Published in final edited form as:

J Acquir Immune Defic Syndr. 2010 March 1; 53(3): 338–347. doi:10.1097/QAI.0b013e3181c7a245.

Provider-Focused Intervention Increases Adherence-Related Dialogue, But Does Not Improve Antiretroviral Therapy Adherence in Persons with HIV

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Abstract

Background—Physicians' limited knowledge of patients' antiretroviral adherence may reduce their ability to perform effective adherence counseling.

Methods—We conducted a randomized, cross-over study of an intervention to improve physicians' knowledge of patients' antiretroviral adherence. The intervention was a report given to the physician prior to a routine office visit that included data on: MEMS and self-reported data on antiretroviral adherence, patients' beliefs about antiretroviral therapy, reasons for missed doses, alcohol and drug use, and depression. We audio-recorded one intervention and one control visit for each patient to analyze differences in adherence related dialogue.

Results—156 patients were randomized, and 106 completed all 5 study visits. Paired audio-recorded visits were available for 58 patients. Using a linear regression model that adjusted for site and baseline MEMS adherence, adherence following intervention visits did not differ significantly from control visits (2.0% higher, $p=0.31$, 95% CI -1.95% – 5.9%). There was a trend toward more total adherence-related utterances (median of 76 vs. 49.5, $p=0.07$) and a significant increase in utterances about the current regimen (median of 51.5 vs. 32.5, $p=0.0002$) in intervention compared with control visits. However less than 10% of adherence-related utterances were classified as “problem solving” in content, and one third of physicians' problem solving utterances were directive in nature.

Conclusions—Receipt of a detailed report prior to clinic visits containing data about adherence and other factors did not improve patients' antiretroviral adherence. Analyses of patient-provider dialogue suggests that providers who care for persons with HIV may benefit from training in adherence counseling techniques.

Keywords

patient compliance; randomized controlled trial; physician-patient relations; HIV infections/drug therapy; communication; electronic monitoring

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These findings were presented in abstract form at the Second International Conference on HIV Treatment Adherence, Jersey City, NJ, March 28-20, 2007.

Introduction

As many as 1.2 million Americans have HIV infection. Fortunately, antiretroviral therapy (ART) can change HIV infection from a progressive and fatal condition to a chronic illness.¹⁻⁶ Unfortunately, for a number of reasons, including that fact that ART has multiple toxicities and must be continued indefinitely, many people do not adhere optimally.⁷⁻¹² Suboptimal adherence may result not only in disease progression and worsening health status, but also in drug resistance, often to multiple classes of antiretrovirals.^{11,13-15} Improving ART adherence is thus of vital clinical and public health importance.

The World Health Organization described five “interacting dimensions” that affect adherence, including social and economic dimension factors, condition-specific factors, therapy-related factors, patient factors, and factors related to the health care team, including provider-patient interactions.¹⁶ A number of interventions can improve adherence to HIV antiretroviral medications,¹⁷ but virtually all of the interventions reported to date have focused on patients. We therefore developed an intervention focused on providers.

This intervention was based on a few simple premises. First, that good provider decision making about ART therapy requires accurate data, both about adherence, and about factors related to adherence such as drug use; second, that providers do not reliably predict patients' adherence, as a number of studies have demonstrated;¹⁸⁻²² and third, that providers have relatively little time or infrastructure in the course of regular office visits to systematically collect such data. We hypothesized that better data would produce more adherence-related dialogue, and in particular more dialogue that had an adherence problem solving character. Our strategy was to provide comprehensive adherence data in the form of a short report to providers at the time of a routine outpatient visit. This report included adherence data from the Medication Event Monitoring System, or MEMS. To test the efficacy of this intervention, we conducted a randomized, cross-over, intervention trial at five sites, including two academic medical centers, a community health center, a general medicine practice, and a private infectious diseases practice.

Methods

Patients

Eligibility requirements included current use of HIV antiretrovirals, a detectable HIV RNA at the most recent clinical visit (a non-detectable viral load was an exclusion criterion), willingness to use an electronic pill bottle cap for one of the ART medications for the duration of the study, and fluency in English. All patients signed written informed consent, and the study was approved by the local Institutional Review Boards and Ethics Committees of all participating sites. Participating providers (n=41) included 40 physicians and 1 physician assistant. We therefore use the term “provider” throughout.

Study design and data collection

A diagram of the study design is shown in Figure 1. There were 6 study visits: a baseline visit, four visits shortly before (median of 8 days) a provider visit (visits 1-4), and a final study visit 6-12 weeks after their fourth provider visit. At each study visit patients completed a survey that asked about various behaviors related to medication adherence or possible non-adherence, and electronic adherence data from the MEMS cap (<http://www.aardexgroup.com/>) was downloaded. During the intervention phase, the data collected at the study visit were summarized in a 3-page report that was given to the provider before each intervention visit. The report included data on self-reported adherence, MEMS adherence, reminder use, beliefs about ART, reasons for missed doses, alcohol and drug use, and depression. Patients were

randomized to 2 groups. The first group received the report prior to 2 consecutive provider visits, followed by 2 visits with no report (the cross over). The second group received no report for 2 visits, followed by 2 visits with the report (the cross over). Providers decided how to use the report; no specific responses to the report were required. The Clinicaltrials.gov identifier is NCT00870792.

Enrollment occurred between 11/18/02 and 1/31/05. Of the 282 persons referred to study coordinators, 220 (78%) agreed to discuss participation with them. Of those, 197 (90%) enrolled, and 156 (79%) successfully completed a run-in period (median of 57 days) designed to test willingness to use the MEMS caps, and were randomized. The number of patients and the number of follow-up visits completed are shown in Fig. 2: 156 (1 visit), 141 (2 visits), 126 (3 visits), 114 (4 visits) and 106 (5 visits). Assignment to intervention first or control first did not predict dropout, suggesting that study drop out did not bias our comparisons. In addition, no study variables (including baseline MEMS and self reported adherence) predicted treatment assignment, suggesting that the randomization was valid.

We made an audio-recording of the first and third provider visits (one intervention, and one control visit). Of the 126 who completed 3 study visits, paired, audio-recorded visits were available and assessable for 58 patients (46%). Thirty-one (53%) were in the intervention first arm and 27 (47%) were in the control first arm. Forty-six (37%) had only one recorded visit, and 10 (8%) had no recorded visits. Reasons for the unavailability of usable recordings included patient refusal, provider refusal, poor quality recording, incomplete recordings, and multiple providers participating in the visit. There were no differences ($p>0.05$) between the patients for whom we did and did not have paired recorded visits on the following characteristics: age, gender, race, education, marital status, percent homeless, sexual orientation, employment, HIV risk factor, physical or mental health status, depression, or beliefs about the usefulness of HIV antiretroviral therapies.

Study Variables

Patient characteristics—Patient characteristics were assessed by self-report at the enrollment visit. Race/ethnicity categories were White, Black, Hispanic, Asian, and other. Education categories included seventh grade or less, high school graduate, college graduate, and higher education graduate. We classified work status as part-time or full-time versus unemployed, and sexual orientation as homosexual, heterosexual or other. Patients also reported how often in the last 30 days they had had a drink (never to daily), and when they drank, the number of drinks they usually had.²³ We classified as “heavy drinkers” those who reported drinking 3 or 4 times a week (or more), and who reported having 3 or 4 drinks when they did drink. We also asked how often in the last 30 days they had had 5 or more drinks in a row (never to daily), and classified as “heavy drinkers” those who reported doing this 3 or 4 times a week or more. To assess drug use, patients were asked whether they had ever used cocaine or heroin, and if so, whether they had used in the last six months.²³ Those who had used in the last six months were classified as “current” drug users. Patients also reported HIV transmission risk factors and whether they were living in a shelter. We used a DSM-IV compatible instrument, the Primary Care Screener for Affective Disorder (PC-SAD), to assess depression.²⁴⁻²⁵ Functional status was assessed using the Medical Outcomes Study Short Form 12-item Survey (SF-12),²⁶ which produces both physical and mental health component scores.

MEMS adherence—We used the Medication Event Monitoring System (MEMS) to monitor adherence with one of the patient's antiretroviral medications. We chose which antiretroviral to monitor with the following priorities: twice a day single or boosted protease inhibitor, twice a day NNRTI, once a day PI, once a day NNRTI, twice a day NRTI, once a day NRTI, once a

day NtRTI. MEMS caps have a pressure-activated microprocessor that records the date and time of each bottle opening and closure. We developed a measure of “covered time” to summarize the MEMS adherence data. To calculate covered time, we assumed that patients were “covered,” meaning that they likely had therapeutic serum levels of the drug, for 15 hours after each dose of a twice-a-day medication, and for 27 hours after a once a day medication. That is, for each dosing regimen we allowed a 3 hour grace period. We did not attempt to make this grace period different for different antiretrovirals. “Uncovered time” accumulated from the end of the grace period to the time that the next dose was taken. Using this approach, we can determine the amount of uncovered time in minutes that are accrued between any two time points. Covered time is expressed as a percentage $((\text{total minutes in an interval} - \text{uncovered minutes in an interval}) / \text{total minutes in an interval}) * 100$, with zero percent representing no adherence, and 100 percent representing optimal adherence. In analyses we used adherence measured over the whole intervention or control period, that is, from the time of randomization to the time of cross over, or the time of cross-over to the final study visit.

Self-reported adherence—For self-reported adherence we used a rating item shown in previous analyses to be most associated with MEMS.²⁷ Patients were asked, “Rate your ability to take all your medications as prescribed” (six categories: very poor, poor, fair, good, very good, and excellent). The reference period was the last month.

Plasma HIV RNA viral loads—We reviewed patients' medical records for plasma HIV viral RNA data. Of the 643 study visits, we found HIV RNA data from the previous 30 days in 488 (76%).

Coding variables from audio-recorded visits—Recordings were analyzed using a system called the Generalized Medical Interaction Analysis System (GMIAS). A unique feature of GMIAS is that it assigns each utterance both a topic code and a speech act code.²⁸ Topic codes include physical health, psychosocial health, logistics, physical exam, studies and trials, socializing, HIV antiretrovirals, non-HIV pharmacotherapy, non-allopathic treatments, and non-pharmacological treatments (e.g., surgeries). Because we were particularly interested in ART adherence, subcodes within the ART adherence topic code were developed, including adherence with the current regimen, side effects, prescribing details, and problem solving. Problem solving utterances are utterances that concern specific strategies for improving adherence, such as using reminder notes and adjusting the patient's schedule. Speech act codes represent the social act embodied in an utterance, such as questioning, giving information, conversation management, showing empathy, directives (urging action), commissives (indicating action), humor, and social ritual.

For example, giving information is divided into two major sub-categories. “Representatives” are assertions of intersubjective reality, statements of facts about the world; while “expressives” are statements about the speaker's state of mind, beliefs, opinions and feelings. Because symptom reports are normally treated as factual and the speaker's purpose in making them is not self-revelation, we classify them as representatives. Examples of representative utterances would be “It hurts when I swallow,” or “This condition is called peripheral neuropathy.” Self-reports of behavior are coded as a sub-category of representative, e.g., “I think I was late one hour [on a medication dose].” Examples of expressives are “I hope you feel good about what you have accomplished,” and “It makes a lot of difference [to have a once-a-day regimen] because it's easier.” Directives include “It is very important to use protection,” and “If your appetite is bad then don't take a lot of foods that are filling.” For more detail on GMIAS speech act codes see the Appendix.

Note that each of these speech act codes has a technical meaning that may differ from how it might be understood colloquially. For example, whereas in normal conversation “giving

information” might describe much of what doctors do, here it has a more specific meaning. The codes are hierarchical, that is they may be subdivided into categories of greater specificity, and both topic and speech act codes can have several levels of hierarchy. Evidence for the reliability and validity of the GMIAS has been previously described.²⁹

To measure inter rater reliability, we compared the codes of each of 3 coders, after training, with the codes of the system developer (MBL), and calculated both percent agreements and kappas.³⁰ Mean percent agreement (kappa) for the first, second, and third digits of the topic codes were 82.7% (0.80), 89.6 (0.87), and 82.7% (0.80), respectively; and for speech act codes were 74.4 (0.71), 79.9 (0.75), and 74.4 (0.72). Kappa statistics of 0.61 – 0.80 are considered “substantial.”³⁰

Analyses

For analysis of our primary study outcome, MEMS adherence, we measured percent adherence in two time periods – between the first doctor visit and the crossover doctor visit (the primary outcome), and between the crossover visit and the end of the study (the crossover outcome). For the analysis of each period, we considered a number of possible covariates. These included baseline data such as MEMS adherence prior to the first doctor visit, self-reported baseline adherence, the mental component of the SF-12, and site, as well as an indicator of treatment or control in the period. We also had a number of other variables describing age and gender, sexuality, route of infection, depression, PTSD, and substance abuse. Due to the randomized design, treatment is theoretically uncorrelated with any covariate, and covariates could be chosen to optimize power. If randomization failed because some patients dropped out, the results would be biased only if the same factors were related to both dropout and outcomes, and if we neglected to consider these factors. Baseline adherence, the mental component of the SF-12, and site were significant predictors of outcomes, so we controlled for those factors. None of the other variables mentioned above were significant predictors of outcomes, and no factors significantly predicted dropout. Log viral loads, a secondary endpoint, were analyzed similarly.

The crossover outcome was not analyzed as a primary outcome because patients in the crossover control group had already received the intervention, and that could have affected their behavior during the crossover period. However, if the intervention effect were small then it could be tested with extra power by analyzing both outcomes as separate but correlated observations. We attempted the latter in a number of ways including regression analysis and a “mixed model” regression (Stata 9) similar to repeated measures ANOVA. These should be viewed as sensitivity tests.

In order to make sure we were not missing something such as a strong but temporary effect early in the first intervention period, we also constructed a graph of adherence over time based on the relationships with the visit time. To graphically represent adherence over time in the 2 study groups (intervention first, then control; control first, then intervention), we used time forward from a given provider visit, and time backward from the next provider visit as anchors. For each between-visit interval for each patient, we created five time points: one week after the initial visit (point 1), one week before the subsequent visit (point 5), and the midpoint between the two visits (point 3). The midpoint between points 1 and 3 was point 2, and the midpoint between points 3 and 5 was point 4. The median between-visit interval was 63 days (25th – 75th percentile, 42 – 92 days).

To better understand how the intervention operated, we used the codes from the GMIAS to compare intervention and control groups for the 58 participants for whom we had paired, usable audiotapes. We hypothesized that intervention visits would have more ART adherence related dialogue (i.e., more total utterances) and in particular more problem solving dialogue. We were

also interested in examining the distribution of speech acts for ART adherence utterances. We hypothesized that intervention visits would have more total utterances that were classified as questions and provision of information by providers than control visits. Utterance counts tended to be skewed, so we used the signed rank test to compare the number of utterances in the ART topic code in intervention and control groups. Finally, we were interested in understanding the role relationships or interactional dynamic within the ART topic code, so we examined the distribution (percentage) of speech act codes within the ART adherence topic code, distinguishing between problem solving and other ART topic code utterances, for both participants and providers, again using the signed rank test.

Results

Patient Characteristics

The mean age of patients was 42 years, 24% were female (Table 1). Fifty-one percent were white, 26% were African American, 19% were Hispanic, and 4% were classified as “other.” Seven percent lived in a shelter or were homeless, 32% were working full time, and 24% screened positive for depression at study entry. The median pre-study viral load was 3.6 copies/mm³ (non-detectable viral load was an exclusion criterion).

Comparison of adherence in intervention and control groups

In analyses that compared the intervention and control groups before the cross-over, adherence in the intervention group was greater than that seen in the control group, but the difference was not statistically significant (2.0 points, 95% confidence interval -5.1 to 9.1, $p=0.57$). When taking the cross-over into account, the difference favoring the intervention was still insignificant (2.0 points, 95% confidence interval of -1.95 to 5.9, $p=0.32$). Similar results were seen using self-reported adherence, and in analyses of viral loads (data not shown).

Figure 3 is a graphical representation of adherence over time in the two groups. In the Figure, Dr. Visits 1 and 2 occur in the first phase of the study; then patients cross over, and visits 3 and 4 occur in the second phase of the study. The closed dots are those who had the intervention first, and then the control; the open dots had the control first, then the intervention. The analyses described in the previous paragraph examine average adherence over the whole intervention and control periods, and Figure 3 shows that there are no within period changes in adherence patterns that such an averaging might have missed.

Characteristics of patient-provider dialogue in intervention and control groups

Intervention visits had more total utterances than control groups (median of 360 vs. 311.5, $p=0.03$, Table 2). There was a trend toward more ART adherence related utterances in the intervention group (median 76 vs. 49.5, $p=0.07$), and, within that group, significantly more utterances related to the current regimen (median 51.5 vs. 32.5, $p=0.0002$). However, there were no differences in the number of utterances in the side effects or ART prescribing subgroups. Finally, there were more problem solving utterances in the intervention compared with the control groups ($p=0.05$). Note, however, that the medians for both groups were zero. That is, in half or more of the visits in both intervention and control groups there were no utterances coded as having ART problem solving content.

To further characterize the ART adherence dialogue, we examined the distribution of speech act codes for patients and for providers (Table 3) and within the ART adherence topic code. There were no differences in number of patients' speech acts comparing interventions and controls, either in the total number of utterances or within any particular type of speech act. There was a trend toward more patient information giving utterances ($p=0.13$) in the intervention group. Note that in both intervention and control columns patients ask almost no

questions, and very few patient utterances were classified as expressions of comprehension or knowledge, or expressions of values, beliefs, desires or goals.

In contrast, there are a number of intervention-related differences in provider speech acts (Table 3). There are more total provider utterances (median of 41 vs. 27, $p=0.05$) and more information giving utterances (23 vs. 10, $p=0.03$) in the intervention compared with the control group. Within information giving, there were more provider expressions of values, beliefs, desires, and goals in the intervention compared with the control group (median of 3 vs. 2, $p=0.01$). In addition, there were more provider directives (median of 3 vs. 1, $p=0.01$). Note that providers in the intervention group did not ask more questions than those in the control group ($p=0.7$), and that there were almost no utterances in either the intervention or control group that showed empathy.

Table 4 compares the pattern of speech acts between ART problem solving utterance and all other ART-related topics, for patients and providers. Table 2 showed that even though there were more problem solving utterances in the intervention than in the control group, that the median number of utterances was zero, so there is relatively little problem solving dialogue over all. Table 4 shows that there are significant differences between the pattern of dialogue for problem solving and other ART related dialogue. Patients give less information (median of 66.7% vs 83.2% of utterances, $p=0.0017$) in problem-solving vs. non-problem solving ART related topic codes. Physicians do less information giving (median of 36.4% vs. 50.8% of utterances, $p=0.028$), show less empathy (median of 0% vs. 0%, $p=0.002$), and make far more directive statements (median of 32.6% vs. 7.7% of utterances, $p<0.0001$) in problem-solving vs. non-problem solving ART related topic codes.

We created the topic code of adherence problem solving because the GMIA developers noted that in discussion of ARV adherence, physicians frequently expressed non-specific exhortations, or reminded patients of unpleasant consequences of non-adherence. Less commonly, the conversation focused on specific reasons for non-adherence and methods for overcoming them, whether initiated by provider or patient. These two strategies seem to be based on different assumptions about why patients are or are not adherent: the first that it is largely a question of motivation, perhaps influenced by beliefs; the second that patients face practical challenges which can be addressed instrumentally. This distinction seemed sharp enough to merit capturing in the coding. An example of a general discussion of non-adherence would be:

D: I tell ya I'm I think in some ways you've been living on borrowed time the way you're, the way you haven't been taking your medicines.

P: I know I know I know. I need to be a strong girl.

D: Well... You're not gonna, you know you can only play the odds so long.

An example of a problem-solving dialogue would be:

D: What would you say the worse problem is that would make you miss every now and then?

P: Um, going to church and doing my girls' hair. I was trying to get ready at the time, church started at (Undecipherable) ...

D: ...So just go leave yourself a note on your pillow or something to-- it doesn't have to-- a little smiley face, whatever to help remind you to take your meds.

Note the typically directive nature of the problem solving excerpt.

Discussion

The provider-focused intervention that we tested, designed to give providers a strong evidence base with which to conduct adherence counseling, did not improve patients' antiretroviral adherence. There was a trend toward an intervention effect, but the average effect size, 2.0 percentage points, was quite small, and we do not believe that an effect of this magnitude is clinically important, even if our study had greater power and the result were statistically significant. The 95% confidence interval ranged from -1.95 to 5.9 percentage points, but even a 5.9% increase in adherence is a relatively small effect; therefore we do not believe that the study was underpowered.

Our analysis of patient-provider dialogue may explain why the intervention was not successful. As hypothesized, the intervention did indeed increase certain aspects of ART related dialogue – specifically utterances related to adherence with the current regimen and ART problem solving – but adherence did not improve. One possible explanation is that this is not a large enough increment in discussion to improve adherence, and we cannot disprove this possibility. However, our data suggest another possible explanation: that providers' approach to improving adherence was ineffective.

While the amount of adherence dialogue increased in the intervention group, very little of that dialogue was problem solving in nature. In fact, the median number of adherence utterances in both groups was zero, so problem solving was rarely practiced as a strategy. If providers were not trying to solve patients' adherence problems, what were they doing? Our analysis of speech acts within the ART adherence topic code suggests that the intervention did not prompt providers to ask more questions, give more information, show more empathy, or suggest more patient actions. Rather, a large fraction of providers' utterances were directive: that is, providers were urging or indicating that patients should undertake certain actions. At best these directives can be exhortations to patients to bring forth their best efforts to achieve an important, even life-saving goal. But these directives tended to have a scolding or lecturing quality. This was clearly not an effective strategy.

Several recent articles that use qualitative methods have pointed to dynamics in patient-provider relationships related to ART adherence that both help explain, and support, our findings. Tugenberg et al.³¹ interviewed patients, who described the “paradoxical effects” of physicians' emphasis on perfect adherence. That is, some patients responded positively to physicians' insistence on perfect adherence; but others became discouraged, and rather than sharing their difficulties taking ART, they concealed them from their physicians. Some patients even described discontinuing clinic visits or stopping medications altogether to avoid being “lectured” to. Barfod et al.³² studied physicians in both San Francisco and Denmark by observing all of a physician's visits for a day, and then conducting a semi-structured interview with the physician about the observed visits. They found that although adherence was mentioned in more than half the visits, in depth discussions were rare, and were almost never initiated by patients. When physicians brought up adherence, they felt awkward in doing so, and patients' responses were usually brief and of low perceived believability. Malta et al.³³ conducted in-depth interviews of 40 Brazilian HIV physicians who described uncertainty about how to discuss adherence, reluctance to discuss ART side effects, and avoidance of the topic. Gerbert et al.³⁴ reported that the providers they interviewed did not have time for a thorough review of adherence – they usually only had time to ask about missed doses.

Our findings disprove an important premise that informed the design of this study – that HIV providers have the skills necessary to effectively counsel patients about ART adherence, but lack accurate and timely information about adherence itself and other key variables that affect adherence such as depression and substance abuse. While it may be true that accurate and

timely information is necessary, in this study it was far from sufficient to improve patients' adherence outcomes. We believe that our results provide empiric support for the assertion that providers need training in adherence counseling in order to achieve better adherence results, as others have previously suggested.^{31,33,35,36}

Efforts to develop and test methods to train physicians in adherence counseling are needed. A number of clinical trials of specific interventions have shown that it is possible to improve ART adherence in persons with HIV infection, but overall the magnitude of the improvements was small, and in a meta analysis, these increments in adherence were not substantial enough to significantly improve viral load outcomes.¹⁷⁻³⁷ A variety of approaches were used in the trials included in this meta analysis, including patient education and case management, modified directly observed therapy, contingency management, provision of social support, and using technologies (e.g., beepers). Interventionists included a variety of types of persons, such as nurses, pharmacists, and peers, but physicians were only mentioned as possible interventionists in two papers.^{38,39} While evidence supports the assertion that physicians can be trained to improve overall communications skills,⁴⁰⁻⁵⁰ we could not find any literature that reports on efforts to train physicians in adherence counseling. This is particularly challenging because for treating physicians because ART adherence counseling for persons with HIV infection needs to take place during routine office visits, which usually last between 15 and 30 minutes.⁵¹ While adherence interventions funded by research grants such as those included in the meta analysis by Simoni et al.¹⁷ show promise, it is not clear how these interventions, which can be labor intensive, can be funded on a sustained basis to become part of routine clinical care. In this context, the importance of training treating physicians, and other treating providers such as nurse practitioners and physician assistants,⁵² in adherence counseling takes on added urgency.

These results also demonstrate the usefulness of the GMIAS as an analytic tool. While a variety of other systems exist to code audio-recorded visits,^{53,54} none that we are aware of is designed to capture adherence content. The GMIAS can easily be generalized to apply to other conditions and other medications, and may be useful to other researchers interested in adherence dialogue.

The design we chose has inherent limitations. We implemented this intervention in the course of routine clinical practice, and while providers welcomed additional data to inform their clinical decision making and interactions with patients, providers at participating sites did not want to participate in a more protocol-driven or directive approach that required certain types of clinical reactions to the data collected because of concerns that it would be too time consuming. Thus, the "strength" of the intervention depended on the time, interest, and skills of individual physicians, and probably also on the unpredictable characteristics of providers' clinical schedules on the day that patients had intervention visits. While a more structured intervention might have been desirable from a research design point of view, it was not practical. This is a challenge for any intervention that takes place as part of routine clinical care. In part because of these challenges, most of the interventions to improve ART adherence that have been tested previously have been patient-focused, with interventions that occur outside of routine office visits, but as previously noted, these effects of patient-focused interventions have been relatively weak.¹⁷ To produce robust and sustainable change in patients' ART adherence behavior, interventions may require combined provider and patient-focused approaches.

It is also possible that providers needed more time to develop a comprehensive approach to the data presented in the reports. For example, our results might have been different if providers had received the intervention report for more than 2 consecutive visits, or if we had followed patients' adherence after receiving the intervention reports for a longer period of time. We were able to obtain paired, analyzable audio-recordings for only 58 study participants, and we would

have had more power had we been able to obtain a larger number. But we show that these 58 were not different from those in whom we could not do such analyses, so we do not believe that this biased our analyses. Finally, it is possible that our physician-focused approach would have gotten more traction in other clinical settings, or other regions of the country. But given that our intervention took place in five very different clinical settings, representing the types of practices in which patients in the US generally get HIV care, we think that this is unlikely.

In summary, this physician-focused intervention produced statistically significant increases in the amount of ART adherence-related patient-provider dialogue, but the intervention overall did not result in improvements in patients' adherence. Analysis of the content and speech acts of the ART related dialogue that we did observe showed a paucity of problem solving dialogue and a directive approach on the part of physicians which was not successful. Adherence is a serious problem for all chronic medications,^{16,55} which argues that improved physician skills in this area are fundamental not just to HIV care, but to the modern day practice of medicine. However we know relatively little about how such training should be conducted, and the development and testing of creative approaches to this problem are needed.

Acknowledgments

This work was supported by grants from the National Institute on Drug Abuse (R01DA015679, R21MH073420), the National Institute for Mental Health (R21MH073420), the Lifespan/Tufts/Brown Centers for AIDS Research (P30AI042853), and the National Center for Research Resources (K24 RR020300).

Appendix

Speech Act Classes	Explanation
Questions	Including open-ended, closed-ended, and leading ("You don't have any nausea?") questions.
Information giving	
Factual information	Assertions about "intersubjective reality"; or statements which have a truth value. Includes symptom reports as these are normally treated as factual by the physician and the speaker's purpose is not principally self-revelation.
Comprehension or knowledge	Assertions that the speaker does or did, or does not or did not, know or understand something.
Values, beliefs, desires, goals	Assertions about the speaker's inner state. "Facts" verifiable only by insight or inner experience.
Conversation management	Utterances which refer to the discourse or function to control it. The most common is what we call a "facilitative utterance," which corresponds to what is sometimes called a "back channel" utterance. These are brief interjections – such as "uh huh" or "okay" – which indicate that the speaker is listening and continues to yield the floor to the interlocutor.
Showing empathy	Only utterances which overtly express empathy are given this code, although an observer might feel that a speaker is being empathic while performing other speech acts, based on tone of voice or body language.
Directives	These are utterances explicitly intended to control or influence the behavior of the interlocutor, divided into modes such as recommending, ordering, requesting, and approving or encouraging reported behavior. Because physicians often couch directives in terms that superficially look like expressives, e.g. "I'd like for you to ... " or "I wish you would ...," we established a code for this as a directive.
Comissives	Promises or expressions of the speaker's future intentions.
Humor	These can only be coded here because their meaning as a social act is unrelated to their manifest content, e.g. "Why

Speech Act Classes	Explanation
	did the chicken cross the road?" is not a question. Utterances which can properly be interpreted as expressives, but also have an ironic or humorous edge which might provoke laughter, are coded in the appropriate expressive category. This is a residual.
Social ritual	These are "politeness" words such as hello, thank you, you're welcome, etc. Greetings such as "How are you?" and the ritualistic responses are coded here. These are generally readily distinguishable from sincere inquiries about the interlocutor's well being

Reference List

1. Palella FJJ, Delaney KM, Moorman AC, et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV Outpatient Study Investigators. *N Engl J Med* 1998;338(13):853–860. [PubMed: 9516219]
2. Hogg RS, Heath KV, Yip B, et al. Improved survival among HIV-infected individuals following initiation of antiretroviral therapy. *JAMA* 1998;279(6):450–454. [PubMed: 9466638]
3. Ledergerber B, Egger M, Opravil M, et al. Clinical progression and virological failure on highly active antiretroviral therapy in HIV-1 patients: a prospective cohort study. Swiss HIV Cohort Study. *Lancet* 1999;353(9156):863–868. [PubMed: 10093977]
4. Egger M, Hirschel B, Francioli P, et al. Impact of new antiretroviral combination therapies in HIV infected patients in Switzerland: prospective multicentre study. Swiss HIV Cohort Study. *BMJ* 1997;315(7117):1194–1199. [PubMed: 9393221]
5. Marins JR, Jamal LF, Chen SY, et al. Dramatic improvement in survival among adult Brazilian AIDS patients. *AIDS* 2003;17(11):1675–1682. [PubMed: 12853750]
6. Sterne JA, Hernan MA, Ledergerber B, et al. Long-term effectiveness of potent antiretroviral therapy in preventing AIDS and death: a prospective cohort study. *Lancet* 2005;366(9483):378–384. [PubMed: 16054937]
7. Paterson DL, Swindells S, Mohr J, et al. Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. *Ann Intern Med* 2000;133(1):21–30. [PubMed: 10877736]
8. Hogg, R.; Yip, B.; O'Shaughnessy, M., et al. Non-adherence to triple combination therapy is predictive of AIDS progression and death in HIV-positive men and women. The XIII International AIDS Conference; Durban, South Africa. July 9–14, 2000; 2000.
9. Arntsen JH, Grant RW, Demas PA, et al. Adherence with antiretroviral therapy in HIV-infected drug users. *Journal of General Internal Medicine* 1999;14(7)
10. Kleeberger CA, Phair JP, Strathdee SA, et al. Determinants of heterogeneous adherence to HIV-antiretroviral therapies in the Multicenter AIDS Cohort Study. *J Acquir Immune Defic Syndr* 2001;26(1):82–92. [PubMed: 11176272]
11. Bangsberg DR, Hecht FM, Charlebois ED, et al. Adherence to protease inhibitors, HIV-1 viral load, and development of drug resistance in an indigent population. *AIDS* 2000;14(4):357–366. [PubMed: 10770537]
12. Stone VE, Hogan JW, Schuman P, et al. Antiretroviral regimen complexity, self-reported adherence, and HIV patients' understanding of their regimens: survey of women in the her study. *J Acquir Immune Defic Syndr* 2001;28(2):124–131. [PubMed: 11588505]
13. Gallego O, de MC, Perez-Elias MJ, et al. Drug resistance in patients experiencing early virological failure under a triple combination including indinavir. *AIDS* 2001;15(13):1701–1706. [PubMed: 11546946]
14. Wensing AM, van d V, Angarano G, et al. Prevalence of drug-resistant HIV-1 variants in untreated individuals in Europe: implications for clinical management. *J Infect Dis* 2005;192(6):958–966. [PubMed: 16107947]
15. Pillay D, Green H, Matthias R, et al. Estimating HIV-1 drug resistance in antiretroviral-treated individuals in the United Kingdom. *J Infect Dis* 2005;192(6):967–973. [PubMed: 16107948]

16. World Health Organization. Adherence to Long-Term Therapies. Geneva: World Health Organization; 2003.
17. Simoni JM, Pearson CR, Pantalone DW, et al. Efficacy of Interventions in Improving Highly Active Antiretroviral Therapy Adherence and HIV-1 RNA Viral Load: A Meta-Analytic Review of Randomized Controlled Trials. *J Acquir Immune Defic Syndr* 2006;43:S23–S35. [PubMed: 17133201]
18. Bangsberg DR, Hecht FM, Clague H, et al. Provider assessment of adherence to HIV antiretroviral therapy. *J Acquir Immune Defic Syndr* 2001;26(5):435–442. [PubMed: 11391162]
19. Roth HP, Caron HS. Accuracy of doctors' estimates and patients' statements on adherence to a drug regimen. *Clin Pharmacol Ther* 1978;23(3):361–370. [PubMed: 627144]
20. Caron HS, Roth HP. Patients' cooperation with a medical regimen. Difficulties in identifying the noncooperator. *JAMA* 1968;203(11):922–926. [PubMed: 5694313]
21. Wagner JH, Justice AC, Chesney M, et al. Patient- and provider-reported adherence: toward a clinically useful approach to measuring antiretroviral adherence. *J Clin Epidemiol* 2001;54:S91–S98. [PubMed: 11750214]
22. Gross R, Bilker WB, Friedman HM, et al. Provider inaccuracy in assessing adherence and outcomes with newly initiated antiretroviral therapy. *AIDS* 2002;16(13):1835–1837. [PubMed: 12218400]
23. Chesney MA, Ickovics JR, Chambers DB, et al. Self-reported adherence to antiretroviral medications among participants in HIV clinical trials: the AACTG adherence instruments. Patient Care Committee & Adherence Working Group of the Outcomes Committee of the Adult AIDS Clinical Trials Group (AACTG). *AIDS Care* 2000;12(3):255–266. [PubMed: 10928201]
24. Rogers WH, Wilson IB, Bungay KM, et al. Assessing the performance of a new depression screener for primary care (PC-SAD). *J Clin Epidemiol* 2002;55(2):164–175. [PubMed: 11809355]
25. Rogers WH, Adler DA, Bungay KM, et al. Depression screening instruments made good severity measures in a cross-sectional analysis. *J Clin Epidemiol* 2005;58(4):370–377. [PubMed: 15862723]
26. Ware JJ, Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Med Care* 1996;34(3):220–233. [PubMed: 8628042]
27. Lu M, Safren SA, Skolnik PR, et al. Optimal Recall Period and Response Task for Self-Reported HIV Medication Adherence. *AIDS Behav* 2008;12(1):86–94. [PubMed: 17577653]
28. Laws, MB.; Lu, M.; Coady, W., et al. Impact of an Intervention on Physician-patient Dialogue Related to Antiretroviral (ARV) Adherence. Oral presentation, 3rd International Conference on HIV Treatment Adherence; Jersey City, NJ. March 17-18, 2008; 2008.
29. Laws, MB.; Lu, M.; Bradshaw, Y., et al. Physician communication styles and their association with antiretroviral adherence. XVII International AIDS Conference; Mexico City. August 3-8, 2008; 2008. #THPE0141
30. Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics* 1977;33(1):159–174. [PubMed: 843571]
31. Tugenberg T, Ware NC, Wyatt M. Paradoxical Effects of Clinician Emphasis on Adherence to Combination Antiretroviral Therapy for HIV/AIDS. *AIDS Patient Care & STDS* 2006;20:269–274. [PubMed: 16623625]
32. Barford TS, Hecht FM, Rubow C, et al. Physicians' communication with patients about adherence to HIV medication in San Francisco and Copenhagen: a qualitative study using Grounded Theory. *BMC Health Serv Res* 2006;6:154. [PubMed: 17144910]
33. Malta M, Petersen ML, Clair S, et al. Adherence to antiretroviral therapy: a qualitative study with physicians from Rio de Janeiro, Brazil. *Cad Saude Publica, Rio De Janeiro* 2005;21(5):1424–1432.
34. Gerbert B, Bronstone A, Clanon K, et al. Combination antiretroviral therapy: health care providers confront emerging dilemmas. *AIDS Care* 2000;12(4):409–421. [PubMed: 11091774]
35. Golin CE, Smith SR, Reif S. Adherence counseling practices of generalist and specialist physicians caring for people living with HIV/AIDS in North Carolina. *J Gen Intern Med* 2004;19(1):16–27. [PubMed: 14748856]
36. Harman JJ, Amico KR, Johnson BT. Standard of care: promoting antiretroviral adherence in clinical care. *AIDS Care* 2005;17(2):237–251. [PubMed: 15763717]
37. Simoni JM, Amico KR, Pearson CR, et al. Strategies for promoting adherence to antiretroviral therapy: a review of the literature. *Curr Infect Dis Rep* 2008;10(6):515–521. [PubMed: 18945394]

38. Rathbun RC, Farmer KC, Stephens JR, et al. Impact of an adherence clinic on behavioral outcomes and virologic response in treatment of HIV infection: a prospective, randomized, controlled pilot study. *Clin Ther* 2005;27(2):199–209. [PubMed: 15811483]
39. Goujard C, Bernard N, Sohier N, et al. Impact of a patient education program on adherence to HIV medication: a randomized clinical trial. *J Acquir Immune Defic Syndr* 2003;34(2):191–194. [PubMed: 14526208]
40. Roter DL.; Hall, JA. Doctors talking with patients. patients talking with doctors. Westport, Connecticut: Auburn House; 1992.
41. Gordon, GH.; Rost, K. Evaluating a faculty development course on medical interviewing. In: Lipkin, M., Jr; Putnam, SM.; Lazare, A., editors. *The Medical Interview: Clinical Care, Education, and Research*. New York: Springer-Verlag; 1995. p. 436-447.
42. Thompson, TL.; Parrott, R. Interpersonal communication and health. In: Knapp, ML.; Daly, JA., editors. *Handbook of Interpersonal Communication*. 3rd. Thousand Oaks: SAGE Publications; 2002. p. 680-725.
43. Roter DL, Cole KA, Kern DE, et al. An evaluation of residency training in interviewing skills and the psychosocial domain of medical practice. *J Gen Intern Med* 1990;5(4):347–354. [PubMed: 2197377]
44. Levinson W, Roter D. The effects of two continuing medical education programs on communication skills of practicing primary care physicians. *J Gen Intern Med* 1993;8(6):318–324. [PubMed: 8320576]
45. van Dulmen AM, van Weert JC. Effects of gynaecological education on interpersonal communication skills. *BJOG* 2001;108(5):485–491. [PubMed: 11368134]
46. van Dulmen AM, Holl RA. Effects of continuing paediatric education in interpersonal communication skills. *Eur J Pediatr* 2000;159(7):489–495. [PubMed: 10923220]
47. Moral RR, Alamo MM, Jurado MA, et al. Effectiveness of a learner-centred training programme for primary care physicians in using a patient-centred consultation style. *Fam Pract* 2001;18(1):60–63. [PubMed: 11145630]
48. Sliwa JA, Makoul G, Betts H. Rehabilitation-specific communication skills training: improving the physician-patient relationship. *Am J Phys Med Rehabil* 2002;81(2):126–132. [PubMed: 11807349]
49. Hulsman RL, Ros WJ, Winnubst JA, et al. The effectiveness of a computer-assisted instruction programme on communication skills of medical specialists in oncology. *Med Educ* 2002;36(2):125–134. [PubMed: 11869439]
50. Roter DL, Hall JA, Kern DE, et al. Improving physicians' interviewing skills and reducing patients' emotional distress. A randomized clinical trial. *Arch Intern Med* 1995;155(17):1877–1884. [PubMed: 7677554]
51. Wilson IB, Landon BE, Ding L, et al. A National Study of the Relationship of Care Site HIV Specialization to Early Adoption of Highly Active Antiretroviral Therapy. *Med Care* 2005;43(1):12–20. [PubMed: 15626929]
52. Wilson IB, Landon BE, Hirschhorn LR, et al. Quality of HIV care provided by nurse practitioners, physician assistants, and physicians. *Ann Intern Med* 2005;143(10):729–736. [PubMed: 16287794]
53. Stiles, WB.; Putnam, SM. Coding Categories for Investigating Medical Interviews: A metaclassification. In: Lipkin, M., Jr; Putnam, SM.; Lazare, A., editors. *The Medical Interview: Clinical Care, Education, and Research*. New York: Springer-Verlag; 1995. p. 489-494.
54. Rimal RN. Analyzing the physician-patient interaction: an overview of six methods and future research directions. *Health Commun* 2001;13(1):89–99. [PubMed: 11370926]
55. Osterberg L, Blaschke T. Adherence to medication. *N Engl J Med* 2005;353(5):487–497. [PubMed: 16079372]

Figure 1.
Study design.

Figure 2.
Study enrollment using CONSORT format.

Figure 3.
Adherence in the two study groups: intervention then control, and control then intervention.

Table 1*Patient characteristics (N=156)*

Characteristic	
Age (mean years (SD))	42.1 (7.5)
Gender (% female)	23.7
Race (%)	
White	51.0
African American	25.8
Hispanic	19.4
Other	3.8
Education	
Grade school	5.8
High school	51.9
College or beyond	42.3
Marital status	
Single	56.4
Married	9.6
Other	34.0
Housing (% living in shelter or homeless)	7.1
Sexual orientation	
Heterosexual	49.4
Men who have sex with men	44.9
Bisexual	5.7
Employment (% working full time)	32.1
HIV risk factor (%)	
Sex with a man	56.4
Sex with a woman	12.2
Injecting drugs	14.7
Other	16.7
Physical Component Score [*] (mean (SD))	45.7 (10.0)
Mental Component Score [*] (mean (SD))	43.0 (12.0)
Depression (% with 5 or greater symptoms)	24.4
HIV therapies "definitely worth taking" (%)	79.5
Monitored medication (top 5 monitored medications, # (%))	
Lopinavir/ritonavir	31 (19.9)
Efavirenz	28 (18.0)
Lamivudine/zidovudine	10 (6.4)
Abacavir/lamivudine/zidovudine	9 (5.8)
Nelfinavir	8 (5.1)
Log ₁₀ pre-randomization HIV RNA (copies/mm ³) ^{**}	3.6 (1.2)

* From the Medical Outcomes Study Short Form 12-item survey

**
Non-detectable viral load was an exclusion criterion for this study.

Table 2

Comparison (median [25th, 75th percentile]) between the total (*patient* plus provider) number of utterances in control and intervention visits by topic code.

Topic Codes	Intervention (N=58)	Control(N=58)	P-value *
Physical health	120.5 [68, 210]	97 [55, 167]	0.14
Psychosocial	24 [0, 53]	6 [0, 59]	0.77
Logistics	43.5 [18, 78]	40.5 [14, 72]	0.35
Physical exam	5 [0, 11]	5 [0, 12]	0.83
Studies/Trials	4 [0, 15]	0 [0, 5]	0.001
Socializing	11 [5, 21]	9 [5, 22]	0.27
ART related	76 [52, 127]	49.5 [28, 113]	0.07
Adherence, current regimen	51.5 [37, 77]	32.5 [17, 52]	0.0002
ART side effects	0 [0, 11]	0 [0, 8]	0.96
ART prescribing	0 [0, 15]	0 [0, 17]	1.00
ART problem solving	0 [0, 12]	0 [0, 2]	0.05
Pharmacological, non-ART	13.5 [6, 59]	23.5 [9, 58]	0.71
Non-Allopathic	0 [0, 0]	0 [0, 0]	0.50
Non-pharmaceutical	0 [0, 2]	0 [0, 4]	0.46
Total utterances	360 [258, 531]	311.5 [239, 492]	0.03

* Signed rank test

Table 3

Number of *patient* and provider utterances (median [25th, 75th percentile]) in the ART topic code by speech act; control and intervention visits (N=58) are compared

Speech Act Codes	Patient Utterances			Provider Utterances		
	Intervention	Control	P-value *	Intervention	Control	P-value *
Questions	1 [0, 2]	1 [0, 3]	0.84	8 [4, 13]	7 [4, 12]	0.34
Information giving	21 [14, 39]	18 [8, 33]	0.13	23 [11, 39]	10 [4, 28]	0.03
Factual information	19 [12, 30]	13 [5, 26]	0.13	17 [6, 32]	6 [2, 21]	0.07
Comprehension or knowledge	1 [0, 3]	1 [0, 2]	0.13	1 [0, 2]	0 [0, 1]	0.13
Values, beliefs, desires, goals	2 [1, 5]	2 [0, 5]	0.79	3 [1, 8]	2 [0, 5]	0.01
Conversation management	3 [2, 8]	1 [0, 8]	0.20	5 [3, 9]	4 [2, 10]	0.39
Showing empathy	0 [0, 0]	0 [0, 0]	n/a	0 [0, 0]	0 [0, 0]	0.7
Directives	0 [0, 0]	0 [0, 0]	0.56	3 [1, 7]	1 [0, 5]	0.01
Commissives	0 [0, 1]	0 [0, 1]	0.15	0 [0, 2]	0 [0, 0]	0.06
Humor	0 [0, 0]	0 [0, 0]	1.0	0 [0, 0]	0 [0, 0]	0.98
Social ritual	0 [0, 0]	0 [0, 0]	n/a	0 [0, 0]	0 [0, 0]	1.0
Total utterances	30 [19, 48]	23 [9, 43]	0.11	41 [25, 69]	27 [15, 49]	0.0469

* Signed rank test

Table 4

This table shows the distribution (percent, median [25th, 75th percentiles]) of speech act codes within the ART problem solving topic code by *patient* and provider. Of the 58 pairs, only 34 had any utterances in the problem solving topic code, and only these 34 are shown here.

Speech Act Codes	Patient Utterances (N=34)			Provider Utterances (N=34)		
	ART-related, not including problem-solving	Problem-solving	P-value*	ART-related, not including problem-solving	Problem-solving	P-value*
Questions (%)	2.6 [0, 8.2]	0 [0, 5]	0.80	21.3 [13.6, 29.9]	14.5 [0, 28.3]	0.082
Information giving (%)	83.2 [75.1, 90.6]	66.7 [12.5, 90.9]	0.0017	50.8 [35.6, 60.2]	36.4 [18.2, 60]	0.028
Factual information (%)	66.1 [58, 76.6]	47.3 [0, 70]	0.0009	38.5 [25.7, 47.3]	32.6 [7.5, 41.7]	0.094
Comprehension or knowledge (%)	3.1 [0, 7.6]	0 [0, 0]	<.0001	2.4 [0, 5.3]	0 [0, 0]	<.0001
Values, beliefs, desires, goals (%)	8.1 [5.3, 13]	0 [0, 13.5]	0.55	7.8 [4.8, 12.3]	0 [0, 12.5]	0.046
Conversation management (%)	10.2 [4.8, 15.8]	0 [0, 16.2]	0.67	16 [10.5, 20.9]	8.7 [0, 14.3]	0.0007
Showing empathy (%)	0 [0, 0]	0 [0, 0]	NA	0 [0, 1]	0 [0, 0]	0.002
Directives (%)	0 [0, 0]	0 [0, 0]	0.57	7.7 [3.2, 13.8]	32.6 [12.5, 50]	<.0001
Commissives (%)	0 [0, 2.8]	0 [0, 10]	0.0057	0 [0, 2.5]	0 [0, 0]	0.96
Humor (%)	0 [0, 0]	0 [0, 0]	0.25	0 [0, 0]	0 [0, 0]	0.25
Social ritual (%)	0 [0, 0]	0 [0, 0]	0.25	0 [0, 0]	0 [0, 0]	1.00
Total utterances (%)	100	100		100	100	
Total utterances (number)	61 [40, 87]	4.5 [2, 11]	<.0001	82 [53, 125]	11 [5, 22]	<.0001

* Signed Rank Test