention increases adherence-related dialogue but does not improve antiretroviral therapy adherence in persons with HIV. J Acquir Immune Defic Syndr. 2010;53:338-47. [PMID: 20048680]

108.**Garcia R, Pondé M, Lima M, Souza AR, Stolze SM, Badaró R.** Lack of effect of motivation on the adherence of HIV-positive/AIDS patients to antiretroviral treatment. Braz J Infect Dis. 2005;9:494-9. [PMID: 16410944]

109.**Javanbakht M, Prosser P, Grimes T, Weinstein M, Farthing C.** Efficacy of an individualized adherence support program with contingent reinforcement among nonadherent HIV-positive patients: results from a randomized trial. J Int Assoc Physicians AIDS Care. 2006;5:143-50. [PMID: 17101806]

110.**Remien RH, Stirratt MJ, Dolezal C, Dognin JS, Wagner GJ, Carballo-Dieguez A, et al.** Couple-focused support to improve HIV medication adherence: a randomized controlled trial. AIDS. 2005;19:807-14. [PMID: 15867495]

111.**Koenig LJ, Pals SL, Bush T, Pratt Palmore M, Stratford D, Ellerbrock TV.** Randomized controlled trial of an intervention to prevent adherence failure among HIV-infected patients initiating antiretroviral therapy. Health Psychol. 2008;27:159-69. [PMID: 18377134]

112.**Chiou PY, Kuo BI, Lee MB, Chen YM, Chuang P, Lin LC.** A programme of symptom management for improving quality of life and drug adherence in AIDS/HIV patients. J Adv Nurs. 2006;55:169-79. [PMID: 16866809]

113.**Kalichman SC, Cherry C, Kalichman MO, Amaral CM, White D, Pope H, et al.** Integrated behavioral intervention to improve HIV/AIDS treatment adherence and reduce HIV transmission. Am J Public Health. 2011;101:531-8. [PMID: 21233431]

114.**van Servellen G, Nyamathi A, Carpio F, Pearce D, Garcia-Teague L, Herrera G, et al.** Effects of a treatment adherence enhancement program on health literacy, patient-provider relationships, and adherence to HAART among low-income HIV-positive Spanish-speaking Latinos. AIDS Patient Care STDS. 2005;19:745-59. [PMID: 16283835]

115.**Antoni MH, Carrico AW, Durán RE, Spitzer S, Penedo F, Ironson G, et al.** Randomized clinical trial of cognitive behavioral stress management on human immunodeficiency virus viral load in gay men treated with highly active antiretroviral therapy. Psychosom Med. 2006;68:143-51. [PMID: 16449425]

116.**Berger S, Schad T, von Wyl V, Ehlert U, Zellweger C, Furrer H, et al.** Effects of cognitive behavioral stress management on HIV-1 RNA, CD4 cell counts and psychosocial parameters of HIV-infected persons. AIDS. 2008;22:767-75. [PMID: 18356607]

117.**Sampaio-Sa M, Page-Shafer K, Bangsberg DR, Evans J, Dourado Mde L, Teixeira C, et al.** 100% adherence study: educational workshops vs. video sessions to improve adherence among ART-naïve patients in Salvador, Brazil. AIDS Behav. 2008;12:S54-62. [PMID: 18512141]

118.**Frick P, Tapia K, Grant P, Novotny M, Kerzee J.** The effect of a multidisciplinary program on HAART adherence. AIDS Patient Care STDS. 2006;20:511-24. [PMID: 16839250]

119.**Chang LW, Kagaayi J, Nakigozi G, Ssempijja V, Packer AH, Serwadda D, et al.** Effect of peer health workers on AIDS care in Rakai, Uganda: a cluster-randomized trial. PLoS One. 2010;5:e10923. [PMID: 20532194]

120.**Mugusi F, Mugusi S, Bakari M, Hejdemann B, Josiah R, Janabi M, et al.** Enhancing adherence to antiretroviral therapy at the HIV clinic in resource constrained countries; the Tanzanian experience. Trop Med Int Health. 2009;14:1226-32. [PMID: 19732408]

121.**Muñoz M, Finnegan K, Zeladita J, Caldas A, Sanchez E, Callacna M, et al.** Community-based DOT-HAART accompaniment in an urban resource-poor setting. AIDS Behav. 2010;14:721-30. [PMID: 19370409]

122.**Nachega JB, Chaisson RE, Goliath R, Efron A, Chaudhary MA, Ram M, et al.** Randomized controlled trial of trained patient-nominated treatment supporters providing partial directly observed antiretroviral therapy. AIDS. 2010;24:1273-80. [PMID: 20453627]

123.**Pearson CR, Micek MA, Simoni JM, Hoff PD, Matediana E, Martin DP, et al.** Randomized control trial of peer-delivered, modified directly observed therapy for HAART in Mozambique. J Acquir Immune Defic Syndr. 2007;46:238-44. [PMID: 17693890]

124.**Ruiz I, Olry A, López MA, Prada JL, Causse M.** Prospective, randomized, two-arm controlled study to evaluate two interventions to improve adherence to

antiretroviral therapy in Spain. Enferm Infecc Microbiol Clin. 2010;28:409–15. [PMID: 20381924]

125.**Simoni JM, Pantalone DW, Plummer MD, Huang B.** A randomized controlled trial of a peer support intervention targeting antiretroviral medication adherence and depressive symptomatology in HIV-positive men and women. Health Psychol. 2007;26:488–95. [PMID: 17605569]

126.**Simoni JM, Huh D, Frick PA, Pearson CR, Andrasik MP, Dunbar PJ, et al.** Peer support and pager messaging to promote antiretroviral modifying therapy in Seattle: a randomized controlled trial. J Acquir Immune Defic Syndr. 2009;52:465–473. [PMID: 19911481]

127.**Taiwo BO, Idoko JA, Welty LJ, Otoh I, Job G, Iyaji PG, et al.** Assessing the viorologic and adherence benefits of patient-selected HIV treatment partners in a resource-limited setting. J Acquir Immune Defic Syndr. 2010;54:85–92. [PMID: 20418724]

128.**Matovu F, Wabwire D, Nakibuuka J, Mubiru M, Bagenda D, Musoke P, et al.** Efficacy of using peer counselors and nurses to support adherence to HAART among HIV-1-infected patients at the prevention of MTCT program, Mulago Hospital, Kampala, Uganda: a randomized non-inferiority interventional trial. Presented at the 18th Conference on Retroviruses and Opportunistic Infections, Boston, Massachusetts, 27 February–2 March 2011. Paper no. 1016.

129.**Sanne I, Orrell C, Fox MP, Conradie F, Ive P, Zeinecker J, et al; CIPRA-SA Study Team.** Nurse versus doctor management of HIV-infected patients receiving antiretroviral therapy (CIPRA-SA): a randomised non-inferiority trial. Lancet. 2010;376:33–40. [PMID: 20557927]

130.**Kipp W, Konde-Lule J, Saunders LD, Alibhai A, Houston S, Rubaale T, et al.** Results of a community-based antiretroviral treatment program for HIV-1 infection in Western Uganda. Curr HIV Res. 2010;8:179–85. [PMID: 20163349]

131.**Wolitski RJ, Kidder DP, Pals SL, Royal S, Aidala A, Stall R, et al; Housing and Health Study Team.** Randomized trial of the effects of housing assistance on the health and risk behaviors of homeless and unstably housed people living with HIV. AIDS Behav. 2010;14:493–503. [PMID: 19949848]

132.**Cantrell RA, Sinkala M, Megazinni K, Lawson-Marriott S, Washington S, Chi BH, et al.** A pilot study of food supplementation to improve adherence to antiretroviral therapy among food-insecure adults in Lusaka, Zambia. J Acquir Immune Defic Syndr. 2008;49:190–5. [PMID: 18769349]

133.**Serrano C, Laporte R, Ide M, Nouhou Y, de Truchis P, Rouveix E, et al.** Family nutritional support improves survival, immune restoration and adherence in HIV patients receiving ART in developing country. Asia Pac J Clin Nutr. 2010;19:68–75. [PMID: 20199989]

134.**Andersen M, Hockman E, Smereck G, Tinsley J, Milfort D, Wilcox R, et al.** Retaining women in HIV medical care. J Assoc Nurses AIDS Care. 2007;18:33–41. [PMID: 17570298]

135.**Hirsch JD, Rosenquist A, Best BM, Miller TA, Gilmer TP.** Evaluation of the first year of a pilot program in community pharmacy: HIV/AIDS medication therapy management for Medi-Cal beneficiaries. J Manag Care Pharm. 2009;15:32–41. [PMID: 19125548]

136.**Gross R, Tierney C, Andrade A, Lalama C, Rosenkranz S, Eshleman SH, et al; AIDS Clinical Trials Group A5073 Study Team.** Modified directly observed antiretroviral therapy compared with self-administered therapy in treatment-naive HIV-1-infected patients: a randomized trial. Arch Intern Med. 2009;169:1224–32. [PMID: 19597072]

137.**Wohl AR, Garland WH, Valencia R, Squires K, Witt MD, Kovacs A, et al.** A randomized trial of directly administered antiretroviral therapy and adherence case management intervention. Clin Infect Dis. 2006;42:1619–27. [PMID: 16652320]

138.**Sarna A, Luchters S, Geibel S, Chersich MF, Munyao P, Kaai S, et al.** Short- and long-term efficacy of modified directly observed antiretroviral treatment in Mombasa, Kenya: a randomized trial. J Acquir Immune Defic Syndr. 2008;48:611–9. [PMID: 18645509]

139.**Idoko JA, Agbaji O, Agaba P, Akolo C, Inuwa B, Hassan Z, et al.** Direct observation therapy-highly active antiretroviral therapy in a resource-limited setting: the use of community treatment support can be effective. Int J STD AIDS. 2007;18:760–3. [PMID: 18005510]

140.**World Heath Organization.** Antiretroviral drugs for treating pregnant women and preventing HIV infections in infants: recommendations for a public health approach (2010 version). Geneva, Switzerland: World Health Organization; 2010.

141.**Laine C, Newschaffer CJ, Zhang D, Cosler L, Hauck WW, Turner BJ.** Adherence to antiretroviral therapy by pregnant women infected with human immunodeficiency virus: a pharmacy claims-based analysis. Obstet Gynecol. 2000;95:167-73. [PMID: 10674574]

142.**Leisegang R, Nachega JB, Hislop M, Maartens G.** The impact of pregnancy on adherence to and default from ART. Presented at the 18th Conference on Retroviruses and Opportunistic Infections, Boston, Massachusetts, 27 February-March 2 2011. Abstract 1021.

143.**Mellins CA, Chu C, Malee K, Allison S, Smith R, Harris L, et al.** Adherence to antiretroviral treatment among pregnant and postpartum HIV-infected women. AIDS Care. 2008;20:958-68. [PMID: 18608073]

144.**Stringer JS, Sinkala M, Stout JP, Goldenberg RL, Acosta EP, Chapman V, et al.** Comparison of two strategies for administering nevirapine to prevent perinatal HIV transmission in high-prevalence, resource-poor settings. J Acquir Immune Defic Syndr. 2003;32:506-13. [PMID: 12679702]

145.**Megazzini KM, Sinkala M, Vermund SH, Redden DT, Krebs DW, Acosta EP, et al.** A cluster-randomized trial of enhanced labor ward-based PMTCT services to increase nevirapine coverage in Lusaka, Zambia. AIDS. 2010;24:447-55. [PMID: 19926959]

146.**Altice FL, Kamarulzaman A, Soriano VV, Schechter M, Friedland GH.** Treatment of medical, psychiatric, and substance-use comorbidities in people infected with HIV who use drugs. Lancet. 2010;376:367-87. [PMID: 20650518]

147.**Altice FL, Bruce RD, Lucas GM, Lum PJ, Korthuis PT, Flanigan TP, et al; BHIVES Collaborative.** HIV treatment outcomes among HIV-infected, opioid-dependent patients receiving buprenorphine/naloxone treatment within HIV clinical care settings: results from a multisite study. J Acquir Immune Defic Syndr. 2011;56 Suppl 1:S22-32. [PMID: 21317590]

148.**Margolin A, Avants SK, Warburton LA, Hawkins KA, Shi J.** A randomized clinical trial of a manual-guided risk reduction intervention for HIV-positive injection drug users. Health Psychol. 2003;22:223-8. [PMID: 12683743]

149.**Palepu A, Tyndall MW, Joy R, Kerr T, Wood E, Press N, et al.** Antiretroviral adherence and HIV treatment outcomes among HIV/HCV co-infected injection drug users: the role of methadone maintenance therapy. Drug Alcohol Depend. 2006;84:188-94. [PMID: 16542797]

150.**Uhlmann S, Milloy MJ, Kerr T, Zhang R, Guillemi S, Marsh D, et al.** Methadone maintenance therapy promotes initiation of antiretroviral therapy among injection drug users. Addiction. 2010;105:907-13. [PMID: 20331553]

151.**Roux P, Carrieri MP, Villes V, Dellamonica P, Poizot-Martin I, Ravaux I, et al; MANIF2000 cohort study group.** The impact of methadone or buprenorphine treatment and ongoing injection on highly active antiretroviral therapy (HAART) adherence: evidence from the MANIF2000 cohort study. Addiction. 2008;103:1828-36. [PMID: 18778390]

152.**Springer SA, Chen S, Altice FL.** Improved HIV and substance abuse treatment outcomes for released HIV-infected prisoners: the impact of buprenorphine treatment. J Urban Health. 2010;87:592-602. [PMID: 20177974]

153.**Lucas GM, Chaudhry A, Hsu J, Woodson T, Lau B, Olsen Y, et al.** Clinic-based treatment of opioid-dependent HIV-infected patients versus referral to an opioid treatment program: A randomized trial. Ann Intern Med. 2010;152:704-11. [PMID: 20513828]

154.**Altice FL, Maru DS, Bruce RD, Springer SA, Friedland GH.** Superiority of directly administered antiretroviral therapy over self-administered therapy among HIV-infected drug users: a prospective, randomized, controlled trial. Clin Infect Dis. 2007;45:770-8. [PMID: 17712763]

155.**Altice FL, Tehrani AS, Qiu JJ, Herme M, Springer SA.** Directly administered antiretroviral therapy (DAART) is superior to self-administered therapy (SAT) among released HIV+ prisoners: results from a randomized controlled trial (RCT). Presented at the 18th Conference on Retroviruses and Opportunistic Infections, Boston, Massachusetts, 27 February-2 March 2011-. Abstract no. 543.

156.**Macalino GE, Hogan JW, Mitty JA, Bazerman LB, Delong AK, Loewenthal H, et al.** A randomized clinical trial of community-based directly observed therapy as an adherence intervention for HAART among substance users. AIDS. 2007;21:1473-7. [PMID: 17589194]

157.**Maru DS, Bruce RD, Walton M, Springer SA, Altice FL.** Persistence of virological benefits following directly administered antiretroviral therapy among drug users: results from a randomized controlled trial. J Acquir Immune Defic Syndr. 2009;50:176-81. [PMID: 19131891]

158.**Babudieri S, Aceti A, D'Offizi GP, Carbonara S, Starnini G.** Directly observed

therapy to treat HIV infection in prisoners [Letter]. JAMA. 2000;284:179–80. [PMID: 10889588]

159.**Lucas GM, Weidle PJ, Hader S, Moore RD.** Directly administered antiretroviral therapy in an urban methadone maintenance clinic: a nonrandomized comparative study. Clin Infect Dis. 2004;38 Suppl 5:S409–13. [PMID: 15156431]

160.**Mitty JA, Macalino GE, Bazerman LB, Loewenthal HG, Hogan JW, MacLeod CJ, et al.** The use of community-based modified directly observed therapy for the treatment of HIV-infected persons. J Acquir Immune Defic Syndr. 2005;39:545–50. [PMID: 16044005]

161.**Berg KM, Litwin A, Li X, Heo M, Arnsten JH.** Directly observed antiretroviral therapy improves adherence and viral load in drug users attending methadone maintenance clinics: a randomized controlled trial. Drug Alcohol Depend. 2011;113:192–9. [PMID: 20832196]

162.**Clarke S, Keenan E, Ryan M, Barry M, Mulcahy F.** Directly observed antiretroviral therapy for injection drug users with HIV infection. AIDS Read. 2002;12:305–7, 312–6. [PMID: 12161852]

163.**Lucas GM, Mullen BA, Weidle PJ, Hader S, McCaul ME, Moore RD.** Directly administered antiretroviral therapy in methadone clinics is associated with improved HIV treatment outcomes, compared with outcomes among concurrent comparison groups. Clin Infect Dis. 2006;42:1628–35. [PMID: 16652321]

164.**Conway B, Prasad J, Reynolds R, Farley J, Jones M, Jutha S, et al.** Directly observed therapy for the management of HIV-infected patients in a methadone program. Clin Infect Dis. 2004;38 Suppl 5:S402–8. [PMID: 15156430]

165.**Gonzalez JS, Batchelder AW, Psaros C, Safren SA.** Depression and HIV/AIDS treatment nonadherence: a review and meta-analysis. J Acquir Immune Defic Syndr. 2011;58:181–7. [PMID: 21857529]

166.**Safren SA, O'Cleirigh C, Tan JY, Raminani SR, Reilly LC, Otto MW, et al.** A randomized controlled trial of cognitive behavioral therapy for adherence and depression (CBT-AD) in HIV-infected individuals. Health Psychol. 2009;28:1–10. [PMID: 19210012]

167.**Weiss SM, Tobin JN, Antoni M, Ironson G, Ishii M, Vaughn A, et al; SMART/EST Women's Project Team.** Enhancing the health of women living with HIV: the SMART/EST Women's Project. Int J Womens Health. 2011;3:63–77. [PMID: 21445376]

168.**Horberg MA, Silverberg MJ, Hurley LB, Towner WJ, Klein DB, Bersoff-Matcha S, et al.** Effects of depression and selective serotonin reuptake inhibitor use on adherence to highly active antiretroviral therapy and on clinical outcomes in HIV-infected patients. J Acquir Immune Defic Syndr. 2008;47:384–90. [PMID: 18091609]

169.**Tsai AC, Weiser SD, Petersen ML, Ragland K, Kushel MB, Bangsberg DR.** A marginal structural model to estimate the causal effect of antidepressant medication treatment on viral suppression among homeless and marginally housed persons with HIV. Arch Gen Psychiatry. 2010;67:1282–90. [PMID: 21135328]

170.**Yun LW, Maravi M, Kobayashi JS, Barton PL, Davidson AJ.** Antidepressant treatment improves adherence to antiretroviral therapy among depressed HIV-infected patients. J Acquir Immune Defic Syndr. 2005;38:432–8. [PMID: 15764960]

171.**Jürgens R, Nowak M, Day M.** HIV and incarceration: prisons and detention. J Int AIDS Soc. 2011;14:26. [PMID: 21595957]

172.**Seal DW.** HIV-related issues and concerns for imprisoned persons throughout the world. Curr Opin Psychiatry. 2005;18:530–5. [PMID: 16639113]

173.**Chen RY, Accortt NA, Westfall AO, Mugavero MJ, Raper JL, Cloud GA, et al.** Distribution of health care expenditures for HIV-infected patients. Clin Infect Dis. 2006;42:1003–10. [PMID: 16511767]

174.**Hammett T, Kennedy S, Kuck S.** National Survey of Infectious Diseases in Correctional Facilities: HIV and Sexually Transmitted Diseases: US Department of Justice. March 2007. Report No. NCJ 217736. Accessed at www.ncjrs.gov/pdffiles1/nij/grants/217736.pdf on 14 May 2010.

175.**Zaller N, Thurmond P, Rich JD.** Limited spending: an analysis of correctional expenditures on antiretrovirals for HIV-infected prisoners. Public Health Rep. 2007;122:49–54. [PMID: 17236608]

176.**Baillargeon J, Giordano TP, Rich JD, Wu ZH, Wells K, Pollock BH, et al.** Accessing antiretroviral therapy following release from prison. JAMA. 2009;301:848–57. [PMID: 19244192]

177.**Inés SM, Moralejo L, Marcos M, Fuertes A, Luna G.** Adherence to highly active

antiretroviral therapy in HIV-infected inmates. Curr HIV Res. 2008;6:164-70. [PMID: 18336264]

178.**Pontali E.** Antiretroviral treatment in correctional facilities. HIV Clin Trials. 2005;6:25-37. [PMID: 15765308]

179.**Rosen DL, Golin CE, Schoenbach VJ, Stephenson BL, Wohl DA, Gurkin B, et al.** Availability of and access to medical services among HIV-infected inmates incarcerated in North Carolina county jails. J Health Care Poor Underserved. 2004;15:413-25. [PMID: 15453178]

180.**Small W, Wood E, Betteridge G, Montaner J, Kerr T.** The impact of incarceration upon adherence to HIV treatment among HIV-positive injection drug users: a qualitative study. AIDS Care. 2009;21:708-14. [PMID: 19806487]

181.**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;203:1215-21. [PMID: 21459814]

182.**Springer SA, Pesanti E, Hodges J, Macura T, Doros G, Altice FL.** Effectiveness of antiretroviral therapy among HIV-infected prisoners: reincarceration and the lack of sustained benefit after release to the community. Clin Infect Dis. 2004;38:1754-60. [PMID: 15227623]

183.**Stephenson BL, Wohl DA, Golin CE, Tien HC, Stewart P, Kaplan AH.** Effect of release from prison and re-incarceration on the viral loads of HIV-infected individuals. Public Health Rep. 2005;120:84-8. [PMID: 15736336]

184.**Grodensky GC, Golin C, Sunil A, White B, Cole S, Wohl D, et al.** Effect on antiretroviral adherence of directly observed therapy (DOT) versus keep-on-my-person medication (KOM) among HIV-infected prisoners: the DOT-KOM Study. Presented at the 4th International Conference on HIV Treatment Adherence, Miami, Florida, 5-7 April 2011. Oral Abstract no. 280.

185.**Robertson MJ, Clark RA, Charlebois ED, Tulsky J, Long HL, Bangsberg DR, et al.** HIV seroprevalence among homeless and marginally housed adults in San Francisco. Am J Public Health. 2004;94:1207-17. [PMID: 15226145]

186.**Mostashari F, Riley E, Selwyn PA, Altice FL.** Acceptance and adherence with antiretroviral therapy among HIV-infected women in a correctional facility. J Acquir Immune Defic Syndr Hum Retrovirol. 1998;18:341-8. [PMID: 9704939]

187.**Weiser SD, Frongillo EA, Ragland K, Hogg RS, Riley ED, Bangsberg DR.** Food insecurity is associated with incomplete HIV RNA suppression among homeless and marginally housed HIV-infected individuals in San Francisco. J Gen Intern Med. 2009;24:14-20. [PMID: 18953617]

188.**Moss AR, Hahn JA, Perry S, Charlebois ED, Guzman D, Clark RA, et al.** Adherence to highly active antiretroviral therapy in the homeless population in San Francisco: a prospective study. Clin Infect Dis. 2004;39:1190-8. [PMID: 15486844]

189.**Kushel MB, Colfax G, Ragland K, Heineman A, Palacio H, Bangsberg DR.** Case management is associated with improved antiretroviral adherence and CD4+ cell counts in homeless and marginally housed individuals with HIV infection. Clin Infect Dis. 2006;43:234-42. [PMID: 16779752]

190.**Martin S, Elliott-DeSorbo DK, Wolters PL, Toledo-Tamula MA, Roby G, Zeichner S, et al.** Patient, caregiver and regimen characteristics associated with adherence to highly active antiretroviral therapy among HIV-infected children and adolescents. Pediatr Infect Dis J. 2007;26:61-7. [PMID: 17195708]

191.**Reddington C, Cohen J, Baldillo A, Toye M, Smith D, Kneut C, et al.** Adherence to medication regimens among children with human immunodeficiency virus infection. Pediatr Infect Dis J. 2000;19:1148-53. [PMID: 11144374]

192.**Dowshen N, D'Angelo L.** Health care transition for youth living with HIV/AIDS. Pediatrics. 2011;128:762-71. [PMID: 21930548]

193.**Agwu AL, Fleishman JA, Korthuis PT, Siberry GK, Ellen JM, Gaur AH, et al; HIV Research Network.** Disparities in antiretroviral treatment: a comparison of behaviorally HIV-infected youth and adults in the HIV Research Network. J Acquir Immune Defic Syndr. 2011;58:100-7. [PMID: 21637114]

194.**Ryscavage P, Anderson EJ, Sutton SH, Reddy S, Taiwo B.** Clinical outcomes of adolescents and young adults in adult HIV care. J Acquir Immune Defic Syndr. 2011;58:193-7. [PMID: 21826014]

195.**Davila J, Miertschin N, Sansgiry S, Mitts B, Parkinson-Windross D, Henley C, et al.** Centralization of HIV services in HIV+ African-American and Hispanic youth improves retention in care. Presented at the 5th International Conference on HIV Treatment Adherence, Miami, Florida, 23-25 May 2010. Oral Abstract no. 62911.

196.**Wohl AR, Garland WH, Wu J, Au CW, Boger A, Dierst-Davies R, et al.** A youth-focused case management intervention to engage and retain young gay men of color in HIV care. AIDS Care. 2011;23:988-97. [PMID: 21390879]

197.**Ellis DA, Naar-King S, Cunningham PB, Secord E.** Use of multisystemic therapy to improve antiretroviral adherence and health outcomes in HIV-infected pediatric patients: evaluation of a pilot program. AIDS Patient Care STDS. 2006;20:112-21. [PMID: 16475892]

198.**Naar-King S, Parsons JT, Murphy DA, Chen X, Harris DR, Belzer ME.** Improving health outcomes for youth living with the human immunodeficiency virus: a multisite randomized trial of a motivational intervention targeting multiple risk behaviors. Arch Pediatr Adolesc Med. 2009;163:1092-8. [PMID: 19996045]

199.**Berrien VM, Salazar JC, Reynolds E, McKay K; HIV Medication Adherence Intervention Group.** Adherence to antiretroviral therapy in HIV-infected pediatric patients improves with home-based intensive nursing intervention. AIDS Patient Care STDS. 2004;18:355-63. [PMID: 15294086]

200.**Lyon ME, Trexler C, Akpan-Townsend C, Pao M, Selden K, Fletcher J, et al.** A family group approach to increasing adherence to therapy in HIV-infected youths: results of a pilot project. AIDS Patient Care STDS. 2003;17:299-308. [PMID: 12880493]

201.**Rotheram-Borus MJ, Swendeman D, Comulada WS, Weiss RE, Lee M, Lightfoot M.** Prevention for substance-using HIV-positive young people: telephone and in-person delivery. J Acquir Immune Defic Syndr. 2004;37 Suppl 2:S68-77. [PMID: 15385902]

202.**Garvie PA, Lensing S, Rai SN.** Efficacy of a pill-swallowing training intervention to improve antiretroviral medication adherence in pediatric patients with HIV/AIDS. Pediatrics. 2007;119:e893-9. [PMID: 17353298]

203.**Glikman D, Walsh L, Valkenburg J, Mangat PD, Marcinak JF.** Hospital-based directly observed therapy for HIV-infected children and adolescents to assess adherence to antiretroviral medications. Pediatrics. 2007;119:e1142-8. [PMID: 17452493]

204.**McKeegan K, Ramsden D, Prebus O, Rutstein RM.** A pilot program of health worker- or nurse-provided directly observed therapy for nonadherent youth with perinatally acquired HIV. Presented at the 6th International Conference on HIV Treatment Adherence, Miami, Florida, 22-24 May 2011. Poster Abstract no. 70043.

205.**Myung P, Pugatch D, Brady MF, Many P, Harwell JI, Lurie M, et al.** Directly observed highly active antiretroviral therapy for HIV-infected children in Cambodia. Am J Public Health. 2007;97:974-7. [PMID: 17463375]

206.**Craw JA, Gardner LI, Marks G, Rapp RC, Bosshart J, Duffus WA, et al.** Brief strengths-based case management promotes entry into HIV medical care: results of the antiretroviral treatment access study-II. J Acquir Immune Defic Syndr. 2008;47:597-606. [PMID: 18285714]

207.**Horstmann E, Brown J, Islam F, Buck J, Agins BD.** Retaining HIV-infected patients in care: Where are we? Where do we go from here? Clin Infect Dis. 2010;50:752-61. [PMID: 20121413]

208.**Rajabiun S, Cabral H, Tobias C, Relf M.** Program design and evaluation strategies for the Special Projects of National Significance Outreach Initiative. AIDS Patient Care STDS. 2007;21 Suppl 1:S9-19. [PMID: 17563295]

209.**Rigsby MO, Rosen MI, Beauvais JE, Cramer JA, Rainey PM, O'Malley SS, et al.** Cue-dose training with monetary reinforcement: pilot study of an antiretroviral adherence intervention. J Gen Intern Med. 2000;15:841-7. [PMID: 11119180]

210.**Rosen MI, Dieckhaus K, McMahon TJ, Valdes B, Petry NM, Cramer J, et al.** Improved adherence with contingency management. AIDS Patient Care STDS. 2007;21:30-40. [PMID: 17263651]

211.**Llibre JM, Arribas JR, Domingo P, Gatell JM, Lozano F, Santos JR, et al; Spanish Group for FDAC Evaluation.** Clinical implications of fixed-dose coformulations of antiretrovirals on the outcome of HIV-1 therapy. AIDS. 2011;25:1683-90. [PMID: 21673556]

212.**Petry NM, Weinstock J, Alessi SM, Lewis MW, Dieckhaus K.** Group-based randomized trial of contingencies for health and abstinence in HIV patients. J Consult Clin Psychol. 2010;78:89-97. [PMID: 20099954]

213.**Cunningham CO, Sohler NL, Cooperman NA, Berg KM, Litwin AH, Arnsten JH.** Strategies to improve access to and utilization of health care services and adherence to antiretroviral therapy among HIV-infected drug users. Subst Use Misuse. 2011;46:218-32. [PMID: 21303242]

214.**Sullivan LE, Barry D, Moore BA, Chawarski MC, Tetrault JM, Pantalon MV, et al.** A trial of integrated buprenorphine/naloxone and HIV clinical care. Clin Infect Dis. 2006;43 Suppl 4:S184-90. [PMID: 17109305]

215.**Broadhead RS, Heckathorn DD, Altice FL, van Hulst Y, Carbone M, Friedland GH, et al.** Increasing drug users' adherence to HIV treatment: results of a peer-driven intervention feasibility study. Soc Sci Med. 2002;55:235-46. [PMID: 12144138]

216.**Deering KN, Shannon K, Sinclair H, Parsad D, Gilbert E, Tyndall MW.** Piloting a peer-driven intervention model to increase access and adherence to antiretroviral therapy and HIV care among street-entrenched HIV-positive women in Vancouver. AIDS Patient Care STDS. 2009;23:603-9. [PMID: 19591602]

217.**Feaster DJ, Mitrani VB, Burns MJ, McCabe BE, Brincks AM, Rodriguez AE, et al.** A randomized controlled trial of Structural Ecosystems Therapy for HIV medication adherence and substance abuse relapse prevention. Drug Alcohol Depend. 2010;111:227-34. [PMID: 20538417]

218.**Purcell DW, Latka MH, Metsch LR, Latkin CA, Gómez CA, Mizuno Y, et al; for the INSPIRE Study Team.** Results from a randomized controlled trial of a peer-mentoring intervention to reduce HIV transmission and increase access to care and adherence to HIV medications among HIV-seropositive injection drug users. J Acquir Immune Defic Syndr. 2007;46 Suppl 2:S35-47. [PMID: 18089983]

219.**Samet JH, Horton NJ, Meli S, Dukes K, Tripps T, Sullivan L, et al.** A randomized controlled trial to enhance antiretroviral therapy adherence in patients with a history of alcohol problems. Antivir Ther. 2005;10:83-93. [PMID: 15751766]

220.**Williams AB, Fennie KP, Bova CA, Burgess JD, Danvers KA, Dieckhaus KD.** Home visits to improve adherence to highly active antiretroviral therapy: a randomized controlled trial. J Acquir Immune Defic Syndr. 2006;42:314-21. [PMID: 16770291]

221.**Copenhaver M, Chowdhury S, Altice FL.** Adaptation of an evidence-based intervention targeting HIV-infected prisoners transitioning to the community: the process and outcome of formative research for the Positive Living Using Safety (PLUS) intervention. AIDS Patient Care STDS. 2009;23:277-87. [PMID: 19260773]

222.**Klein SJ, O'Connell DA, Devore BS, Wright LN, Birkhead GS.** Building an HIV continuum for inmates: New York State's criminal justice initiative. AIDS Educ Prev. 2002;14:114-23. [PMID: 12413199]

223.**Rich JD, Holmes L, Salas C, Macalino G, Davis D, Ryczek J, et al.** Successful linkage of medical care and community services for HIV-positive offenders being released from prison. J Urban Health. 2001;78:279-89. [PMID: 11419581]

224.**Wohl DA, Scheyett A, Golin CE, White B, Matuszewski J, Bowling M, et al.** Intensive case management before and after prison release is no more effective than comprehensive pre-release discharge planning in linking HIV-infected prisoners to care: a randomized trial. AIDS Behav. 2011;15:356-64. [PMID: 21042930]

225.**Belzer ME, Fuchs DN, Luftman GS, Tucker DJ.** Antiretroviral adherence issues among HIV-positive adolescents and young adults. J Adolesc Health. 1999;25:316-9. [PMID: 10551660]

226.**Macdonell KE, Naar-King S, Murphy DA, Parsons JT, Huszti H.** Situational temptation for HIV medication adherence in high-risk youth. AIDS Patient Care STDS. 2011;25:47-52. [PMID: 21162691]

227.**Murphy DA, Sarr M, Durako SJ, Moscicki AB, Wilson CM, Muenz LR; Adolescent Medicine HIV/AIDS Research Network.** Barriers to HAART adherence among human immunodeficiency virus-infected adolescents. Arch Pediatr Adolesc Med. 2003;157:249-55. [PMID: 12622674]

228.**Naar-King S, Templin T, Wright K, Frey M, Parsons JT, Lam P.** Psychosocial factors and medication adherence in HIV-positive youth. AIDS Patient Care STDS. 2006;20:44-7. [PMID: 16426155]

229.**Rao D, Kekwaletswe TC, Hosek S, Martinez J, Rodriguez F.** Stigma and social barriers to medication adherence with urban youth living with HIV. AIDS Care. 2007;19:28-33. [PMID: 17129855]

230.**Brackis-Cott E, Mellins CA, Abrams E, Reval T, Dolezal C.** Pediatric HIV medication adherence: the views of medical providers from two primary care programs. J Pediatr Health Care. 2003;17:252-60. [PMID: 14576630]

231.**Marhefka SL, Tepper VJ, Brown JL, Farley JJ.** Caregiver psychosocial characteristics and children's adherence to antiretroviral therapy. AIDS Patient Care STDS. 2006;20:429-37. [PMID: 16789856]

232.**Mellins CA, Brackis-Cott E, Dolezal C, Abrams EJ.** The role of psychosocial

and family factors in adherence to antiretroviral treatment in human immunodeficiency virus-infected children. Pediatr Infect Dis J. 2004;23:1035-41. [PMID: 15545859]

233.**Hightow-Weidman LB, Jones K, Wohl AR, Futterman D, Outlaw A, Phillips G 2nd, et al; YMSM of Color SPNS Initiative Study Group.** Early linkage and retention in care: findings from the outreach, linkage, and retention in care initiative among young men of color who have sex with men. AIDS Patient Care STDS. 2011;25 Suppl 1:S31-8. [PMID: 21711141]

234.**Martinez J, Bell D, Dodds S, Shaw K, Siciliano C, Walker LE, et al.** Transitioning youths into care: linking identified HIV-infected youth at outreach sites in the community to hospital-based clinics and or community-based health centers. J Adolesc Health. 2003;33:23-30. [PMID: 12888284]

235.**Antiretroviral Therapy Cohort Collaboration.** Causes of death in HIV-1-infected patients treated with antiretroviral therapy, 1996-2006: collaborative analysis of 13 HIV cohort studies. Clin Infect Dis. 2010;50:1387-96. [PMID: 20380565]

236.**Grunfeld C, Delaney JA, Wanke C, Currier JS, Scherzer R, Biggs ML, et al.** Preclinical atherosclerosis due to HIV infection: carotid intima-medial thickness measurements from the FRAM study. AIDS. 2009;23:1841-9. [PMID: 19455012]

237.**Mocroft A, Reiss P, Gasiorowski J, Ledergerber B, Kowalska J, Chiesi A, et al; EuroSIDA Study Group.** Serious fatal and nonfatal non-AIDS-defining illnesses in Europe. J Acquir Immune Defic Syndr. 2010;55:262-70. [PMID: 20700060]

238.**El-Sadr WM, Lundgren JD, Neaton JD, Gordin F, Abrams D, Arduino RC, et al; Strategies for Management of Antiretroviral Therapy (SMART) Study Group.** CD4+ count-guided interruption of antiretroviral treatment. N Engl J Med. 2006;355:2283-96. [PMID: 17135583]

239.**Currier JS, Lundgren JD, Carr A, Klein D, Sabin CA, Sax PE, et al; Working Group 2.** Epidemiological evidence for cardiovascular disease in HIV-infected patients and relationship to highly active antiretroviral therapy. Circulation. 2008;118:e29-35. [PMID: 18566319]

240.**Friis-Møller N, Reiss P, Sabin CA, Weber R, Monforte A, El-Sadr W, et al; DAD Study Group.** Class of antiretroviral drugs and the risk of myocardial infarction. N Engl J Med. 2007;356:1723-35. [PMID: 17460226]

241.**Dubé MP, Sattler FR.** Inflammation and complications of HIV disease [Editorial]. J Infect Dis. 2010;201:1783-5. [PMID: 20446849]

242.**Barbaro G.** Cardiovascular manifestations of HIV infection. Circulation. 2002;106:1420-5. [PMID: 12221062]

243.**Kalra S, Kalra B, Agrawal N, Unnikrishnan A.** Understanding diabetes in patients with HIV/AIDS. Diabetol Metab Syndr. 2011;3:2. [PMID: 21232158]

244.**Friedland G.** Infectious disease comorbidities adversely affecting substance users with HIV: hepatitis C and tuberculosis. J Acquir Immune Defic Syndr. 2010;55 Suppl 1:S37-42. [PMID: 21045598]

245.**Baeten J, Celum C, for the Partners PrEP Study Team.** Antiretroviral pre-exposure prophylaxis for HIV-1 prevention among heterosexual African men and women: the Partners PrEP Study. Presented at the 6th International AIDS Society Conference on HIV Pathogenesis, Treatment and Prevention, Rome, Italy, 17-20 July 2011. Abstract MOAX0106.

246.**Grant RM, Lama JR, Anderson PL, McMahan V, Liu AY, Vargas L, et al; iPrEx Study Team.** Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. N Engl J Med. 2010;363:2587-99. [PMID: 21091279]

247.**Thigpen MC, Kebaabetswa PM, Smith DK, Segolodi TM, Soud FA, Chillag K, et al.** Daily oral antiretroviral use for the prevention of HIV infection in heterosexually active young adults in Botswana: results from the TDF2 study. Presented at the 6th International AIDS Society Conference on HIV Pathogenesis, Treatment and Prevention, Rome, Italy, 17-20 July 2011 Abstract WELBC01.

248.**Abdool Karim Q, Abdool Karim SS, Frohlich JA, Grobler AC, Baxter C, Mansoor LE, et al; CAPRISA 004 Trial Group.** Effectiveness and safety of tenofovir gel, an antiretroviral microbicide, for the prevention of HIV infection in women. Science. 2010;329:1168-74. [PMID: 20643915]

249.**U.S. Department of Health and Human Services.** Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. HHS Panel on Antiretroviral Guidelines for Adults and Adolescents—A Working Group of the Office of AIDS Research Advisory Council (OARAC). Washington, DC: U.S. Department of Health and Human Services; 2011. Accessed at http://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-treatment-guidelines/0/ on 19 December 2011.

250.**European AIDS Clinical Society (EACS).** Guidelines. Version 6.0. October 2011. Accessed at www.europeanaidsclinicalsociety.org/images/stories/EACS-Pdf/eacsguidelines-v6_english.pdf .

251.**Thompson MA, Aberg JA, Cahn P, Montaner JS, Rizzardini G, Telenti A, et al; International AIDS Society-.** Antiretroviral treatment of adult HIV infection: 2010 recommendations of the International AIDS Society- panel. JAMA. 2010;304:321-33. [PMID: 20639566]

252.**World Health Organization.** Antiretroviral therapy for HIV infection in adults and adolescents: recommendations for a public health approach, 2010 revision. Geneva, Switzerland. 2010. Accessed at http://whqlibdoc.who.int/publications/2010/9789241599764_eng.pdf.

253.**Brouwers MC, Kho ME, Browman GP, Burgers JS, Cluzeau F, Feder G, et al; AGREE Next Steps Consortium.** AGREE II: advancing guideline development, reporting, and evaluation in health care. Prev Med. 2010;51:421-4. [PMID: 20728466]

254.**Laine C, Taichman DB, Mulrow C.** Trustworthy clinical guidelines [Editorial]. Ann Intern Med. 2011;154:774-5. [PMID: 21646561]

255.**Whiting P, Rutjes AW, Reitsma JB, Bossuyt PM, Kleijnen J.** The development of QUADAS: a tool for the quality assessment of studies of diagnostic accuracy included in systematic reviews. BMC Med Res Methodol. 2003;3:25. [PMID: 14606960]

256.**Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al; GRADE Working Group.** GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ. 2008;336:924-6. [PMID: 18436948]

257.**Qaseem A, Snow V, Owens DK, Shekelle P; Clinical Guidelines Committee of the American College of Physicians.** The development of clinical practice guidelines and guidance statements of the American College of Physicians: summary of methods. Ann Intern Med. 2010;153:194-9. [PMID: 20679562]

258.Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy. 2009. Accessed at http://srdta.cochrane.org/handbook-dta-reviews on 19 December 2011.

259.**Higgins J, Green S.** Cochrane Handbook for Systematic Reviews of Interventions 5.1.0 [updated March 2011]. 2011. Accessed at www.cochrane.org/training/cochrane-handbook on 19 December 2011.

260.**Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al.** The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Accessed at www.ohri.ca/programs/clinical_epidemiology/oxford.asp on 19 December 2011.