
Complex HIV Treatment Regimens and Patient Quality of Life

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Abstract

Recent advances in the treatment of HIV/AIDS have led to medical improvements for persons living with the virus. As a result, many now think of HIV infection as a chronic rather than a terminal illness. Along with this shift comes the understanding that individuals now live with treatments that require long-term adherence to regimens that are often complex, time consuming, and not without deleterious side effects. The greater life expectancy, nature of new treatments and their dependence on regimented adherence has recently led to the investigation of psychosocial variables loosely categorized as quality of life (QOL). Although there has been relatively little research on the topic in relation to new HIV therapies, what is known is that QOL – with all of its complications and dimensions – appears to play an essential role in HIV and HIV treatment. Moreover, QOL would seem to be a most worthwhile component to further investigations of improved therapies and betterment for the lives of infected individuals. The following literature review discusses these issues, highlights key research findings, and provides directions for further research.

Recent developments in the management of HIV/AIDS have brought about dramatic alterations in the lives of persons infected by the virus. The introduction of more effective treatments, especially highly active antiretroviral therapy regimens (HAART) have not only resulted in lower viral loads, but also made significant impacts on morbidity and mortality (Altice & Friedland, 1998; Faber & McDaniel, 1999; Holzemer, Henry, Portillo, & Miramontes, 2000; Jeffe, Meredith, Mundy, & Fraser, 1998; Singh et al., 1999). In fact, as Singh et al. state, "The remarkable success of the newer antiretroviral therapeutic regimens, with their

ability to achieve durable suppression of HIV replication, have transformed HIV infection into a chronic manageable disease" (p. 824). Antiretroviral medications are documented in the prolonging survival of individuals infected with HIV and, hence, in the status change of the disorder to one requiring long-term management and continued ongoing treatment (Bright, 1999; Jeffe et al., 1998). This is noteworthy in that ongoing treatment is the often daunting and complex nature of the regimens that are part of HAART (Altice & Friedland, 1998; Bright, 1999; Holzemer et al., 1999). Further, these complicated and time-consuming treatments require rigorous adherence, with a medication cut-off point typically stipulated at 80% of doses taken for an adherence/nonadherence distinction (Rabkin & Chesney, 1999; Williams, 1999). Conscientious maintenance is necessary in order to achieve full treatment effect and avoid increased viral loads, and the possibility of viral mutation and resistance (Holzemer et al., 1999; Holzemer et al., 2000; Mostashiri, Riley, Selwyn, & Altice, 1998; Singh et al., 1999). The transition of HIV infection to a chronic disorder involving relatively complex treatments dependent on diligent patient adherence raises the need to consider how these treatments affect psychological integrity and the quality of life (QOL) of infected individuals.

QOL includes dimensions of well-being spanning the physical, mental, and social, and including a diversity of aspects from direct symptomology and daily functioning to work performance and emotional status (Anderson, Hollenberg, & Williams, 1999; Cramer, 1999; Keith & Schalock, 1992, 1994). Medical diagnoses and treatments have implications that extend beyond the disease or infirmity, however; as Cramer notes, such matters are "often not brought to the attention of the physician" (p. S52). However, in the context of HIV/AIDS, QOL concerns are particularly relevant because they have been directly correlated with adherence to treatment regimens (Anderson et al., 1999; Holzemer et al., 1999; Holzemer et al., 2000; Mostashiri et al., 1998; Pequegnat & Stover, 1999; Singh et al., 1999). Predictors of increased adherence include patient self-reports of having a meaningful life, feeling comfortable and well cared for, using their time wisely, and taking time for important things (Holzemer, 1999). Similarly, Singh et al. report that

social and psychological factors are significant and fundamentally influential variables in adherence to medical therapy. Conversely, decreases in adherence rates have been correlated with factors ranging from negative attributions regarding medications (Aversa, Kimberlin, & Segal, 1998) to complexity of treatment regimens (Altice & Friedland, 1998). QOL considerations are affected by HIV treatments, and in turn affect these same treatments. In essence, it is a transactional process. The need to better understand QOL issues as contributing to the complex interplay between HIV infection, HAART, and the lives of persons living with the virus is the focus of this paper.

Although QOL has been considered in some recent investigations correlating various factors to adherence rates among patients undergoing HAART, the inclusion of psychosocial experiences is relatively novel. The majority of research to date has centred on advancing medical interventions and treatments, with efforts to understand the greater implications of these new therapies only now coming to the fore. It is argued here that consideration of the impact HIV therapies have on patient QOL and how those concerns influence therapeutic issues such as adherence rates is a necessary component to informing health care providers, pharmaceutical researchers, and other professionals working to improve treatments. Although investigations of other illnesses can and ought to inform this line of inquiry, the unique nature of HIV and HAART arguably requires additional investigation and focused attention. As a prerequisite to advocating for QOL research, recent changes in treatment regimens and HIV status are discussed, along with the significance of adherence and the role QOL plays for persons living with HIV/AIDS.

CHANGES IN TREATMENT/CHANGES IN STATUS

The development of new and more potent antiretroviral medications of various pharmacological classes (see, for example, Bright's (1999) description of current anti-HIV drugs) has led to significant changes in treatment regimens. Fundamental to these treatments has been the use of combined approaches, whereby a number of different medications are promoted in tandem. These combined regimens form the cornerstone of HAART and are cited as greatly reducing viral loads, decreasing hospitalization, and improving survival (Altice & Friedland, 1998; Jeffe et al., 1998; Kalichman, 2000). For example, Rabkin and Chesney (1999) cite clinical trials that put success rates (defined as undetectable viral loads) between 65 and 85%. The impact of HAART has been so pronounced that many believe HIV infection itself has undergone a change in status consideration.

With the dramatic effects of HAART and the greatly improved medical condition experienced by many of the individuals who have access to these therapies, there has been a shift in referring to the infection from one that is terminal to one that is chronic (Altice & Friedland, 1998; Singh et al., 1999). For example, Altice and Friedland state that "For many, HIV disease has been transformed into a manageable chronic disease" (p. 503). The transformation attributed to these treatment measures has extended life expectancy to the point where management has become longitudinal. With the prospect of patients following long-term medical regimens, the need to consider QOL questions arises – especially in reference to these treatments. This is particularly true in the case of HAART, where adherence to the dictates of treatment is fundamental for achieving full therapeutic benefit, and for avoiding potentially harmful outcomes (i.e., viral mutation and resistance).

ISSUES OF ADHERENCE

The opening paragraph of a recent paper by Mostashari et al. (1998) begins with "Newer and more potent antiretroviral therapy for HIV infection has increased the importance of adherence to medical therapy by HIV infected individuals" (p. 341). Similarly, Holzemer et al. (2000) argue that "these therapies require unprecedented levels of medication adherence" (p. 36). The emphasized need for vigilance in following prescribed HAART regimens is underscored because of the severe consequences of nonadherence. Failure in attending to the prescribed course of treatment and lapses in taking medications have been found to markedly increase the risk of incomplete viral suppression and the development of drug-resistant viral strains (that may subsequently be transmitted to others), narrow the choices of drugs if the initial regimen is unsuccessful, decrease CD4 cell counts and so forth (Altice & Friedland, 1998; Bright, 1999; Holzemer et al., 1999; Rabkin & Chesney, 1999; Singh et al., 1999; Williams, 1999). In fact, based on a review of recent findings, Altice and Friedland report that adherence predicts which patients may achieve nondetectable viral levels.

The significance of adherence in HAART is noted in several recent papers and investigations assessing the causes and possible interventions related to adherence rates among HIV patients (Holzemer et al., 1999; Holzemer et al., 2000; Singh, 1999). One set of authors (Altice & Friedland, 1998) has gone so far as to coin this the "era of adherence." In this era, one facet that has repeatedly come to be recognized is the relationship between adherence to what is a complex daily medical regimen and larger QOL factors.

QUALITY OF LIFE

When considering QOL factors in regards to HAART, an essential notion is the interaction of these variables within the total life-view of the individual. That is to say, while treatment regimens have an undeniable impact on QOL, an individual's QOL in turn has a direct connection to HAART, particularly in the realm of adherence. The interaction is not unidirectional. The inclusion of the individual person affected by HIV renders this relationship multidimensional and transactional. However, for the sake of organization and with the goal of achieving clarity, HAART and QOL variables are discussed sequentially, despite the artificial nature of doing so.

HAART variables. There are several facets of HAART that have been directly implicated in QOL and adherence rates. Perhaps the most notable component of these treatments is the relative complexity of the regimens. The requirements placed on patients following HAART have been described as "daunting" and "demanding," with greater complexity correlated with decreased adherence (Altice & Friedland, 1998; Bright, 1999; Singh et al., 1999). Commonly prescribed treatments are depicted as requiring a substantial sum of daily medications in a number of specified doses (Altice & Friedland, 1999; Bright, 1999). A typical regimen, for example, may require upwards of 28 capsules per day for each protease inhibitor, taken in divided doses, some with meals some on an empty stomach, others with high fat intake and so forth (Pequegnat & Stover, 1999; Rabkin & Chesney, 1999). In addition, various medications require refrigeration, are susceptible to high humidity, must be taken at room temperature, or are otherwise dependent on particular requirements that may severely limit the mobility and flexibility of patient activities and lifestyle (Pequegnat & Stover, 1999; Rabkin & Chesney, 1999). When one considers that this is carried on daily over the longterm, complete adherence becomes a difficult task. Moreover, QOL issues are illuminated in light of the ongoing routine that becomes so all pervasive in the everyday lives of persons on HAART. This in turn has implications for adherence rates.

Noting that few prescribed regimens are as complicated and disturbing to the daily lives of individuals as HIV therapies, Holzemer et al. (1999) reviewed several investigations of HAART adherence rates. They conclude that rates varied widely, with figures ranging from 50% adherence and 58% nonadherence to 30% of patients reporting missing an HAART dose in the preceding three days. The authors state that clearly "Patients are struggling with the challenge of being 100% compliant" (p. 186). This is of particular con-

cern and importance considering that Holzemer et al. (1999) further report that missed doses in HAART appear to be extremely unforgiving, with evidence of increased viral loads after foregoing only two days of medications. Nonetheless, remaining faithful to HAART is a difficult undertaking made more so by the side effects of the drugs themselves.

When considering the association between the adverse physical effects of medications and overall QOL, Anderson et al. (1999) note that side effects "play a predominant role in the success of treatment, as adverse effects may lead to partial or total noncompliance with a prescribed treatment regimen" (p. 693). They further state that such side effects can adversely affect QOL factors from everyday functioning to emotional condition. This point is particularly salient in light of the identified reactions, which have been noted to include such factors as nausea, vomiting, circumoral numbness, kidney stones, diarrhea, rashes, fatigue, peripheral neuropathy, diabetes, and a host of other adverse conditions (Pequegnat & Stover, 1999; Rabkin & Chesney, 1999). As stated by Pequegnat and Stover, "People may not want to live with the symptoms and limited QOL if they do not believe in the efficacy claims made for the new therapies" (p. 187). Similarly, if treatment effects are thought to be more invasive and deleterious than current disease status, adherence to HAART is questionable.

Beyond the severity of possible reactions, an investigation of the perceived effects of medications, by Aversa et al. (1998) noted that, "The perceptions that antiretrovirals have negative effects on daily functioning may contribute to quality of life perceptions above and beyond the actual level of symptomology being experienced" (p. 206). They conclude, "The results indicate that, for persons taking antiretrovirals, much of the variance in their quality of life can be explained by the limitations they attribute to the medications over and above their appraisal of their physical health status" (p. 212). Side effects of medications reflected directly in symptoms or in perceived effects and attributed limitations are intertwined with QOL, adherence, and, in turn, success of treatment. Again, overall QOL arises as a significant factor being affected by and affecting treatments that are described as requiring "diligent life-long adherence and often causing debilitating side effects" (Kalichman, 2000, p. 40). Added to this are further prohibitive variables and barriers to adherence relevant to HAART.

While adverse reactions to medications correlate with adherence rates, other factors play a role in the interaction between adherence and QOL. It ought to be noted that these have been informed by investiga-

tions of various chronic illnesses and that they are applicable to an array of treatments, including HAART. Identified as barriers – and, consequently, also facilitators – to adherence are such noted characteristics as patient beliefs, knowledge and expectations regarding treatment/efficacy, homelessness, substance abuse, the presence of psychiatric disorders, education/understanding regarding the disease/treatment, and so forth (Rabkin & Chesney, 1999; Williams, 1999). Additional factors include such matters as prohibitive medication costs, fear of social stigma, personal circumstances, and a host of other particular considerations. For example, in a qualitative analysis of children and families with HIV, Roberts and Cairns (1999) describe a parent deviating from the prescribed treatment regimen so that her child could participate normally in social overnight outings. Williams summarizes the nebulous interplay between the multitude of variables when he writes, “Adherence is a complex personal, interpersonal, and social behavior that is influenced by a variety of factors acting on an individual level...” (p. 119). This becomes particularly apparent when considering some of the influential QOL variables identified in the literature.

QOL variables. As noted above, investigations of the psychosocial components connected with HAART are relatively recent undertakings, with the sparse information available tending to centre on adherence research. Nonetheless, the available data from investigations of other illnesses and the limited research on HAART underscore several key QOL areas found related to HIV treatment regimens.

Investigations of adherence rates and QOL factors have repeatedly identified the significance of social supports in the lives of HIV-infected individuals (Altice & Friedland, 1998; Holzemer et al., 1999; Holzemer et al., 2000; Mostashari et al., 1998; Singh, 1999). Social supports and closely related factors such as stable living conditions provide the necessary contact and personal environment in which to better cope with the illness and its treatment. In a recent investigation of HAART adherence, Singh et al. found social support to be among the key factors influencing adherence rates. They speculate that “Social support may enhance adherence, either directly (through encouragement, reassurance, reinforcement, systematic cues, bolstering of competence, and motivation), or indirectly (by buffering the effect of those variables that might interfere with adherence, e.g., life’s stresses, anxiety and depression)” (p. 828). The authors conclude that satisfaction with overall support is significantly correlated with adherence. Likewise, in their investigation of adherence and acceptance of HAART among incarcer-

ated HIV-infected women, Mostashari et al. found that interpersonal relationships were most strongly associated with medication adherence. Specifically identified were support from peers (seeking help when feeling “down” and interpersonal trust) and the characteristics of the physician/patient relationship.

The patient/physician or client/provider relationship as well as satisfaction with health care treatment in general has been identified as a significant variable contributing to adherence (Holzemer et al., 1999; Holzemer et al., 2000; Mostashari et al., 1998). For example, Holzemer et al. (2000) cite several investigations indicating that clients more engaged with their health care providers and having a positive rapport indicated greater adherence to treatment regimens and provider advice. Similarly, Mostashari et al. found that individuals who felt most comfortable speaking with their physicians were more likely to remain adherent to therapy. A supportive and informative relationship between health care providers and clients fosters a situation of trust and acceptance not unlike other interpersonal connections. The relationship between client and provider raises issues directly related to HAART, QOL, and adherence, including matters of trust, confidence, and knowledge. Not surprisingly, issues such as lack of information, treatment satisfaction, and satisfaction with informational support contribute to a decline in adherence (Holzemer et al., 1999; Singh et al., 1999). In turn, interpersonal supports, be they more formal relations with health care providers or the personal support of family and peers, are influenced by medical regimens, treatment efficacy, perceptions of effects, and so forth. The interaction between disease, treatment, and QOL factors finds its way into several other areas identified in investigations of adherence.

Other variables that have been implicated in HAART adherence rates include depression, cherishing the environment (how participants felt about the world, including such factors as whether they have a meaningful life, use their time wisely, and take time for important things), coping styles, motivation, helplessness, and other psychosocial factors (Holzemer et al., 1999; Singh et al., 1999). Focusing on the category of cherishing the environment, Holzemer et al. (1999) state that this “should remind clinicians that their patients’ total world view affects their ability to adhere to medications, follow advice, or keep appointments. Simply writing prescriptions for medications with little attention to the patients’ environment has a strong potential for failure” (p. 194). Discussing the assessment considerations associated with HAART, Faber and McDaniel (1999) highlight several aspects of QOL that are particularly relevant to this communi-

ty. Included are psychological components such as changing self and role definitions (including healthy vs. ill, living opposed to dying, independence vs. dependence), life trajectory (life choices, priorities, aspirations, goals) and hope-fear dilemmas (such as optimism vs. uncertainty). The authors further note psychosocial variables such as access to treatment (particularly for individuals without the financial means or adequate insurance), challenges of adherence, and risk behaviour practice. The need to consider overall QOL in matters of HIV treatment and HAART adherence would seem to be a relevant avenue of investigation for researchers concerned not only with improved adherence rates but better lives for individuals infected with HIV. The complex and multifarious interplay between disease, treatment, and QOL is suggested from the limited investigations to date. Further uncovering these relationships appears to be the next step.

SUMMARY

Recent advances in the treatment of HIV/AIDS, particularly HAART, have led to dramatic medical improvements for persons living with the virus. What some have called the "stunning benefits" of HAART have resulted in a transition whereby HIV infection is now considered a "manageable chronic disease" (Altice & Friedland, 1998, p. 503). Along with this shift comes the understanding that individuals accessing HAART now live with treatments that require long-term adherence to regimens that are often complex, time consuming, and not without deleterious side effects (Altice & Friedland, 1998; Bright, 1999; Holzemer et al., 1999; Rabkin & Chesney, 1999; Williams, 1999). Further, the success of HAART depends on diligent and unforgiving client adherence in order to achieve its full benefits (Holzemer et al., 1999; Holzemer et al., 2000; Mostashiri, Riley, Selwyn, & Altice, 1998; Singh et al., 1999). The result is that individuals are undergoing lengthy treatments that require the conscientious maintenance of regimens that are relatively intrusive and complicating to their daily lives.

The greater life expectancy, nature of HAART and its dependence on regimented adherence has recently led to the investigation of psychosocial variables loosely categorized as QOL. Although there is a general paucity of information on the relationship between HIV, HAART, and overall QOL, the necessity to understand and improve adherence rates has resulted in the identification of some interacting variables. Notable are such factors directly related to treatments as complexity of regimen, side effects, and knowledge of medications (Altice & Friedland, 1998; Anderson et al., 1999; Avera et al., 1998; Bright, 1999; Kalichman,

2000; Singh et al., 1999). More interpersonally, matters of social support, client/provider relationships, depression, cherishing the environment, and so forth are noted to be correlated with adherence (Altice & Friedland, 1998; Holzemer et al., 1999; Holzemer et al., 2000; Mostashari et al., 1998; Singh et al., 1999). An important caveat here is that the interaction of these variables is not unidirectional, with HIV symptomatology, treatment effects, side effects, and QOL influencing and being influenced by each other. However, the nature of these relationships is not well understood. What is known is that QOL, with all of its complications and dimensions, appears to play an essential role in HIV and HIV treatment, and would seem to be a most worthwhile component to further investigations of improved therapies and betterment for the lives of infected individuals.

SUGGESTIONS FOR RESEARCH

In any investigation of treatment effects, but especially in the consideration of such influences on QOL, Anderson et al. (1999) claim that both physical symptoms and psychosocial factors should be evaluated. This has been noted in recent QOL measures and assessment considerations related to HAART (e.g., in Faber & McDaniel, 1999, and Pequegnat & Stover, 1999). These measures provide for the inclusion of such diverse clusters as psychological, psychosocial, and biomedical indicators (Faber & McDaniel, 1999). Similar factors such as side effects and intrusiveness of medical regimens, return to work and financial concern, role resumption/retention, social support/independence, as well as sexuality and self-concept have also been proposed (Pequegnat & Stover, 1999). As Pequegnat and Stover note, the identification of QOL measures specific to the needs and lives of persons with HIV is a flagged area for further research.

Future research addressing improvements in HIV treatments has much to be gained from investigating the diversity of personal and social variables that are part and parcel of QOL. The use of in-depth, semi-structured interviews and other qualitative measures stand to inform survey data on adherence and medical information concerning treatment effects. In turn, knowledge gleaned from such inquiry offers the potential to construct individualized regimens more suited to the long-term needs of persons with HIV. This fits well with the suggestion made by Bright (1999) that "Tailoring of the regimen, when possible, to the patients schedule and needs is mandatory" (p. 372). Examination of the influences HAART exudes on overall QOL is a necessary step to improving treatment regimens. This is seen as a means to informing adherence concerns and coming to understand how

QOL factors interact with treatment and how improved regimens and therapies might be constructed.

As we move towards a new era in HIV/AIDS treatment, Altice and Friedland (1998) state that "Interventions that promote adherence to anti-HIV therapies are urgently needed" and that "...strategies be implemented on the basis of what little is known and what is reasonably likely to be effective" (p. 503-504). It is argued here that understanding of QOL issues provides a fundamental link to informing those strategies and improving the lives of persons who must face the daily routine of coping with HIV and its treatments.

Résumé

Les progrès récents que connaît le traitement du VIH/sida ont conduit à des améliorations sur le plan médical chez les personnes qui sont porteuses du virus. Si bien que plusieurs croient maintenant que l'infection au VIH est une maladie chronique, plutôt qu'une maladie fatale. Ce changement d'attitude s'accompagne d'une nouvelle réalité, à savoir que les personnes pour survivre à la maladie doivent suivre des traitements qui exigent une observance à long terme d'un schéma posologique souvent complexe et chronophage et qui n'exclut pas des effets secondaires nocifs. L'augmentation de l'espérance de vie, la nature des nouveaux traitements et les conditions d'observance thérapeutique qu'ils supposent, ont mené tout récemment à des recherches sur les variables psychosociales que l'on classe *grosso modo* dans la catégorie de la qualité de vie. Même s'il n'existe que peu de travaux de recherche sur les nouvelles thérapies anti-VIH, on sait déjà que la qualité de vie – et toutes ses dimensions et complications – semble jouer un rôle essentiel dans le traitement du VIH et du sida. De surcroît, la qualité de vie pourrait être vue comme un élément extrêmement déterminant de toute nouvelle recherche qui examinerait ces thérapies perfectionnées et le mieux-être, chez les personnes atteintes. Les auteurs présentent pour finir une recension des écrits qui abordent ces questions, mettent en évidence des résultats de recherche importants et offrent des orientations pour les travaux de recherche futurs.

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