National Institute for Mental Health (NIMH) / International Association for Physicians in AIDS Care (IAPAC) – International Conference on HIV Treatment Adherence Jersey City, New Jersey, USA March 9-10, 2006: Trip Report

Abiola Johnson

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About RPM Plus

The Rational Pharmaceutical Management Plus (RPM Plus) Program, funded by the U.S. Agency for International Development (cooperative agreement HRN-A-00-00-00016-00), works in more than 20 developing countries to provide technical assistance to strengthen drug and health commodity management systems. The program offers technical guidance and assists in strategy development and program implementation both in improving the availability of health commodities—pharmaceuticals, vaccines, supplies, and basic medical equipment—of assured quality for maternal and child health, HIV/AIDS, infectious diseases, and family planning and in promoting the appropriate use of health commodities in the public and private sectors.

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Abstract

The National Institute for Mental Health and the International Association for Physicians in AIDS Care organized an international conference on HIV treatment adherence in Jersey City, New Jersey from March 8-10, 2006. The goal of the conference was to provide a forum where the latest developments in HIV treatment adherence are discussed and highlighted. RPM Plus had 2 poster presentations at the conference based on the adherence activities that had been carried out under SO4 using FY03 funds; the 2 posters were as follows:

1. Interventions to enhance the use of VCT and PMTCT services: how to improve adherence to ART – a survey of developing countries’ experience
2. Interventions to improve adherence to ART – A review

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Key Words

HIV Treatment, Adherence, Interventions
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## ACRONYMS

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Full Form</th>
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<tbody>
<tr>
<td>AIDS</td>
<td>Acquired Immune Deficiency Syndrome</td>
</tr>
<tr>
<td>ART</td>
<td>Antiretroviral Therapy</td>
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<tr>
<td>ARV</td>
<td>Antiretroviral Treatment</td>
</tr>
<tr>
<td>HIV</td>
<td>Human immunodeficiency virus</td>
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<tr>
<td>IAPAC</td>
<td>International Association for Physicians in AIDS Care</td>
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<tr>
<td>INCIID</td>
<td>InterNational Council on Infertility Information Dissemination, Inc</td>
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<tr>
<td>INRUD</td>
<td>International Network for Rational Use of Drugs</td>
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<tr>
<td>MSH</td>
<td>Management Sciences for Health</td>
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<tr>
<td>NIMH</td>
<td>National Institute for Mental Health</td>
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<tr>
<td>PMTCT</td>
<td>Preventing Mother-To-Child-Transmission</td>
</tr>
<tr>
<td>RCT</td>
<td>Randomized Controlled Trials</td>
</tr>
<tr>
<td>RPM Plus</td>
<td>Rational Pharmaceutical Management Plus</td>
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<tr>
<td>USAID</td>
<td>United States Agency for International Development</td>
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<tr>
<td>VCT</td>
<td>Voluntary Counseling and Testing</td>
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</table>
Adherence to ART has been defined as “the ability of the person living with HIV/AIDS to be involved in choosing, starting, managing and maintaining a given therapeutic combination medication regimen to control viral (HIV) replication and improve immune function”\textsuperscript{1}. High levels of adherence are essential to keeping the HIV-positive individual alive and to slowing the development of ART-resistant strains of the virus. ART resistance has been reported in many recent studies of newly infected HIV+ patients\textsuperscript{2,3}, including treatment-naïve individuals\textsuperscript{4}.

There is evidence from studies in a few resource-constrained countries\textsuperscript{5,6,7,8,9} that show that high levels of adherence, often higher than in developed countries, can be achieved, even, in some cases, where patients must pay for drugs. However, some of these studies have been criticized, due to evidence that they require a relatively strict exclusion criteria as well as the fact that the study populations tend to be urban with above average education and income, which is not generally the profile of the average patient in a resource-constrained setting.

With no agreed upon consensus or gold standard among physicians treating patients with HIV as far as establishing an optimum adherence level\textsuperscript{10} or an ideal method for measuring adherence, maintaining high levels of adherence becomes a required goal of the patient and the physician when it comes to measuring and monitoring patient ART adherence levels.

\textsuperscript{1} Jani AA 9ed.) Adherence to HIV treatment regimens: recommendations for best practices. Available at: http://www.apha.org/ppp/hiv/Best_Practices.pdf
\textsuperscript{2} Salomon, H.; M.A. Wainberg; B. Brenner; Y. Quan; D. Rouleau; P. Cote; R. LeBlanc; E. Lefebvre; B. Spira; C. Tsoukas; R-P Sekaly; B. Conway; D. Mayers; J-P Routy; Investigators of the Quebec Primary Infection Study Prevalence of HIV-1 resistant to antiretroviral in 81 individuals newly infected by sexual contact or injecting drug use. AIDS 2000: 14 F17-23
\textsuperscript{3} Boden, D.; A. Hurley; L. Zhang; Y. Cao, Y. Guo, E. Jones; J. Tsay; J. Ip; C. Farthing, K. Limoli; N. Parkin, M. Markowitz. . HIV-1 drug resistance in newly infected individuals. JAMA 1999, 282:1135-1149
\textsuperscript{6} Orrell C., D.R. Bangsberg, M. Badri and R. Wood. Adherence is not a barrier to successful ART in South Africa AIDS 2003, 17: 1369-1375
\textsuperscript{8} Oyugi J, Byakika-Tusiime J B, Charlebois E, Kityo C, Mugerwa R, Mugenyi P and Bangsberg D 2004 Multiple validated measures of adherence indicate high levels of adherence to generic Hivantiretroviral therapy in resource-limited settings JAIDS 36(5) 1100-1102
\textsuperscript{9} Oyugi J.H., J.T. Byakika, K. Ragland, P. Mugenyi, C. Kityo, R. Mugerwa and D.R. Bangsberg. Treatment outcomes and adherence to generic Triomune and Maxivir therapy in Kampala, Uganda. XV International AIDS conference, Bangkok, 11-16 July 2004 [WeOrB1323] and personal communication
\textsuperscript{10} Though most studies recommend an adherence level of greater than or equal to 95% of all doses.
Purpose of Trip

As part of RPM Plus’ work in improving HIV treatment adherence which has included a desktop literature search on the interventions to improve HIV treatment adherence, administration of a survey on factors enhancing and inhibiting proper access and use of HIV treatment facilities, RPM Plus attended this conference in order to disseminate the work that has been done so far in terms of research to improve adherence and also to participate in discussions with other individuals and organizations who are involved in the treatment of HIV-infected patients. Among the goals of attending the conference, RPM Plus intends to consider new findings from research on HIV treatment adherence and discuss the challenges and strides made in HIV treatment adherence.

Scope of Work for Abiola Johnson

- Present a poster entitled *Interventions to enhance the use of VCT and PMTCT services: How to improve access to ART – Survey of developing country experience*
- Present a poster entitled *Interventions to improve adherence to antiretroviral therapy: A Review*
- Attend workshops, plenary sessions and roundtable discussion and participate in discussions addressing interventions to improve HIV treatment adherence
Friday March 10, 2006
Poster presentation *Interventions to enhance the use of VCT and PMTCT services: How to improve access to ART – Survey of developing country experience* (Poster is included as Annex 1)

Scale-up of HIV/AIDS treatment services in resource-constrained settings, even when antiretroviral medications are available there are considerable challenges such as:

- Encouraging individuals to come forward for testing through VCT programs
- Encouraging HIV positive mothers to complete treatment for their newborns as part of PMTCT
- Encouraging patients on ART to adhere to treatment consistently

The poster presented by Abiola Johnson on behalf of the RPM Plus HIV/AIDS team summarized the study that was carried out as part of the research on interventions to improve adherence to HIV treatment. The objective of the study was to gather information from developing countries on interventions being planned or used in VCT, PMTCT and ART programs. Twelve participating organizations from resource-constrained settings responded to the survey and described a wide number of interventions for improving adherence to ART and for enhancing the use of VCT and/or PMTCT services including travel support, adherence aids, medical and nutritional support and patient and provider education interventions

Friday March 10, 2006
Poster presentation *Interventions to improve adherence to antiretroviral therapy – a review* (Poster is included as Annex 2)

The poster presented by Abiola Johnson on behalf of the RPM Plus HIV/AIDS team summarized the study that was carried out as part of the research on interventions to improve adherence to HIV treatment. The objective of the study was to conduct a desktop research to document approaches to improving adherence to ART and consider how the lessons learned from high-income settings can be applied to HIV/AIDS programs in resource-constrained settings. The result of the research was the classification of most interventions into sub-categories including – Directly Observed Therapy (DOT) and Modified- DOT (M-DOT), Social Support, Educational Interventions, Incentives and Technological devices

**Collaborators and Partners**

Below is a list of the sessions attended during the conference and a summary of presentations

- Plenary Session- Panel Discussion: Reaching adherence goals –
  1. Re-evaluating the 95% [adherence] goal - David Bangsberg
     95% was an important public health goal which had a cost and also had various risk factors. Research has shown that patients of African origin have a better metabolism of NNRTIs. However, the presenter also pointed out that treatment discontinuation/interruption may lead to severe resistance and it is important to minimize resistance especially in cases where one medication is being use. The presenter’s recommendation is that the treatment focus should be on more medications in addition to improving the 95% adherence level
2. Pediatric HIV – Barriers and facilitators to achieving ART adherence in the United States – Claude Ann Mellins (Columbia University)
Profile of HIV-infected children categorizes them in terms of race, poverty as well as substance abuse. There is a multigenerational adversity plaguing the children who are HIV-infected in the US. This includes young people with high and negative psychological factors and neurological health issues. All these combine to decrease the level of adherence achieved by the children. In addition, while age is a factor that counts against the level of adherence achieved, two-thirds of these children were not aware of their HIV sero-status. The presenter also noted that knowledge of their serostatus often ultimately led to non-adherence. Some of the major barriers include non-acceptance of diagnosis and complexity of the regimen. In other words, the near-perfect adherence recommended by experts is often not just difficult, but also impossible. The presenter concluded that while knowledge and motivational-based interventions are important, they are not sufficient, as such, interventions being developed should also explore mental health issues which children are faced with (this is particularly important in children 9-16 years of age). In addition, efforts need to be made to reduce the complexity and toxicity of the drug regimens.

3. Linkage to care to treat HIV-infected patients – Timothy Flannigan
The presenter shared evidence from a number of studies which had concluded that ARV resistance is not a major determinant of clinical disease progression. One of these studies used M-DOT as an intervention to target substance-users who were failing therapy (i.e. had less than optimum adherence levels), the results were that there was no development of resistance. The most important issues to focus on, according to the presenter, were models of care that work. This includes engaging patients in care in a timely manner, taking into consideration differences in community and culture – in other words, what works in X place will not work in Y place. The presenter also emphasized using short-term but effective interventions which bear in mind the instability in certain communities.

4. Barriers to adherence in resource-poor setting – Joia Mukherjee (affiliated with Brigham and Women’s Hospital but working with HIV-infected patients in Haiti) – The presenter pointed out that even in cases where ART is provided free-of-charge, additional out-of-pocket costs which the patient is faced with often serve as a barrier to adherence. A number of interventions were discussed which were being used to help patients adhere properly to treatment, these include – behavior change interventions, incentives (including the threat of jail time to patients who fail to adhere properly), social support and a number of enablers. Interventions for health care providers included basic training in HIV treatment which should have a long-term focus, an example was cited of a pediatrician who had trained in Haiti but had never had the opportunity to treat an HIV-infected child for a number of reasons, until the introduction of basic training and the provision of pediatric medications.

11 Mitty Jennifer, Mwaburi D, Macalino G, Caliendo A, Bazerman L and Flanigan T. 2006 Improved virologic outcomes and less resistance for HAART-experienced substance users receiving modified directly observed therapy-Results from a randomized controlled trial 13th Conference on Retroviruses and Opportunistic Infections. Denver, Colorado [abstract 622a]
Workshop and Specialty Topics – Methodological issues in design of adherence interventions from on-going and randomized controlled trials. The workshop session was moderated by Margaret Chesney. Presenters included Steven Safren who discussed the lessons learned from RCTs, Glenn Wagner who discussed cognitive-behavioral interventions to enhance adherence to ART, Nancy Reynolds who evaluated lessons learned from coordinating RCTs. Recommendations which came out of this workshop session included:

a. Developing a module/program to inform funding review committees on the essential requirements in terms of adherence for HIV treatment regimens in order to redirect the current focus which is not favorable

b. Analyze the factors which enable certain [non-HIV treatment] programs to succeed in improving levels of adherence and examine what lessons can be learned from them in order to develop programs – examples cited include programs under INCIID

c. Allow treatment sites/centers to determine which approaches work for them – promotion of a participatory approach

Poster Sessions – There were several posters presented but the author was not able to see all of them being a presenter herself. One of those which she was able to see was ‘HIV Adherence Training for Substance Abuse Counselors: Client Discussions and Health Advocacy’ which concluded that in tackling adherence issues the counselor needs to take into consideration all of the co-related issues that the HIV-positive substance abuser is faced with.

More proceedings on the NIMH/IAPAC international conference on HIV treatment adherence are available on the website at http://www.iapac.org/home.asp?pid=6514
NEXT STEPS

Immediate Follow-up Activities
RPM Plus is working on developing another survey in collaboration with INRUD which will be administered in East African countries and will focus on adherence monitoring and promotion in order to learn which facilities/programs/projects in these countries have established adherence monitoring mechanisms and also which facilities/programs/projects use interventions to improve/promote adherence. In addition, the motivations mapping tool - developed by the RPM Plus TB team in collaboration with other partners - will be adapted to HIV treatment settings and will serve as an adherence promotion planning tool.

Recommendations
It is recommended that USAID continue the funding of related activities in terms of research for improving adherence and developing interventions or innovative approaches in the direction of improving adherence because as more and more countries are receiving ARVs as part of the HIV treatment programs, adherence is bound to be a challenge, more so given that there are no established rules set by health care providers and physicians in terms of what the gold standard for measuring and monitoring adherence should be.

Agreement or Understandings with Counterparts
NIMH/IAPAC have decided to make this conference an annual event to take place in the US and also to include not just physicians in AIDS care but various stakeholders in the HIV treatment programs who are working to improve adherence in patients on ART.
ANNEX 1. POSTER PRESENTATION

Interventions to Enhance the use of VCT and PMTCT Services—How to Improve Adherence to ART—
Survey of Developing Countries’ Experience

A. Bith and A. Johnson, Management Sciences for Health

Background
Scale-up of HIV/AIDS treatment services in resource-constrained settings is gradually becoming a reality despite the potential barriers such as stigma and the high cost of treatment. However, even where antiretroviral medications appear to be accessible and affordable, considerable challenges remain such as—
- Encouraging individuals to come forward for testing and treatment through voluntary counseling and testing programs (VCT).
- Encouraging Behavior change messages to complete treatment for their needs and as part of prevention of mother-to-child transmission (PMTCT) interventions.
- Encouraging patients on antiretroviral treatment (ART) to adhere to treatment both consistently and for the rest of their lives.

Study Objective
Gather information from developing countries on interventions being used or planned in VCT, PMTCT, and ART programs.

Methodology
In April 2004, the Management Sciences for Health (MSH) Rational Pharmaceutical Management (RPM) Plan Program sent an electronic survey via e-mail to 127 individuals, civil and public and private organizations worldwide that had been identified as working in resource-constrained settings. In addition to the e-mail, information on the survey was posted to appropriate forums and to the MSH/RPM Plan website.

Results
Twelve participating organizations, all from resource-constrained settings, responded to the survey. They were prompted to describe interventions they are using to improve adherence to ART—
- Travel support
- Adherence aids (pill boxes)
- Patient education interventions (adherence counseling prior to starting treatment)
- Interventions targeted to the client/patient

Enhancing the use of VCT and/or PMTCT services—
- Travel, food, or financial support
- Medical and nutritional support
- Patient and provider education interventions (such as HIV/AIDS awareness seminars)

Interventions targeted to the provider and the caregiver.

Lessons Learned
- Diverse public and private organizations are providing HIV/AIDS services in resource-constrained settings.
- Direct financial costs, such as the cost of medications and laboratory tests, are becoming less of a barrier to accessing VCT, PMTCT, and ART services.
- HIV/AIDS treatment programs recognize that barriers exist for access to services and treatment. To improve clients’ health, they are planning and implementing a variety of innovative interventions to increase the use of VCT or PMTCT services or to improve adherence to ART.

Next Steps
- RPM Plan is administering another survey directly addressing service providers.
- This survey will concentrate on ART adherence and not focus on infrastructure and supply chains unfamiliar to HIV/AIDS service providers.
- RPM Plan is planning to develop improved adherence monitoring and promotion systems.

For more information—
Web: www.msh.org/rpmplus
E-mail: rpmpplus@msh.org

Summary of Interventions Described by Survey Participants

<table>
<thead>
<tr>
<th>Country</th>
<th>Type of Organization</th>
<th>Type(s) of Service Provided</th>
<th>Description of Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>India</td>
<td>Private hospital</td>
<td>ART</td>
<td>Education, adherence aids, adherence aids at pill boxes</td>
</tr>
<tr>
<td>Bangladesh</td>
<td>Community-based organization (CBO)</td>
<td>VCT, PMTCT</td>
<td>Education, adherence aids, adherence aids at pill boxes</td>
</tr>
<tr>
<td>Kenya</td>
<td>National hospital, GPO, and workplace program</td>
<td>VCT, PMTCT, ART</td>
<td>Education, adherence aids, adherence aids at pill boxes</td>
</tr>
<tr>
<td>Kenya</td>
<td>District hospital</td>
<td>VCT, PMTCT, ART</td>
<td>Education, adherence aids, adherence aids at pill boxes</td>
</tr>
<tr>
<td>Kenya</td>
<td>Regional hospital</td>
<td>VCT, PMTCT, ART</td>
<td>Education, adherence aids, adherence aids at pill boxes</td>
</tr>
<tr>
<td>Ghana</td>
<td>Non-governmental organization (NGO)</td>
<td>VCT, PMTCT</td>
<td>Education, adherence aids, adherence aids at pill boxes</td>
</tr>
<tr>
<td>Nigeria</td>
<td>NGO</td>
<td>VCT, PMTCT, ART</td>
<td>Education, adherence aids, adherence aids at pill boxes</td>
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<tr>
<td>Nigeria</td>
<td>NGO</td>
<td>VCT, PMTCT, ART</td>
<td>Education, adherence aids, adherence aids at pill boxes</td>
</tr>
<tr>
<td>South Africa</td>
<td>Private organization</td>
<td>ART</td>
<td>Education, adherence aids, adherence aids at pill boxes</td>
</tr>
<tr>
<td>South Africa</td>
<td>Private non-profit manufacturer</td>
<td>VCT, PMTCT</td>
<td>Education, adherence aids, adherence aids at pill boxes</td>
</tr>
<tr>
<td>Tanzania</td>
<td>Regional and local government</td>
<td>VCT, PMTCT, ART</td>
<td>Education, adherence aids, adherence aids at pill boxes</td>
</tr>
<tr>
<td>Tanzania</td>
<td>NGO</td>
<td>VCT, PMTCT, ART</td>
<td>Education, adherence aids, adherence aids at pill boxes</td>
</tr>
</tbody>
</table>

This poster was made possible through support provided by the U.S. Agency for International Development, under the terms of Cooperative Agreement Number NOV-A-00-00-00416-00.

The opinions expressed herein are those of the authors and do not necessarily reflect the views of the U.S. Agency for International Development.
ANNEX 2. POSTER PRESENTATION

Interventions to improve adherence to Antiretroviral therapy – A review

Background
Access to affordable antiretroviral therapy (ART) is slowly becoming a reality for HIV-positive individuals in resource-constrained settings. With increased availability and access comes the challenge of promoting adherence to treatment. Considerable evidence exists from both high-income and resource-constrained settings on the common barriers to optimal ART adherence. Little evidence is available on how interventions are addressing these barriers—especially from resource-constrained settings.

Objective
The objective of this review is to document approaches to improving adherence to ART and to consider how lessons from high-income settings can be applied in resource-constrained settings.

Methodology
Management Sciences for Health’s Rational Pharmaceutical Management Program (RPM) has pilot tested MEDLINE/PubMed using both Medical Subject Headings (MeSH) and non-MeSH terms related to ART, HIV, health behaviors, behavioral and health education interventions, and patient acceptance of health care. The literature search, which was completed between March and July 2004, was limited to articles between 1995 and 2004.

Findings
- More than 100 articles were initially identified, of which 43 described interventions to improve adherence.
- Twenty-one of the 43 articles were abstracts—most full papers in peer-reviewed journals.
- Very few of the 43 articles described interventions from resource-constrained areas; almost none of the studies referenced were rigorously evaluated.
- Six of the 43 articles were from resource-constrained settings—Cameroun, Republique de Congo, South Africa, and Thailand.

Conclusions
- Inadequate adherence monitoring may have contributed to the lack of evaluation of many interventions—this highlights the importance of monitoring to promote adherence interventions.
- Cost-effectiveness of adherence interventions was rarely addressed.
- As ART becomes more widely available, programs should document, evaluate, and disseminate their experiences with promoting ART adherence to enable other programs to benefit from lessons learned.