

Updates from Barcelona:

I. Overview of Adherence

The focus of current research has shifted from descriptive to predictive studies. An excellent example is the wide-based study of Hinkin et al.¹ In this study, not only diagnosed comorbidities, CD4 and viral load counts, and gender were examined; also the more social based factors of health beliefs, education, neuropsychiatric dysfunction and specific types of substance abuse were subjected to regression analysis. Positive predictors of medication adherence included intention to adhere and self efficacy, demonstrating a shift in focus from the physiologic factors to the psychological and functional factors. Identification of drug abuse as a negative predictor while failing to identify the effect of alcohol abuse on adherence provides yet another social-medical link.

Likewise, Ekstrand et al.² demonstrated negative effects on adherence of substance abuse, depression, psychological distress, lack of personal organization and unstructured lives. This is supported by a large study (n=206 initial) of HAART naïve patients in an inner city environment conducted by Koenig et al.³ in which perceived autonomy and “autonomy supportive health care context” were identified as significant predictors. In yet another study, based on a comparable size (n=300) sample of gay men, the only significant predictor of overall HIV disease progression was the qualitative face-to-face interview describing medication adherence and measures of viral load⁴.

The shift to predictive studies occurs in the context of a shift to more social-based interventions and approaches. Specifics of identification of factors, design of interventions, and even the evaluation of electronic monitoring are conducted in this context.

II. HAART

Changes too old to be new—editorial update should be based on more recent conference.

III. Adherence Measurement Strategies

Measurement was addressed at the Barcelona conference in two ways: first from the overall effectiveness as demonstrated by CD4 and viral load counts and second in terms of internal validity. It is this second focus that represents a new approach. In prior settings, the introduction of electronic monitoring was hailed as the answer to all concerns with measurement of adherence. Currently this is being questioned from within the ‘gold standard’ and in comparison with other measures.

In a direct analysis of the effectiveness of the use of electronic monitoring devices (EMD), several problems were identified. These included 41% of the sample who reported removing more than one dose at a time and 26% who reported opening the EMD

but not taking the medication. Additional “social problems” and conflict with pill box use were identified as significant factors negatively affecting the usefulness and validity of EMD measures.⁵ A comparative study by Deschamps et al.⁶ concluded with the recommendation that while electronic monitoring is sensitive and reliable, triangulation of different methods is recommended in research and clinical practice. Findings are summarized in the following table.

Diagnostic value methods (EEM = gold standard)	Prevalence NC	Sensitivity	Specificity	False + result	False - result	+ Pred value	- Pred value	Accuracy
Self-report: (T1) intake med	17%	27%	90%	10%	73%	67%	62%	63%
Self-report: (T1) regularity	41%	40%	58%	42%	60%	43%	55%	50%
Self-report: (T3)	5%	6%	96%	4%	94%	50%	61%	60%
Collateral report: (T1)	25%	24%	76%	24%	76%	40%	59%	55%
Collateral report: (T3)	28%	29%	73%	27%	71%	42%	61%	56%

In another study reported by the SPNS adherence collaboration, correlations between a number of self report adherence measures were found in a diverse population.

Baseline Measure	Missed dose on 3-day recall	No missed doses on 3-day recall	P value
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Days/week with missed dose=0/<1 per week	28%	81%	.001
Last time missed=>1mo or never	3%	66%	.001
Difficulty taking on time=never/rarely	58%	88%	.001
ART-related side effect	61%	28%	.001
"A lot" of difficulty taking ART due to side effects	23%	3%	.001
Any side effects	61%	28%	.001

Hirschhorn et al.⁷

In a study using pager reminder with an electronic pill cap, it was concluded that “more intensive intervention” would be required for patients with adherence problems. (Safren et al.)⁸ A study comparing a “low literacy self-report tool compared to electronic monitoring (Kunches et al.)⁹ presents an interesting approach; however the use of the instrument with a population consisting of 96% college educated patients leaves unanswered the question of efficacy in low literacy populations.

Based on a review of presentations at the Barcelona conference, it is evident that a multi-faceted approach is more effective than electronic monitoring alone. Thus there is identified a need for more extensive research on measurement effectiveness, and particularly on possible barrier effects of technology intensive measurement and adherence interventions .

IV. Factors Impacting Treatment Adherence

Presentations at the AIDS 2002 conference related to factors impacting treatment adherence reflected the shift from descriptive to predictive studies. While descriptive studies continue to identify the comorbidities and demographic factors that affect adherence, others target barriers to adherence as predictive.

Demographic factors do continue to be identified as significant in identifying target groups for intervention. In a study designed to identify predictors of adherence in an inner city population, Mannheimer et al.⁹ identified Latino ethnicity (independent of literacy and education level) as a positive predictor. Depression, substance abuse and other psychosocial factors were identified as negative predictors.

Gender was identified as a significant factor, with a study by Sorensen et al.¹⁰ addressing not only medication adherence but also clinic visits as measures of treatment adherence. Gender was found to be related to low adherence by self report. Older age for females was a positive factor as was less drug abuse. Depression, particularly in women, was identified as a negative factor. The results detail a lack of significant gender differences in alcohol use, medication knowledge, adverse effects, adherence to food requirements or

social support, while both genders demonstrated higher rates of missed doses (but not of clinic visits) when side effects were identified as problems. These findings are supported by a study in which participants were not identified geographically or socioeconomically, in which age was found to be a strong predictor.¹ The effect of “symptom bothersomeness” was assessed by Corless et al.¹⁹. Gender was also significant in the findings from this study. Intensity of symptoms was associated with forgetting to take medications, and discontinuing medications. Women were significantly more bothered by symptoms that were men.

Of particular interest to care providers is the finding that there is low agreement between provider estimate and self report of adherence. Perkins¹¹ and Mannheimer et al.¹² found that depression, other psychiatric problems and homelessness significantly impacted adherence; however the only positive correlate between patient and provider assessment was between lower HIV RNA level and higher CD4 counts.

The shift to a more psychosocial approach to predicting adherence is evident in the work of Silverio et al.¹³ Psychosocial factors of job loss, family abandonment, cost of transportation, extreme poverty, depression, stress, and addiction were identified as barriers to adherence in a diverse sample of HIV positive individuals in Argentina. Among drug users in Los Angeles, low adherence was found to be associated with concern about dependence on medications, interest in alternative therapies, lack of daily routine, and concern about concurrent illegal drug use and medication (Longshore¹⁴).

Exploration of adherence in special populations also yields primarily psychosocial factors as barriers. In an extensive study of imprisoned persons, Catz et al.¹⁶ identified confidentiality concerns (75%), limited social support (57%), interference from prison rules (53%) and systems issues including refill problems, medication storage, and coordination with meal times.

This address to psychosocial predictors extends to studies of youth as well. Hosek et al.¹⁵ Depression, and lower age of first marijuana use were found to be significant predictors of poor adherence. An incidental finding that 69% of the sample had not begun the developmental shift from concrete thinking to formal or abstract reasoning may serve as a basis for future adult studies.

It is evident that identification of predictive factors of adherence, both positive and negative, has shifted to the psychosocial from the more direct emphasis on timing and pill burden. The AIDS 2002 Barcelona conference presentation reflect this shift.

V. Adherence Models and Other Disease Entities

The use of therapeutic approaches to enhance adherence continue to be based primarily on tuberculosis treatment models. In projects in South Africa (Jack et al.¹⁷) and Zambia (Ayles et al.¹⁸) adherence models used with tuberculosis were piloted for patients with HIV in high TB incidence areas. While the START study¹⁷ found directly observed therapy to be effective, the use of a TB preventive therapy approach in Zambia¹⁸ yielded

information on factors significantly associated with adherence. These included health beliefs, the role of stigma, and hunger.

There is a dearth of new material on adaptation of models developed originally for use with other disease entities. While directly observed therapy is used in a wide variety of settings, from technologically sophisticated health care systems to those with marginal resources, adaptation of older models has been replaced by the creation of new models for the enhancement of adherence to HAART.

VI. Current and Practical Approaches to Medication Adherence

In studies conducted with a wide range of geographic, socio-economic, and cultural populations, individuation of intervention is identified as the primary provider goal for improvement of adherence. Whether patients are adherent (Waters et al.²⁰) or non-adherent (Carmona et al.²¹) recommendations include the use of individual counselors or support persons who are part of a multidisciplinary team.

In discussion of a program “Stick with It” developed for impoverished urban populations in resource rich countries, Evans et al.²² employed intensive one-on-one counseling, support, nutritional intervention, and peer intervention to deal with shame and denial. This discussion does not include analysis of success of adherence interventions, but provides a model for development of services.

Development of resource systems may also be a significant part of the interdisciplinary one-to-one intervention widely recommended. The “HIVCareNet” web site designed by Jani²³ serves as a resource that can be individualized for clients, targeting practical as well as psychological support needs. Weiss et al.²⁴ note that there is little information on the characteristics of successful programs. Identified as of probably significance is the provision of adherence support in the same place as the clinic. While this seems obvious it may represent a shift away from dichotomous thinking about psychosocial/medical approaches that heralds an era of more coordinated care.

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