‘The Sufficiency of Hope’
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In his annual New Year’s message, IAPAC President/CEO José M. Zuniga offers his perspectives on an American philosopher’s conceptual framework of belief, hope, and religion; and delivers a message of hope that humanity shun excessive fear of error, undue caution, and unwarranted suspicion—all of which can lead us to suspect our common humanity, be contemptuous of mankind’s common sense, and mistrust mankind’s general tendency toward improving the human condition.
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Like most people, I look forward to each December, not so much because of the holiday season (which each year becomes increasingly fraught with commercially induced stress and, at least in recent years, subject to global warming [no snow again this year in Chicago!]), but because of the time it affords me to catch up with old acquaintances and friends, as well as a stack of books collecting dust on my nightstand. One such book was American philosopher James Muyskens’ “The Sufficiency of Hope,” which was given to me by a new friend I made during a trip to Botswana last year. While not the type of book I would normally read on an overcast Saturday lying on the couch, I was intrigued enough to read the book from cover to cover because of its pertinence, not only for the professional theorist, but also for those of us who regularly attempt to reconcile our convictions with contemporary philosophy.

Muyskens posits that most people hope the world is the way they believe it is. That is, most people hope that their view of the world is right. They usually do not hope for the truth about things to be much better than what they suppose it is. Sometimes this hope is a factor in causing the belief; sometimes this hope stems from the desire to be right about our belief; and in some cases this hope may follow the belief (i.e., we become accustomed to a particular view of the world and finally come to prefer that view). It seems that most people, especially most philosophers, would rather be perceived to be right than have the world turn out to be even different than their theories allow. They might not admit this outright, but one sees in their writings no signs that they hope they are wrong, and that the world is, in the case of those with a cynical perspective, better than they have supposed. You rarely hear them say: “This is a somewhat grim view I have proposed, and I hope very much that I am wrong, but I am driven to this view by solid considerations.”

The late British philosopher A.J. Ayer is reported to have said shortly before his death that he certainly “hoped in” the finality of death, in spite of having had a “near-death experience,” which “slightly weakened my conviction that my genuine death... will be the end of me, though I continue to hope that it will be.” [He reversed himself a few days later, saying that, “What I should have said is that my experiences have weakened, not my belief that there is no life after death, but my inflexible attitude toward that belief.”]

But what about those people who hope the world is a better place than their theories permit? I have always been curious to know how many agnostics, for example, are regretful that the existence of God is not supported by historical or scientific evidence, and how many permit themselves to hope for God’s existence (and to what degree they do so). Also, are there people who believe in God who are more or less sorry that he exists? Certainly many people who believe in God fear that their thoughts and acts put them in danger of his wrath or, heaven forbid, eternal damnation.

There have always been people who believe that there is inadequate evidence for “supernature,” whether in the form of a specific God or some vague notion of an afterlife. Supposing there is indeed little evidence for God, this raises an intriguing question: Would there be anything epistemologically aberrant in permitting oneself, while not believing in God’s existence, to hope for it? In “The Sufficiency of Hope,” Muyskens makes the curious argument that such hope is not only epistemologically permissible, but that an agnostic may actually be a sincere adherent to a specific religious faith—whether Christian, Muslim, Jewish, Hindu, or other—based upon this hope. According to Muyskens, an agnostic who honestly does not believe there is enough evidence of God’s existence or inexistence to make a judgment either way, is entitled to do two things: 1) he can hope his religion (e.g., Christianity) is true; and 2) he can be a Christian—a full-fledged, praying, worshiping Christian—based merely upon his hope and without “believing” in God in the usual sense of the term “believing.” This is a strange but important thesis. In this instance, an agnostic Christian says, I do not know if God exists; I neither believe nor disbelieve in his existence, but I do hope he exists,
and I will pray to him in the hope that he exists. Muyskens argues that faith has always meant something like this. It has always meant we cannot know; and when people say they believe without knowing, this means, in effect, they are hoping, or at least this is what it should mean.

I would argue it is no different in principle—and really is strikingly similar in many ways—to a person speaking long and tenderly to a loved one in a coma. We do not know or have much evidence that a comatose individual is hearing us, but sometimes we hope he or she can, and sometimes people live out that hope by acting on it with a determined resolution. Not only does this acting out of hope give comfort, but there is a chance the hope is being fulfilled, that is, that words are reaching the mind for which they are intended. This is like praying, so at least Muyskens suggests.

According to Muyskens, ordinary believers who fully believe in the existence of God are living in “epistemological sin.” Based upon his interpretation, there is not enough evidence to warrant actual belief. Only hope is warranted. Ideally, then, there would be millions and millions of Christians (Muslims, Jews, Hindus, and others), not one of whom believed in the existence of God (or Allah, Brahma, Vishnu, Shiva, or Shakti) or the afterlife, but all praying and worshipping, preaching and serving, all in the hope that God is there, but never lapsing into actual belief. Such a person might weep with joy at the great mercy God had shown to him in his life, provided he did not actually think God had done it, but in the hope that God had done it. No doubt many of these people would occasionally feel a temptation to think, “Sometimes I feel so sure it is all true.” or “Yes, that happens. But be strong and resist the temptation; it is very wrong to believe without sufficient evidence.” (Or is it possible that we can be permitted to enjoy the feeling of conviction provided we abstain from actual belief? “I feel sure it is true, but of course I neither know nor believe such a thing.”)

Essentially, Muyskens’ position is that when certain conditions exist, we have a right to hope for things which we do not know to be true, and which we have no right to affirm are true or to believe are true, or even to have faith in (except insofar as faith is understood as hope). He argues that religious faith is best understood as a kind of legitimate hope rather than an unsupported and illegitimate belief. The conditions that characterize legitimate, permissible hope include: 1) that which is hoped for must at least be possible; 2) we can rightly hope only for good things, not for evil things; 3) we naturally only hope for things we believe to be in our real interest; and 4) if that for which we hope pre-supposes other things, those things should be supported by evidence. Notice we do not need a preponderance of evidence of that for which we only hope, but background beliefs involved in the hope must themselves be supported by evidence. (I am not clear why these background conditions cannot, in and of themselves, be hoped for, and I suppose they can be, provided one is conscious that they too are merely hopes and provided they also meet these conditions.)

Muyskens argues further that hope is a matter of degrees. Strong hopes are a function of two factors: the strength of our desire, and the strength of the evidence. For example, a person may strongly hope for the survival of a loved one even if the chances appear dim—or in the case of the global AIDS pandemic, you and I may strongly hope for the survival of those most vulnerable, even if the odds of success are stacked against our collective efforts to save and protect them. If support by evidence becomes preponderant, our hope may become belief. But intensity of desire alone would never justify this transformation of hope into belief, for which strength of evidence is required. In addition, there are cases where we have a duty to hope, and other cases where hope is justified by its possible self-fulfilling nature. In other words, the right to believe becomes more defensible when discussed in terms of the right to hope.

What are we to make of Muyskens’ theory? Three weeks after reading his book—and a number of deep conversations later—I would put the case this way, without delving too far into my own religious beliefs. The world we live in may easily be interpreted in either a natural or a supernatural way. Looked at in one way, the world can be interpreted as an endlessly complex machine. Looked at in another way, the world can, with equal coherence, be interpreted as God’s creation. Either way, we are forced to believe in the existence of the outside world (that which we observe from our narrow, internal worldview), as well as the reality of yesterday and the likelihood of tomorrow.

As I launch into my professional and personal endeavors for 2007, and having re-read the concluding chapter of Muyskens’ book during a break from writing this Report from the President, I have to ask myself whether he is right when he says that hope is all we can legitimately have. In stressing hope, he is very close to putting his finger on a pivotal consideration. We have many alternatives other than believing and disbelieving something. Muyskens observes the importance of hope as an alternative to belief. But there are other alternatives to belief. Besides hope there is also adopting a policy, taking a stance, and making up one’s mind, which need only rely on desire, not hope or faith. I think it likely that all these are much closer to what we have meant by faith than hope; hope being too weak a word. In a rich language such as English, and in all languages, near-synonyms of belief can express complex variations on the theme. Hope is a second cousin of belief; a different idea, but in the same extended family. Similarly for such concepts as supposing, positing, knowing, wishing, and/or trusting, it is unlikely that the meaning of these words can ever be precisely pinned down because the meaning varies in countless subtle ways with the context in which the word appears.

What does the 26th year of our global battle against HIV/AIDS hold? I can well imagine an individual saying: “If you ask me if I believe good will exists to end the scourge of HIV/AIDS, or if I believe in human charity to mitigate the suffering of millions ravaged by HIV disease, I cannot give you a straightforward answer. I believe good will exists, and I believe in human charity. In fact, I am confident, even if at times reality shakes my confidence. Sometimes I am doubtful of the truth of certain aspects of our individual and collective response to the devastation wrought by HIV/AIDS (not to mention poverty, hunger, other diseases, and social upheaval). And, sometimes it is not so much the truth of the matter that is in question as how it ought to be understood. But if I am forced to average out all those times and give you the sort of general answer the question merits, I would have to answer that I hope it is all true; I am supposing for practical purposes that it is true; and in some sense I think it is true.”
In preparing for my decade anniversary as President/CEO of the International Association of Physicians in AIDS Care (IAPAC), I also wonder whether one could enjoy a feeling of conviction without believing 100% that the unlikely is possible. A policeman or prosecutor may feel quite sure that an individual committed a crime, but of course neither the policeman nor the prosecutor may proceed legally against that individual on that basis alone. They may pursue leads connected with the crime based upon their gut feelings, and lacking any other leads this would appear unobjectionable. I may feel sure that the concept of certifying every HIV/AIDS-treating physician in the world is of the utmost importance, and could well alter the practice of HIV medicine forever. There may be scarce objective evidence for this belief, but I can see no reason why I should not indulge my feeling and give way to actual belief. Is this always and everywhere epistemologically faulty? Is it any different, in principle, than believing that a creative “spirit” lies behind the material universe?

I believe that hope, supposing, accepting, taking a stance, and making up one’s mind are not gradations of but indeed close variations on belief. Why should people resist this temptation to let a stance or hope shade over into belief? In my mind, the degree to which this temptation ought to be resisted is highly exaggerated. The plea for caution is usually based upon the danger of believing with insufficient evidence, or, worse, self-deception. Certainly we cannot approve of self-deception, wishful thinking, Pollyanna-ishness, or believing falsehoods. These are the dangers which fascinate Muyskens, and which have preoccupied all the tough-minded thinkers of our philosophical tradition. But a resolute, clear-eyed individual who understands the risks, but has made up his mind to suppose for practical purposes, to hope for, and have some confidence, in the final meaningfulness of the universe, the final triumph of justice, human perfectibility—to name but a few “idealistic” beliefs—is hardly to be compared to a compulsive neurotic who fiercely and passionately ignores, for example, all signs that he is an alcoholic and frantically rejects the entreaties of others to help himself.

We could argue that error must be shunned; that a great source of error is our tendency to believe pleasant things without sufficient evidence; that a hard-nosed, realistic, scientific assessment of the human condition presents us with no good reason for accepting an idealized interpretation of the world. We could therefore conclude that the basic reason so many people do accept such an interpretation has to do with wishful thinking. With exactly as much reason, however, we could conclude the precise opposite. Most people think too small. We know that people are capable of far more than they often imagine themselves to be. We know that the slings and arrows of fortune that browbeat and discourage people, conspire to lower our hopes and expectations. If we had a more lively appreciation of our own potential (individual and collective), if hope were alive and strong in us all, if we dared to dream great dreams, most the world could live at a level far above what is presently supposed. A hard world discourages people. People are more prone to qualms, mistrust, and doubt than they are to excessive optimism. It is our doubts that hold us back, not our dreams, visions, and hopes.

As we continue our struggle against those forces that degrade the human condition, I hope that we will shun excessive fear of error, undue caution, and unwarranted suspicion; and that we will avoid interpreting our world in a pessimistic, skeptical, and mistrustful way which leads to a self-fulfilling undervaluation of our potential. Indeed, it is this pessimistic and mistrustful vision that leads us to suspect our common humanity, be contemptuous of mankind’s common sense, and mistrust mankind’s general tendency toward improving the human condition.

José M. Zuniga is President/CEO of the International Association of Physicians in AIDS Care, and Editor-in-Chief of the IAPAC Monthly.

References
Visit www.iapac.org to learn about how you may join the International Association of Physicians in AIDS Care (IAPAC) in advocating our patients’ right to quality HIV/AIDS care and support.
The GALEN Study Guide features 100 multiple-choice, best-answer format questions similar to those that make up the GALEN Certification Examination. The study guide includes answer rationale and a sample examination bubble-sheet so that clinicians interested in writing the GALEN Certification Examination may self-assess their knowledge in the 12 areas of HIV medicine covered by the examination.

Produced in collaboration with the US National Institutes of Health (NIH), the GALEN Study Guide is a useful tool to measure and strengthen clinicians’ ability to pass the GALEN Certification Examination with a score of 70% or better. Visit www.iapac.org to order your GALEN Study Guide today!
The recently-approved protease inhibitor (PI), darunavir (DRV), boosted by ritonavir (RTV) and in combination with an optimal background regimen, continues to show itself to be safe and potent, according to three studies presented at the Frontiers in Drug Development for Antiretroviral Therapies (DART) conference, held December 10-14, 2006, in Cancun, Mexico. At 48 weeks, a total of 45% of over 450 POWER 1, 2, and 3 study participants had a plasma viral load below 50 copies/ml, with short- and longer-term side effects and toxicities comparable to most first-line boosted PIs.

**POWER 1, 2, 3**

Some 24- and 48-week results from all three POWER studies—have previously been reported, but these new reports include more detailed results, in particular adverse event data.

POWER 1 and 2 were randomized, controlled studies in which 131 highly treatment-experienced participants were randomized to DRV/RTV 600 mg/100 mg twice-daily, and another 124 highly treatment-experienced participants received any other approved RTV-boosted PI along with an optimized background regimen—which included two or more nucleoside reverse transcriptase inhibitors (NRTIs) and/or enfuvirtide (ENF). POWER 3 was a combination of two open-label, non-randomized, rollover studies comprising a total of 324 highly treatment-experienced participants who received DRV/RTV 600 mg/100 mg twice daily along with an optimized background regimen.

**Toxicity and side effects**

The most commonly reported adverse events in participants on DRV/RTV in all three POWER studies were mild-to-moderate diarrhea, nausea, and headache. A total of 9% of those on DRV/RTV in POWER 1 and 2 discontinued due to adverse events compared with 5% on other RTV-boosted PIs. In POWER 3, 25% of participants experienced a grade 3 or 4 laboratory adverse event (although not all of these might have been due to DRV/RTV alone). A total of 7% experienced high amylase (a predictor of pancreatitis); another 6% had high triglycerides and/or high blood sugar; 4% had high total cholesterol; and around 3% had unusually high liver function tests. However only 2% discontinued due to adverse events. Although 14% experienced diarrhea and 10% experienced nausea in POWER 3, the investigators say that there was “no [DRV/RTV] dose relationship...observed and there was no clear relationship between...dose and the frequency or severity of [adverse events].”

Triglyceride levels were above normal for all POWER 1 and 2 participants at baseline. By week 48, mean triglyceride levels were 24% lower in those on DRV/RTV and 25% for those on other boosted PIs. Mean low-density lipoprotein (LDL), high-density lipoprotein (HDL), and total cholesterol levels remained within normal ranges.

**Virological results**

At week 48, 45% of the pooled POWER 1, 2 and 3 participants had viral loads below 50 copies/ml; and more than 90% who had reached this point at week 24 continued to remain undetectable at week 48.

A total of 62% on DRV/RTV in POWER 1 and 2 (and 61% in POWER 3) had at least a one-log reduction in viral load from baseline at week 48. Furthermore, 73% of POWER 1 and 2 participants on DRV/RTV, and 82% of POWER 3 participants, who had achieved a greater than one-log drop in viral load at week 24—but not an undetectable viral load—maintained or improved their virologic response by week 48.

**Efficacy predictors**

Week 48 efficacy was analyzed by various phenotypic and genotypic resistance tests. When examining baseline phenotypic fold change to DRV/RTV undetectable viral load at week 48 was achieved by 54% of participants with a 10-fold or lower change at baseline, compared with 28% and 14% of patients with a 10- to 40-fold change, and a greater than 40-fold change, respectively.

A total of 53% of participants with two or fewer DRV-associated PI mutations achieved an undetectable viral load at week 48, compared with 20% of participants with three or more DRV-associated PI mutations. Similarly, 54% of participants with two or more active NRTIs in their optimized background regimen achieved an undetectable viral load at week 48.

**Utility of ENF**

In participants with one or more DRV-associated mutations at baseline, ENF made no apparent contribution to potency (62% versus 64% with undetectable viral loads at week 48 in those who used ENF for the first time compared with those who did not use ENF). However, the...
participants who did not use ENF appeared to be less treatment-experienced than those who did, since they had a higher mean CD4 count and more active NRTIs in their optimized background regimen at baseline (198 cells/mm$^3$ versus 112 cells/mm$^3$, and 41% versus 22% with two or more active NRTIs, respectively).

Enfuvirtide made much more of an impact in those with two or more DRV-associated mutations at baseline. A total of 62% of participants with two DRV-associated mutations who used ENF for the first time achieved an undetectable viral load, compared with 40% who did not use ENF. And 43% of participants with three or more DRV-associated mutations who used ENF for the first time achieved an undetectable load, compared with 14% who did not use ENF.

Real world experience
A fourth DRV presentation, from an HIV clinic in Houston, found that real world results of DRV/RTV in the drug’s Expanded Access Program were similar to—or even better than—those of the pooled POWER studies.$^4$

Here, 38 individuals (average age 48, mostly white males, two coinfected with hepatitis C virus [HCV]) with limited or no treatment options (on average they had received 11 prior antiretroviral drugs); more than 95% had burned through three or more PIs—including tipranavir (TPV) for one in three—and 39% had previously taken ENF. They received twice-daily DRV/RTV 600 mg/100 mg along with a variety of other antiretroviral drugs. Of the 23 who took ENF, 15 had not taken it before.

By October 2006, all had been on DRV for at least 12 weeks, and 23 had used the drug for 24 weeks. At baseline, mean viral load and median CD4 count were 126,775 copies/mL and 144 cells/mm$^3$, respectively.

Nine adverse events were considered “possibly related to” DRV: two mild rashes; one mild bout of nausea; two abnormal (grade 2) liver function tests; one high (grade 2) total cholesterol test; one very high (grade 3) triglyceride test; one increased (grade 2) creatinine level; and one increased (grade 2) total bilirubin.

Another two serious events occurred that were considered unrelated to DRV: one ENF injection-related hematoma requiring surgery, and one death.

After 12 weeks, 54% achieved a viral load below 50 copies/mL. At week 24, 11 of the 22 for whom data were reported (50%) were undetectable—10 had achieved this by week 12. Total mean viral load reduction at week 24 was 2.17 log$_{10}$ copies/mL, and the mean CD4 count increase was 109 cells/mm$^3$ Of the 22 patients with CD4 data at baseline and at week 24, 42% had CD4 counts below 50 cells/mm$^3$ at baseline. By week 24, 80% had CD4 counts above 100 cells/mm$^3$.

References

Delaying maternal NVP-based ART more effective

Keith Alcorn

Women who received single-dose nevirapine (NVP) at the time of childbirth had better outcomes from a NVP-based triple combination antiretroviral regimen if they started antiretroviral therapy (ART) more than six months after delivery, according to results of a study publishing in the January 11, 2007, edition of the New England Journal of Medicine.

Concern about the effectiveness of NVP-based ART for women previously exposed to NVP at the time of delivery centers around the risk that a single dose of the drug may be enough to cause long-lasting resistance. This is because NVP levels can take 10 to 14 days after a single dose to fall below the limits of detection in many women, and throughout this period the potential exists for NVP-resistant virus to emerge.

In order to study the effect of peripartum NVP exposure on subsequent response to NVP-based ART, US researchers from the Botswana-Harvard School of Public Health AIDS Initiative conducted a prospective observational study in Botswana that included 218 postpartum, HIV-infected women who had received NVP or placebo at delivery plus a short course of zidovudine (ZDV) during pregnancy in the previous MASHI study.

Sixty women started NVP-based ART within six months of giving birth, and the remaining women began the regimen after that time had passed. Of the 60 women who started NVP-based ART within six months of giving birth, 24 had received a single dose of NVP during labor, while 36 had received a placebo. (All of the women in the study were given ZDV from 34 weeks into their pregnancies through delivery; similar to NVP, ZDV reduces HIV transmission from mother to child.) Of the women in this group who received a single dose of NVP during labor, 41.7% subsequently experienced virologic failure within a half a year of starting ART—compared to zero percent among the women in this group who had received placebo during delivery ($P < 0.0001$). Similar differences were found at follow-up visits one and two years after ART had started.

In contrast, there were no statistically significant differences in failure rates within the women who delayed ART for six months—regardless of whether they had received a single dose of NVP during labor. This group (and additional women who have joined the study since) continues to be followed to ensure that no differences emerge as the women receive treatment over a longer period of time.

According to the investigators, “these results translate into very clear policy for
how to treat AIDS in new mothers who received [NVP] to protect their infants. If you can wait six months to administer NVP-based ART, do so. If not, treat only with combinations of drugs that do not contain NVP or NVP-related drugs. Implementing this policy can improve the health of women who need AIDS treatment.”

Advice about NVP-based regimens also applies to efavirenz (EFV)-based regimens, since NVP and EFV are cross resistant.

Treatment response was also measured among 30 infants in the study who received NVP-based ART. More than three-quarters of the 15 infants who were exposed to single-dose NVP as newborns did not respond adequately to the triple-drug treatment (compared with 9.1% of the 15 infants without prior NVP exposure). While these results raise concerns regarding the use of NVP-based ART for infants following single-dose NVP exposure, the group of infants studied was small, and additional data among infants is needed.

The investigators conclude that, “women who need combination ART for their own health during pregnancy should absolutely receive combination ART whenever possible. However, single-dose NVP remains important in preventing mother-to-child transmission of HIV in many locales where it is still the only intervention available. This study provides some important guidance and measured reassurance regarding the timing and effectiveness of NVP-based [ART] for the many women with AIDS who previously received single-dose NVP in labor.”

Reference

Michael Carter

Frequent methamphetamine use, primary NNRTI resistance

Frequent methamphetamine use is associated with primary resistance to nonnucleoside reverse transcriptase inhibitors (NNRTIs) in gay men, according to a San Francisco study published in the January 11, 2007, edition of AIDS. The study’s investigators speculate that poor adherence to antiretroviral therapy (ART) by gay men on “meth binges” may lead to the development of NNRTI-resistant HIV which is then transmitted to other methamphetamine-using gay men who engage in unprotected sex.

Investigators from the University of California, San Francisco wanted to see if methamphetamine use was associated with primary drug resistance in a cohort of 287 gay men recently infected with HIV. Their study was prompted by the case of the “New York patient” who was thought to have become infected with a highly resistant strain of HIV via unprotected sex under the influence of methamphetamine. In addition, high rates of methamphetamine use have been reported by gay men in the United States, and several American studies have found an association between risky sexual behavior and methamphetamine use among gay men. The investigators therefore believed it was plausible that methamphetamine could be implicated in the transmission of drug-resistant HIV.

All the study participants had been infected with HIV within the previous 12 months. They completed structured interviews to assess their HIV risk behavior and drug use in the six months prior to HIV seroconversion. None of the individuals included in the investigators’ analysis was on ART. Genotypic resistance tests were performed to see if the individuals had primary HIV drug resistance.

Over a quarter (83 individuals, 28%) of men reported methamphetamine use in the previous 30 days, and frequent (weekly or more) methamphetamine use was reported by 12% of men. Resistance to at least one antiretroviral drug was present in 77 individuals (26%). The investigators found that men who reported frequent methamphetamine use had a higher prevalence of primary drug resistance (34%) than men who used methamphetamine monthly (21%), or who reported never using methamphetamine (25%).

The investigators, controlling for factors including ethnicity, number of sex partners, and the use of other illicit drugs, then performed further statistical analysis. Frequent methamphetamine use remained significantly associated with resistance to any antiretroviral drug ($P=0.006$). No such relationship was established for infrequent use of the illicit drug. The investigators next conducted a set of analyses to see if the use of methamphetamine was associated with primary resistance to any particular class of antiretroviral drug. Controlling for the same factors as in their first analysis, they found a strong association between frequent use of methamphetamine and resistance to NNRTIs ($P=0.03$). No association was found between infrequent use of methamphetamine use and NNRTI resistance, or between frequent and infrequent use of the drug and resistance to protease inhibitors (PIs) or nucleoside reverse transcriptase inhibitors (NRTIs).

“Our results…suggest that methamphetamine may be an important cofactor in the transmission of NNRTI resistance in this population.” The authors note that an earlier study found users of methamphetamine disrupted their adherence to ART during “meth binge episodes” lasting 24 to 72 hours. They speculate, “repeated cycles of such behavior could result in the emergence of drug resistance because of spasmodic treatment interruptions.” They add that, “the convergence of treatment interruptions and high-risk behavior could be responsible for the high rates of resistance we report here.”

Reference
Now published by

in association with IAPAC, the editors invite manuscripts pertaining to the aims and scope of the journal mentioned below.

The journal publishes original research and research reviews and includes the following regular sections:

- **Pharma Reviews:** Descriptions of specific drug actions, indications, contraindications, and so forth
- **Diagnostic Test Reviews:** Descriptions of new testing procedures for identifying HIV/AIDS
- **Country Profiles:** Overviews of how individual nations and their governments are addressing the AIDS epidemic
- **Program Reviews and Evaluations:** Review and analysis of a specific program (at any level) for AIDS health prevention, education, or treatment
The introduction of antiretroviral therapy (ART) has been credited with extending the lifespan of people living with HIV/AIDS. However, its efficacy relies on access to treatment and excellent adherence, which has proven to be a serious challenge to those receiving highly active antiretroviral therapy (HAART). Regimens are often complicated, can require dietary restrictions, and may lead to adverse effects. Non-adherence to ART in adult populations has been shown to range from 33% to 88%, depending on how adherence is defined and evaluated. Research indicates that consistently high levels of adherence are necessary for reliable viral suppression and prevention of resistance, disease progression, and death. As successful treatment requires exceptional adherence to ART, interventions to improve and maintain adherence are needed.

Several studies have been conducted that examine factors affecting adherence to HAART. We used a novel methodology to synthesize the information from these studies by performing a systematic review on all the literature available in this field using content analysis, particularly focusing on the currently existing qualitative studies and examining their generalizability through quantitative data. We examined both developed and developing nation patient populations.
Search strategy
We performed a systematic, all-language literature search for all qualitative studies and quantitative surveys that addressed barriers and motivators influencing adherence to antiretroviral (ARV) regimens in HIV-positive patients. We searched the following databases: AMED (inception to June 2005), Campbell Collaboration (inception to June 2005), CinAhl (inception to June 2005), Cochrane Library (inception to June 2005), Embase (inception to June 2005), ERIC (inception to June 2005), MedLine (inception to June 2005), and NHS EED (inception to June 2005). Unpublished studies were also sought using the search terms “adherence” and “HIV” on www.clinicaltrials.gov, the UK National Research Register, and conference abstracts from international conference Web sites: International AIDS Society conferences (inception to 2005) and Conferences on Retroviruses and Opportunistic Infections (inception to 2005). Our search strategy combined terms that represented attitudes, barriers, and anxieties. Our search vocabulary included “HIV or AIDS,” “compliance or adherence,” “factors or determinant or barriers,” “motivate or facilitate,” and “HAART or antiretroviral.” We supplemented this search by reviewing the bibliographies of key papers.

Study selection
Two members of the study team independently reviewed the abstracts. Eligible studies met the following criteria: 1) reported an original research study, 2) contained content addressing barriers or facilitators to ART adherence, and 3) were either a qualitative study or quantitative survey. The studies were divided to represent developed or developing nations, as according to the United Nations Human Development Index (HDI). The HDI is a composite index that measures a country’s average achievements in three basic aspects of human development: longevity, knowledge, and standard of living.

Data extraction
Two reviewers independently extracted data and appraised both quality and content. From an initial review of qualitative studies, a coding template was iteratively developed to categorize key barriers to adherence to HAART. The reviewers then conducted a second review of the papers and identified whether they contained the barriers present in the complete template. At each stage of the data abstraction, the reviewers discussed the studies to determine consensus regarding the identification and coding of themes. We analyzed the themes presented in the qualitative studies. After the initial viewing of the selected articles, these themes were grouped into categories. Barriers and facilitators fell under the following subheadings: 1) patient-related, 2) beliefs about medication, 3) daily schedules, and 4) interpersonal factors/relationships. To determine the extent to which these themes exist in the wider communities of developed and developing nations, the reviewers then abstracted data from the survey studies to determine if the issues addressed in the qualitative studies had been asked about in the surveys. We abstracted data on the prevalence of the issues as reported in the surveys.

We extracted data on the quality of both qualitative and quantitative studies using pre-determined criteria for quality. We previously reported our rationale for assessing the quality of qualitative studies and in this study have extended our quality assessment to examine quantitative surveys. Although no formal criteria exist for appraising the quality of surveys, we a priori determined that the following criteria are important across surveys: 1) the survey included members of the target community in the preparation of the survey tool, 2) the survey instrument was assessed for face validity, 3) the survey population was randomly selected, 4) a rationale for determining the response rate was provided, and 4) the investigators attempted to contact non-responders. We did not propose a cut-off score for higher-quality surveys versus lower-quality surveys.

Statistical analysis
We measured chance-adjusted inter-rater agreement for eligibility using the K statistic. When information on proportions was available in the quantitative studies, we first stabilized the variances of the raw proportions (r/n) using a Freeman-Tukey-type arcsine square-root transformation, and then conducted weighted analysis of studies using methods described by Fleiss. The pooled proportion is calculated as the back-transform of the weighted mean of the transformed proportions, using inverse arcsine variance weights for the fixed-effects model and DerSimonian-Laird weights for the random-effects model. The random-effects model recognizes that the studies are a sample of all potential studies and incorporates an additional between-study component to the estimate of variability. Thus, larger studies with smaller variances have relatively more impact on the final estimate. We present the weighted mean with 95% confidence intervals, with lower confidence intervals truncated at zero. The I² statistic was calculated as a measure of the proportion of the overall variation in the meta-analyses that was attributable to between-study heterogeneity.
in developing countries included four from Brazil, 57, 68, 78, 85 and one each from Uganda, 57 Côte d’Ivoire, 63 South Africa, 82 Malawi, 96 Botswana, 52 Costa Rica, 94 Romania, 50 and China. 77

**Barriers and facilitators (developed countries): themes from qualitative studies**

**Barriers.** Thirty-three individual themes of barriers were recorded in 34 qualitative studies.

- **Patient-related:** Thirteen barriers were patient-related and included: a fear of disclosure and wanting to avoid taking medications in public places (23/34); 18, 20, 22-25, 27-29, 31-33, 35-37, 40, 42, 44, 45, 49-51, 108 feeling depressed, hopeless, or overwhelmed (18/34); 19, 23-26, 29, 31, 33-36, 40, 41, 43, 45, 46, 49, 50 having a concurrent addiction (14/34); 23, 24, 27, 31, 33, 36-39, 42, 49-51, 81 and forgetting to take medication at the specified time (11/34); 20, 24, 25, 28, 31, 33-37, 40, 44, 50. Other barriers include: being suspicious of treatment/medical establishment (9/34); 21, 26, 35-36, 38, 41, 42, 50 wanting to be free of medications or preferring a natural approach (10/34); 20, 21, 29, 31, 32, 37, 44, 50, 54, 108 feeling that treatment is a reminder of HIV status (8/34); 18, 32, 38, 39, 41, 43, 49, 54 wanting to be in control (7/34); 28, 31, 37, 38, 41, 54, 108 not understanding treatment instructions (5/34); 31, 33, 36, 38, 42 still having doubt or not being able to accept HIV status (5/34); 18, 33, 42, 44, 51 and a lack of self-worth (4/34); 35, 43, 44, 51. Financial constraints, 31, 42, 46 being homeless, 40, 42 and having other concurrent illnesses affecting adherence were also cited.

- **Beliefs about medication:** There were eight reported barriers pertaining to beliefs/perceptions about medications. Some common barriers in this category included: side effects (either real or anticipated) (27/34); 18, 20, 21, 23-32, 35, 37, 38, 41-46, 48-50, 54, 108 complicated regimens (12/34); 18, 22, 23, 26-28, 32, 42, 48-50, 54 and the taste, size, dosing frequency, and/or pill count (12/34); 18, 20, 23, 25, 29, 45, 48-50, 54. In nine studies, when patients prescribed HAART felt healthy, adherence was often negatively affected. 22, 24, 25, 29, 32, 33, 38, 43, 44. Other barriers included: doubting the efficacy of HAART (7/34); 21, 23, 25, 26, 42, 45, 46 having a decreased quality of life (6/34); 20, 24, 25, 38, 42, 46 uncertainty of long-term effects (6/34); 30, 32, 45, 46, 48, 49 and unwanted changes in body image (5/34). 18, 28, 37, 45, 54

- **Daily schedules:** Nine common barriers were related to daily schedules and included: disruptions in routine or having a chaotic schedule (16/34); 15, 22, 23, 25, 27, 30, 37, 39, 45, 54, 108 finding HAART too inconvenient or difficult to incorporate (14/34); 19, 20, 27-29, 31, 32, 37, 38, 41, 44, 46, 48, 54, 108 and difficulties coordinating adherence with work, family, or care-giving responsibilities.
Individuals in seven studies found it difficult to balance the numerous strict dietary requirements associated with HAART. Six studies cited sleeping through a dose. Other barriers included: being away from home and not bringing medication. Sixteen studies reported learning to balance HAART with daily schedules as a facilitator of adherence. Twelve studies reported having a trusting relationship with a health care provider as a facilitator of adherence. Twenty-three studies noted a lack of trust or a dislike of a patient’s health care provider as an impediment to adherence. Ten studies noted social isolation. Nine studies noted negative publicity regarding HAART or the medical establishment. Finally, five studies noted that having a discouraging social network often deterred patients from successful adherence.

**Facilitators.** Fourteen factors facilitating successful adherence to HAART were abstracted.

- **Patient-related:** Patient-related facilitators included having self-worth (15/23), medication taking priority over substance use (4/23), and seeing positive results when adhering to HAART (6/23). Also, those patients who had accepted their HIV-seropositivity reported improved adherence (8/23).

- **Beliefs about medication:** The most common motivator (12/23) to adherence is a belief in the efficacy of HAART and “having faith” in the treatment. Other motivators included understanding the need for compliance (9/23), difficulty understanding both treatment instructions and the need for compliance; and the presence of concurrent diseases or illnesses, including malnutrition.

- **Daily schedules:** Twelve studies reported learning to balance HAART with daily schedules as a facilitator of adherence. Having a routine in which taking antiretrovirals could be easily incorporated (11/23) and making use of reminder tools (7/23) are both reported to be effective tools for optimizing adherence.

- **Interpersonal relationships:** Positive interpersonal relationships were reported as necessary for successful adherence. Having a trusting relationship with a health care provider was reported as a facilitator of adherence in 17 studies. In addition, openly disclosing HIV status to family and friends and having a strong support network was reported as influential to adherence (18/23). Other motivators included: living for someone, especially, children (9/23); being actively involved in treatment decision making (4/23); and using friends and family as reminders (6/23).

**Common themes from surveys and quantitative studies**

Figure 2 displays the pooled results of studies assessing barriers and reporting proportions of responders. There were three barriers described in qualitative reports but not in the quantitative studies. These were: having suspicions regarding HAART, wanting to be in control, and doubting or having difficulty accepting one’s HIV status.

**Barriers (developing countries): themes from qualitative studies**

As there were only two studies identified, we describe the findings here. Eighteen specific barriers are cited in two studies.

- **Patient-related:** The most common patient-related barriers were: having a co-existing substance addiction, simply forgetting, and financial constraints. Other barriers affecting adherence incorporated: a fear of disclosure; difficulty understanding both treatment instructions and the need for compliance; and the presence of concurrent diseases or illnesses, including malnutrition.

- **Beliefs about medication:** Barriers reflective of patient beliefs regarding antiretrovirals included: side effects (either real or anticipated); complicated regimens; taste, size, and frequency of dosing; having doubts about HAART efficacy; feeling fine or healthy; a decreased quality of life while taking medications, or feeling too sick; and being uncertain about potential long-term effects of HIV treatment.

- **Daily schedules:** Trouble incorporating work and family responsibilities with HAART was seen as a barrier to adherence in both studies. Traveling long distances to receive treatment was common, and not surprisingly, transportation difficulties were often reported to be a major hindrance to adherence (2/2). Other barriers included running out of medications or having an irregular supply.
away from home; and being too busy or distracted to properly comply. No studies mentioned interpersonal relationships as a barrier to adherence in this population. No facilitators to adherence were discussed in any study in a developing country setting.

### Themes from surveys and quantitative studies
Ten surveys were found in developing country settings (Figure 3). No quantitative study enquired of difficulties with morning or afternoon doses, work and family responsibilities, or listed inconvenience as a barrier.

### Table 1. Study characteristics

<table>
<thead>
<tr>
<th>Reference</th>
<th>Country</th>
<th>Population</th>
<th>Focus of study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abel, 2003</td>
<td>US</td>
<td>n = 6; 100% women; (2 African-American, 1 Hispanic, 3 white)</td>
<td>Factors that influence adherence to ART were explored from perspective of women</td>
</tr>
<tr>
<td>Adamian, 2004</td>
<td>US</td>
<td>n = 20; 14 men/6 women (18 African-American, 1 white, 1 multiracial)</td>
<td>Pilot study to assess patients' perceptions of and attitudes toward the motivational interviewing session</td>
</tr>
<tr>
<td>Adam, 2003</td>
<td>Canada</td>
<td>n = 35; 31 men/4 women (no ethnicity info given)</td>
<td>Paper examines difficulties with ART adherence particularly related to dosing schedules and food prohibitions with the structure of everyday lives</td>
</tr>
<tr>
<td>Aversa, 1996</td>
<td>US</td>
<td>n = 99; 74 men/24 women (71% white: 25% African-American: 4% Hispanic)</td>
<td>Study examines variables related to alteration of ART regimens, independent of medical advice</td>
</tr>
<tr>
<td>Barton Laws, 2000</td>
<td>US</td>
<td>n = 25 (sub-sample from group of 61); 17 men/8 women (9 Euro-American, 3 African-American, 12 Latino/Latina, 1 Portuguese)</td>
<td>Describe patients' medication taking behavior and factors related to non-adherence</td>
</tr>
<tr>
<td>Brigido, 2001</td>
<td>Brazil</td>
<td>n = 182; 126 men/56 women</td>
<td>To assess if adherence to antiretroviral medication would correlate to clinical and laboratory outcomes</td>
</tr>
<tr>
<td>Golin, 2002</td>
<td>US</td>
<td>n = 24; 16 men/8 women (12 Euro-American: 12 white)</td>
<td>To understand barriers to ART adherence faced by patients living with HIV in the southeastern US</td>
</tr>
<tr>
<td>Goode, 2003</td>
<td>Australia</td>
<td>n = 18 (11 boys/7 girls) (no ethnicity info given)</td>
<td>To examine beliefs about pediatric HAART from the caregivers' perspective in addition to examining these beliefs in relation to the day-to-day lives of children and their families</td>
</tr>
<tr>
<td>Graney, 2003</td>
<td>US</td>
<td>n = 67; 44 men/13 women (82% African-American)</td>
<td>Study seeks to document relationships between HIV/AIDS medication regimen adherence and characteristics of the regimen itself, social factors, psychological factors, and healthcare practitioner factors</td>
</tr>
<tr>
<td>Hammami, 2004</td>
<td>Belgium</td>
<td>n = 11; caregivers; 8 mother, 1 adoptive parent; 2 self-care; age 0.25 to 18.75 y</td>
<td>To understand adherence behavior in a pediatric population, as reported by caregiver</td>
</tr>
<tr>
<td>Hills, 2003</td>
<td>US</td>
<td>n = 78 (no demographic/ethnicity given specific to study; only general clinic population)</td>
<td>Explore patterns and explanations of adherence to ART from the patients' perspective</td>
</tr>
<tr>
<td>Johnston-Roberts, 2003</td>
<td>US</td>
<td>n = 20; 100% women (50% Hispanic, 35% African-American, 15% white)</td>
<td>Explore, using HIV-positive women's own recollections collected in diary format, how and why women intentionally fail to adhere to ART</td>
</tr>
<tr>
<td>Johnston-Roberts, 2002</td>
<td>US</td>
<td>n = 28; 15 men/13 women (46% white, 36% African-American, 14% Hispanic, 4% other)</td>
<td>Explore the connections between HIV-positive patients' adherence to antiretroviral medication regimens and their beliefs about and satisfaction with their primary care physicians</td>
</tr>
<tr>
<td>Johnston-Roberts, 2001</td>
<td>US</td>
<td>n = 38; 100% women (50% Hispanic, 35% African-American, 15% white)</td>
<td>Explore, from HIV-positive women's own perspectives, the barriers they faced in adhering to combination ARV regimens</td>
</tr>
<tr>
<td>Kaopua, 2004</td>
<td>US</td>
<td>n = 80; 57 men/23 women (40 Native Hawaiian, 40 white)</td>
<td>To understand HAART adherence among Native Hawaiians, a group with historic difficulty in using Western healthcare services because of cultural conflict</td>
</tr>
<tr>
<td>Kemppainen, 2004</td>
<td>US</td>
<td>n = 46; 38 men/8 women (12 African-American, 24 white, 5 Hispanic, and 5 mixed)</td>
<td>To identify factors and circumstances that influence the ability of persons with HIV/AIDS and severe mental illness to comply with ART regimens</td>
</tr>
<tr>
<td>Kitzman, 2004</td>
<td>US</td>
<td>n = 14152; 96 men/56 women (47 white, 40 Latino/Latina, 60 African-American, 5 other)</td>
<td>To understand whether and how HAART affects views and patterns of disclosure and how disclosure interacts with treatment decisions</td>
</tr>
<tr>
<td>Malcolm, 2003</td>
<td>US</td>
<td>n = 44; 28 men/16 women (17 &quot;people of color/27 white)</td>
<td>Examine the health-related attitudes and beliefs of HIV/AIDS patients with excellent adherence to HAART and how they differ from those of patients with suboptimal adherence</td>
</tr>
<tr>
<td>Meytie-Agustoni, 2000</td>
<td>Switzerland</td>
<td>n = 37; 25 men/12 women (no ethnicity information given)</td>
<td>Explore patients' perceptions of HAART</td>
</tr>
<tr>
<td>Reference</td>
<td>Country</td>
<td>Population</td>
<td>Focus of study</td>
</tr>
<tr>
<td>-------------</td>
<td>---------</td>
<td>----------------------------------------------------------------------------</td>
<td>--------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Miller, 2002</td>
<td>US</td>
<td>n = 30; 23 men/7 women (21 Latino, 7 African-American, 2 white)</td>
<td>Assessed barriers to adherence to ARV regimens by conducting focus groups and asking patients about their preferences for different aspects of ARV regimens</td>
</tr>
<tr>
<td>Misener, 1998</td>
<td>US</td>
<td>n = 22; 100% women (18 African-American, 4 white)</td>
<td>To describe the influences affecting decisions made by women in the southern US to accept and adhere to ART</td>
</tr>
<tr>
<td>Murphy, 2003</td>
<td>US</td>
<td>n = 81; 45 men/36 women (22% Central American, 61% Mexican, 6% Mexican-American or Chicano, 1% South American, 4% mixed, and 5% other)</td>
<td>Three aims: (1) to determine what barriers impede adherence, (2) what strategies facilitate adherence, and (3) investigate the health care provider-patient relationship and how it may affect adherence</td>
</tr>
<tr>
<td>Murphy, 2000</td>
<td>US</td>
<td>n = 39; 27 men/12 women (3% Asian/Pacific Islander, 44% African-American, 6% Latino, 3% Native American, 39% white, 6% other or mixed)</td>
<td>Determine what strategies facilitate adherence, determine what barriers prevent adherence, and investigate the health care provider-patient relationship and how it may affect adherence</td>
</tr>
<tr>
<td>Oggins, 2003</td>
<td>US</td>
<td>n = 62; 40 men/22 women (21 African-American, 7 Asian, 2 Haitian, 12 Latino/Latina, 9 European American, 11 Native American)</td>
<td>To explore the reasons for low adherence to HIV-medication regimens among ethnic minority groups</td>
</tr>
<tr>
<td>Powell-Cope, 2003</td>
<td>US</td>
<td>n = 24; 100% women (22 African-American, 2 white)</td>
<td>To obtain complementary data on the complex set of beliefs, attitudes, and behaviors that are related to adherence in indigent, substance-abusing women</td>
</tr>
<tr>
<td>Proctor, 1999</td>
<td>US</td>
<td>n = 39; 27 men/12 women (19 white, 16 African-American, 4 Hispanic)</td>
<td>To understand the barriers to adherence to HAART faced by people living with HIV/AIDS</td>
</tr>
<tr>
<td>Reback, 2003</td>
<td>US</td>
<td>n = 23; 100% men (87% white, 19% Latino, 4% Native American)</td>
<td>To understand the meaning of reported HIV medication adherence among gay and bisexual men who are dependent on or use methamphetamine</td>
</tr>
<tr>
<td>Remien, 2003</td>
<td>US</td>
<td>n = 110; 70 men/40 women (33% white, 31% Hispanic, 43% African-American, 2% other)</td>
<td>To present qualitative data relating to adherence to antiretroviral therapy for HIV disease from a diverse sample in four US cities</td>
</tr>
<tr>
<td>Richter, 2002</td>
<td>US</td>
<td>n = 33; 100% women, 100% African-American</td>
<td>To examine attitudes and beliefs of African-American women of child-bearing age living with HIV, about pregnancy and ART</td>
</tr>
<tr>
<td>Ryan, 2003</td>
<td>US</td>
<td>n = 27; 21 men/6 women (64% African-American)</td>
<td>Exploratory study examines the contextual factors that lead to episodic non-adherence to HAART</td>
</tr>
<tr>
<td>Sankar, 2002</td>
<td>US</td>
<td>n = 15; 100% women (100% African-American)</td>
<td>To identify sources of authority that either promote or discourage adherence, also, to explore how women resolve conflicts between conflicting sources of influence</td>
</tr>
<tr>
<td>Schilder, 2001</td>
<td>Canada</td>
<td>n = 47; 27 gay men, 10 bisexual men, 10 transgendered men (16 First Nations, 31 white, 1 Asian, 1 Latino, 1 French Canadian, 1 Jewish)</td>
<td>To characterize the relationship between identity and healthcare experiences (including ART utilization) among HIV-positive sexual minority males</td>
</tr>
<tr>
<td>Stone, 1998</td>
<td>US</td>
<td>n = 56; 28 men/28 women (16 African-American, 12 Latino/Latina, 28 white containing PIs)</td>
<td>To gather qualitative data regarding HIV/AIDS patients’ perspectives about HIV-1 protease inhibitors and about their experiences taking and adhering to regimens</td>
</tr>
<tr>
<td>Weiser, 2003</td>
<td>Botswana</td>
<td>n = 109; 54 men/55 women (no ethnicity information given)</td>
<td>To improve antiretroviral therapy treatment delivery, social, cultural, and structural determinants of treatment adherence were studied</td>
</tr>
<tr>
<td>Westerfelt, 2004</td>
<td>US</td>
<td>n = 21; 100% men, 100% white</td>
<td>To explore adherence issues among HIV-positive individuals to provide information to design interventions to help individuals achieve higher rates of adherence to ART</td>
</tr>
<tr>
<td>Wilson, 2002</td>
<td>US</td>
<td>n = 66; 90% men/10% women (50% white, 27.3% African-American, 10.6% Hispanic, 4.5% Native American, 1.5% Filipino, 4.5% other)</td>
<td>To explain how ethnically diverse men and women infected with HIV manage their interacting symptom clusters and medication side effects as well as their treatment adherence choices</td>
</tr>
<tr>
<td>Witteveen, 2002</td>
<td>The Netherlands</td>
<td>n = 147; 16 men/11 women (ethnicity not given)</td>
<td>To provide better insights to the extent of adherence to HAART in “hard drug” users</td>
</tr>
<tr>
<td>Wood, 2004</td>
<td>US</td>
<td>n = 36; 100% women (19 Latina, 10 Euro-American, 5 African-American, 2 Cape Verdean)</td>
<td>The study seeks to better understand the patterns, barriers, and facilitators to medication adherence in women caring for children</td>
</tr>
</tbody>
</table>

Source: doi:10.1371/journal.pmed.0030438.t001  PLoS Medicine | www.plosmedicine.org
Figure 2. Barriers reported in developed countries

<table>
<thead>
<tr>
<th>Barriers</th>
<th>Total number of studies</th>
<th>Number of pooled studies</th>
<th>n</th>
<th>% (95% CI)</th>
<th>I²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fear of disclosure</td>
<td>17</td>
<td>13</td>
<td>1,423</td>
<td>20 (12 to 28)</td>
<td>96.3</td>
</tr>
<tr>
<td>Feeling overwhelmed</td>
<td>16</td>
<td>11</td>
<td>1,436</td>
<td>21 (14 to 29)</td>
<td>90.4</td>
</tr>
<tr>
<td>Substance abuse</td>
<td>10</td>
<td>9</td>
<td>964</td>
<td>13 (9 to 16)</td>
<td>60.3</td>
</tr>
<tr>
<td>Simply forgot</td>
<td>18</td>
<td>17</td>
<td>2,146</td>
<td>37 (31 to 42)</td>
<td>84.0</td>
</tr>
<tr>
<td>Suspicious of treatment</td>
<td>1</td>
<td>1</td>
<td>126</td>
<td>21 (15 to 28) *</td>
<td></td>
</tr>
<tr>
<td>Want to be free of meds</td>
<td>5</td>
<td>4</td>
<td>488</td>
<td>11 (9 to 15)</td>
<td>8.4</td>
</tr>
<tr>
<td>Treatment reminder of HIV</td>
<td>10</td>
<td>7</td>
<td>709</td>
<td>33 (13 to 58)</td>
<td>97.9</td>
</tr>
<tr>
<td>Don’t understand treatment</td>
<td>9</td>
<td>5</td>
<td>476</td>
<td>23 (11 to 39)</td>
<td>91.7</td>
</tr>
<tr>
<td>Financial constraints</td>
<td>3</td>
<td>1</td>
<td>214</td>
<td>1 (0 to 3)   *</td>
<td></td>
</tr>
<tr>
<td>Homeless/concurrent illness</td>
<td>2</td>
<td>2</td>
<td>345</td>
<td>2 (0 to 6)</td>
<td>68.1</td>
</tr>
<tr>
<td>Side effects</td>
<td>27</td>
<td>15</td>
<td>1,655</td>
<td>22 (16 to 30)</td>
<td>91.0</td>
</tr>
<tr>
<td>Regimens too complicated</td>
<td>13</td>
<td>5</td>
<td>369</td>
<td>25 (7 to 49)</td>
<td>95.7</td>
</tr>
<tr>
<td>Taste sizing frequency of dosing</td>
<td>20</td>
<td>13</td>
<td>1,577</td>
<td>24 (14 to 36)</td>
<td>96.5</td>
</tr>
<tr>
<td>Doubts about efficacy</td>
<td>16</td>
<td>8</td>
<td>654</td>
<td>9 (6 to 11)</td>
<td>14.4</td>
</tr>
<tr>
<td>Felt fine/healthy</td>
<td>6</td>
<td>5</td>
<td>612</td>
<td>21 (15 to 28)</td>
<td>66.4</td>
</tr>
<tr>
<td>Decreased quality of life</td>
<td>18</td>
<td>12</td>
<td>1,571</td>
<td>19 (13 to 27)</td>
<td>92.1</td>
</tr>
<tr>
<td>Uncertainty</td>
<td>2</td>
<td>2</td>
<td>205</td>
<td>57 (29 to 82)</td>
<td>94.0</td>
</tr>
<tr>
<td>Too toxic</td>
<td>9</td>
<td>7</td>
<td>958</td>
<td>12 (9-16)</td>
<td>61.6</td>
</tr>
<tr>
<td>Disruption/chaotic routine</td>
<td>17</td>
<td>9</td>
<td>1,204</td>
<td>23 (15 to 33)</td>
<td>92.2</td>
</tr>
<tr>
<td>Inconvenient</td>
<td>18</td>
<td>12</td>
<td>1,656</td>
<td>27 (18 to 36)</td>
<td>94.5</td>
</tr>
<tr>
<td>Work/family responsibilities</td>
<td>2</td>
<td>1</td>
<td>65</td>
<td>32 (22 to 44) *</td>
<td></td>
</tr>
<tr>
<td>Dietary requirements</td>
<td>6</td>
<td>2</td>
<td>288</td>
<td>26 (7 to 50)</td>
<td>95.2</td>
</tr>
<tr>
<td>Fell asleep</td>
<td>13</td>
<td>10</td>
<td>1,217</td>
<td>28 (23 to 33)</td>
<td>67.6</td>
</tr>
<tr>
<td>Being away from home</td>
<td>22</td>
<td>17</td>
<td>2,028</td>
<td>28 (21 to 36)</td>
<td>93.2</td>
</tr>
<tr>
<td>Too busy/distressed</td>
<td>17</td>
<td>12</td>
<td>1,288</td>
<td>32 (25 to 39)</td>
<td>86.6</td>
</tr>
<tr>
<td>Pharmacy problems</td>
<td>12</td>
<td>8</td>
<td>1,200</td>
<td>15 (8 to 24)</td>
<td>92.9</td>
</tr>
<tr>
<td>Transportation problems</td>
<td>3</td>
<td>1</td>
<td>13</td>
<td>39 (18 to 64) *</td>
<td></td>
</tr>
<tr>
<td>Social isolation</td>
<td>7</td>
<td>1</td>
<td>70</td>
<td>49 (37 to 60) *</td>
<td></td>
</tr>
</tbody>
</table>

Proportion (%) of pooled responses
Figure 3. **Barriers reported in developing countries**

<table>
<thead>
<tr>
<th>Barriers</th>
<th>Total number of studies</th>
<th>Number of pooled studies</th>
<th>n</th>
<th>% (95% CI)</th>
<th>I²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fear of disclosure</td>
<td>2</td>
<td>2</td>
<td>202</td>
<td>19 (14 to 25)</td>
<td>0</td>
</tr>
<tr>
<td>Feeling overwhelmed</td>
<td>3</td>
<td>1</td>
<td>136</td>
<td>10 (5 to 16)</td>
<td>*</td>
</tr>
<tr>
<td>Simply forgot</td>
<td>5</td>
<td>5</td>
<td>603</td>
<td>36 (19 to 55)</td>
<td>95.7</td>
</tr>
<tr>
<td>Suspicious of treatment</td>
<td>1</td>
<td>1</td>
<td>40</td>
<td>8 (3 to 20)</td>
<td>*</td>
</tr>
<tr>
<td>Want to be free of meds</td>
<td>2</td>
<td>2</td>
<td>179</td>
<td>7 (4 to 11)</td>
<td>0</td>
</tr>
<tr>
<td>Don’t understand treatment</td>
<td>4</td>
<td>4</td>
<td>397</td>
<td>20 (11 to 31)</td>
<td>81.5</td>
</tr>
<tr>
<td>Financial constraints</td>
<td>2</td>
<td>2</td>
<td>240</td>
<td>52 (16 to 88)</td>
<td>97.5</td>
</tr>
<tr>
<td>Homeless/other illness</td>
<td>1</td>
<td>1</td>
<td>134</td>
<td>2 (1 to 6)</td>
<td>*</td>
</tr>
<tr>
<td>Side effects</td>
<td>6</td>
<td>5</td>
<td>555</td>
<td>11 (5 to 18)</td>
<td>84.8</td>
</tr>
<tr>
<td>Regimens too complicated</td>
<td>4</td>
<td>4</td>
<td>355</td>
<td>12 (5 to 21)</td>
<td>77.5</td>
</tr>
<tr>
<td>Taste/size frequency of dosing</td>
<td>3</td>
<td>1</td>
<td>136</td>
<td>4 (2 to 8)</td>
<td>*</td>
</tr>
<tr>
<td>Felt fine/healthy</td>
<td>2</td>
<td>1</td>
<td>136</td>
<td>8 (5 to 14)</td>
<td>*</td>
</tr>
<tr>
<td>Decreased quality of life</td>
<td>3</td>
<td>2</td>
<td>343</td>
<td>15 (12 to 19)</td>
<td>0</td>
</tr>
<tr>
<td>Uncertainty</td>
<td>1</td>
<td>1</td>
<td>16</td>
<td>13 (3 to 36)</td>
<td>*</td>
</tr>
<tr>
<td>Disruption/chaotic routine</td>
<td>3</td>
<td>2</td>
<td>224</td>
<td>15 (11 to 20)</td>
<td>0</td>
</tr>
<tr>
<td>Fell asleep</td>
<td>3</td>
<td>3</td>
<td>363</td>
<td>18 (8 to 31)</td>
<td>88.6</td>
</tr>
<tr>
<td>Being away from home</td>
<td>6</td>
<td>5</td>
<td>440</td>
<td>21 (13 to 31)</td>
<td>80.8</td>
</tr>
<tr>
<td>Too busy/distracted</td>
<td>3</td>
<td>3</td>
<td>358</td>
<td>22 (4 to 49)</td>
<td>96.7</td>
</tr>
<tr>
<td>Pharmacy/irregular supply</td>
<td>7</td>
<td>7</td>
<td>637</td>
<td>22 (10 to 36)</td>
<td>92.9</td>
</tr>
<tr>
<td>Negative view of provider</td>
<td>1</td>
<td>1</td>
<td>207</td>
<td>13 (9 to 18)</td>
<td>*</td>
</tr>
</tbody>
</table>

Proportion (%) of pooled responses
To our knowledge, this is the first systematic review to examine the concerns of HIV-positive patients to maintaining adherence. We found that fear of disclosure, forgetfulness, a lack of understanding of treatment benefits, complicated regimens, and being away from their medications were consistent barriers to adherence across developed and developing nations. More common to developing settings were issues of access, including financial constraints and a disruption in access to medications. While there is a tremendous paucity of qualitative research in developing settings, our findings indicate that many barriers to adherence can be addressed with patients through discussion and education regarding treatment benefits to health. In developing settings, access to medications is the greatest concern. Indeed, discussion in both economic settings may alleviate patients’ suspicions regarding treatment and address practical barriers to improve adherence. This study should also be used to guide the development of interventions aiming to improve adherence in any setting.

This study has several important strengths. The methods we employed to tabulate these findings come from a multi-step process. We first systematically identified qualitative and quantitative studies examining the questions. We then extracted the themes from the qualitative studies and determined which of them were sampled in the quantitative studies. Finally, we synthesized the available quantitative data. By systematically determining the existence and prevalence of barriers in multiple qualitative and quantitative studies, we believe that stronger inferences can be made into patient-related adherence obstacles and facilitators. We have previously demonstrated that surveys benefit from systematically examining qualitative studies, as this improves content validity. To this end, our review of qualitative studies identified several key themes addressing barriers to adherence that were not examined in larger quantitative studies. The presence of barriers in more than one qualitative study, consisting of populations of patients representing different patient populations, supports the conclusion that these barriers are somewhat applicable. Our meta-analysis of survey data is a relatively new process that we have previously demonstrated and can permit stronger inferences into the generalizability of our findings. Finally, our criteria to assess the quality of both qualitative studies and surveys are a new contribution to the methodological literature. Recognizing that the absence of reporting particular methodological criteria may not reflect what was actually conducted during a study, we invite discussion regarding the relative usefulness and applicability of these criteria.

This work has several limitations. We aimed to reduce reviewer bias by conducting abstraction independently, in duplicate. We cannot, however, know to what extent we may miss themes or to what extent reporting bias of the original report may have contributed. We emphasize that our methodology is specific but not sensitive for identifying themes. Reporting bias in the included manuscripts may have limited our ability to identify all barriers and facilitators to adherence. A broad range of economic and social conditions fall under the HDI. It would be wrong to assume that all individuals living in a HDI-categorized “developed” nation are in a better economic situation than all individuals living in a “developing” nation. Detailed information pertaining to this was rarely available in the original reports included in this review. It is possible that surveys used in developing nations were similar to surveys used in developed nations. However, the validity of these surveys in developing settings may not be appropriate, and we press for further qualitative research on this topic. Detailed population descriptions (e.g., education level) and the regional conditions from which this study is produced (e.g., gross national product) would benefit interpretation of future studies in this field. There are several interpretations of appropriate adherence and execution of drug regimens. We did not evaluate patients’ perceptions of what “adherence” means to them, whether it meant acceptance, execution, or persistence of drug therapy. In our meta-analyses of pooled survey data, we found large heterogeneity (as displayed by the $I^2$ values in Figures 2 and 3), indicating large variation between the surveys. Very little methodological literature deals with pooling proportions, and our findings call for further exploration to determine the importance of this heterogeneity. Finally, there were few studies in developing countries that examined early adopters to ART. These individuals may not be representative of the larger epidemic and may not have experienced longer-term side effects of therapy.

It is important to note that the qualitative studies generated a richer spectrum of barriers and facilitators than did the quantitative studies. Qualitative studies are superior at identifying patient-important barriers and facilitators. We would submit that the ideal study of adherence would be one that occurs across several phases and incorporates both qualitative and quantitative elements. For example, to avoid biasing one’s investigation with a priori assumptions about what may be important factors relating to adherence in a given population, it is logical to commence a study with qualitative research, thereby allowing the local population to tell the researchers what they believe to be important barriers, rather than the reverse. By using questionnaires developed in settings that are economically or culturally foreseeably different, the surveys force respondents to answer potentially irrelevant questions.
Clearly, the evidence base for barriers and facilitators of adherence is far richer from developed countries than from developing countries. In our analysis we found only two qualitative studies published from developing nation settings. This is sadly paradoxical, given that the vast majority of HIV-positive patients live in the developing world, and over the coming decades will constitute a growing proportion, and probably the majority, of the world’s HAART recipients. Consequently, we see further research on HAART adherence in developing countries that incorporates both qualitative and quantitative elements as a priority.

Our findings should influence adherence program delivery systems in developing settings. We found that issues such as fear of disclosure, suspicions about treatment, forgetfulness, and irregular supply were important barriers identified by large proportions of the populations studied. It seems appropriate that before mandating any adherence program, such as disclosure or accompagnateurs, opportunities should be provided for individuals who require opting out.16,17 Further, in developing settings, the reliability of medication access is an important adherence barrier that individuals have little opportunity to facilitate. Patient-level adherence can be determined only when a steady supply of medication exists.

We identified a broad range of barriers and facilitators to adherence. These barriers should be inferred as guides for interventional research to improve adherence rates. Given the many factors tabulated in this review, clinicians should use this information to engage in open discussion with patients to promote adherence and identify barriers and facilitators within their own populations. The methodology we used to pool the quantitative data is novel and may prove a useful methodological tool for generalizing patient-important issues.

Editor’s Note: Reprinted with permission from PLoS Medicine (first e-published November 21, 2006).

References
A comparison of three highly active antiretroviral treatment strategies consisting of non-nucleoside reverse transcriptase inhibitors, protease inhibitors, or both in the presence of nucleoside reverse transcriptase inhibitors as initial therapy (CPCRA 058 FIRST Study): A long-term randomized trial


BACKGROUND: Long-term data from randomised trials on the consequences of treatment with a protease inhibitor (PI), non-nucleoside reverse transcriptase inhibitor (NNRTI), or both are lacking. Here, we report results from the FIRST trial, which compared initial treatment strategies for clinical, immunological, and virological outcomes. METHODS: Between 1999 and 2002, 1,397 antiretroviral-treatment-naive patients, presenting at 18 clinical trial units with 80 research sites in the USA, were randomly assigned in a ratio of 1:1:1 to a protease inhibitor (PI) strategy (PI plus nucleoside reverse transcriptase inhibitor [NRTI]; n = 470), a non-nucleoside reverse transcriptase inhibitor (NNRTI) strategy (NNRTI plus NRTI; n = 463), or a three-class strategy (PI plus NNRTI plus NRTI; n = 464). Primary endpoints were a composite of an AIDS-defining event, death, or CD4 cell count decline to less than 200 cells/mm$^3$ for the PI versus NNRTI comparison, and average change in CD4 cell count at or after 32 months for the three-class versus combined two-class comparison. Analyses were by intention-to-treat. This study is registered ClinicalTrials.gov, number NCT00000922.

FINDINGS: 1,397 patients were assessed for the composite endpoint. A total of 388 participants developed the composite endpoint, 302 developed AIDS or died, and 186 died. NNRTI versus PI hazard ratios (HRs) for the composite endpoint, for AIDS or death, for death, and for virological failure were 1.02 (95% CI 0.79-1.31), 1.07 (0.80 to 1.41), 0.95 (0.66 to 1.37), and 0.66 (0.56 to 0.78), respectively. One thousand one hundred ninety-six (1,196) patients were assessed for the three-class versus combined two-class primary endpoint. Mean change in CD4 cell count at or after 32 months was +234 cells/mm$^3$ and +227 cells/mm$^3$ for the three-class and the combined two-class strategies (P=0.62), respectively. HRs (three-class versus combined two-class) for AIDS or death and virological failure were 1.15 (0.91-1.45) and 0.87 (0.75-1.00), respectively. HRs (three-class versus combined two-class) for AIDS or death were similar for participants with baseline CD4 cell counts of 200 cells/mm$^3$ or less and of more than 200 cells/mm$^3$ (P=0.38 for interaction), and for participants with baseline HIV RNA concentrations less than 10,000 copies/mL and 100,000 copies/mL or more (P=0.26 for interaction). Participants assigned the three-class strategy were significantly more likely to discontinue treatment because of toxic effects than were those assigned to the two-class strategies (HR 1.58; P < 0.0001).

INTERPRETATION: Initial treatment with either an NNRTI-based regimen or a PI-based regimen, but not both together, is a good strategy for long-term antiretroviral management in treatment-naive patients with HIV.

Lancet. 2006;368(9553):2107-2109.

Clinical Infectious Diseases

CD4 cell count six years after commencement of highly active antiretroviral therapy in persons with sustained virologic suppression

Moore RD, Keruly JC.

BACKGROUND: Sustained suppression of the human immunodeficiency virus (HIV) type 1 RNA load with the use of highly active antiretroviral therapy (HAART) results in immunologic improvement, but it is not clear whether the CD4 cell count increases to normal levels or whether it reaches a less-than-normal plateau. We characterized the increase in the CD4 cell count in patients in clinical practice who maintained sustained viral suppression for up to six years. METHODS: All patients were from the Johns Hopkins HIV Clinical Cohort, a longitudinal observational study of patients receiving primary HIV care in Baltimore, Maryland, who were observed for more than one year while receiving HAART and who had sustained suppression of the HIV RNA load at <400 copies/mL. We analyzed annual change in the CD4 cell count for up to six years after the start of HAART, stratified by baseline CD4 cell counts of ≤200 cells/µL, 201 cells/µL to 350 cells/µL, >350 cells/µL, and we assessed the development of clinical events (death and new immunodeficiency syndrome-defining illness) by Kaplan-Meier analysis.

RESULTS: A total of 655 patients were observed for a median of 46 months (range, 13 to 72 months). The median change from baseline to most recent CD4 cell count was +274 cells/µL, with 92% of patients having an increase in CD4 cell count. By six years, the median CD4 cell count was 493 cells/µL among patients with baseline CD4 cell counts ≤200 cells/µL, 508 cells/µL among those with baseline CD4 cell counts of 201 cells/µL to 350 cells/µL, and 829 cells/µL among those with baseline CD4 cell counts >350 cells/µL. In addition to baseline CD4 cell count, injection drug use and older age were associated with a lesser CD4 cell count response, and duration of therapy was associated with a greater CD4 cell count response. CONCLUSION: Only patients with baseline CD4 cell counts >350 cells/µL returned to near-normal CD4 cell counts after six years of follow-up. Significant increases were observed in all CD4 cell count strata during the first year, but there was a lower plateau CD4 cell count at lower baseline CD4 cell strata. These data suggest that waiting to start HAART at lower CD4 cell counts will result in the CD4 cell count not returning to normal levels.

Clin Infect Dis. 2007;44(3):441-446.

ABSTRACTS

Pediatric Infectious Disease Journal

Patient, caregiver, and regimen characteristics associated with adherence to highly active antiretroviral therapy among HIV-infected children and adolescents

Martin S, Elliott-Desorbo DK, Wolters PL, et al.

BACKGROUND: This study assesses the relationship between child and caregiver perceptions of medication responsibility, disease knowledge, regimen complexity and adherence to highly active antiretroviral therapy among HIV-positive children. We also examine the association of adherence to child and caregiver demographic characteristics and surrogate markers of HIV disease. METHODS: For this six-month longitudinal study, 24 HIV-positive children (mean age=14.0 years) being treated with highly active antiretroviral therapy and their caregivers completed measures of medication responsibility and disease knowledge. Medication Event Monitoring System caps calculated adherence across months 1 through 3 (time 1) and 4 through 6 (time 2). RESULTS: Medication Event Monitoring System data revealed adherence rates of 81% at time 1 and 79% at time 2. Only 8% (n=2) of child-caregiver pairs reported complete agreement regarding who held responsibility for medication-related tasks. Patients’ responsibility for medication was correlated with age based on child (r=0.51) and caregiver (r=0.57; Ps < 0.05) perceptions, although their regimen knowledge was not. Greater regimen knowledge among caregivers and fewer child-caregiver discrepancies about medication responsibility predicted better adherence (adjusted r=0.45). Finally, adherence was correlated with CD4 percentages at time 1 (r=0.50) and viral load at time 1 (r=-0.56) and time 2 (r=-0.68; Ps < 0.05). CONCLUSIONS: Medication adherence among HIV-infected children is lower than required for optimal viral suppression. Adherence is related to surrogate markers of HIV disease but not to child or caregiver demographic variables. Responsibilities for medication-related tasks should be clarified among family members, regimen knowledge should be emphasized and caregivers should avoid assigning treatment responsibility to a child prematurely.

Focus on Hepatitis

Michael Carter

Coinfection with hepatitis C virus (HCV) increases the risk of cardiovascular disease (CVD) in HIV-positive patients, according to a study published in the January 11, 2007, edition of the journal AIDS. The investigators found that the relationship between HCV infection and increased CVD risk, such as hardening of the arteries, stroke and heart attack, persisted even when they adjusted for factors including age, gender, race, blood pressure, drug use, and smoking. Numerous studies have found a connection between chronic infections and an increased risk for CVD. However, there are conflicting data regarding any such association and infection with HCV.

Heart disease is an increasing concern for HIV-positive patients, many of whom are benefiting from the prolonged prognosis that antiretroviral therapy makes possible. But this means that some individuals are now living long enough to develop cardiovascular illnesses, and an association has been found between the use of antiretroviral therapy and a long-term risk of increased metabolic disorders and heart disease. In addition, many HIV-positive patients (as many as 30% in some cohorts) are HCV-coinfected. The investigators from the HIV-Live (HIV-Longitudinal Interrelationships of Viruses and Ethanol) study therefore wished to see if there was any association between chronic infections and an increased risk for CVD. However, there are conflicting data regarding any such association and infection with HCV.

A total of 395 individuals were included in the investigators’ analysis. Exactly half of the study population was HCV-coinfected. Patients were asked to complete a questionnaire about their health and specify if their physicians had ever been told them that they had atherosclerosis; had a stroke; or, had a heart attack. Data were also gathered on the patients’ age, gender, race, current CD4 count, weight, adherence to antiretroviral therapy, blood pressure, alcohol consumption, drug use, and housing status. Patients were also asked to state if they had diabetes, renal disease, or lipodystrophy.

HIV/HCV-coinfected individuals were significantly older than HIV-monoinfected patients (44 versus 41 years), and had a higher prevalence of health complaints, including diabetes (10% versus 4%), cirrhosis (10% versus 3%), heart attack (7% versus 1%), and CVD (11% versus 3%). All these differences were statistically significant (P < 0.05).

After adjusting their results for age, the association between HCV coinfection and both CVD and heart attack persisted (OR: 4.65 and 12.86, respectively). The investigators then looked to see if any possible confounding factors including gender, race, alcohol consumption, current CD4 count, antiretroviral therapy, lipodystrophy, or the use of illicit substances such as crack, cocaine, or injected drugs affected these results. They write, “When individual cofounders were added separately to the age-adjusted models, the relationship between [HCV] and [CVD] remained unchanged.”

The investigators acknowledge that their study had limitations, in particular that patients were asked to self-report their health histories. Nevertheless, they conclude that, “among HIV-infected individuals, coinfection with [HCV] may be independently associated with an increased risk of [CVD].”

References

Editor's Note: Reprinted with permission from www.aidsmap.com (first e-published January 4, 2007)
Adherence to medical treatment for HIV/AIDS, including highly active antiretroviral therapy (HAART) is an essential determinant of treatment success or failure. Yet, we have much to learn about measurement and intervention for adherence—it is a complex challenge that requires multidisciplinary cooperation among providers, researchers, government agencies, and patients.

Visit www.iapac.org for complete information.
Conference Goal
The goal of this conference is to provide an international forum for the presentation and discussion of state-of-the-science HIV treatment adherence research, as well as current behavioral and clinical perspectives in practicum. Our ultimate hope is that this dialogue translates into evidence-based implementation of approaches for real world clinical and community settings. This activity is targeted to physicians, nurses, pharmacists, psychologists, social workers, researchers, and other healthcare professionals with an interest in the treatment of HIV/AIDS.

Dates to Remember
Exhibitor registration deadline February 15, 2007
Hotel room reservation cut-off February 15, 2007
(Hyatt Regency Hotel, Jersey City, NJ)
Advanced registration ends* March 15, 2007
Late/onsite registration ends* March 30, 2007
* Space is limited. Registration will be processed on a first-come, first-served basis.

Registration
Register online at www.iapac.org.

Accommodations
The Hyatt Regency Hotel is located in Jersey City, New Jersey, directly across the river from Manhattan. The conference room rate is $215. Visit www.iapac.org to make your reservation.

Conference Planning and Funding
Conference content is coordinated by the Planning Committee, led by the hosts, the International Association of Physicians In AIDS Care (IAPAC) and the National Institute of Mental Health (NIMH). This activity is funded through support from the NIMH, National Institute on Drug Abuse (NIDA), and the Office of AIDS Research (OAR) at the US National Institutes of Health (NIH). Additional support has been provided through educational grants from Bristol-Myers Squibb and Gilead Sciences (as of December 15, 2006).

Conference Objectives
After attending this conference, participants will be able to:
- Identify successes and challenges in HIV treatment adherence in various settings and populations worldwide
- Understand behavioral and clinical aspects of adherence that reflect a variety of HIV treatment team perspectives (e.g., patients, physicians, pharmacists, nurses, mental health professionals, adherence specialists)
- Describe the relationships between adherence, pharmacokinetics, viral suppression, and resistance
- Understand the implications of adherence for HIV prevention and public health
- Identify adherence interventions and assessment tools that can be integrated into patient care, including in resource-limited settings

Continuing Education
Continuing education credit for the conference is being provided through a joint sponsorship between IAPAC and the Discovery Institute of Medical Education (DIME). DIME is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians. DIME designates this educational activity for a maximum of 15.75 AMA PRA Category 1 Credit(s). Physicians should only claim credit commensurate with the extent of their participation in the activity.

DIME is accredited by the Accreditation Council for Pharmacy Education (ACPE) as a provider of continuing pharmacy education. This program has been assigned the ACPE Universal Program Number 246-999-07-001-L02 and has been approved for 15.75 contact hours, 1.575 CEUs of continuing education credit.
An application for approval for nursing contact hours has been submitted to the Illinois Nurses Association Approver Unit. Continuing education for psychologists and social workers has been applied for.
Who are your mentors or real life heroes?
I’d have to say Jonathan Mann, for all of the energy and inspiration he gave me over the years. And Quentin Young, Bobby Cohen, Jack Raba, and Pat Logan, who taught me how to be a county hospital doctor; and Ron Sable, Gordy Schiff, and Mardge Cohen, the most principled people I have ever known.

With what historical figure do you most identify?
My dad.

Who are your favorite authors, painters, and/or composers?
Authors: I have a fondness for Larry McMurtry, John LeCarre, Pablo Neruda, and Arundati Roy. What’s the deal with this question excluding musicians? Anyway, there are too many to list: Bonnie Raitt and Jeffrey Orayema, Wolfgang Amadeus Mozart and Miles Davis, Bob Dylan and Ravi Shankar, Ludwig van Beethoven and the Blind Boys of Alabama, Patsy Kline and Carlos Santana, Ladysmith Black Mambazo and Gillian Welch, Louis Armstrong and Ben Folds, David Byrne and Johan Sebastian Bach, the Beach Boys and Billie Holiday, Peter Gabriel and John Coltrane and Aretha Franklin… The best music, though, is the tune you just finished playing, and the one you’re about to begin.

If you could have chosen to live during any time period in human history, which would it be?
This one right here.

If you did not have the option of becoming a physician, what would you have likely become, given the opportunity?
A musician, or maybe a cook.

In your opinion, what are the greatest achievements and failures of humanity?
Achievements: Elimination of smallpox and, on a smaller scale, the reversal of the Chicago River, which was a great public health achievement in alleviating typhoid fever. Also, the fact that women put up with men... Failure: Negligence toward the HIV epidemic and preventable childhood illnesses in the developing world by the developed world, as well as the failure of men and women to rise above our dark sides.

What is your prediction as to the future of our planet one full decade from present day?
I’d like to think that the growing idea that loss of life in the developing world to preventable and treatable conditions is unacceptable will continue to grow and spread. This will continue to encourage not only an effort to provide antiretroviral drugs, but also to fight malaria and tuberculosis, preventable childhood diseases, and, finally, poverty and starvation in the world.
The laws have been signed and they are now effective... We can’t watch our people die, and their patents have been here for so long.

Thailand’s Minister of Health, Mongkol na Songkhla, quoted in a January 25, 2007, Reuters report entitled, “Thailand Stuns Drug Firms with Generic Licenses,” in which he announced the government is issuing compulsory licenses to allow the production of generic versions of the two patented drugs: Kaletra (lopinavir) and Plavix (clopidogrel bisulfate). The government issued its first compulsory license, for Stocrin (efavirenz), in November 2006. That country’s Pharmaceutical Research and Manufacturers Association (PReMA) wrote to Prime Minister Surayud Chulanont to ask that no further compulsory licenses be issued. But Mongkol moved forward, claiming that the industry is “reaping colossal benefit from us.” He added that generic copies from Chinese or Indian firms would be up to 90% less expensive than the patented versions. Brand-name pharmaceutical companies protested that they had not been informed in advance of the decision, which they said could cause some companies to leave Thailand.

One of the strongest predictors of whether or not the teens disclosed their sexual orientation was whether the physician had discussed sex with them at all. Very few physicians were regularly discussing sexuality, even though sex is one of the major developmental challenges and health risks at that age.

Gareth D. Meckler of Portland’s Oregon Health and Sciences University and co-author of a recent US survey that found the majority of openly gay teens are not apt to freely discuss their sexuality their physician, according to a January 3, 2007, Reuters report. In the study, researchers from the RAND Corporation and the University of California, Los Angeles (UCLA) surveyed 131 lesbian, gay, and bisexual teens ages 14-18 attending the “Models of Pride Youth Conference.” Ninety percent had seen their physician within the previous two years, and two-thirds had visited their physician within the past year. Among those surveyed, 70% reported being “out” to everyone or nearly everyone they knew. But while 66% acknowledged it was important for their physician to know about their sexual orientation, only 35% said their own physician knows they are gay, lesbian, or bisexual. In cases where the teens had disclosed to their physician, the physician brought up the issue only 21% of the time. When asked what physicians could do to facilitate a discussion about sexuality, 64% of teens said, “Just ask me.” The full report, “Nondisclosure of Sexual Orientation to a Physician Among a Sample of Gay, Lesbian, and Bisexual Youth,” was published in a recent issue of the Archives of Pediatrics & Adolescent Medicine [2006;160(12):1248-1254].

I haven’t seen this overall realization, like “Houston, we have a problem.”

US Rep. Donald M. Payne (D-NJ), Co-Chair of the Congressional Caribbean Caucus, quoted in a January 21, 2007, Associated Press report about the one-day Caribbean Summit on HIV/AIDS held in St. Croix, during which health officials said widespread ignorance about HIV disease and discrimination against those living with HIV/AIDS are hampering regional control efforts. Excluding Cuba, the Caribbean has the second-highest rate of infection after sub-Saharan Africa. An estimated 500,000 people in the region, or 2.4% of the total population, are infected. In 2005, around 24,000 people in the Caribbean died of AIDS-related illnesses, making it the leading cause of death among people ages 15 to 44. Payne called on the 15-member Caribbean Community (Caricom) to do more to secure international funding for controlling the spread of HIV disease, lest predictions from economists at the University of the West Indies showing that failing to slow HIV/AIDS will have a major impact on Caribbean economies, come true.

It’s not just enrolling people on therapy. It’s people who will die—they’re gone.

Mark Dybul, US Global AIDS Coordinator and in charge of the US President’s Emergency Plan for AIDS Relief (PEPFAR), quoted in a January 12, 2007, San Francisco Chronicle article about the implications of how an impasse over budget priorities left the Republican-controlled 109th US Congress to adjourn in December 2006 with budget resolutions freezing most federal programs, including PEPFAR, at 2006 funding levels through September 2007. Unless the Democratic-controlled 110th US Congress revisits PEPFAR funding by mid-February 2007, PEPFAR will be unable to fulfill the planned expansion of antiretroviral therapy access or programs to prevent mother-to-child transmission (MTCT) of HIV. According to Dybul, PEPFAR was to enroll 350,000 more patients on antiretroviral therapy this year, at 50,000 new patients per month. Most of the new patients to be treated are Africans. Dybul stated that from 110,000 to 175,000 patients will die without antiretroviral therapy, and that an estimated 23,000 children would become infected if Congress does not fully fund PEPFAR, as MTCT services “will pretty much have to halt.”
WHY DOES KEVIN BACON WEAR THE BRACELET?

He wears it to raise desperately needed funds for HIV/AIDS care services, education and vaccine development. Over half a million people have chosen to wear The Bracelet. What about you?

Available at: The Body Shop; Kenneth Cole; Virgin Megastore; Ben Bridge Jewelers and other fine retailers. Or visit us at WWW.UNTIL.ORG or call 1-800-88-UNTIL to order.