EFFICACY OF LONG-TERM PSYCHOTHERAPY IN THE MANAGEMENT OF PERSONS LIVING WITH HIV/AIDS

J. GERRY MUGFORD

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EFFICACY OF LONG-TERM PSYCHOTHERAPY IN THE MANAGEMENT OF PERSONS LIVING WITH HIV/AIDS

By

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Abstract

Background

Since recognition of acquired immunodeficiency syndrome (AIDS) in 1981, an estimated 60 million people, worldwide, have been infected with HIV, and an estimated 25 million people have died of AIDS. In Canada almost 50,000 people are believed to be HIV positive, and each year over 2000 new infections are reported to the Centre for Infectious Disease Prevention and Control (CIDPC).

It is unknown whether long-term psychotherapy can prevent psychological dysfunction in HIV/AIDS patients.

The objective of this randomized controlled trial (RCT) was to determine the impact of long-term psychotherapy on depression, the primary outcome measure, hopelessness, coping skills, and CD4 counts in a group of HIV positive subjects who were heterogeneous in respect to their HIV infection, and level of psychological health.

Methods

HIV positive adults at a tertiary referral centre were randomly assigned to receive either long-term psychotherapy (N=16), or no psychotherapy with crisis intervention (N=14), irrespective of initial psychological health.

Results

The mean age was 30 years, Beck Depression Inventory (BDI) score 22 and CD4 count (cells/μL) 277. At 0, 6 and 12 months, the mean BDI scores were 20, 18 and 26 in the control group, compared to 23 (P = 0.34), 13 (P = 0.016), and 9 (P = 0.006) in the intervention group.

Mean Beck Hopelessness Scale scores (BHS) were 10, 11 and 13 vs. 10 (P = 0.968), 7(P = 0.027), and 6 (P = 0.005).

Coping Inventory for Stressful Situations (CISS) scores were: Task, 52, 53 and 55 vs. 52, (P = 0.906), 55 (P = 0.654) and 59 (P = 0.214); Emotion, 50, 46, 49 vs. 51, (P = 0.846), 49 (P = 0.374) and 43 (P = 0.059); Avoidance, 49, 46 and 46 vs. 51 (P = 0.426), 46, (P = 0.036) and 52 (P = 0.062); Distraction, 25, 23 and 24 vs. 24, (P = 0.708), 25 (P = 0.221) and 25 (P = 0.331); Social Diversion, 15, 14 and 13 vs. 15, (P = 0.640), 17 (P = 0.031) and 17 (P = 0.031).

CD4 counts were 333, 243 and 346 vs. 232 (P = 0.25), 262 (P = 0.09), and 259 (P = 0.764).

Conclusion

Long-term psychotherapy ameliorates depression and hopelessness in persons living with HIV/AIDS. It may also have a preventative effect.

Key words

randomized controlled trial, psychotherapy, HIV/AIDS, depression, hopelessness, HIV prevalence, HIV incidence

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List of Abbreviations

Acquired immunodeficiency syndrome (AIDS)

Active Mycobacterium tuberculosis infection (TB)

Analysis of covariance (ANCOVA)

Bone marrow (B)

Basic Personality Inventory (BPI)

Beck Depression Inventory (BDI)

BECK Hopelessness Scale (BHS)

Canada Communicable Disease Report (CCDR)

Canadian Broadcasting Corporation (CBC)

Canadian Mental Health Association (CMHA)

Canadian Psychiatric Association (CPA)

Center for Epidemiologic Studies Depression scale (CES-D)

Centre for Infectious Disease Prevention and Control (CIDPC)

Clonal Differentiation (CD)

Cognitive-behavioral group therapy (CBGT)

Cognitive Behavioural therapy (CBT)

Cognitive-behavioral stress management (CBSM)

Conception Bay North (CBN)

Coping Inventory for Stressful Situations (CISS)

Cytomegalovirus (CMV)

List of Abbreviations (Continued)

Deoxyribonucleic acid (DNA)

Depression Scale of the Minnesota Multiphasic Personality Inventory (MMPI-D Scale)

Diagnostic and Statistical Manual of Mental Disorders (DSM)

Enzyme immunoassay antibody (EIA)

Enzyme-linked immunoabsorbent assay (ELISA)

Ethylenediamine tetraacitic acid (EDTA)

Experiential group therapy (EGT)

Experiential psychotherapy (EP)

Generalized Anxiety Disorder (GAD)

General Heath Questionnaire (GHQ)

Hamilton Anxiety Rating Scale (HARS)

Hamilton Depression Rating Scale (HRSD)

Hamilton Depression Scale (HAM-D)

Hamilton Depression Rating Scale (HAM-D)

Herpes simplex virus - type 2 (HSV-2)

HIV-1 associated dementia complex (HADC)

Human Investigation Committee (HIC)

Hopkins Symptom Checklist (HSCL)

Human immunodeficiency virus (HIV)

Immunoglobulin E (IgE)

List of Abbreviations (Continued)

Infectious disease (ID)

Injecting drug use (IDU)

Interferon gamma (IFN-gamma)

International Statistical Classification of Diseases and Related Health Problems (ICD-10)

Interpersonal psychotherapy (IPT)

Last Value Carried Forward (LCVF)

Kuder-Richardson (KR-20)

Marlowe-Crowne Social Desirability Scale (M-C)

Men who have had sex with men (MSM)

Million (Mil)

Multidimensional Health Locus of Control Scale (MHLCS)

Multiple sclerosis (MS)

Mycobacterium avium complex (MAC)

Natural killer (NK)

National Institutes of Mental Health (NIMH)

Neurobehavioral Research Centre (HNRC)

Norepinephrine (NE)

North American Nursing Diagnosis Association (NANDA)

Ontario Hospital Insurance Plan (OHIP)

Opportunistic Infection (OI)

List of Abbreviations (Continued)

Perceived Stress Scale (PSS)

Persons living with HIV/AIDS (PWHA)

Pneumocystis carinii pneumonia (PCP)

Polymerase chain reaction test (PCR)

Profile of Mood States (POMS)

Progressive multifocal leukoencephalopathy (JC virus) (PML)

Quality of life (QOL)

Randomized Controlled Trial (RCT)

Ribonucleic acid (RNA)

Social Provisions Scale (SPS)

Structured Interview Guide for the Hamilton Anxiety and Depression (SIGH-AD)

Supportive-expressive group (SEGT)

Supportive psychotherapy (SP)

Symptom Checklist 90 – Revised (SCL-90-R)

Thymus (T)

Texas Inventory of Grief (TIG)

Total mood disturbance (TMD)

United Nations Program on HIV/AIDS (UNAIDS)

United States of America (USA)

University of California, San Diego (UCSD)

List of Abbreviations (Continued)

Viral load (VL)

Ways of Coping Questionnaire (WCQ)

World Health Organization (WHO)

List of Appendices

CHAPTER 1
INTRODUCTION

1.1 Overview of the Chapter Contents

Chapter one of this thesis is intended to provide the reader with information related to establishing a diagnosis of human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS), and provide a brief overview of some of the clinical manifestations of HIV infection. This chapter also presents a global, Canadian, and Newfoundland and Labrador overview of the prevalence of HIV and AIDS infection. Included in this chapter is a summary of the purpose of the Randomized Controlled Trial (RCT), which forms the basis of this thesis.

The intent of chapter two is to provide the reader with information related to the provision of psychotherapy. To help accomplish this, brief definitions of some common psychotherapies are provided. This chapter discusses the psychotherapeutic approach used in the thesis RCT as well as an overview of the literature related to the provision of psychotherapy for persons living with HIV/AIDS. Included in this chapter, is information related to the prevalence and incidence of depression. A review of the major clinical trials related to the thesis RCT primary and secondary outcome measures in patients with HIV disease is presented in this chapter. The review covers the period up to the commencement of the thesis RCT in 1996.

Chapter three describes the tools used to measure depression, hopelessness, coping and CD4 T-cells in the trial subjects. The RCT methodology is also presented in this chapter.

Chapter four provides the baseline descriptions of the trial subjects. This chapter includes the results of the analyses of the primary and secondary outcome measures.

In chapter five the reader is presented with a discussion of the results and implications of the RCT findings related to the primary and secondary outcome measures. In addition, there is discussion of the major clinical trials that were published after the start of the thesis RCT. In this chapter strengths and weaknesses of the trial are presented as well as implications and recommendations for clinical practice and health care provider education.

1.2 Introduction to the Thesis

Since recognition of acquired immunodeficiency syndrome (AIDS) in 1981 among homosexual men in the United States of America (USA) (UNAIDS, 1996) we have witnessed emergence of a disease often assigned labels which have contributed to both a misunderstanding of the demographics of its victims and an underestimation of the magnitude of its global invasiveness. AIDS and its subsequent etiologic label, human immunodeficiency virus (HIV), has worn a variety of unique and oftentimes pejorative descriptors; a disease whose labels were, and sometimes still are, imbued with prejudice,

hate, and fear. Its various labels have also provided indications of the ignorance of the etiology of HIV.

The early 1980s gave us "The Gay Plague" label, which provided a kind of comfort and promise of safety to the heterosexual community, by supporting a belief only Gays were susceptible and heterosexuals were safe from both HIV and AIDS. Within a few years, however, there were noticeably large numbers of HIV positive diagnoses observed in intravenous drug (IV) users and sex trade workers; reinforcing a newer label of "gods punishment for queers, whores and junkies" and again providing a misguided sense of safety in the general population. Even with an increased diagnosis of HIV among heterosexuals in the Haitian community, pejorative labels attached to this community helped blind society to the pervasiveness of HIV and AIDS.

In the early 1990s, when HIV had clearly established itself outside marginalized communities and into the straight community, a more accurate label of "epidemic" became associated with the disease. This newer label more fully implicated the impact of HIV on heterosexuals and homosexuals alike, males and females, young and old, rich and poor, educated and uneducated, marginalized and not. The world was being prepared for the most accurate of the labels assigned to HIV/AIDS.

By the mid nineties HIV had been fully recognized as a "pandemic" and currently HIV /AIDS is the "fourth biggest killer globally" (UNAIDS/WHO, 2001). One of many issues in the management of HIV/AIDS in Canada generally, and in the province of Newfoundland and Labrador in particular, is the relatively low numbers of cases of HIV/AIDS. It is easier to ignore the virulence of this disease with the numbers of

HIV/AIDS infections observed in Canada and Newfoundland and Labrador. With an estimated 48,800 persons living with HIV/AIDS in Canada, and only 134 in Newfoundland and Labrador (Disease Control and Epidemiology Division, Department of Community Services of St. John's, Newfoundland, 2001), it may be possible to underestimate the physical, emotional and social consequences of HIV/AIDS, especially when compared to the impact in places such as sub-Saharan Africa. In that region the impact is difficult to ignore when an estimated 28.1 million adults and children are living with HIV/AIDS (UNAIDS/WHO, 2001). The main mode of transmission is heterosexual contact, almost ensuring increased numbers of seropositive persons. Adding to the main mode of transmission is the fact that 55% of the HIV positive adults are women and this, in conjunction with a lack of antiretroviral therapy, ensures an increase in the number of children born with HIV/AIDS (UNAIDS/WHO, 2001).

HIV/AIDS is a chronic debilitating disease that is blind to race, age, geography, income, sexual orientation and religion; and has become, according to the WHO, a worldwide threat to human health (UNAIDS/WHO, 2001).

1.3 Laboratory Definition of HIV

Human immunodeficiency virus (HIV-1) is a human retrovirus containing ribonucleic acid (RNA) and an enzyme, reverse transcriptase, to transcribe RNA into deoxyribonucleic acid (DNA). HIV is transmitted across the mucocutaneous barrier with extension to regional lymph tissue within days of exposure. Within weeks the infected

individuals experience massive viremia and an acute retroviral syndrome (about 40-70 % of cases) accompanied by widespread dissemination and extensive involvement of lymph tissue. There is an immune response with partial control ascribed to the cyotoxic T-cell response and a humoral response (seroconversion at 6-12 weeks) within weeks to months. About six months to a year after transmission of the virus, the infected individual has persistent HIV replication with relatively constant levels of HIV RNA in the bloodstream; and experiences gradual CD4 cell depletion averaging 50/mm^3/year over a mean of 8-10 years. Eventually there is a massive destruction of the immune system with susceptibility to opportunistic pathogens and tumors, particularly when the CD4 count falls below 200/mm^3 (Bartlet, 1997; Carpenter *et al.*, 2001). HIV-1 is the causative agent in Acquired Immunodeficiency Syndrome (AIDS) (UNAIDS, 1996; Levy 1989).

In addition, there is a recognized second HIV virus, HIV-2, which is associated with a considerably longer clinically latent period than HIV-1 (Markovitz, 1993; Carpenter *et al.*, 2001). This virus, identified in West Africa in the mid 1980s, also results in AIDS. Though HIV-1 and HIV-2 share many biologic and genetic characteristics, they have regulatory and structural genes that are unique. HIV-1 is closely related to the simian immunodeficiency virus (SIV) isolated from a subspecies of chimpanzee; whereas HIV-2 is more closely related to an SIV commonly found in the sooty mangaby (Carpenter *et al.* 2001). Due to the rarity of HIV-2 infections outside the West African region this thesis will focus on the more pervasive and generally referred to form of the virus, HIV-1.

1.4 Establishing a Diagnosis

A diagnosis of HIV is generally made through a positive test result from an enzyme-linked immunoabsorbent assay (ELISA) screening test to detect HIV-1 and HIV-2 antibodies in blood. A reactive screening test must be verified by a second test such as the Western Blot[1].

The current laboratory definition of HIV infection (CDCP, 1999; CDCP Appendix, 1999) is described in terms of a positive test result on a screening test for HIV antibody (e.g., repeatedly reactive enzyme immunoassay), followed by a positive result on a confirmatory (sensitive and more specific) test for HIV antibody (e.g., Western blot or immunofluorescence antibody test) or a positive test result or report of a detectable quantity on any of the following HIV virologic (nonantibody) tests:

- HIV nucleic acid (deoxyribonucleic acid (DNA) or ribonucleic acid (RNA) detection (e.g., polymerase chain reaction (PCR) or plasma HIV- 1 RNA DNA);
- HIV p24 antigen test;
- HIV isolation (viral culture).

In Newfoundland and Labrador, HIV diagnosis is determined in the following manner:

The samples are screened using a highly sensitive enzyme immunoassay antibody (EIA) screen test. If a sample tests positive then a second EIA test, with a high specificity, is

[1] A procedure in which proteins separated by electrophoresis in polyacrylamide gels are transferred (blotted) onto nitrocellulose or nylon membranes and identified by specific complexing with antibodies that are either pre or post-tagged with a labeled secondary protein (Williams & Wilkins, 1995).

conducted. If either of these tests is repeatedly reactive for antibodies or yields indeterminate results then a Western blot test is conducted. If the Western Blot is positive there is a confirmed case of HIV infection. If the Western Blot is negative then no further testing is indicated, unless the person is considered to be at high risk for HIV infection in which case repeat testing is recommended in three to six months. If the Western Blot test is indeterminate then a repeat test is conducted within 3- 6 months.

In the case of infants born to HIV seropositive mothers a slightly different approach is taken to determine the HIV status. Babies born to seropositive mothers will test positive for HIV- antibodies for up to 18 months after birth because of placental transfer of maternal antibodies. In this situation a polymerase chain reaction test (PCR), which is a molecular test for HIV RNA, can be utilized. This test can confirm a diagnosis before the disappearance of maternal antibodies in the baby and can determine if the infant has viral genetic material. Another common test used for infants of seropositive mothers is the p24 antigen test.

HIV and AIDS refer to the continuum of the infection, where HIV reflects the presence of the virus with or without evidence of immune suppression. In Canada, AIDS refers to the presence of an opportunistic infection or other illness indicating immune suppression in a person who is not compromised for reasons other than HIV.

1.5 Sequential Clinical Manifestations of HIV-1 Infection

Within 2 to 8 weeks of initial infection with the HIV virus between 40 and 70 percent of persons experience a mononucleosis-like syndrome. During this acute

retroviral syndrome stage, infected individuals may experience fever, sore throat, lymph node enlargement, rash, arthralgias, fatigue, and headache. These symptoms generally last for several days to 3 weeks. Additionally a short-lived maculopapular rash on the face and trunk is common. Acute self-limited aseptic meningitis is observed in 10 to 20 percent of patients. The acute retroviral syndrome varies greatly in both duration and severity. During this stage, HIV antibody is generally not detectable and HIV infection is detected by plasma HIV RNA or p24 antigen assays (Carpenter *et al.*, 2001).

In untreated people, the acute retroviral syndrome stage is usually followed by a slow nonlinear progression to severe immunodeficiency marked by progressive depletion of CD4 cells. Approximately 50 % of untreated individuals develop AIDS within 10 years of HIV infection; 30 % have milder symptoms; and less than 20 % are asymptomatic 10 years after infection.

Major life threatening Opportunistic Infections (OIs) seldom occur until the CD4 cell count is below 200 cells/mm^3. At this stage infected individuals are at high risk of OIs [e.g., Pneumocystis carinii pneumonia (PCP)] and neoplasms.

CD4 counts below 50 cells/mm^3 indicate profound immunosuppression. HIV immunosuppressed individuals frequently experience OIs and neoplasms; most common and potentially preventable are cytomegalovirus (CMV) retinitis, toxoplasmosis, and disseminated Mycobacterium avium complex (MAC). Ineffective antiretroviral therapy at this stage of illness is associated with high mortality within the subsequent 24 to 36 months.

With the substantial improvements in disease management, particularly through the introduction of antiretroviral treatments, it is widely believed that, in the presence of active treatment, life expectancy more than doubles for HIV infected persons. Recent estimates show a decline in mortality since 1995 from 29.4 per 100 person-years to 8.8 per 100 person-years (Palella, Delaney, Moorman, *et al.* 1998). In addition to Opportunistic Infections (OI) and neoplasms, patients may experience a variety of dertamologic conditions (Carpenter, Flanigan & Lederman, (2001) (Table 1.1). Patients may also experience HIV-1 associated dementia complex (HADC), mood disorders and HIV wasting syndrome (Brouillette & Citron, (1997). These outcomes vary in terms of frequency and severity. Following a diagnosis of HIV many patients can expect to experience a variety of complicating illnesses, many of which are painful and life threatening, severely impacting quality of life.

Table 1.1: Common Dermatologic Conditions in HIV

Herpes simplex [cold sore or genital herpes]
Herpes zoster [shingles]
Staphylococcal folliculitis
Bacilliary angiomatosis
Molluscum contagiosum
Seborrheic dermatitis
Psoriasis
Candidal dermatitis

Table 1.2, adapted from Carpenter *et al.* (2001) provides a list of the opportunistic infections (OI) and neoplasms associated with HIV disease. It also indicates both the

CD4 cell count levels at which the various OIs and neoplasms generally occur, as well as estimates of their frequency of occurrence. Infections may reoccur or progress during the course of disease.

Table. 1.2: CD4 Cell Counts and Frequencies of AIDS Associated OIs and Neoplasms

CD4 Count Cells/mm^3	Opportunistic Infection or Neoplasm	Frequency
	Protozoan	
200-100	• Pneumocystis carinii pneumonia (PCP)	20-60
<100	• Toxoplasma gondii encephalitis	5-25
<100	• Cryptosporidium parvum enteritis (> 1 month)	2-10
<100	• Isospora belli enteritis (> 1 month)	2-10
	Fungal	
200-100	• Disseminated histoplasmosis[1]	0-20
200-100	• Disseminated coccidioidomycosis[1]	0-20
<100	• Candida esophagitis	15-20
<100	• Cryptococcus neoformans meningitis	3-5
	Bacterial	
500-200	• Active Mycobacterium tuberculosis infection (TB)	2-20
500-200	• Recurrent bacterial pneumonia	15-20
<100	• Disseminated Mycobacterium avium complex (MAC)	20-35
<100	• Recurrent Salmonella septicemia	2-10
	Viral	
500-200	• Chronic (> 1 month) mucocutaneous herpes simplex virus infection	40-70
500-200	• Chronic (> 1 month) esophageal herpes simplex virus infection	40-70
200-100	• Progressive multifocal leukoencephalopathy (JC virus) (PML)	2-3
<100	• Cytomegalovirus retinitis (CMV)	20-35
<100	• Cytomegalovirus esophagitis	4-8
<100	• Cytomegalovirus colitis	4-8

Table. 1.2: CD4 Cell Counts and Frequencies of AIDS Associated OIs and Neoplasms (Continued)

CD4 Count Cells/mm^3	Opportunistic Infection or Neoplasm	Frequency
<100	Helminths[2] • Strongyloidiasis (disseminated beyond the gastrointestinal tract)	Rare
	Neoplasms	
500-200	• Kaposi's sarcoma (person < 60 years old) mucocutaneous	15-30 M[3]
200-100	visceral	3-8 M
500-200	• Invasive carcinoma of the cervix	1-2 F[4]
200-100	• High-grade, B-cell non-Hodgkin's lymphoma[2] • Undifferentiated non-Hodgkin's lymphoma	2-5
<100	• Immunoblastic sarcoma[2] • Primary brain lymphoma	3-6

1. Endemic areas
2. Not specific to CD4 count.
3. Usually seen in men.
4. Only seen in women (Related to human papilloma virus.)

The frequency of all opportunistic infections and neoplasms decrease with viral control and immunologic reconstitution following effective anti-retroviral therapy. Many of the infections can be managed or prevented with specific antimicrobial prophylaxis. The neoplasms must be managed through specific cancer protocols but increased survival is dependent on HIV control (Palella, Delaney, Moorman, *et al.* 1998; Carpenter, Flanigan & Lederman, (2001).

1.6 Implications and Understanding of CD4 T-lymphocytes and Viral Load

The generation of an effective immune response is highly dependent on the presence and type of white blood cell known as the lymphocyte. Lymphocytes are one of

the white blood cells produced in bone marrow. They are small, featureless cells with few cytoplasmic organelles and condensed nuclear chromatin. Lymphocytes require contact with a foreign antigen to trigger their proliferation and differentiation into their specialized functions. Lymphocytes possess unique antigen-binding cell surface receptors, and can mediate the defining immunological attributes of specificity, diversity, memory, and self/nonself recognition.

The two major populations of lymphocytes that circulate in the blood and reside in various lymphoid organs are T lymphocytes and B lymphocytes. T lymphocytes mature in the thymus and are responsible for the cell-mediated arm of the immune response, whereas B lymphocytes mature in the bone marrow and, upon encounter with specific antigen, produce antibody molecules which mediate the humoral arm of the immune response. Helper T cells and cytotoxic T cells are two well-defined subpopulations of T lymphocytes, and are distinguished by the presence of CD4 membrane receptors (CD4+) on their surfaces for helper cells and CD8 membrane receptors (CD8+) for cytotoxic cells. When CD4+ T lymphocytes are activated they secrete various growth factors called cytokines, which play a critical role in activating the various cells that participate in immune responses. The generation of both antibody-mediated and cell-mediated immunity depends on the activation of CD4+ helper T lymphocytes. These cells function as the central control element for most immune responses. The human immunodeficiency virus is able to infect human cells that express the CD4 receptor on their surface. HIV binds to the CD4 receptor, and with the aid of a co-receptor, fuses with the cell membrane gaining entry into the cell commencing a

process that destroys the CD4 cell. For more detailed information on CD4 T cells see Janeway et al. (1999), or a similar immunobiology text. The normal range for CD4 T cells is 700-1100 cells/mm^3 (Hannet *et al.*, 1992).

Viral load (VL), measured in copies/mL, is a measurement of the levels of HIV RNA in blood plasma of an HIV-infected individual. Like the CD4 cells, it is used both as a marker of disease severity and a guide to therapy. In conjunction with CD4 cell counts, virus load measures provide prognostic information, which is used to help determine when to implement and when to change antiretroviral therapy. Table 1.3 extracted from Carpenter *et al.* (2001) effectively demonstrates the relationship of CD4 cell counts and VL levels to disease progression.

Table 1.3: Guidelines for the Initiation of Antiretroviral Therapy in HIV+ Patients

Clinical Category	CD4+ T Cell Count and HIV RNA	Recommendations
Symptomatic (AIDS, thrush, unexplained fever)	Any values	Treatment generally recommended
Asymptomatic	CD4+ T cells < 350 mm^3 or HIV RNA > 30,000 copies/mL	Treatment recommended
Asymptomatic	CD4+ T cells between 350 and 500 and HIV RNA between 10,000 and 30,000	Treatment should be considered based on prognosis for disease free survival.
Asymptomatic	CD4+ T cells > 500 mm^3 and HIV RNA < 10,000 copies/mL	Most clinicians would delay therapy and observe; however some would treat under certain conditions.

1.7 Global profile of HIV and AIDS

The goal of the following section of this thesis is to present a numerical representation of the Global, Canadian and Newfoundland and Labrador face of HIV/AIDS, for both the period 1996, when this Randomized Controlled Trial (RCT) was begun, and the current presentation of the disease, determined from the 2001HIV/AIDS estimates. Where appropriate, cumulative estimates of HIV/AIDS data are presented first. These data will be followed by estimates specific to the time periods under discussion, 1996 and 2001. Where data are available and the distinction between HIV and AIDS is considered appropriate for understanding issues, data will be presented separately for the two conditions.

The UNAIDS/WHO 2001 AIDS epidemic update presents a disturbing picture of the twenty-first century presence of HIV/AIDS. The global prevalence rate for adults is 1.2 %, with rates for various countries ranging from a low of 0.1 % to a high of 8.4 %. Since its discovery an estimated 60 million people have been infected with HIV and an estimated 25 million people have died of AIDS (UNAIDS/WHO, 2001).

If we take into account the number of people estimated to have been infected with HIV and to have died from AIDS prior to 1996, we see a reasonably clear picture of the changing face of HIV/AIDS from 1996 to 2001 (Table 1.4).

Table 1.4: Comparisons of Global Estimates of HIV/AIDS Infection - 1996 and 2001

	1996				2001			
	Males	Females	Children	**Total in millions**	Males	Females	Children	**Total in millions**
HIV prevalence	12.6 mil.	9.2 mil.	830,000	**22.6**	19.6 mil.	17.6 mil.	2.7 mil.	**40.0**
HIV incidence [1]			400.000	**3.1**	2.5 mil	1.8 mil.	800,000	**5.0** [2]
AIDS deaths per yr.	650,000	470,000	350,000	**1.5**	1.3 mil.	1.1 mil.	580,000	**3.0**

[1] UNWHO 1996 report does not provide estimates for males and females separately but reports almost half the 2.7 million new infections occur in women.

[2] Figures do not tally due to UNAIDS/WHO rounding.

The global picture of HIV/AIDS in 2001 reveals an estimated 40 million people, worldwide, were living with HIV/AIDS, an increase of 17.4 million from the 1996 estimates. Of this total population, males accounted for 19.6 million, females 17.6 million, and children 2.7 million. These figures represent an increase of 7 million, 8.4 million, and 1.9 million respectively compared to the 1996 estimates. The number of females with HIV/AIDS increased by 48 % and women, currently, account for 44 % of global HIV/AIDS infection. Similarly, reports of the number of new cases of HIV/AIDS demonstrate an increase from 1996 figures compared to 2001, 3.1 million vs. 5.0 million

respectively. The number of deaths attributed to AIDS doubled in 2001 compared to the 1996 figures; 3.0 million vs. 1.5 million (Table 1.4).

Not only are millions of lives lost annually to HIV/AIDS, but millions of new infections also occur each year. Over a third of people living with HIV are aged 15 to 24 and it is believed by the UNAIDS and WHO that most of them are unaware they carry the virus (UNAIDS WHO, 2001). It is reasonable to conclude that HIV has not only severely impacted the quality of life of people worldwide, but is becoming increasingly invasive.

1.8 Canadian Profile of HIV and AIDS

The following profile of HIV in Canada has been derived from Health Canada Population and Public Health Branch publications and reflects the most current government data available. The statistical information has been derived primarily from the Canada Communicable Disease Report (CCDR) - Volume 26-23, December 2000, the HIV/AIDS Epidemiology Update, May 2001 and the HIV and AIDS in Canada Surveillance Report to December 31, 2001, (April 2002). It should be noted that data used to arrive at numbers related to HIV/AIDS in Canada are extracted from surveillance data reported to the Centre for Infectious Disease Prevention and Control (CIDPC) to December 31, 2001. Additionally, utilizing reported positive HIV tests and AIDS cases underestimates the number of persons living with HIV/AIDS. The inaccuracies of this kind of reporting are reflected in that the data represent only a portion of the true number

of HIV positive individuals; specifically those who come forward for testing, are diagnosed, and are reported as HIV positive to CIDPC. Data collected as a function of reported positive results will not capture cases of HIV that have not been tested, and will reflect inaccuracies due to underreporting, delayed reporting, and changes in testing behavior, such as who comes forward for testing. In addition, the number of positive test reports in a given year is not an estimate of the number of new infections occurring in that year because most of the individuals would have been infected in previous years and the majority of individuals newly infected in that year will be diagnosed years later. The CIDPC estimates 15,000 Canadians are HIV positive but unaware of their infection because they have not come forward for testing (Division of HIV/AIDS Epidemiology and Surveillance, Bureau of HIV/AIDS, STD and TB, April 2000).

Less than 0.01 % of HIV in Canada is attributed to positive test results on children (defined as under 15 years of age). For the period January 1996 to December 2001, 264 new test results were reported, and only 15 cases in 2001. Additionally, the number of cases of HIV positive children has been declining since 1995 (Health Canada HIV and AIDS in Canada, 2002). With respect to statistics involving HIV/AIDS infection in children, only very general information will be provided, and this thesis will generally report Canadian demographics in terms of males and females and the numeric values for each will include children under 15 years of age. This decision was taken primarily because the focus of this thesis was HIV infection in adults. This decision was reinforced by the relatively small numbers of reported cases of HIV infection in children in Canada, statements by Health Canada that HIV test reports for children contain inaccuracies in

both data collection and reporting, and statements by Health Canada that there is a lack of uniformity in provincial reporting of cases involving persons under age 15.

Except where specified the information in the following sections, unless otherwise indicated, has been extracted from Canadian HIV surveillance data and covers the period to December 31, 2001. The estimates are calculated utilizing the number of reported HIV positive test results. The national prevalence information, however, will be based on estimates calculated by CIDPC. With this in mind, a reasonable representation of the number of Canadians living with HIV/AIDS in both the 1996 time period and the present can still be examined.

Canada began formal collection and analysis of HIV/AIDS related data in November of 1985. In 1996, at the beginning of this RCT, there were an estimated 40,100 Canadians living with HIV/AIDS. The vast majority, 35,500, were males, with females accounting for 4,600 cases. In 1999, the latest period for which Health Canada provides prevalence and incidence figures, there are an estimated 49,800 people living with HIV/AIDS in Canada, with males accounting for over 86.3 % of cases (Table 1.5). The adult prevalence rate is 0.3 %.

Table 1.5 Comparisons of Canadian Estimates of HIV/AIDS - 1996 and 1999[1]

	1996			1999		
	Males	Females	**Total**	Males	Females	**Total**
HIV prevalence	35,500.	4,600	**40,100[2]**	43,000.	6,800	**49,800[2]**
HIV incidence	3,250	950	**4,200**	3,270	920	**4,190**

[1] Canadian prevalence and incidence related estimates are only available to the end of 1999.

[2] Includes those living with AIDS.

In 1996, Health Canada estimated 4,200 new HIV infections, with males accounting for 77.4 % and females 22.6 % of cases. There was little change in the estimates of new infections for the period 1999 (Table 1.5).

At the start of this clinical trial there was a cumulative total of approximately 29,750 males with HIV positive test reports, making up 88.5 % of HIV infections. Females totaled 3,881 positive test reports comprising approximately 11.5 % of HIV in Canada. As of 2001, the cumulative number of HIV positive test results was 50,259. Of this number 49,562 are adults, and 697 children under 15. Currently, adults comprise almost 99 % of the cumulative number of positive test results. There was a decrease of 2.9 % in the 2001 proportion of males with positive test results compared to 1996 (Table 1.6). In 2001, 85.6 percent of all adult tests results were found in males, with females accounting for 14.4 %. Over 72 % of adult HIV infection is seen in persons between 20 and 39 years old.

Table 1.6: Comparisons of Canadian HIV/AIDS Surveillance Data – 1996 and 2001

	1996			2001		
	Males	Females	**Total**	Males	Females	**Total**
Cumulative Positive HIV tests	29,750	3,881	**38,593** [1]	38,101	6,411	**50,259** [2]
Cumulative AIDS cases	14,488	1136	**15,624**	16,519	1,501	**18,026** [3]
Cumulative AIDS deaths [4]			**11,321**			**12,538**
HIV incidence	1,988	541	**2,785** [5]	1,601	535	**2,172** [6]
AIDS incidence	939	137	**1,076**	184	35	**221** [7]
AIDS deaths per year [4]			**1042**			**81**

[1] The total for males plus females included 4962 results with gender unreported.

[2] The total for males plus females included 5747 results with gender unreported.

[3] Includes 6 cases where gender is unreported.

[4] CIDCP did not provide AIDS deaths by gender.

[5] Total includes 256 cases where gender is unreported.

[6] Total includes 36 cases where gender is unreported.

[7] Total includes 2 cases where gender is unreported.

In 1996, 1,988 new cases of HIV were reported for males and 541 new positive tests for females. By the end of 2001, 2,172 new cases of HIV were reported to CIDPC (Table 1.6). There was a 24 % increase in the numbers of persons living with HIV in Canada between 1996 and 2001. It should be noted, however, this increase reflects not only new diagnoses but also a decline in AIDS deaths due to improved treatments. However, despite concentrated efforts through health updates, the media and education

programs, 14,168 new positive results were reported during this period. Since 1996 there has been a 21.8 % drop in the annual numbers of new diagnosis and the number of new cases has remained relatively constant (Table 1.7).

Table 1.7: Annual Number of Reported New HIV Diagnosis -1996 to 2001

	1996	1997	1998	1999	2000	2001
Males	1,982	1,781	1,746	1,653	1,557	1601
Females	540	457	493	545	494	535
Total[1]	**2,778**	**2,537**	**2,322**	**2,240**	**2,119**	**2172**

[1] Males plus females is less than the grand total due to test reports with gender unreported.

Males continue to be the largest group with positive HIV tests, though a disturbing statistic is the increase in the annual percentage of females with positive test results. Between 1985 and 1994 females represented only 9.9 % of the positive test results but constitute 25% of adult positive results since 1999.

We have witnessed a steady increase in the proportion of positive test results from heterosexuals, who traditionally represented 7.5 % from 1985 to 1994 and now account for 32.8 %.

Another trend is the decline in the proportion of HIV positive test results for men who have had sex with men (MSM). Before 1994, this group accounted for 74.7 % of HIV infection. A decline to 36.8 % from 1997 to 1999 has been observed. This decline,

however, has been followed by an increase to 41.8 % in 2000 and a decrease to 36.6 % for 2001.

In 1996 injecting drug use (IDU) accounted for 33.7 % of new cases of HIV infection, but currently accounts for 24.6 % of new cases.

Given that 25 % of HIV test reports provide ethnicity information, in combination with the fact that ethnicity data for positive test results was really only available since 1998, only limited observations can be made regarding HIV and ethnicity. What can be concluded, with caution, is that 64.2 % of HIV positive test results are seen in whites, 17.7 % aboriginal persons, and 18.1 % in non-white non-aboriginal persons. In the black population 74.7 % of infection is attributed to heterosexual contact and more than 50 % of these HIV infections are associated with infection occurring outside Canada. As a consequence, conclusions regarding HIV and ethnicity need to be considered in lieu of the contribution to the numbers of HIV infections directly related to immigration.

Since the beginning of the epidemic in the early 1980s, 18,026 AIDS cases have been reported to CIDPC. Adult males make up the largest proportion of cumulative AIDS cases at approximately 92.2 %, however, there is an observed overall decline in the number of males with AIDS. The proportion for adult females has risen from 8.3 % at the start of 1996 to a high of 16.2 % in 1999. Currently, 2001, the rate for adult females is 15.7 %. Over 40 % of the annually reported AIDS cases are persons between 30 and 39 years of age.

In 1996, the cumulative total of reported cases of AIDS was 15,624, with males accounting for 14,488 and females 1136. The cumulative number of reported AIDS cases

for 2001 revealed an increase of 2,402 cases. Adult males totaled 16,519 and adult females 1,501 (Table 1.6). There were 221 cases of AIDS reported in 2001, compared to a total of 1,076 new cases of AIDS in 1996 (Table 1.6).

The proportion of reported AIDS cases attributed to heterosexual transmission has been increasing since 1996 and reached a level of 35.6 % in 2001.

The proportion of AIDS cases in the category MSM has steadily declined up to 1996. Despite fluctuations in the proportions between 1996 and 2000, estimates for 2001 indicate 44.6 % of AIDS cases can be attributed to this category.

The proportion of AIDS cases associated with IDU has risen steadily from 2.3 % between 1979 and 1991 to 29.1 % in 1999. It currently is calculated to represent 14.4 % of AIDS cases.

Whites have historically represented the largest proportion of reported AIDS cases in Canada, however, the proportion of whites declined from 82 % at the start of the research project in 1996 to 66.0 % in 2001. The decrease amongst whites is contrasted to the increase among racial minorities. In 2001, 33.9 % of AIDS cases were seen in ethnic groups compared to 17.9 % in 1996. Aboriginals make up 2.8 % and Blacks make up 2 % of our population yet these two groups represented 13.4 and 7.3 % respectively of AIDS cases in Canada in 2001. Though only 5% of AIDS cases are attributed to Asians the cases in this population have been steadily increasing since 1996 from 2.4 to 5.0 %. A more detailed breakdown of ethnic status of AIDS in Canada is shown in Table 1.8.

Table 1.8: Canadian AIDS Ethnicity 2001

White	Black	Aboriginal	Asian	Latin American	Other/not reported	
66.0 %	**13.4 %**	**7.3 %**	**5.0 %**	**2.4 %**	**5.9 %**	**100%**

There were an estimated cumulative total of 11,321 deaths attributed to AIDS by the end of 1996. Deaths, in Canada, due to AIDS accounted for a minimum of 12,538 in 2001, an increase of 1217 deaths (Table 1.6).

The total number of reported AIDS cases per year has declined over the past 10 years from 1556 cases in 1991 to 221 in 2001. A similar pattern has been observed in AIDS deaths, particularly since 1996, where number of deaths has declined from 1,042 in 1996 to 81 in 2001. The most likely explanations for this decrease are use of prophylactic treatment of opportunistic infections and development of effective antiretroviral treatments, which have slowed or prevented the progression from HIV to AIDS. Additionally, it is felt by agencies such as Health Canada (Health Canada, 2000) that increased underreporting and reporting delays may explain some of the decline of AIDS cases in Canada.

Particularly relevant to this thesis are the implications for psychotherapy as a result of increased life expectancy of persons infected with HIV. With lifetime estimates of the prevalence of depression as high as 30 %, and prevalence of depression in persons living with HIV estimated to be higher than the general population, there is a need for interventions aimed at improving psychological well being of persons living with HIV and AIDS.

1.9 Newfoundland and Labrador Profile of HIV and AIDS

The following information was obtained from the Disease Control and Epidemiology Division, Department of Health and Community Services of St. John's, Newfoundland and Labrador, (2001) and Health Canada, Population and Public Health Branch, (2002).

In 1996, of the 175 recorded cases of HIV/AIDS, 79.4 % (139) were males and 20.6 % (36) females. This differs from the national figures for 1996 where women represented only 11.5 % of positive test results and males 88.5 %. Since Newfoundland and Labrador began collecting HIV and AIDS surveillance data in 1984, 210 HIV infections have been reported. This figure represents 0.4 % of the Canadian cumulative positive tests reports, though Newfoundland and Labrador accounts for only .016 % of the population of Canada. Males accounted for 77.6 % (163) and females 22.4 % (47) of cases of HIV (Table 1.9). Again, these values are different than the national percentages where males account for 88.5 % and females account for 11.5 % of HIV infections.

Table 1.9: Newfoundland and Labrador HIV/AIDS Surveillance Data 1996 and 2001

	1996			2001		
	Males	Females	**Total**	Males	Females	**Total**
Cumulative positive HIV tests	139	36	**175**	163	47	**210**
Cumulative AIDS cases	55	11	**66**	67	18	**85**
Cumulative AIDS deaths[1]						**76**
HIV incidence	8	2	**10**	5	0	**5**
AIDS incidence	5	2	**7**	2	0	**2**

[1] Information related to AIDS deaths by year is unavailable.

There were 10 new reports in 1996 with males accounting for 8 cases and females 2. From 1996 to December 31, 2001 there was an increase of 35 positive test results. Five reported positive HIV test results occurred in 2001 alone, all attributed to males (Table 1.9).

By 1996, 66 cases of AIDS had been reported in Newfoundland and Labrador with males making up 83.3 % (55) of the reports and females 16.7 % (11). During this same period the national percentages for AIDS were 92.7 % for males and 7.3 % for females. By December 31, 2001, there was an increase of 19 cases of AIDS, bringing the total of reported AIDS cases in Newfoundland and Labrador to 85. Of the 85 cases, males make up 78.8 % (67) and females 21.2 % (18) (Table 1.9). During this same period the national percentages for AIDS was 85.3 % attributed to males and 14.7 % to females.

In 1996 there were 7 new diagnoses of AIDS, with males totaling 5 cases and females 2. There were 2 new diagnoses of AIDS in 2001, with both in males (Table 1.9).

From the period 1987, when the first Newfoundland and Labrador AIDS deaths were recorded and since reporting had begun in 1984, a total of 62 deaths have been attributed directly to AIDS. Of the above 210 HIV positive cases 76 are known to have died, with 13 having died elsewhere or from causes other than AIDS. No information is available for one of the deaths (Table 1.10).

Table 1.10: Cumulative Deaths Among Newfoundland and Labrador AIDS Cases to December 2001

NF AIDS cases with deaths attributed to AIDS	Males Females	52 10
	Sub Total	62
NF AIDS cases with deaths occurring outside NF or attributed to factors other than AIDS		13
NF AIDS case lost to follow-up		1
TOTAL		**76**

Currently, there are an estimated 134 people in Newfoundland and Labrador living with HIV/AIDS. In 1996, some 70 patients were followed routinely by the HIV team. Presently, approximately 90 persons living with HIV/AIDS are treated through three infectious disease (ID) clinics located in the St. John's, Carbonear, and Corner Brook regions of the province.

Based on positive test reports for Newfoundland and Labrador and Labrador, 44 HIV seropositive individuals do not receive routine care through the ID clinics. There are several reasons for the differences in estimates of infections versus numbers of patients

routinely treated. Several patients are treated outside the province because of their fears surrounding confidentiality, some patients are seasonal workers and work several months outside Newfoundland and Labrador and Labrador, three patients reside in other provinces though their treatment is managed from St. John's, two patients reside in the US but return annually to Newfoundland and Labrador for treatment, several patients were diagnosed in Newfoundland and Labrador but live outside the province, a few patients refuse treatment, and some of the HIV positive individuals have moved and their whereabouts are unknown.

1.10 Purpose of the Study

While the prognosis and pharmacological treatment for patients with HIV/AIDS is well documented, the impact of the disease on the individual's psychological well-being is less well-known. Members of the HIV clinical team at the Infectious Disease Clinic in St. John's have documented that both symptomatic and asymptomatic HIV-positive patients report frequent feelings of depression and hopelessness and on many occasions have requested psychological intervention to assist in dealing with these emotions. These feelings were often exacerbated due to the negative reaction of communities within the province to individuals living in their midst with AIDS/HIV.

Though, the number of HIV/AIDS patients in Newfoundland and Labrador may appear small in comparison to Canada and the world, the impact on many individuals and communities has been substantial. Early on, the stigma of HIV and AIDS was so

punishing, that patients dying of AIDS pleaded with health providers to say they were dying of cancer or pneumonia. Many patients, even during hospitalization with AIDS, told family members diseases other than AIDS were responsible for their illness. One gentleman, upon the death of his brother, pleaded to have the primary diagnosis of AIDS be kept secret so that he and the rest of the family would still be accepted in their community. In another community, a financially successful family was forced to accept social assistance because the local people would no longer purchase services from a man whose child had HIV. Another woman buried her two sons, both in their thirties; her grief was in no way trivial. In another community, the funeral of one of its infants was followed by the funeral of his young father, and both have left behind a wife/mother also infected with HIV. When research demonstrated the high prevalence of HIV in women from the Conception Bay North (CBN) region, the national media labeled this area the "AIDS capital of Newfoundland and Labrador." Some members of these communities felt so ashamed when they had to say they lived in the area that they claimed to be from a different region, rather than risk the social ostracism that could accompany residing in CBN. The labeling of the community caused the Red Cross to suspend blood donations from CBN, increasing both peoples' embarrassment and the negative national publicity. Currently, at least one HIV positive individual still fears the AIDS label, and claims to friends and strangers alike to be dying of cancer. These are only a few of the stories associated with HIV and AIDS and many more stories of shame and despair have been heard and told throughout this province.

Not every outcome associated with a diagnosis of HIV/AIDS has resulted in isolation and ostracism; and with time, experience, and education there has been an increased sensitivity to the plight of living with HIV and AIDS. In many families and communities tremendous love and support was provided to persons infected and affected by HIV. Some people continue to provide, supportive care and financial assistance to patients and their caregivers to help cope with the burden of HIV disease. Despite this support, the grief is undeniable, as communities throughout this province cope with HIV infection and bury citizens who have succumbed to AIDS.

This trial was undertaken to investigate whether the provision of scheduled psychotherapy, incorporated into HIV disease management, would lead to a decrease in feelings of depression and hopelessness in patients living with HIV infection. Before this RCT was undertaken, patients were referred for a psychotherapeutic intervention when either of the HIV infectious disease specialists felt they appeared severely depressed or when they were examined in a hospital emergency department as a result of a suicide attempt or they threatened to commit suicide. The aim of the study reported in this thesis was to compare the effectiveness of this approach, which is referred to as "crisis intervention", to a model where patients received psychotherapy independent of measures and observations of their psychological well-being.

1.11 Study goals

It was within the social context discussed above, and an effort to better understand how to effectively treat the psychological impact on individuals living with HIV/AIDS, that this study was undertaken. Prior to start of this RCT in 1996, there was little research evidence related to the provision of psychotherapy to HIV/AIDS patients for the management of depression, and no evidence could be found that examined the effect of long-term psychotherapy on persons living with HIV disease. The bulk of research examined the impact of providing counselling related to safe sex practices and disease disclosure as well as suggested a role for support groups for persons infected and affected by HIV disease. It was clear from the literature that psychosocial interventions reduced the distress associated with confirmation of a diagnosis of HIV/AIDS and that pre and post-test counselling should be a part of the routine management of HIV testing.

Extensive research also examined the role of psychotherapy in changing risk behaviors of HIV infected persons. Again, there was evidence that psychotherapy might be beneficial in reducing risk behaviors in high-risk groups.

Much of the research investigating the role of psychotherapy was conducted using gay or bisexual males, patients who had a diagnosis of depression, and patients who were HIV asymptomatic. In addition, the studies used small numbers of subjects. No studies could be found examining the effects of the provision of long-term psychotherapy in a sample of subjects who were heterogeneous in respect to the mechanism of HIV infection, gender and level of psychological health.

The RCT reported in this thesis was initiated in 1996, by the author of this thesis, to determine whether long-term psychotherapy can prevent psychological dysfunction in HIV/AIDS patients. This researcher wished to look at the effects of providing psychotherapy for a minimum of six months to a diverse group of persons living with HIV/AIDS. The objective was to determine the impact of long-term psychotherapy on depression, the primary outcome measure, as well as the secondary measures of hopelessness, coping skills and CD4 cell counts. The subjects for the trial were a group of HIV positive patients who were heterogeneous in relation to their HIV infection and level of psychological health. The study results have important implications for psychotherapy in the management of HIV disease.

1.12 Research Questions

The primary outcome measure in the RCT discussed in this thesis was the effect on depression scores, measured by the Beck Depression Inventory, in HIV positive persons receiving psychotherapy of six months duration. The question under investigation can be represented in the following way:

- In persons living with HIV disease, does the provision of six months of psychotherapy lead to less depression, as measured by the Beck Depression Inventory, compared to a crisis intervention only model of psychotherapy delivery?

In addition to the primary question, several secondary outcome measures were of interest to this researcher. These are reflected in the following questions:

- In persons living with HIV disease, does the provision of twelve months of psychotherapy lead to less depression, as measured by the Beck Depression Inventory, compared to a crisis intervention only model of psychotherapy delivery?
- In persons living with HIV disease, does the provision of six and twelve months of psychotherapy lead to less hopelessness, as measured by the Beck Hopelessness Scale, compared to a crisis intervention only model of psychotherapy delivery?
- In persons living with HIV disease, does the provision of six and twelve months of psychotherapy lead to improved coping skills, as measured by the Coping Inventory for Stressful Situations, compared to a crisis intervention only model of psychotherapy delivery?
- In persons living with HIV disease, does the provision of six and twelve months of psychotherapy lead to an increase in CD4 T-cell counts compared to a crisis intervention only model of psychotherapy delivery?

CHAPTER 2

PSYCHOTHERAPY – AN OVERVIEW

2.1 Increasing Role for Psychotherapy

In the past few decades psychotherapy has played an increasing role in the management of a number of chronic illnesses. Health care providers and patients report improved clinical outcomes when the patients' psychological well-being is addressed as part of the treatment protocol. In fact, evidence of the attention being paid to psychosocial aspects of health care are seen in the increasing number of clinical trials that examine quality of life outcome measures. Many experts point to a destigmatization of psychotherapy (O'Connor & Yalom, 1997). Irvin D Yalom, professor emeritus of Psychiatry, Stanford University emphasized the enhanced role of psychotherapy in the last decade of the twentieth century: "Psychotherapy was becoming more mainstream, more available, and more acceptable to larger segments of the American public" (O'Connor & Yalom, 1997) (p. ix). Yalom also speaks of a growing intolerance by society of the "noxious long term effects" of trauma and an increasing demand from the public for access to counselling facilities and for the provision of adequate counselling services in health care plans (O'Connor &Yalom, 1997) (p. x). Numerous experts and professional associations in the field of psychotherapy are also echoing this need for an increased role for psychotherapy in the management of chronic diseases (Gabbard, 1994; Shea 1998; O'Connor & Yalom, 1997).

2.2 Defining psychotherapy

Definitions and descriptions of psychotherapy vary according to the different conceptual frameworks used by different therapists. The definitions provided here are working definitions extracted from the texts: Standards and Guidelines for the Psychotherapies (Cameron, Ennis & Deadman (eds.), 1998) and Psychodynamic Psychiatry in Clinical Practice, The DSM-IV Edition (Gabbard, 1994). In the search for a definition of psychotherapy, one discovers there are at least as many definitions of psychotherapy as there are therapeutic approaches. Wolberg (1977), reviewed thirty-seven definitions of psychotherapy. He provides the following composite definition:

> "Psychotherapy is the treatment, by psychological means, of problems of an emotional nature in which a trained person deliberately establishes a professional relationship with the patient with the object of (1) removing, modifying, or retarding existing symptoms, (2) mediating disturbed patterns of behavior, and (3) promoting positive personality and development" (p. 3).

Organizations, such as the Canadian Psychiatric Association (CPA) and the Ontario Hospital Insurance Plan (OHIP), also provide very reasonable working definitions of psychotherapy (Cameron *et al.*, 1998). A drawback in their definitions is the emphasis of delivery of psychotherapy by a physician rather than "suitably trained person" seen in the more general framework. Bloye and Davies (1999), simply define psychotherapy as a treatment that manages psychological symptoms by using the professional relationship between a patient and a therapist to change feelings, cognition, and behavior (p. 121).

Landau (1986), also recognizes the role of a "suitably trained person" in his more detailed definition of psychotherapy. His definition will be used in this manuscript for its informative content and because it does not limit usage of psychotherapy by the inclusion of physician as therapist:

> "Any form of treatment for mental disorders or emotional disturbances in which a suitably trained person establishes a professional relationship with an identified patient for the purpose of removing or modifying symptoms of the disorder, or of promoting character growth and development so as to strengthen the patient's ability to cope with the problems of living. The relationship established between patient and therapist is used to influence the patient to unlearn old, maladaptive patterns and to learn and test new approaches. Psychotherapy includes guidance, counselling, psychoanalysis, behavior therapy, conditioning, hypnotherapy, and all other forms of treatment in which the major technique employed is communication, rather than drugs or other somatic agents." (p. 2348).

2.3 Brief Descriptions of Some Common Psychotherapies

The following section is intended to provide a general understanding of psychotherapy through brief descriptions of some common orientations, as well as descriptions directly related to the orientation of the psychotherapy provided in this RCT.

There are numerous forms of psychotherapy, however, they can be abstracted into four overlapping, heterogeneous orientations: psychodynamic, cognitive/behavioural, strategic/systems, and experiential (Cameron *et al.*, 1998).

2.3.1 Psychodynamic Psychotherapy

Psychodynamic psychotherapy is expressed through five core concepts: the influence of early-childhood experiences on current adult functioning, the power of unconscious functioning in human behavior, reliance on ego defenses, repetition compulsion, and transference (Book, 1998). Psychodynamic psychotherapy operates on an expressive- supportive continuum. At the expressive end of the continuum the primary goal is significant and substantial character change along a broad perspective. The primary aim of psychodynamic psychotherapy is for the patient to increase their understanding of internal conflict, deficits, and defensive compromises. This heightened understanding is expected to yield increased awareness of affects held by the patient, thus leading to both symptom relief as well as personality change.

2.3.2 Cognitive Behavioural Therapy

The general focus of cognitive behavioural therapy (CBT) is identification of dysfunctional cognitive structures that maintain unrealistic thoughts and images in specific situations. An underlying concept is that perception of events mediates the

response and ultimately determines the quality of adaptation. Treatment focuses on assisting patients in recognizing perceptual and cognitive errors, instructing patients to perceive external problems more realistically, and assisting the patient to cope with the more realistically perceived situations (Antony & Swinson, 1998). In essence, the principal aim of CBT is to change or eliminate existing maladaptive behaviors and help patients to acquire new adaptive behaviors, as well as, enhance current adaptive ones. The mechanism of change in CBT is believed to be related to changes in patients' thoughts and behaviors. These changes in turn lead to decreased distress as well as more effective interactions with others and the environment.

2.3.3 Strategic Systems

According to Freebury et al. (1998), strategic systems psychotherapy concerns itself with modification of behaviour within a given system or modification of the entire system. Insight is seen as antithetical to change unless it is imparted according to a strategic plan. Some of the strategies of this orientation are direct advice, paradoxic injunctions, reframing, symptom prescription, boundary marking, and positive connotation.

2.3.4 Experiential Psychotherapy

The primary aim in experiential psychotherapy is the sharing of feelings and experiences in a non-authoritarian and empathic environment (Freebury et al., 1998). The therapy is predominately ahistorical with the emphasis clearly focused on the "here and now" experience. The data source derives from both the "here and now experience" and the therapist's empathic awareness. Strategies of experiential therapy include abreaction empathy, sharing, identification, imitation, and confrontation.

2.3.5 Eclectic Therapy

Eclectic therapy is the label used to identify the situation in which more than one approach is used with a patient. Generally the therapist, and can include the patient, chooses an orientation which seems the most appropriate at a particular time period, but may also see that another orientation is more appropriate as the therapeutic relationship develops. Additionally, the therapist may see a particular orientation as preparation for another (Clarkin, Frances, & Perry, 1995). Often an orientation may present as the appropriate one for immediate symptom relief yet the goal is to build towards a long-term psychodynamic approach. Eclectic psychotherapy does not presuppose a particular theory of psychopathology (Hoaken and Golombeck, 1998). There is a growing consensus that there is no single approach that is adequate for all clients and there should be consideration given to matching the therapy to the client (Messer & Warren, (1995).

There is mounting evidence that enhanced results may be obtained by tailoring the therapy to the client rather than fitting the client into the mold of one mode of therapy (Beutler & Consoli, 1992; Jones, Cumming, & Horowitz, 1988). Fine and Turner (1991), point out that the therapist with relatively ideological freedom and the motivation to integrate different theories enhances their potential for helping a wider spectrum of families. Miller, Duncan & Hubble (1997), emphasize that evidence makes it clear that the similarities rather than the differences between therapy modalities accounts for most of the change that clients experience in treatment underscoring the belief that the therapist need not be restricted to a specific approach but can incorporate a number of frameworks into treating clients.

An excerpt from Weinberg (1995), summarizes a rationale for an eclectic approach to provision of psychotherapy. He states:

"No psychotherapy is superior to any other, although all are superior to no treatment .... This is the conclusion drawn by authoritative reviews..., and well-controlled outcome studies....This is really quite remarkable, given the claims of unique therapeutic properties made by advocates of the various treatments available today."

In addition to the definitions above, an understanding of psychotherapy can be gained through the general framework for most psychotherapy adapted from an article by Haoken and Golombek (1998). In the therapeutic process the therapist is attempting to provide an atmosphere in which both the patient and the therapist are demonstrably interested in the patient's problems and working towards change. The therapist is

committed to continuously showing interest in the patient's symptoms and goals as well as conveying hope that change is possible. The therapeutic relationship allows for common positive transference expectations to develop and motivate the patient (pp. 228-229).

2.4 Psychotherapeutic Approach Used in the Thesis RCT

The psychotherapeutic orientation adopted in this study can be defined in terms of an eclectic approach. This reflects a belief on the part of the author, and indeed others, that patients are not only unique but may require different types of interventions at different times. Support for an eclectic approach is seen in the following statement expressed by Brouillette & Citron, (1997) " In all cases, psychotherapy should be tailored to the person's needs and capacities" (p. 57). There is little doubt that many different therapies are able to achieve goals established by both the therapist and client. However, it is recognized that one approach may be more appropriate than another with respect to the personality or situation of the individual patient. In addition it has been observed that a therapeutic approach might be used initially to help establish a patient therapist dyad while building towards a different orientation once an effective therapeutic relationship has been established. "The contemporary field of psychotherapy is more pluralistic: many diverse approaches have proven therapeutically effective and the therapist of today is more apt to tailor the therapy to fit the particular clinical needs of each patient" (Yalom, 1997) (p. x).

Throughout the course of this trial, elements of a number of theoretical orientations were incorporated into the psychotherapy sessions, particularly the psychodynamic and cognitive/behavioural models. The interventions are best described as a psychodynamic orientation utilizing a range of expressive-supportive interventions and psychoeducation. To help understand this orientation, a brief description of these terms is provided in sections 2.4.1 and 2.4.2.

To facilitate an understanding of the mechanisms of change in the psychotherapy sessions a list of some of the techniques utilized in the therapy sessions is presented. The techniques related to the psychodynamic orientation included:

Expressive techniques: interpretation, confrontation, clarification, attainment of insight, and attention to the transference relationship; Supportive techniques: emphasis on the therapeutic quality of the relationship, education, counselling, modeling, reframing, and encouragement.

Aspects drawn from the Cognitive Behavioral models include: role-play, modeling, desensitization, homework, "empty chair", relaxation exercise, cognitive restructuring, and graded task assignment.

2.4.1 Psychodynamic Orientation

All psychodynamic psychotherapies belong to what has been called the expressive-supportive continuum (Gabbard, 1994). Individual psychotherapy invariably contains both expressive (insight-oriented) and supportive elements, with one or the other

predominating, depending on the clinical picture at any given stage of treatment. Clinical interventions at both ends of the continuum contribute to good outcomes (Wallerstien, 1986; Luborsky, 1993). When working at the expressive end of the continuum, therapists seek to maximize the patient's ability to self-reflect and, ultimately, achieve mature autonomy by helping patients to understand behaviours, thoughts, and feelings, and to decide for themselves how to direct them. When working at the supportive end, the therapist seeks to support the patient in some way compatible with mature dependence with the goal of helping the patient analyze their doubts and understand the longing for advice.

A list of common interventions utilized at the expressive end of the continuum includes: interpretation, confrontation, clarification, encouragement to elaborate, and empathic validation. On the supportive end the therapist might include advice and praise, affirmation, and limit-setting.

2.4.2. Psychoeducation

Psychoeducation refers to the process of teaching a patient about both their disorder, as well as the rationale for the psychotherapy chosen. It is described by Glen O. Gabbard as a model in which the nature of the patient's deficits and their implications are explained (Gabbard, 1994). Psychoeducation explores with the patient organic contributions to the patient's behaviours. An important aspect of psychoeducation is the involvement of the family, friends and care providers in the psychoeducational process.

Glick *et al.* (1994), provide the following definition: "Psychoeducation as a technique in clinical practice can be defined as the systematic administration by the physician of information about symptoms, aetiology, treatment and course, with the goals of increasing understanding and changing behaviour." The psychoeducation website www.psychoeducation.com (Psycho-Educational Counseling Services, Inc. 2002), provides a clear explanation as well as identifies the goals of psychoeducation interventions. In summary, psychoeducation involves teaching the patient, generally, and where possible, family members, friends, and caregivers about the disease, how to treat it, and how to recognize signs of relapse. Beyond just providing information related to the illness, psychoeducation includes teaching coping strategies, and problem solving skills. Recent research suggests the addition of psychoeducational interventions, for both patients and their families promotes compliance and leads to improved psychological outcomes (Glick *et al*, 1991). Psychoeducation has been shown to be an effective intervention in a variety of illnesses including depression (Dowrick *et al.*, 2000).

2.5 The Therapist Effect

In addition to the common psychotherapies, and closely associated with their outcomes, is one of the most critical aspects of the patient/therapist relationship. This aspect is the personality of the therapist. Extensive study of psychotherapy has demonstrated the personality of the therapist contributes substantially to the success or failure of the therapy (Frank & Frank 1991; Grunebaum, 1983; Strupp, 1987a). Many

therapists believe that the personality of the therapist is one of the most important aspects of therapy, possibly more important than any theoretical approach (Strupp, 1987b). This sentiment is expressed particularly well by Steven A. Caldwell, (1997), "Research suggests that the "real" features of the therapist- the personal qualities and interpersonal skills of the clinician –account for at least as much treatment outcome as specific techniques and theories employed. The meaningful encounter between the therapist and patient is facilitated primarily by the core personhood of the psychotherapist" (p. 16).

Despite the importance of innate ability in the therapist, many people believe some of the attributes of a good therapist can be taught (Strupp 1978b). In a trial to investigate adherence to a National Institutes of Mental Health (NIMH) manualized psychotherapeutic treatment procedure, Markowitz *et al.* (2000) showed, through evaluations by blinded independent raters, that therapists were adherent to the specified treatments after training for those treatment formats. The authors concluded it is possible to reliably train adherence monitors and therapists to deliver specified treatments.

2.6 Psychotherapy in HIV/AIDS

It is not uncommon, when treating persons living with HIV/AIDS, to hear frequent reports of symptoms of mood disturbances (Brouillette & Citron, 1997). Persons living with HIV/AIDS may experience a wide range of neuropsychiatric symptoms, including depressed mood, anxiety, irritability, suicidal ideation, agitation and insomnia (Halman, 2001). Yalom, (1997), provides a rationale for inclusion of psychotherapy in

the treatment of persons living with HIV. He points out a diagnosis of HIV infection is likely to raise strong emotional reactions in the client, and a diagnosis of HIV infection is likely to raise previously unresolved concerns and even historical traumas (p. xxviii). As stated earlier, persons living with HIV/AIDS frequently report symptoms of mood disturbances. (Brouilette & Citron, 1997). Living with HIV/AIDS often means facing a series of crises that often overwhelm a person's usual coping ability. In addition, it has been shown that people with HIV who have previously experienced psychiatric symptoms, are more likely to experience symptoms after HIV infection (Yalom, 1997). An overwhelming characteristic of HIV is its variability in terms of structure and effect on individuals with the virus. One of the outcomes of the variable nature of the disease course is a repetitive cycle of hopelessness, denial, hopelessness, as patients experience changes from physical and psychological good health to poor health and back again (Ostrow, 1997). As David G. Ostrow points out, and this is observed by many providers of psychotherapeutic interventions to persons living with HIV and AIDS, "Thus there is an inherent affective instability that comes with HIV infection and with attempts to gain control over its seemingly inevitable encroachment ..." (p. 34).

Patients living with HIV incur multiple losses, which include health, autonomy, social networks, mental acuity and economic security. A routine observation in the management of HIV treatment is that losses are not paced and many of the losses can happen concurrently or in very rapid succession contributing to decreased psychological well being (Ostrow, 1999). Another observation in the management of persons living with HIV/AIDS (PWHA) is an increase in feelings of demoralization (Treisman,

Angelino, & Hutton, 2001). Demoralization, which is an exaggerated grief state in which the patient has a pervasive sense of sadness, low mood, or hopelessness that interferes with usual activities, is different than depression in that it is not a brain disease and is more likely to respond to psychotherapy than antidepressant medication.

Depressed mood is the most common neuropsychiatric complaint in persons with HIV/AIDS seeking psychiatric evaluation (Halman, 2001). Earlier studies, using self reported measures of depression, found a point prevalence of 20 % to 30 % while studies using standardized interviews found point prevalence of 4 % to 18 % Brouillette & Citron, 1997). According to Perry (1994), low-grade depressive symptoms are frequent in HIV positive individuals and depressive disorders occur in about one in ten.

This variation in estimates of the prevalence of depression in HIV can be explained by several factors. The diagnostic criteria for major depression are felt to lose their specificity in medically ill populations. The variability in the population samples, the variability in the interval defined as point prevalence (1-6 months) and variability in the instruments used to assess psychopathology contribute to the variation in estimates. Also contributing to point prevalence variation is the influence of comorbidity with other psychiatric diagnoses.

Initially, it was felt that depression rates were about the same in HIV positive patients as in the general population, though most of the estimates were based on weak information sources. It is generally accepted that rates for major depression in persons living with HIV are higher than in the general population. More recent studies indicate the prevalence rate of major depression in persons with HIV/AIDS is more likely to be 22

% to 45 % (Halman, 2001). Treisman *et al.* (2001), estimate about 60 % of HIV-infected patients have a depressive episode sometime in their illness. Despite differences in opinion related to prevalence and incidence, there is substantive agreement amongst professionals that psychotherapy in an integral part of the treatment of depression in people living with HIV (Brouilette & Citron, 1997).

2.7 Defining Depression

Depression is generally abstracted into "major depressive episode" and recurrent depressive disorder. Depression is viewed as a disease with a number of what are thought of as "core" symptoms. These symptoms include, a lowering of mood to a degree that would be viewed as abnormal for the particular individual experiencing the mood, loss or reduction in energy, and a loss of interest in, or decrease in enjoyment of, normally pleasurable activities.

To meet International Statistical Classification of Diseases and Related Health Problems, Tenth Edition (ICD-10) criteria for depression, at least two of these core symptoms must be present for at least two weeks. Additional symptoms from the following list can be used to affirm a diagnosis of depression. The list includes: loss of confidence, feelings of guilt, thoughts of suicide, poor concentration, changed sleep, changed appetite, and agitation or retardation.

To aid in an understanding of the severity of depression, mild depression is thought to be present when a total of four symptoms from the two lists are present. For a

diagnosis of moderate depression, at least six symptoms from the two lists should be present. When eight symptoms are present, and includes all three of the core symptoms, the patient is thought of as having a severe depressive episode.

To meet the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) criteria for a Major Depressive episode the patient must experience the presence of five or more symptoms, in the same 2-week period, from a list which includes depressed mood, anhedonia, altered sleep, altered appetite, altered weight, fatigue, psychomotor agitation or retardation, diminished concentration, guilt and suicidality. Additionally at least one of the symptoms must be either depressed mood or anhedonia (absence of pleasure from acts that would ordinarily be pleasurable) and the symptoms cannot be directly explained by general medical condition.

Other depression syndromes include the following:

- Dysthymia, which is chronic and prolonged depressed mood which continues for more than 2 years but does not usually satisfy the criteria for a depressive episode.
- Bipolar Depression, which is characterized by the occurrence of one or more major depressive episodes accompanied by at least one Hypomanic Episode.
- Cyclothymia, which may be thought of as chronic mood swings.
- Adjustment Disorder with Depressed Mood, which is depressed mood, not meeting criteria for a major depression, occurring within two months of definable stressor and remitting within six months of cessation of the stressor.

- Bereavement, characterized by depressed mood after the death of a loved one, which is allowed to meet the criteria for major depression for the first two months.
- Depression Secondary to Psychiatric or General Medical Disorders or to Psychoactive Substances, where the depressive symptoms are secondary to other medical conditions or drugs.
- Depression NOS, which is simply depressed mood which does not meet the criteria for any of the above syndromes.

For more detailed information on these conditions please refer to the American Psychiatric Association (1994), *Diagnostic and Statistical Manual of Mental Disorders,* Fourth Edition, or any professional manual on mental disorders.

Recurrent depressive disorder is established as the diagnosis when the patient experiences two or more episodes of depression.

Rosenbaum (1996) goes beyond the definitions to more clearly express what patients report when they are depressed:

> "Perhaps we should have a different name for the syndrome that drains the zest for living and replaces it with anguish, guilt, pessimism, irritability, and the inability to experience pleasure – a condition that saps the appetite for food as well as for life, blocks access to the sanctuary of sleep, depletes energy and the motivation to rally, and fills the mind with morbid thoughts, including the wish to be dead." (p. 1).

So often, descriptions similar to this, are heard from patients experiencing depression and frequently the words are accompanied by tears and trembling. This, more than an ICD-10 or DSM-IV description, is the face of depression.

2.8 Prevalence and Incidence of Depression

Since so many of us have encountered someone who has experienced depression, it should come as no surprise that it is one of the most common psychiatric illnesses (Canadian Mental Health Association, 1995). It is estimated that between 2.3 % and 3.2 % of men and 4.5 % to 9.3 % of women in western countries suffer from major depressive disorder (U.S. Department of Health and Human Services, 1993). If the minor forms are added to the major depressive episodes category then it is more likely that 10 % of the population suffers from depression (Cassem and Coyle, 2002). A study by Murphy (1990) indicated that 5 % of the Canadian population suffers from depression at any one time.

The overall lifetime prevalence estimates of clinically significant depression range from 15 % to 30 % (Canadian Task Force on the Periodic Health examination, 1990). The point prevalence of depression in the general population has been reported from a low of 3.5 % to a high of 27 % (Canadian Task Force on the Periodic Health examination, 1990). This wide variation is associated with variability in the populations under study, variability due to the assessment tools used, as well as variability of definitions of depression. Reporting depression prevalence information is generally

derived from a diagnostic interview or self-report questionnaires (Canadian Mental Health Association, 1995), and there appears to be higher percentages of depression from self-reported questionnaires (Brouillette & Citron 1997. This may also contribute to the variability in estimates. Even if someone chooses to accept only the lower end of the estimates, there are undoubtedly many millions of people who have experienced, are currently experiencing, or can expect to experience depression.

2.9 Depression in HIV/AIDS

Depression is a major factor associated with decreased quality of life in patients with HIV/AIDS, and major depression is a primary risk factor for suicide in the HIV population, as well as the general population (Fawcett *et al.*, 1990; Rundell *et al.*, 1992). Major depression has been associated with decreased survival in persons living with HIV disease (Mayne *et al.*, 1996) as well as decreased immunological function (Evans *et al.*, 1997).

In summary there appears to be clear evidence of a role for psychotherapy in the management of HIV disease. S.W. Perry (1994), reports that accumulated clinical experience and a couple of systematic studies suggest that psychotherapy alone or in combination with antidepressant drug therapy can be remarkably beneficial in treating HIV-infected patients. "Given the nature of this illness and the stresses associated with it, psychotherapy should be an integral part of psychiatric care for someone living with HIV." (Brouillette & Citron, 1997) (p. 57).

Clearly, the addition of a diagnosis of HIV brings about new psychological issues and exacerbates previous and existing conditions. Depression is a condition strongly associated with living with HIV and AIDS. It seems reasonable to conclude there is a role for psychotherapy in the management of HIV disease.

2.10 Evaluation of the Major Clinical Trials Related to the Primary Outcome Measure of the Thesis RCT

In order to portray an understanding of the role of psychotherapy in the management of HIV disease at the time this trial was undertaken, this section will review the literature up to the period 1996 when the clinical trial, which is the subject of this thesis, was begun. Trials investigating the impact of psychotherapy on HIV and AIDS which were published after the start of this clinical trial, as well as studies directly related to secondary outcome measures, will be presented in the discussion chapter of this document.

The focus of the discussions of the research related to psychotherapy and HIV/AIDS will be concerned with Randomized Controlled Trials. There is non-experimental evidence to support the possibility of benefit due to psychotherapy, but in the presence of experimental evidence from RCTs this researcher chose to limit discussion, generally, to results obtained from this stronger evidence source.

There is an abundance of literature describing psychological issues that confront persons diagnosed with HIV/AIDS. These include: depression, hopelessness, chronic somatic preoccupation, fear of development of illness, debilitation, anger, frustration,

societal ostracism and anxiety (Mulder *et al.*, 1994; Kelly *et al.*, 1993; Perry *et al.*, 1991). Throughout the course of the disease, episodic feelings of depression and hopelessness, a decrease in self-esteem, decreased coping skills, and lower ratings of quality of life may be present. The available literature suggests these outcomes are persistent and a role for psychotherapy is strongly indicated as an integral component of HIV management (Lutgendorf *et al.*, 1994).

There is consensus that a need exists for controlled outcome studies that assess the effects of psychotherapeutic interventions on depression relief in persons living with HIV (Markowitz *et al*, 1995). In their 1995 article Markowitz et al. claim that their trial was the first controlled study of individual psychotherapies for depressed HIV positive patients. This assertion is supported by an extensive literature search undertaken as part of this study.

An initial observational study of 23 adults with HIV infection, by Markowitz et al., 1992, demonstrated a decrease in depression scores in HIV positive patients who met DSM-III- R criteria for nonpsychotic major depression or dysthymia enrolled in an interpersonal psychotherapy (IPT) program lasting 16 sessions. The authors suggest mental health workers should consider IPT as a treatment for depressed HIV positive patients.

There are a number of weaknesses associated with this study. There was no control group, allowing for conclusions that improvements may be explained by factors other than the psychotherapeutic intervention. Time alone could have accounted for the improvement seen in the study subjects. In addition, the sample size was quite small.

Although depression was resolved in 87 % of cases, it was not measured in the same way for all 23 subjects. Five subjects were assessed with the Hamilton Depression Rating Scale (HRSD), whereas 18 were evaluated by therapists' global clinical impressions and patients' subjective assessment. Using different outcome measures for different subjects brings into the question the credibility of the study findings. Two different therapists treated the study subjects and there is no mention of any analysis looking at therapist effects.

All but two subjects were physically asymptomatic, limiting information related to the effects of IPT on symptomatic subjects. Additionally, conclusions cannot be drawn regarding a role for psychotherapy for non-depressed patients living with HIV/AIDS.

Finally, the authors provide no follow-up information regarding the patients, consequently, nothing can be concluded about the lasting effects of IPT on depression in adults living with HIV.

A later randomized controlled trial by Markowitz *et al.* (1995), of 32 gay or bisexual male subjects, showed improved depression scores in HIV-positive patients receiving 16- week interventions of interpersonal psychotherapy or supportive psychotherapy. In addition, the authors observed a potential advantage of interpersonal psychotherapy over supportive therapy.

The subjects in this trial were randomized to either interpersonal psychotherapy or supportive psychotherapy. Analysis of baseline characteristics indicated the groups were similar.

The design of this RCT provides limited credibility to the authors' conclusion that both these psychotherapies can lead to a decrease in depression scores in subjects with HIV disease. One of the major problems with this study is the absence of a control group, thus many factors, other than the psychotherapy, could have accounted for the improvement in the study subjects. Simple passage of time, or enrollment in a trial, or psychological testing, etc. could explain changes, and a control group would have helped address concerns such as these.

Another problem is the homogeneity of the subjects. All subjects were gay or bisexual, asymptomatic and all were males. This limits the generalizabilty of the effects of these two psychotherapies to a heterosexual population, symptomatic population and to females.

All subjects in this trial had a Hamilton Depression Rating Scale score of at least 15 and clinical impression of a DSM-III-R mood disorder. This does not allow for any conclusions regarding the effects of psychotherapy in a HIV population heterogeneous with regards to levels of depression.

In addition, there was no patient follow-up, limiting any conclusion regarding the ability of the short-term interventions to maintain a depression free state. The authors also point out that they used a relatively small sample size.

Targ *et al.* (1994), examined the effects of a 12-week treatment interval of structured group therapy and fluoxetine compared to structured group therapy and placebo in 20 depressed homosexual subjects who met the criterion for major depression or adjustment disorder with depressed mood. Patient demographics were similar at

baseline and subjects were randomized to receive either fluoxetine or placebo and blinded to medications. Subjects were assessed using the Hamilton Depression Scale (HAM-D) and the Profile of Mood States (POMS). Although both groups demonstrated a significant improvement in several measures of depression and anxiety, there were no significant differences on psychological measures between the groups. The authors concluded that by using structured group therapy depressive symptoms can be relieved without a pharmacological intervention.

It is possible, in the absence of a control group, that patients just improved on their own. None of the 20 patients were symptomatic and were included only if they had no concurrent drug or alcohol abuse. This limits conclusions regarding the effectiveness of structured group therapy on symptomatic patients and patients who might have alcohol or drug related problems.

The homogeneity of the trial subjects limits the generalizabilty of the conclusions. The absence of any females or heterosexual subjects could provide support for an argument that the findings only apply to gay males.

Typically there was no mention of follow-up, which could assess the ability of the intervention to maintain absence of depression. The authors also report no differences between groups on CD4+ and CD3+ cell counts.

Mulder *et al.* (1994) investigated the effectiveness of 15-week cognitive behavioral group psychotherapy (CB) and an experiential group psychotherapy (ET) program for 39 HIV-positive homosexual men. Patients were administered the BDI, the General Heath Questionnaire (GHQ) and a Dutch versions of the POMS. Their findings

suggest that psychosocial interventions significantly decreased distress compared to a wait list control group. In addition they found no benefit of one therapy over another, suggesting patients should be allowed to choose their preferred therapy.

Support for the authors' conclusions is strengthened by the fact that patients in this study were randomized to the three experimental conditions: cognitive-behavioral group therapy (CBGT), experiential group therapy (EGT), or a waiting-list control. In addition, the authors state the three groups had similar demographics at baseline.

This study is typical in that the subjects are homosexual males thus limiting generalizations to heterosexuals and females. There was no investigation of any long-term effects of the psychotherapy. All subjects were asymptomatic and had no history of drug or alcohol dependency. This restricts any conclusions related to the success of these interventions for symptomatic patients or patients with drug or alcohol use. In recognition of the fact that alcohol and drug related issues often accompany HIV infection, the study could have been improved by including subjects with these issues.

Kelly *et al.* (1993) compared the outcomes of an eight-session cognitive-behavioural group, eight-session social support group and a comparison group (only administered assessment measures) in 68 depressed predominately homosexual males with HIV infection. Psychological measures were obtained using the Center for Epidemiologic Studies Depression scale (CES-D), the Social Provisions Scale (SPS), the Symptom Checklist 90 – Revised (SCL-90-R), and the Multidimensional Health Locus of Control Scale (MHLCS). Both interventions reduced depression, hostility, and somatization compared to the control group.

Aspects of this trial, such as randomization of subjects to treatment and control conditions, inclusion of symptomatic as well as asymptomatic patients, and patients with history of alcohol and drug use, enhance the generalizabilty of the finding of benefit due to the provision of psychotherapy.

Although 10 females entered the study, they wished to attend only groups with other females and thus were dropped from the analysis, leaving only an analysis conducted on the male patients. It is arguable that data for these women should have been included in the analysis or at least a separate analysis containing both males and females should have been conducted. Again, this limits conclusions that can be drawn regarding the benefits of group psychotherapy for females. A total of 115 subjects were recruited but only 68 had complete follow-up and were included in the analysis. The authors stated that most of the losses were attributable to severe illness. Clearly, the authors' conclusion underrepresented the patients with greater disease severity. It is generally expected that all patients be included in the analysis particularly if there might be a strong association with the primary outcome. The loss of almost 41 % of trial subjects presents a strong challenge to the confidence in the authors' conclusions. As in the preceding trials, only subjects with probable depression entered the study so little can be said about the effects of psychotherapy in nondepressed individuals.

There was a three-month follow-up but only the social support group continued to differ significantly from the comparison subjects. This indicates a need to compare the effects of short versus long-term effectiveness in managing depression in HIV disease.

Over 94 % of subjects were homosexual or bisexual limiting conclusions regarding the effects of these two therapies in heterosexual patients.

2.11 Secondary Outcome Measures

In addition to examining the role of psychotherapy in the treatment of depression in persons living with HIV, secondary issues such as the effects of psychotherapy on hopelessness, coping, and CD4 T lymphocyte cell counts were considered in this study. Though these issues were not of primary interest, they are strongly correlated with psychological well-being and are important considerations in the management of HIV and AIDS.

2.11.1 Hopelessness

Hopelessness is a psychological construct that has been observed to underlie a variety of mental disorders. It is conceptualized as a system of cognitive schemas in which the common denominator is negative expectancy about the short and long term future (Beck & Steer, 1993). Several beliefs are observed in individuals described as hopeless. Hopeless individuals believe nothing will turn out right for them, they will never succeed at what they attempt to do, important goals can never be obtained, and their worst problems will never be solved. The North American Nursing Diagnosis Association (NANDA) describes hopelessness as a subjective state in which an

individual sees limited or no alternatives or personal choices available and is unable to mobilize energy on own behalf (Fortinash & Holoday-Worret, 2000). Some defining characteristics of persons diagnosed as suffering with hopelessness include verbalizations that life, situation, or status seem hopeless or futile, frequent sighing, decreased or absent verbalizations, decreased affect, withdrawal, decreased appetite, increased sleep, lack of involvement in care, lack of interest in significant others.

Hopelessness was assessed in this study because of its' strong association with depression and suicide. In addition to the preceding associations, the clinical team treating HIV/AIDS observed repeated complaints of intense feelings of hopelessness amongst the HIV positive patients. As well, reports of feelings of hopelessness are frequently reported in the HIV/AIDS literature. This researcher felt that interventions, which might decrease hopelessness, would likely improve quality of life.

2.11.2 Coping

Coping has primarily been conceptualized as a response to external stressful or negative events (Endler & Parker, 1990a). The person's responses to the events usually involve conscious strategies. A more precise definition is provided by Folkman (1984) "Coping refers to cognitive and behavioral efforts to master, reduce, or tolerate the internal and/or external demands that are created by the stressful transaction."

Different theoretical orientations affect how coping is defined. Coping is sometimes viewed as a stimulus response relationship, or a product of intrapsychic conflict centering on the persons needs, motives, impulses, or beliefs. Despite differing orientations, most people agree that there is not a simple relationship between stress and coping, that believing an event is controllable does not always lead to reduction in stress and believing that an event is uncontrollable does not always lead to an increase in stress (Thompson, 1981). It has become clear that there is an important relationship between the impact of a stressful event, the coping mechanisms applied and the significance or meaning of the event to the individual experiencing it.

For the purpose of this study, and because it is an underlying assumption of the Coping inventory for Stressful Situations (CISS) used in this study, coping is viewed as having 2 major functions: the regulation of emotions or distress (emotion-focused coping) and the management of the problem that is causing the distress (problem-focused coping).

One of the reasons to measure coping in this patient population is that emotion–oriented and avoidance-oriented coping have been associated with psychopathology, and task-oriented coping has been found to be negatively related to low self esteem, cynicism, depression, and anxiety (Endler & Parker 1990a). Many investigators have observed that psychologically ill persons are prone to use emotion-oriented coping and avoidance-oriented coping strategies more frequently or in preference to task oriented coping strategies, whereas psychologically well persons are prone to using task-oriented coping in preference to other coping strategies.

2.11.3 CD4 T-lymphocytes and Viral load

CD4 cell counts were measured in this trial for two main reasons. When this trial began CD4 T-cell counts were utilized as a measure of disease severity and treatment effectiveness. Perhaps more important, is the role patients have given to CD4 cells as a marker of their health status. Patients viewed their number of CD4 cells as a strong indication of their disease severity and prognosis.

2.12 Summary

In conclusion, at least up to 1996, the evidence from clinical trials investigating the benefits of psychotherapy in treating depression in persons living with HIV/AIDS was limited. Few studies existed and some have methodological concerns. The studies investigated short-term provision of psychotherapy and generally its impact on homosexual males. In 1996 there was definitely a need to examine a role for long-term psychotherapy, the effects on heterosexuals living with HIV, the impact on HIV positive females, and the impact independent of severity of disease. The RCT discussed in this thesis was intended to help address some of these issues.

CHAPTER 3
MATERIALS and METHODS

3.1 Depression Measured in the Thesis Clinical Trial

The revised Beck Depression Inventory (BDI) was utilized to assess depression in the research subjects (Beck & Steer 1993). The revised BDI, developed form the original BDI, by Beck et al. (1961), is a 21-item inventory frequently used to assess somatic, affective, behavioral and cognitive aspects of depression.

Reliability estimates based on Cronbach's coefficient alpha for mixed, single-episode major depression, recurrent-episode major depression, dysthymic, alcoholic, heroin-addicted patients, and nonpsychiatric samples are .86, .80, .86, .79, .90, .88, and .81 respectively.

The BDI has been shown to be able to discriminate between Dysthymic and Major Depressive Disorders as well as differentiate between Generalized Anxiety Disorders and Major Depressive Disorders. The revised BDI has also been shown to be able to differentiate among psychiatric, medical and normal samples.

Numerous studies of the construct validity of the BDI have been conducted with different variables and significant correlations have been observed between constructs hypothesized to be associated with depression (Beck *et al.*, 1988).

A Meta-analysis found a mean Pearson product-moment correlation of .72 between clinical ratings of depression and BDI in psychiatric patients and .60 between

clinical ratings of depression and BDI in nonpsychiatric subjects. In addition, significant correlations with other standardized depression measures have been reported for the BDI. Shafer *et al.* (1985) reported significant correlations between the BDI, Depression Scale of the Minnesota Multiphasic Personality Inventory (MMPI-D Scale), and Zung Self-rating Depression scale with all correlations exceeding .55. BDI has also been correlated with the (Symptom Checklist -90- Revised (SLC-90-R) Depression-Dejection Scale (.76) (Derogatis, 1977). Of particular relevance is the significant correlation (.73) between BDI and the Hamilton Psychiatric Rating Scale for Depression (HRSD). These two scales are amongst the most popular scales used to assess depression and are often used together for evaluating self-reported and clinically observed changes in depression. One advantage of the BDI over HRSD is that it is less likely to overestimate improvement in patients receiving drug therapy or psychotherapy (Edwards *et al.* 1984; Lambert et al. 1986).

BDI is listed by the Canadian Mental Health Association (CMHA) as one of the commonly used scales for measuring depression. (Canadian Mental Health Association, 1995). Others listed by the CMHA are: Zung Self-Assessment Depression Scale, Hamilton Rating Scale, Hopkins Symptom Checklist; Center for Epidemiological Studies Depression Scale, General Health Questionnaire, MacMillan's Health Opinion Survey, Lagner's Scale, Schedule for Affective Disorders and Schizophrenia, Diagnostic Interview Schedule Self-Administered, Structured Clinical Interview for DSM –III-R, Bradburn Affect Balance Scale.

The BDI was chosen for this study for a variety of reasons, which include:

- Its extensive use as a tool to assess depression.

- It has been validated in a psychiatric and non-psychiatric populations.
- Its familiarity amongst professionals and paraprofessionals.
- It has been in use since 1961.
- Improvements in the revised edition were developed in 1971.
- Its recognition as a standardized assessment tool by the CMHA.
- Its past use in trials investigating the impact of psychotherapy in HIV disease.
- The revised BDI scores are not meaningfully related to gender and age.
- Its ease of administration.

There is considerable overlap between the standardized depression questionnaires, and this researcher is unaware of any valid arguments against the use of the BDI to assess depression in patients with HIV infection.

To aid in understanding the scoring of the BDI the following information is beneficial. The maximum possible score is 63 and increasing scores are indicative of increasing levels of depression. A score of 0-9 is considered to be minimal, 10-16, mild, 17-29 moderate, and 30-63 severe depression (Beck, 1993). In arriving at a diagnosis of depression, scores greater than 15 are considered indicative of depression (Beck & Steer, 1993). In conjunction with a BDI above 15, an interview by a trained professional is recommended to confirm presence or absence of depression.

One of the unique features of this trial is that HIV/AIDS patients were included unrelated to presence or absence of symptoms of depression. The depression assessment tool was used to measure individuals after enrolment in the trial.

3.2 Hopelessness Measured in the Thesis Clinical Trial

In this clinical trial, the 20-item BECK Hopelessness Scale (BHS) was used to assess patient feelings of hopelessness. The BHS maintains high internal consistency across clinical samples. The Kuder-Richardson (KR-20) reliabilities for suicide ideators, suicide attempters, alcoholics, heroin addicts, single-episode Major Depression Disorders, recurrent-episode Major Depressive Disorders, Dysthymic Disorders (Beck & Steer, 1993) were, .92, .93, .91, .82, .92, .92, .87 respectively. Durham (1982) reported lower correlations in college students (KR-20 = .65).

Test-retest measures of patients with mixed diagnoses yielded Pearson product-moment correlations after 1 week of .69 and six weeks of .66.

Face validity was established through a review process using several clinicians.

Correlations with clinical ratings of hopelessness were .74. The BHS has been shown to be able to differentiate DSM-III Major Affective Disorders (Major Depression, Dysthymic, etc.) from Generalized Anxiety Disorder (GAD).

The BHS is a standardized measure of hopelessness, and like depression can categorize hopelessness as minimal, mild, moderate, and severe (Beck, 1993). The maximum possible score is 20 and increasing scores are indicative of increasing levels of hopelessness. A score in the range of 0–3 is considered minimal, 4-8 mild, 9-14 moderate, and greater than 14 severe. Beck (1986) reported that hopelessness has

repeatedly been found to be better predictor of suicidal intention than depression. This finding has been supported by Wetzel (1976) and Dyer and Kreitman (1984).

3.3 Coping Measured in the Thesis Clinical Trial

Coping skills were assessed with the Coping Inventory for Stressful Situations (CISS) (Endler & Parker, 1990). An underlying assumption of the CISS is that coping has two major functions: the regulation of emotions or distress (emotion-focused coping) and the management of the problem that is causing the distress (problem-focused coping).

Endler & Parker (1990a) report the alpha coefficients, measuring internal consistency are highly satisfactory across normative groups, though slightly lower, but still highly reliable for psychiatric patients.

Test-retest reliabilities conducted over a six-week period were in the moderate to high range. A similar pattern was seen in mean inter-item correlations indicating internal stability of the scale.

Factor analysis produced three main scales, task-oriented coping, emotion-oriented coping and avoidance-oriented coping. Congruence coefficients above .95 support a conclusion that the factor structure for psychiatric samples and nonpsychiatric samples are the same.

Construct validity was established through comparisons with the Marlowe-Crowne Social Desirability Scale (M-C) and correlation indicated the CISS is not

influenced by social desirability. Additional comparisons with the Ways of Coping Questionnaire (WCQ), Basic Personality Inventory (BPI), MMPI-2, BDI, etc. provide support for the construct validity of the CISS, and support the belief that it is a multidimensional instrument that independently assesses task-oriented coping, emotion-oriented coping, and avoidance-oriented coping in psychiatric and nonpsychiatric populations.

The CISS assessment tool consists of 48 items used to assess task-oriented coping, emotion-oriented coping and avoidance-oriented coping. Avoidance-oriented coping has two subscales: distraction and social diversion. The higher the test score on any one of the five subscales the greater the degree of coping activity for the person on the corresponding coping dimension. A maximum score of 80 can be obtained on each of the three main scales, task, emotion and avoidance. The maximum score on the avoidance subscale distraction is 40 and social diversion 25.

3.4 CD4 T-lymphocytes Measured in the Thesis Clinical Trial

Morning peripheral venous blood samples were collected in ethylenediamine tetraacitic acid (EDTA) tubes from all participants. Lymphocyte counts were determined by whole blood direct immunofluorescence flow cytometry. Comparisons were made utilizing normal rages (700-1100 cells/mm^3), established by Hannett *et al.*, (1992). No additional blood samples were required for this study as routine blood sample analysis was an aspect of standard of care.

3.5 Subjects

The study population consisted of 31 HIV positive adults receiving treatment at the Infectious Diseases Clinic of the Health Care Corporation of St. John's, Newfoundland and Labrador, Canada. Cognitive impairment was the sole exclusion criterion. The Human Investigation Committee (HIC) of Memorial University of Newfoundland and Labrador granted ethics approval for this study. Ultimately, the study sample represented approximately half of the HIV population served by the tertiary referral centre.

Potential subjects were approached by one of the 2 HIV clinical team physician specialists or by the HIV nurse coordinator. After the study was explained to the patient, signed consent, using a form previously approved by HIC, was obtained.

The sample size calculation was based on a standard deviation of the six-month change in BDI of 8 and was powered to detect a change of 10 units over six months with a power of 80 % and an assumed drop out rate of 20 %.

3.6 Therapist

The therapist in this trial, who was also the principal investigator of the RCT and author of this thesis, has both university training as well as extensive participation in continuing professional training in psychotherapy practice. In addition, the therapist has received training specifically related to provision of psychotherapy to persons living with

HIV/AIDS. He has been employed as a therapist in institutional settings, residential counselling and psychotherapy programs, and private practice for over twenty years. Additionally the therapist has been involved in supervision of senior social work student field placements.

3.6.1 Randomization and Stratification

Patients were randomized to one of two groups, psychotherapy (treatment group) or crisis intervention (control group). Balanced block randomization was used, using variable block size of 2, 4, and 6 subjects. A single individual, who was not involved in either the care of the patients, or the study itself, performed the randomization. To address concerns that group availability might influence the order in which patients were recruited by the clinical team, blinding to next group availability was strictly adhered to. Neither the HIV clinical team, patients or research therapist had knowledge of which group successive patients would be assigned.

Patients were stratified according to the severity of their baseline CD4 count; CD4 < 200 or CD4 ≥ 200.

Prior to randomization, the therapist administered the standardized psychological tests. These were repeated at six and twelve months. Test scores were not calculated until the last subject had completed the trial.

3.6.2 Intervention

Patients (N=17) enrolled in the psychotherapy group received routine psychotherapy sessions at a frequency determined by collaboration between the patient and therapist. An eclectic model was used, however the primary orientation was a psychodynamic one utilizing a range of expressive-supportive interventions and psychoeducation. Interventions were given to all patients in person and by telephone. In addition to the above modes of contact, patients who wished to communicate by e-mail had this format incorporated into their interventions. Therapy sessions were scheduled weekly for the first six months of the trial and bi-weekly for the last six months of the trial. In person therapy sessions were approximately 50 minutes duration. The study therapist was available by hospital pager and hospital operator on a 24-hour call basis for the duration of the trial to provide crisis intervention when required.

Patients (N=14) enrolled in the crisis intervention (control) group were provided psychotherapy by the study therapist when it was deemed necessary by the HIV treatment team, and timely access of a psychotherapeutic intervention was unavailable outside the study setting. In addition, control group patients could access psychotherapy services through their primary care physician.

There were challenges to maintaining a control group which could be conceptualized as a "crisis intervention only model" or "current standard of care" model. These concerns focused on whether it was ethical to withhold therapy to a control patient when the HIV clinical team felt an intervention was warranted. Rationalizing that

patients were involved in a RCT and that the control patients still received standard care was felt inadequate by members of the clinical team; hence some control patients were treated by the study therapist when the normal channels could not provide a timely intervention. Thus, in the strictest sense, the control group was not the usual standard of care. Every effort was made to minimize study therapist interventions but such interventions did occur. The most likely effect of these interventions would have been to decrease the likelihood of significant differences between the treatment and control groups. In effect, the significant differences observed between the two groups was, perhaps, even stronger since both groups were receiving enhanced psychological care.

3.6.3 Outcome Measurements

The objective of this study was to compare continuous psychotherapy (the intervention group) to no psychotherapy, except for the purpose of crisis intervention (the control group). The primary outcome measure was the six-month depression score on the BDI. The secondary outcome measures were the 12-month depression score on BDI, the 6 and 12-month hopelessness scores on the BHS, the 6 and 12- month coping skills score on CISS and 6 and 12-month CD4 cell counts.

The primary outcome was evaluated using analysis of covariance (ANCOVA) with the six-month depression score as the dependent variable, baseline depression score and stratification as covariates, and treatment assignment as the comparison variable. The secondary outcome, six and 12-month comparisons were handled similarly. In addition,

the primary and secondary outcome measures were evaluated without stratification as a covariate in the model.

An analysis was also conducted adjusting for gender, age, marital status (described as living with partner in table 4.1), route of transmission and sexual orientation to assess their influence on the primary and secondary outcomes.

The analyses presented in detail in this report did not include dropouts or patients who remained in the trial but who were unavailable at the time of the scheduled psychological testing intervals. All analyses were also performed using the *a priori* scenario of carrying forward the last existing value for missing values.

3.6.4 Selected Issues Explored in Psychotherapy

A wide variety of issues were explored during therapy sessions. There were issues specific to individual patients, such as childhood sexual abuse and common issues such as decline in CD4 T-cell counts and changes in weight. Sessions explored, but were not limited to, feelings of depression, feelings of hopelessness, suicide ideation, physical and sexual abuse, low self esteem, loneliness, fear of pain, fear of abandonment, death, family dynamics, previous sexual history, prescription and non-prescription drug usage, loss of autonomy, loss of ability to procreate, employment, initiation and/or change of antiretroviral therapy, etc.

Primarily, crisis intervention occurred around suicide ideation and/or suicide attempts. Patients often sought an intervention, outside scheduled therapy sessions, when

they described themselves as "feeling totally hopeless" and "having no reason to live" and " happier if they were dead". Notification to patients of significant decline in CD4 cell counts was often a precursor to requests for therapy outside the scheduled sessions.

CHAPTER 4

RESULTS

4.1 Patient Demographics

Between March 1996 and September 1997, 31 subjects were enrolled in the study. The subjects had a mean age of 30 years, mean depression score of 22, mean hopelessness score of 10, mean coping inventory for stressful situations task score of 52, emotion score 51, avoidance score 47, distraction score 24, social diversion, 15 and mean CD4 count of 277 cells/μl. A total of 48.4 % of patients had CD4 counts < 200 cells/μl.

The baseline characteristics of control and intervention patients are shown in Table 4.1. Control group subjects (N=14) were 93 % male (N=13), had a mean age of 33 years, a mean weight of 74.9 kilograms, and mean CD4 T-cell counts of 332.57 cells/μl. Twenty-one percent (N=3) of control subjects were living with a partner, and 71% (N=10) were of homosexual orientation. Thirty-six percent (N=5) were not taking HIV medications, 50% (N=7) were taking two HIV medications, and 14% (N=2) were prescribed triple therapy. Infection was attributed to heterosexual activity in 21% of the control subjects (N=3), homosexual activity in 71% (N=10), blood products in 7% (N=1) and IV drug use in 0%.

Treatment group subjects (N=17) were 65 % male (N=11), had a mean age of 28 years, a mean weight of 69.36 kilograms, and mean CD4 T-cell counts of 231.82 cells/μl.

Thirty-five percent (N=6) of treatment subjects were living with a partner, and 59% (N=10) were of homosexual orientation. Eighteen percent (N=3) were not taking HIV medications, 70% (N=12) were taking two HIV medications, and 12% (N=2) were prescribed triple therapy. Infection was attributed to heterosexual activity in 47% of the treatment subjects (N=8), homosexual activity in 41% (N=7), blood products in 6% (N=1) and IV drug use in 6% (N=1).

Table 4.1: Baseline Characteristics [a]

	CONTROL *(Crisis Intervention)* N = 14	INTERVENTION *(Psychotherapy)* N = 17
Gender		
Male *(%)*	13 (93)	11 (65)
Female *(%)*	1 (7)	6 (35)
Age *Years*	33 (29-37)	28 (26-31)
Weight *Kg*	74.90kg.	69.36kg.
CD4 count *Cells/μL*		
Mean	332.57	231.82
< 200 *(%)*	5 (36)	10 (59)
≥ 200 *(%)*	9 (64)	7 (41)
Living With Partner *(%)*	3 (21)	6 (35)
Homosexual *(%)*	10 (71)	10 (59)
Heterosexual *(%)*	4 (29)	7(41)
Baseline HIV Drugs		
0 *(%)*	5 (36)	3 (18)
2 *(%)*	7 (50)	12 (70)
3 *(%)*	2 (14)	2 (12)
HIV Transmission		
Heterosexual *(%)*	3 (21.43)	8 (47)
Homosexual *(%)*	10 (71.43)	7 (41)
Blood Products *(%)*	1 (7.14)	1 (6)
IV drug use *(%)*	0 (0)	1 (6)

a. Parentheses indicate 95 percent confidence intervals.

The characteristics of control and intervention patients for whom data was available at the 6-month testing interval are shown in Table 4.2. Control group subjects (N=12) were 92% male (N=11), had a mean age of 33 years, a mean weight of 75.99 kilograms, and mean CD4 T-cell counts of 242.92 cells/μl. Seventeen percent (N=2) of control subjects were living with a partner, and 67% (N=8) were of homosexual orientation. Thirty-three percent (N=4) were not taking HIV medications, 50% (N=6) were taking two HIV medications, and 17% (N=2) were prescribed triple therapy. Infection was attributed to heterosexual activity in 25% of the control subjects (N=3), homosexual activity in 67% (N=8), blood products in 8% (N=1) and IV drug use in 0%.

Treatment group subjects (N=14) were 71 % male (N=10), had a mean age of 29 years, a mean weight of 74.28 kilograms, and mean CD4 T-cell counts of 262.15 cells/μl. Thirty-six percent (N=5) of treatment subjects were living with a partner, and 50% (N=7) were of homosexual orientation. Fourteen percent (N=2) were not taking HIV medications, 79% (N=11) were taking two HIV medications, and 7% (N=1) were prescribed triple therapy. Infection was attributed to heterosexual activity in 43% of the treatment subjects (N=6), homosexual activity in 43% (N=6), blood products in 7% (N=1) and IV drug use in 7% (N=1).

Table 4.2: Characteristics of Subjects with Outcome Data at Six Months

	CONTROL *(Crisis Intervention)* N = 12	INTERVENTION *(Psychotherapy)* N = 14
Gender		
Male *(%)*	11 (92)	10 (71)
Female *(%)*	1 (8)	4 (29)
Age *Years*	33	29
Weight *Kg*	75.99kg.	74.28kg.
CD4 count *Cells/μL*		
Mean	242.92	262.15
< 200 *(%)*	6 (50)	7 (50)
≥ 200 *(%)*	6 (50)	7 (50)
Living With Partner *(%)*	2 (17)	5 (36)
Homosexual *(%)*	8 (67)	7 (50)
Heterosexual *(%)*	4 (33)	7(50)
Baseline HIV Drugs		
0 *(%)*	4 (33)	2 (14)
2 *(%)*	6 (50)	11 (79)
3 *(%)*	2 (17)	1 (7)
HIV Transmission		
Heterosexual *(%)*	3 (25)	6 (43)
Homosexual *(%)*	8 (67)	6 (43)
Blood Products *(%)*	1 (8)	1 (7)
IV drug use *(%)*	0 (0)	1 (7

The characteristics of control and intervention patients for whom data was available at the 12-month testing interval are shown in Table 4.3. Control group subjects (N=8) were 87.5% male (N=7), had a mean age of 33 years, a mean weight of 98.9 kilograms, and mean CD4 T-cell counts of 346.38 cells/μl. twenty-five percent (N=2) of control subjects were living with a partner, and 62.5% (N=5) were of homosexual orientation. At baseline, 37.5 percent (N=3) were not taking HIV medications, 37.5% (N=3) were taking two HIV medications, and 25% (N=2) were prescribed triple therapy. Infection was attributed to heterosexual activity in 25% of the control subjects (N=2), homosexual activity in 62.5% (N=5), blood products in 12.5% (N=1) and IV drug use in 0%.

Treatment group subjects (N=11) were 73 % male (N=8), had a mean age of 28 years, a mean weight of 74.66 kilograms, and mean CD4 T-cell counts of 244.00 cells/μl. Thirty-six percent (N=4) of treatment subjects were living with a partner, and 45.5% (N=75) were of homosexual orientation. Eighteen percent (N=2) were not taking HIV medications, 73% (N=8) were taking two HIV medications, and 9% (N=1) were prescribed triple therapy. Infection was attributed to heterosexual activity in 45.46% of the treatment subjects (N=5), homosexual activity in 36.36% (N=4), blood products in 9.09% (N=1) and IV drug use in 9.09% (N=1).

Table 4.3: Characteristics of Subjects with Outcome Data at Twelve Months

	CONTROL *(Crisis Intervention)* N = 8	INTERVENTION *(Psychotherapy)* N = 11
Gender		
Male *(%)*	7 (87.5)	8 (73)
Female *(%)*	1 (12.5)	3 (27)
Age *Years*	33	28
Weight *Kg*	98.9kg.[a]	74.66kg.
CD4 count *Cells/μL*		
Mean	346.38	244.00
< 200 *(%)*	3 (37.5)	6(54.5)
≥ 200 *(%)*	5 (62.5)	5(45.5)
Living With Partner *(%)*	2 (25)	4 (36)
Homosexual *(%)*	5 (62.5)	5 (45.5)
Heterosexual *(%)*	3 (37.5)	6(54.5)
Baseline HIV Drugs		
0 *(%)*	3 (37.5)	2 (18)
2 *(%)*	3 (37.5)	8 (73)
3 *(%)*	2 (25)	1 (9)
HIV Transmission		
Heterosexual *(%)*	2 (25)	5 (45.46)
Homosexual *(%)*	5 (62.5)	4 (36.36)
Blood Products *(%)*	1 (12.5)	1 (9.09)
IV drug use *(%)*	0 (0)	1 (9.09)

a. Weight was only available for one subject in the control group.

Two patients randomized to treatment withdrew immediately after the randomization. One patient confused it with a drug trial being offered at the same time, the other withdrew because of a previous negative experience in a clinical trial. One patient in the treatment group remained in the study but was unavailable at scheduled testing times because of personal travel outside the province. Over the twelve-month follow-up period three subjects in the treatment group, and two in the control group relocated and were unavailable for follow-up.

One control patient withdrew immediately after randomization because he wanted to receive psychotherapy. Three patients in the control group remained in the study but were unavailable at scheduled testing times because of personal travel outside the province.

Six-month data was available for fourteen treatment group subjects and twelve control group subjects whereas 12-month data was available for eleven and eight subjects respectively.

4.2 Study Outcomes

Study outcomes are detailed in Table 4.4, and illustrated in Figures 4.1 to 4. 32.

Table 4.4. P Values of Differences Between Treatment vs. Control at Baseline, Six and Twelve Months [a]

	Baseline	6 Months	12 Months
Beck Depression Inventory			
Control	20 (15-25) [b]	18 (13-23)	26 (12-39)
N	14	12	8
Intervention	23 (18-29) [b]	13 (8-18)	9 (2-15)
N	17	14	11
P value for difference		**P = 0.016**	**P = 0.006**
Beck Hopelessness Scale			
Control	10 (7-13) [b]	11 (8-14)	13 (8-18)
N	14	12	8
Intervention	10 (7-13) [b]	7 (4-10)	6 (2-9)
N	17	14	11
P value for difference		**P = 0.027**	**P = 0.005**
Coping Inventory for Stressful Situations			
Task			
Control	52 (47-58) [b]	53 (47-60)	55 (46-64)
N	14	12	8
Intervention	52 (45-58) [b]	55 (50-60)	59 (52-65)
N	17	14	11
P value for difference		**P = 0.654**	**P = 0.214**
Emotion			
Control	50 (44-56) [b]	46 (40-52)	49 (40-58)
N	14	12	8
Intervention	51 (45-57) [b]	49 (43-55)	43 (36-50)
N	17	14	11
P value for difference		**P = 0.374**	**P = 0.059**

Table 4.4. P Values of Differences Between Treatment vs. Control at Baseline, Six and Twelve Months (Continued) [a]

	Baseline	6 Months	12 Months
Avoidance			
Control	49 (43-55) [b]	46 (45-58)	46 (41-62)
N	14	12	8
Intervention	46 (40-52) [b]	51 (38-54)	52(39-53)
N	17	14	11
P value for difference		**P = 0.036**	**P = 0.062**
Distraction			
Control	25 (20-29) [b]	23 (19-28)	24 (21-28)
N	14	12	8
Intervention	24 (19-28) [b]	25 (22-29)	25 (20-30)
N	17	14	11
P value for difference		**P = 0.221**	**P = 0.331**
Social Diversion			
Control	15 (12-19) [b]	14 (11-17)	13 (10-17)
N	14	12	8
Intervention	15 (12-17) [b]	17 (14-19)	17 (14-21)
N	17	14	11
P value for difference		**P = 0.031**	**P = 0.031**
CD4 count Cells/μL			
Control	333 (186-479) [b]	243(89-396)	346 (117-576)
N	14	12	8
Intervention	232 (116-347) [b]	262(116-408)	259 (115-403)
N	17	13	12
P value for difference		**P = 0.09**	**P = 0.764**

a Data are presented as means with 95% confidence intervals in parentheses.
b There were no statistically significant differences in baseline parameters.

4.2.1 Depression Score Results

Intervention patients showed a significant decrease in Beck Depression Inventory (BDI) scores at 6 ($P = 0.016$) and 12 months ($P = 0.006$), while no improvement was seen in control patients (Figures 4.1 and 4.2).

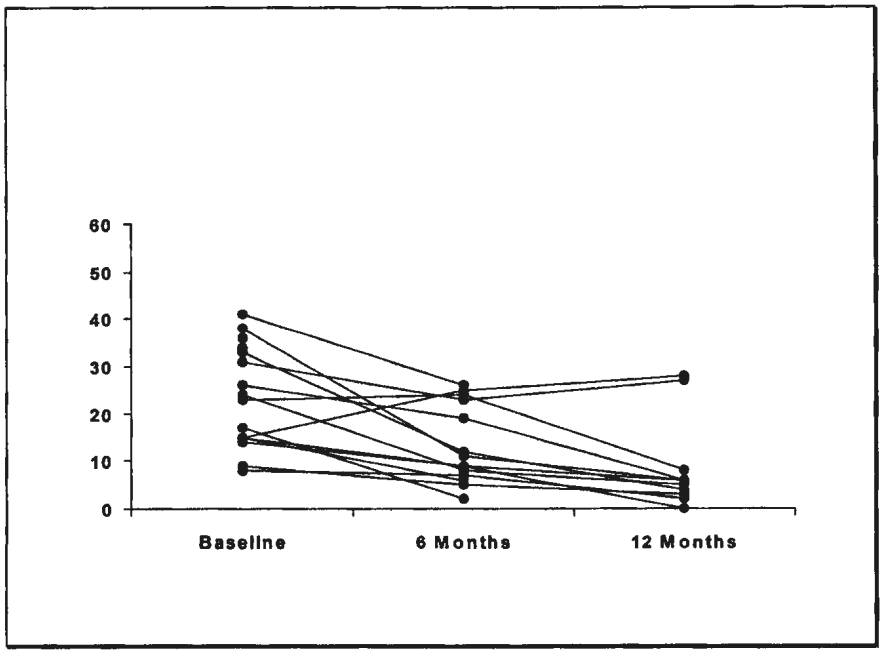

Figure 4.1: Beck Depression Inventory Scores in Treatment Group

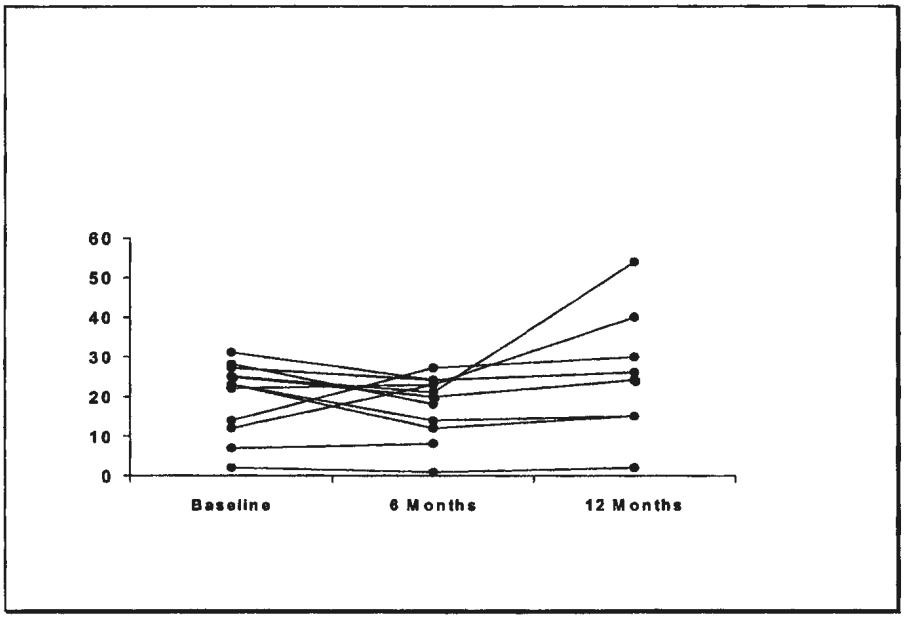

Figure 4.2: Beck Depression Inventory Scores in Control Group

4.2.2 Hopelessness Score Results

A similar pattern was observed in Beck Hopelessness Scale (BHS) scores as was seen in depression scores. Compared to control subjects, the intervention subjects receiving regular psychotherapy showed improved hopelessness scores at 6 ($P = 0.027$) and twelve months ($P = 0.005$) (Figures 4.3 & 4.4).

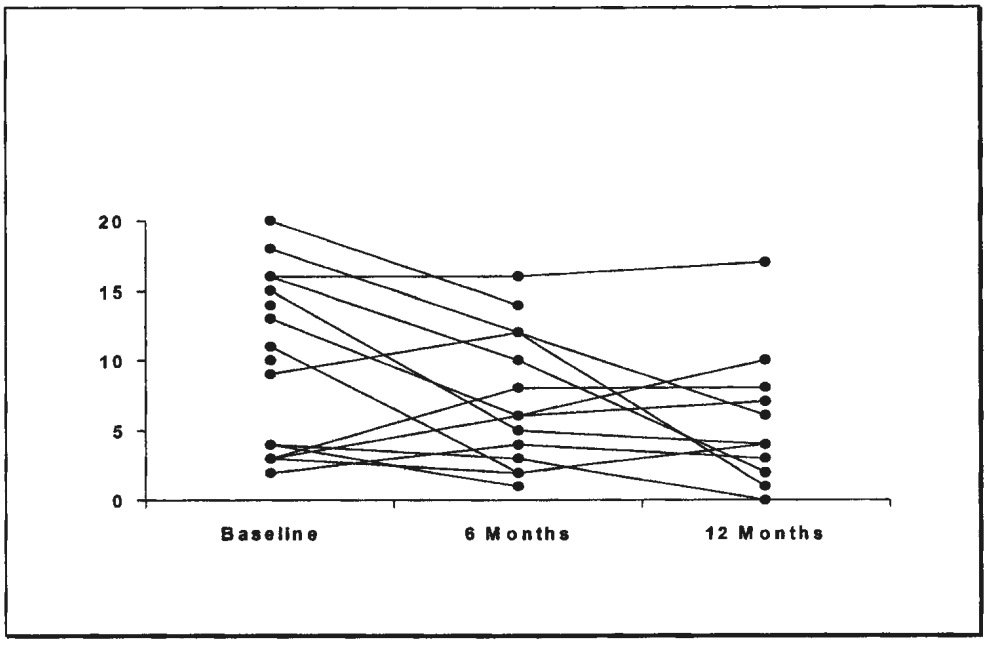

Figure 4.3: Beck Hopelessness Scale Scores in Treatment Group

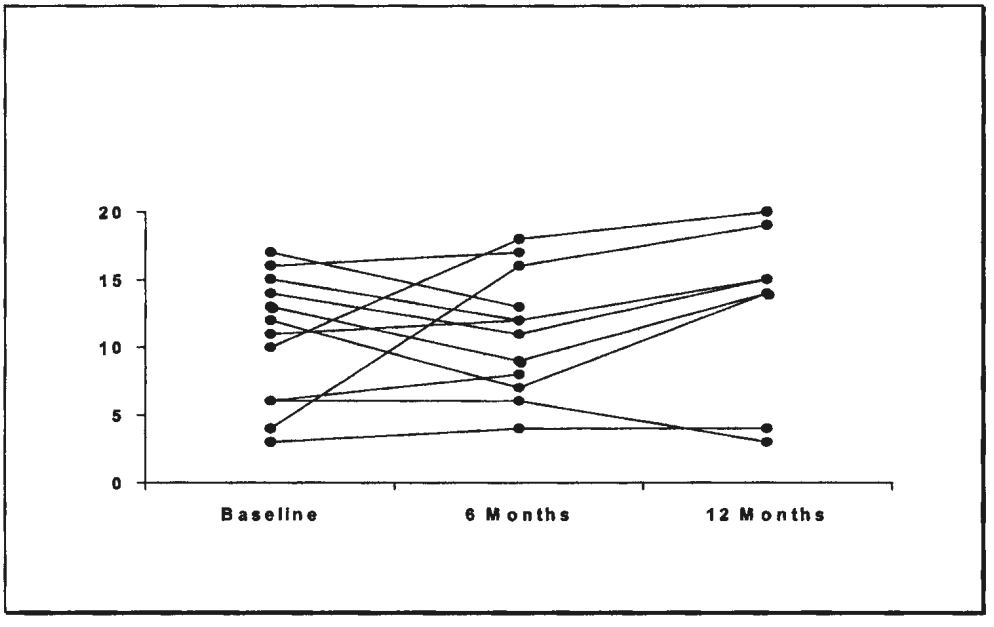

Figure 4.4: Beck Hopelessness Scale Scores in Control Group

4.2.3 Coping Score Results

At six months there were statistically significant differences on avoidance coping (P = 0.036) (Figures 4.9 & 4.10) and social diversion coping (P = 0.031) (Figures 4.13 & 4.14), with the intervention group using more avoidance and social diversion coping.

There was no significant difference at the six-month interval between the psychotherapy and crisis intervention groups on the CISS subscales: task (P = 0.654) (Figures 4.5 & 4.6), emotion (P = 0.374) (Figures 4.7 & 4.8) and distraction (P = 0.221) (Figures 4.11 & 4.12).

The 12-month CISS subscale scores show no difference in groups on task (P = 0.214), emotion (P = 0.059), avoidance (P = 0.062), and distraction (P = 0.331). Only social diversion (P = 0.031) is significant, with the intervention group using more social diversion coping.

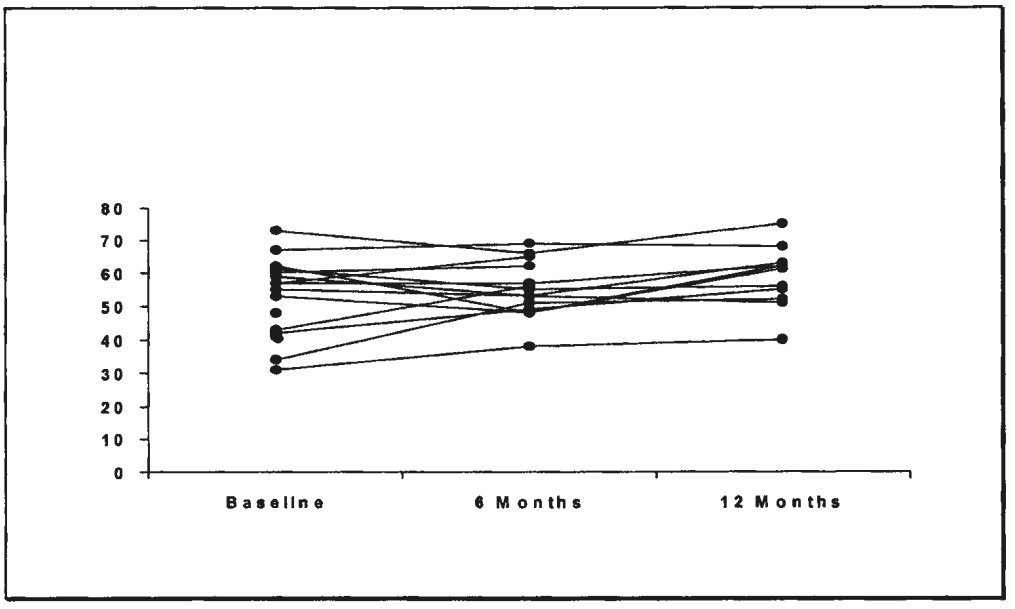

Figure 4.5: Coping Inventory for Stressful Situations: task scores for treatment group

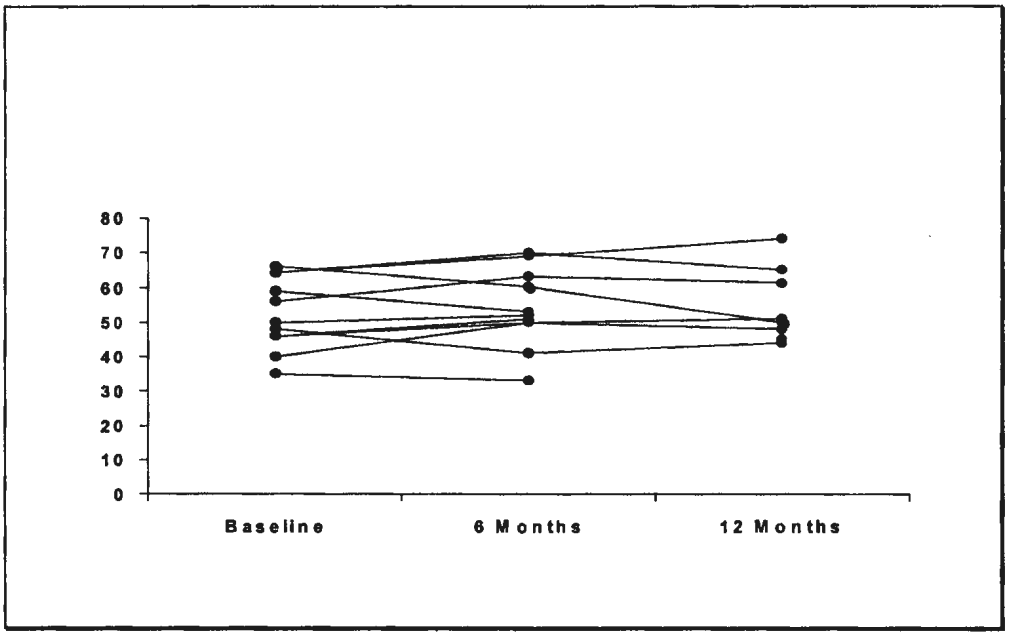

Figure 4.6: Coping Inventory for Stressful Situations: task scores for control group

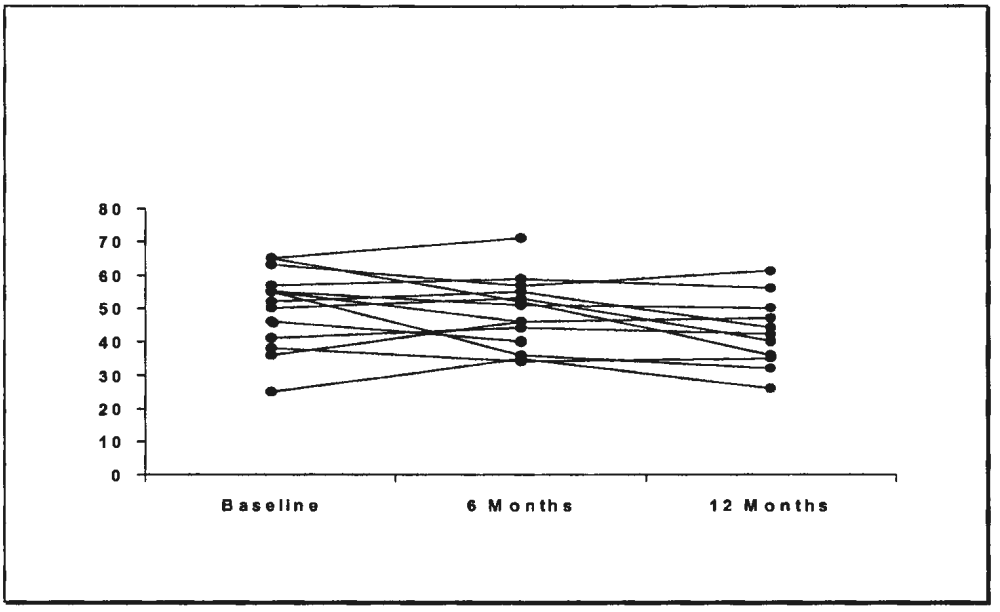

Figure 4.7: Coping Inventory for Stressful Situations: emotion scores for treatment group

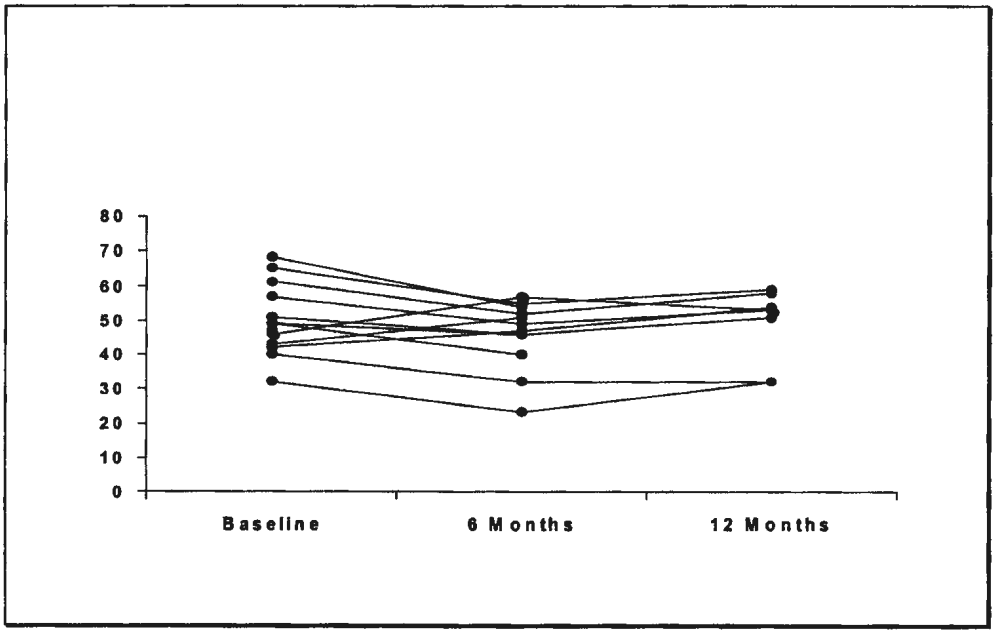

Figure 4.8: Coping Inventory for Stressful Situations: emotion scores for control group

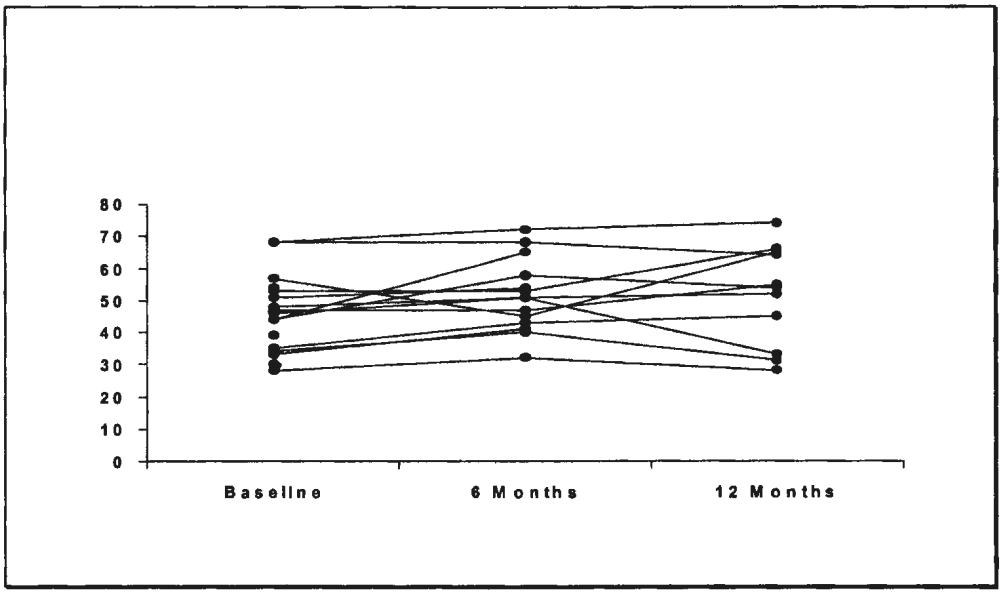

Figure 4.9: Coping Inventory for Stressful Situations: avoidance scores for treatment group

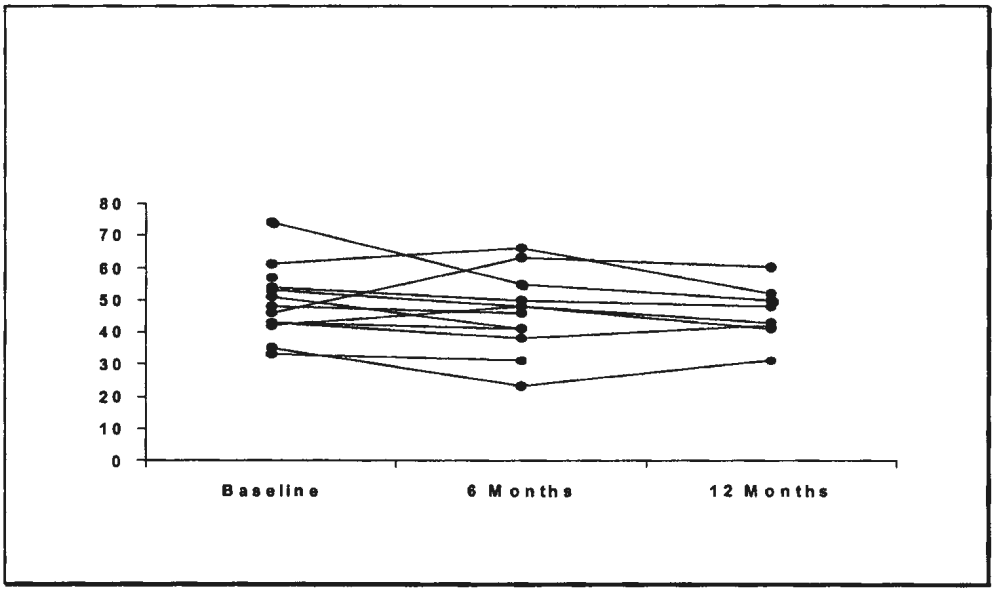

Figure 4.10: Coping Inventory for Stressful Situations: avoidance scores for control group

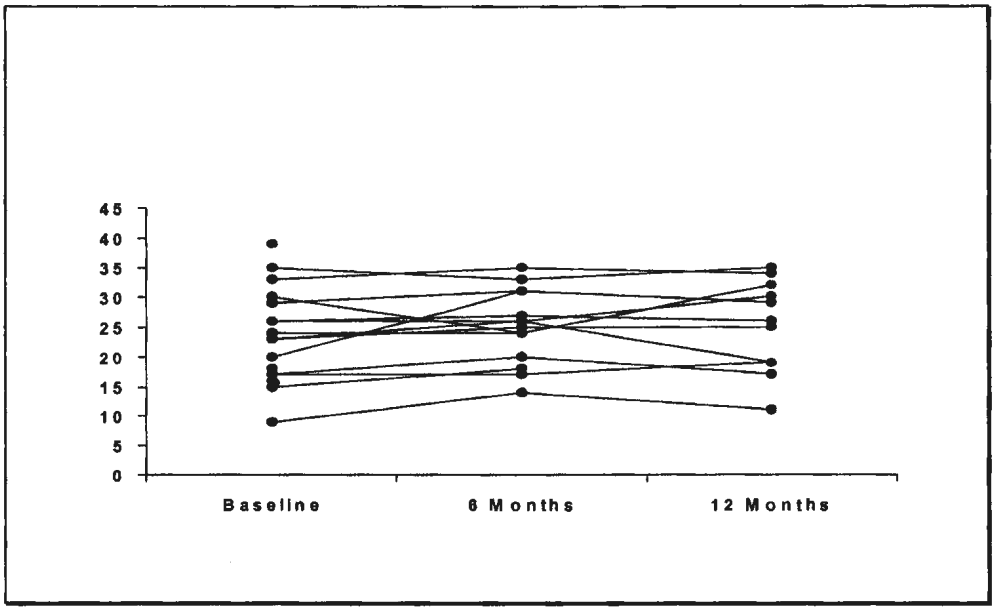

Figure 4.11: Coping Inventory for Stressful Situations: distraction scores for treatment group

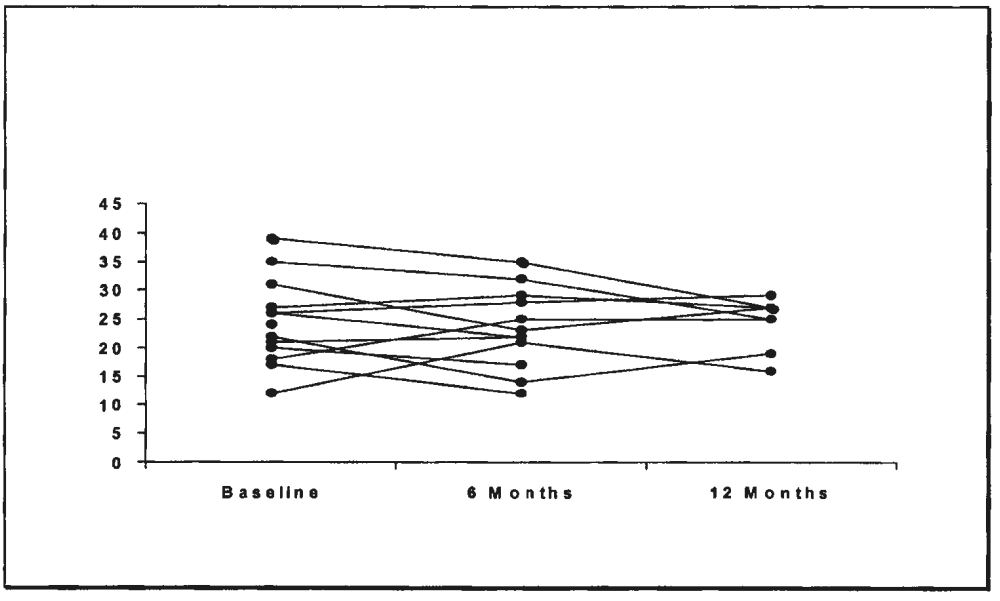

Figure 4.12: Coping Inventory for Stressful Situations: distraction scores for control group

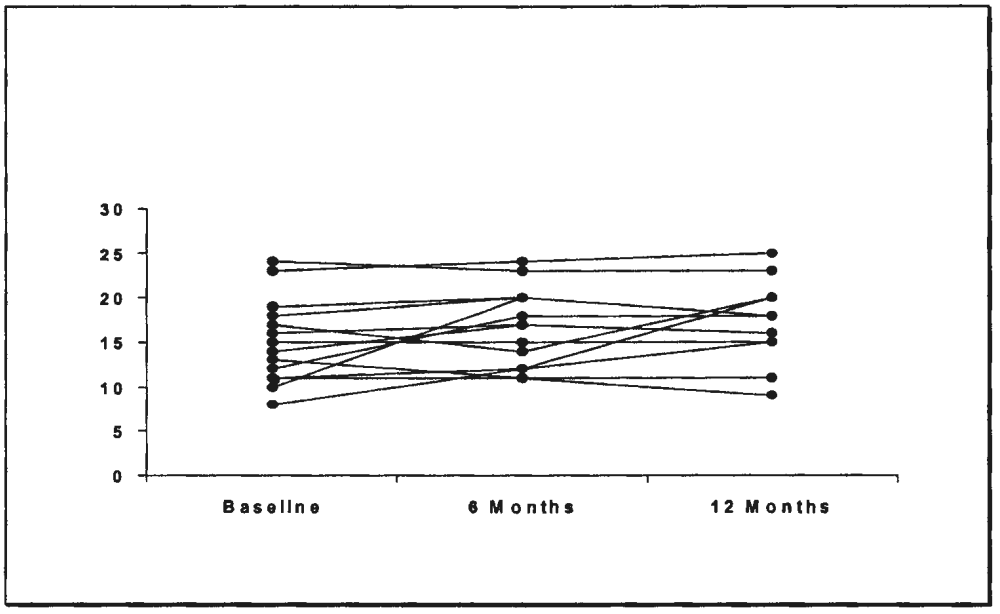

Figure 4.13: Coping Inventory for Stressful Situations: social diversion scores for treatment group

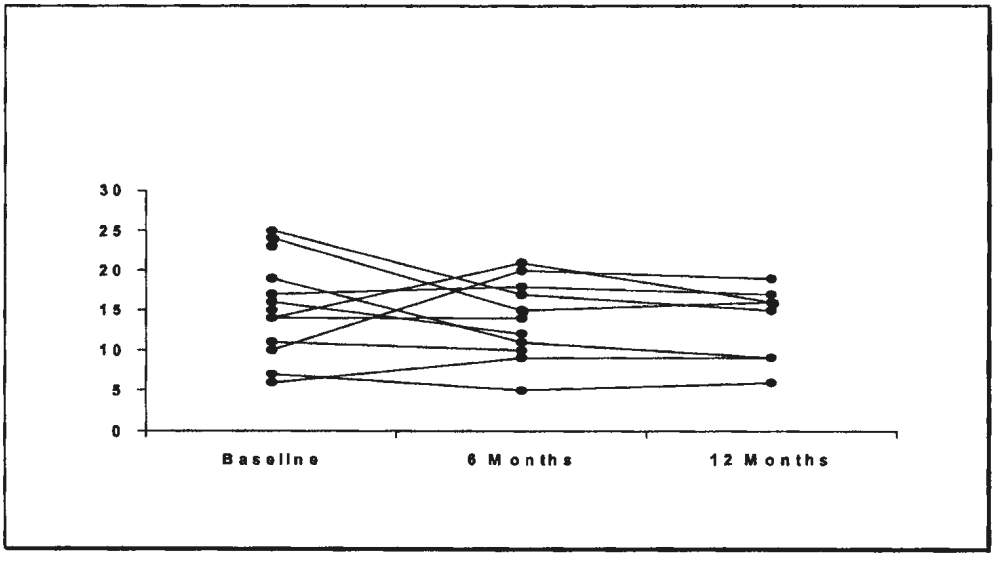

Figure 4.14: Coping Inventory for Stressful Situations: social diversion scores for control group

4.2.4 CD4 T lymphocyte Counts

There was no difference between treatment and control group on CD4+ cell counts at six months (P = 0.09), or 12 months (P = 0.764) (Figures 4.15 & 4.16).

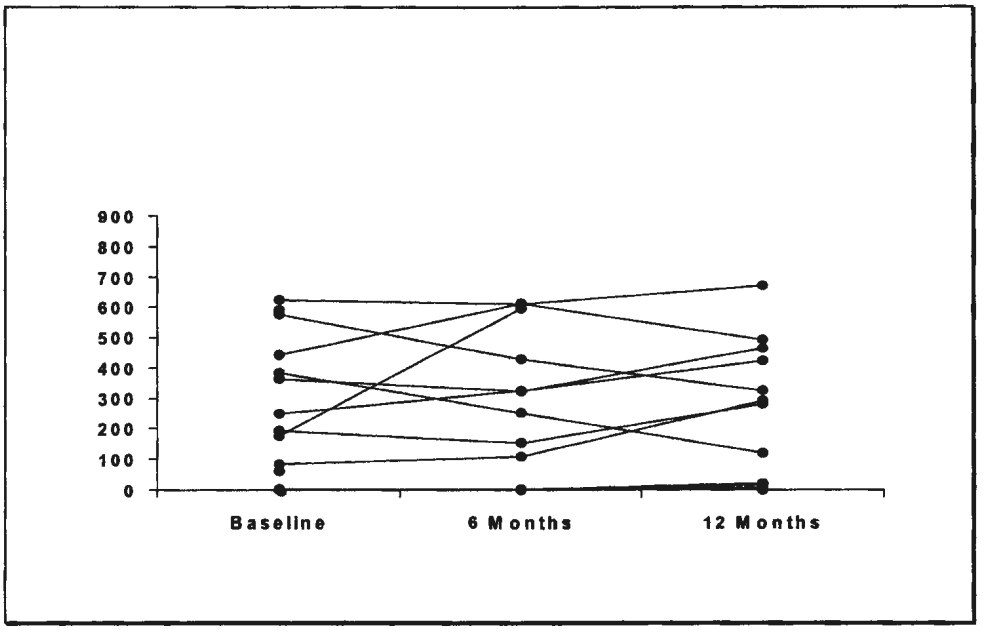

Figure 4.15: CD4 T lymphocyte cell counts in the treatment group

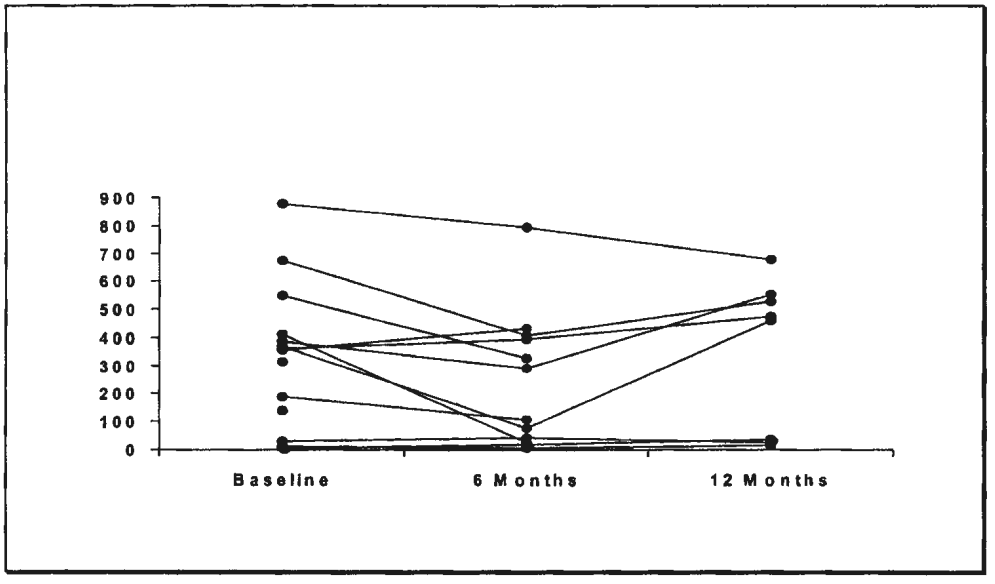

Figure 4.16: CD4 T lymphocyte cell counts in the control group

4.3 Last Value Carried Forward Analysis Results

The conclusions regarding depression, hopelessness and CD4 were unchanged when analyses were performed using the *a priori* scenario of carrying forward the last existing value for missing values (BDI 6, 12months; $p < 0.004$, $p < 0.001$ (Figures 4:17 & 4.18); BHS 6, 12 months; $p < 0.027$, $p < 0.000$ (Figures 4:19 & 4:20); CD4, 6, 12 months; $p < 0.085$; $p < 0.395$ (Figures 4:21 & 4:22).

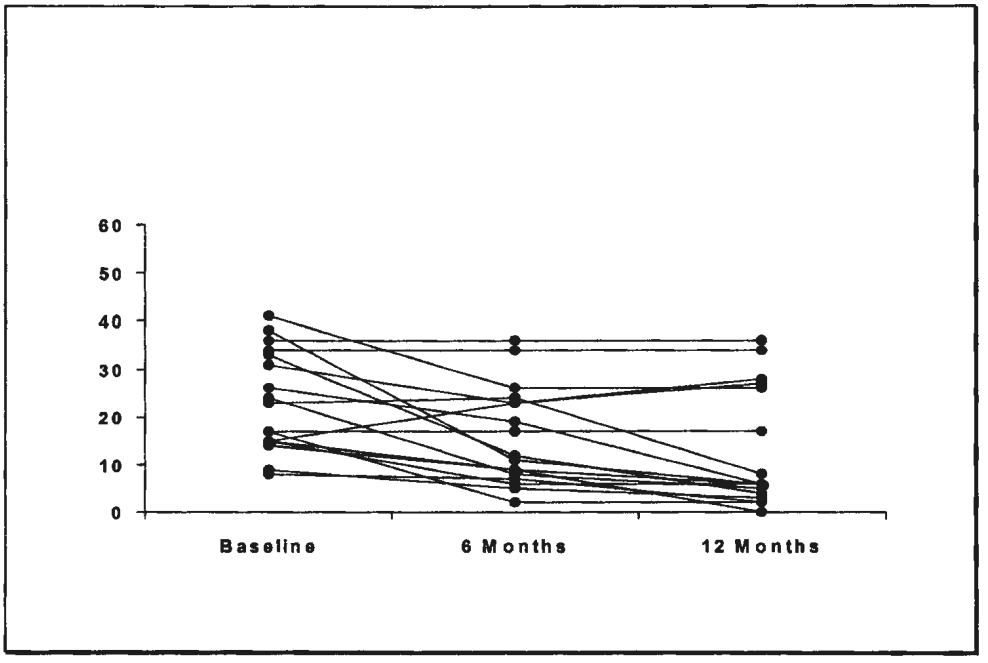

Figure 4.17: LVCF Beck Depression Inventory Scores in Treatment Group

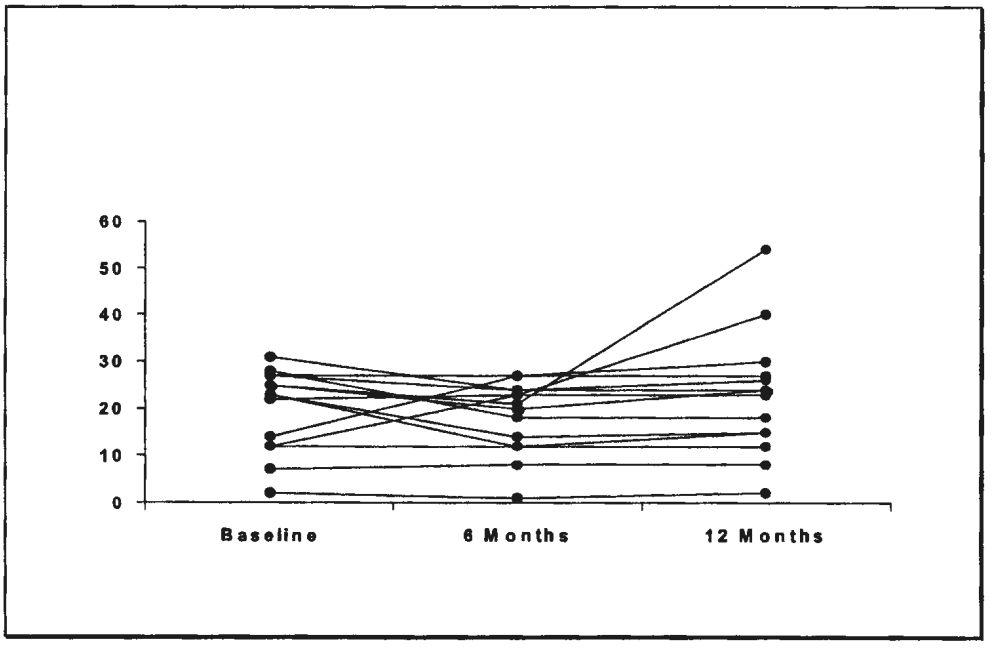

Figure 4.18: LVCF Beck Depression Inventory Scores in Control Group

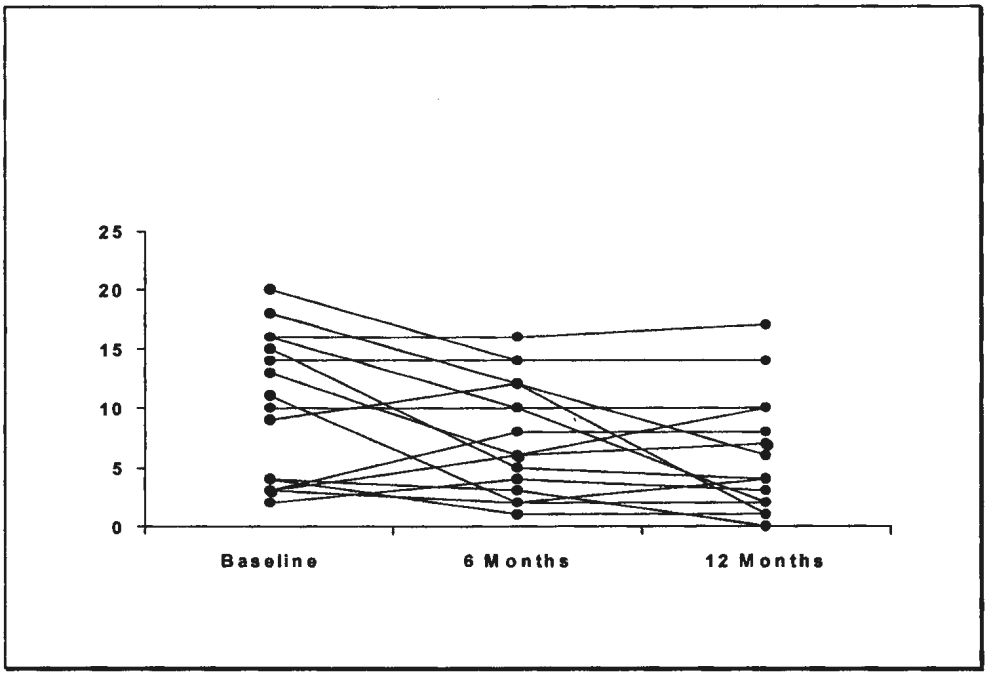

Figure 4.19: LVCF Beck Hopelessness Scale Scores in Treatment Group

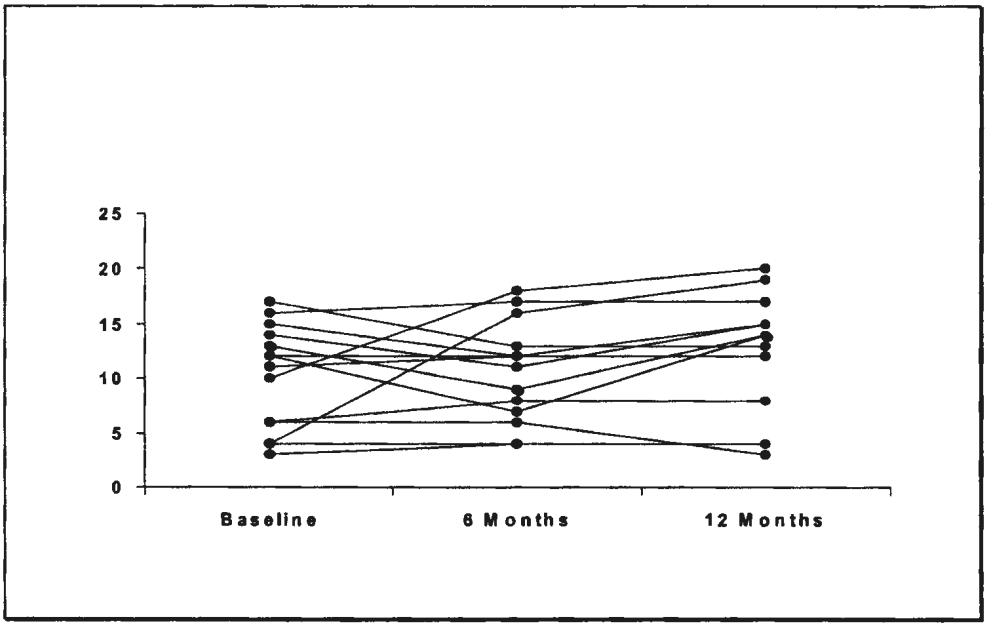

Figure 4.20: LVCF Beck Hopelessness Scale Scores in Control Group

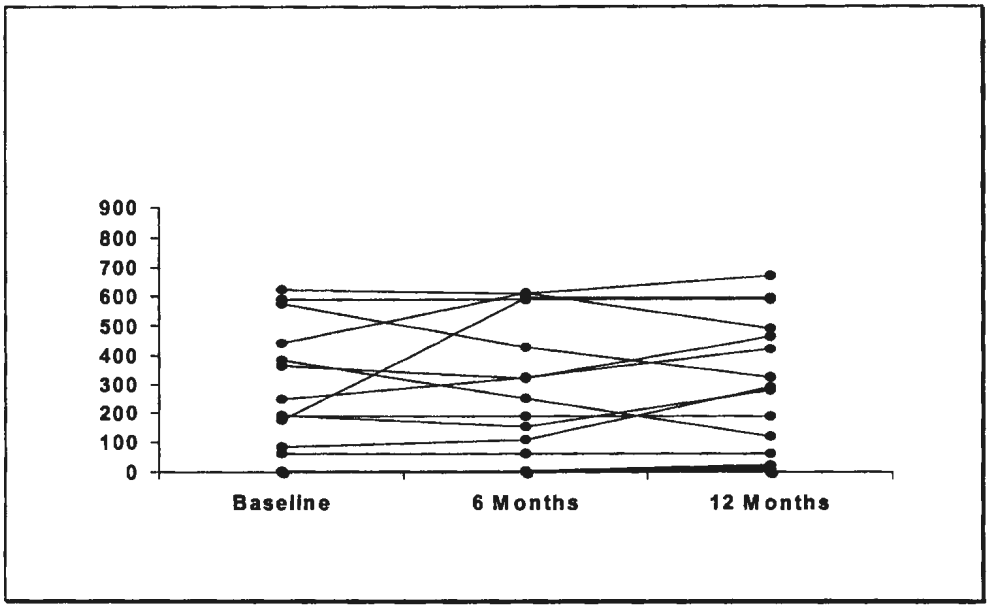

Figure 4.21: LVCF CD4 Cell Counts in Treatment Group

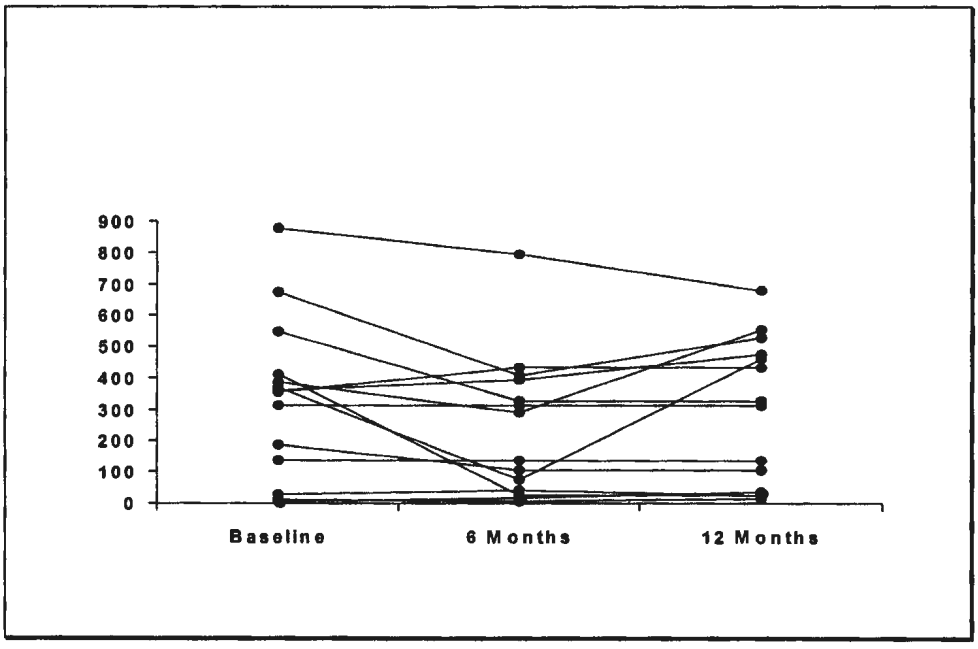

Figure 4.22: LVCF CD4 Cell Counts in Control Group

Results of last value carried forward analyses demonstrated no differences between treatment and control in task coping scores at 6 months, $p = 0.266$, but significantly higher scores in the treatment group at 12mos. $p = 0.010$ (Figures 23 & 24).

Results of last value carried forward analyses demonstrated no differences in emotion scores at 6 and 12 months, $p = 0.584$; $p = 0.202$ (Figures 25 & 26).

Results of last value carried forward analyses demonstrated significantly higher avoidance scores in the treatment group at both 6 and 12 months, $p = 0.015$; $p < 0.003$ (Figures 27 & 28).

Results of last value carried forward analyses demonstrated no differences in distraction scores at 6 and 12 months, $p = 0.377$; $p = 0.126$ (Figures 29 & 30).

Results of last value carried forward analyses demonstrated significantly higher social diversion scores in the treatment group at both 6 and 12 months, $p = 0.008$; $p = 0.001$ (Figures 31& 32).

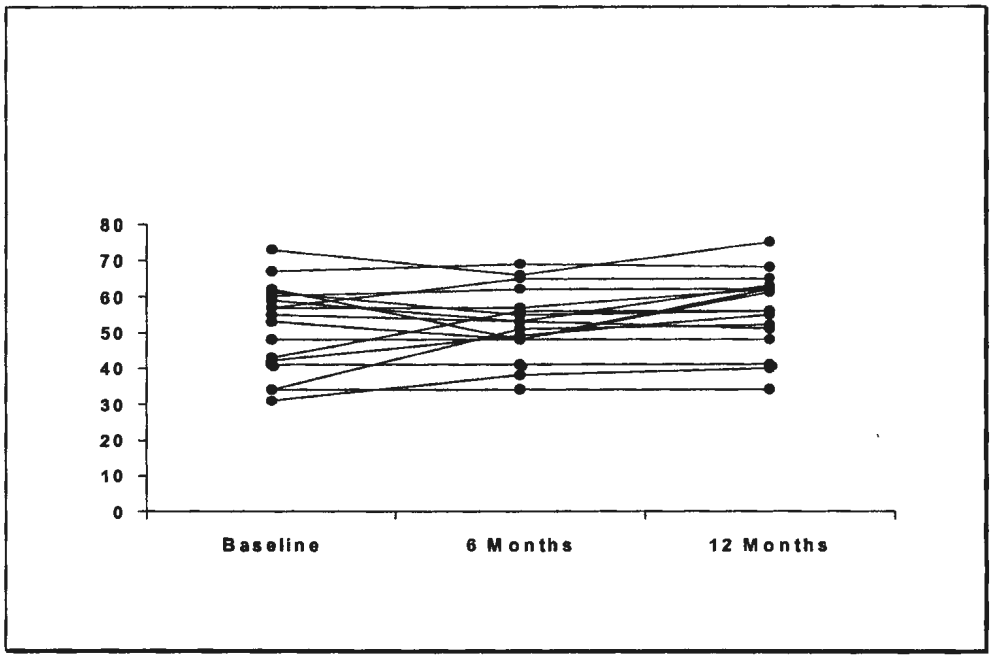

Figure 4.23: LVCF CISS Task Scores in Treatment Group

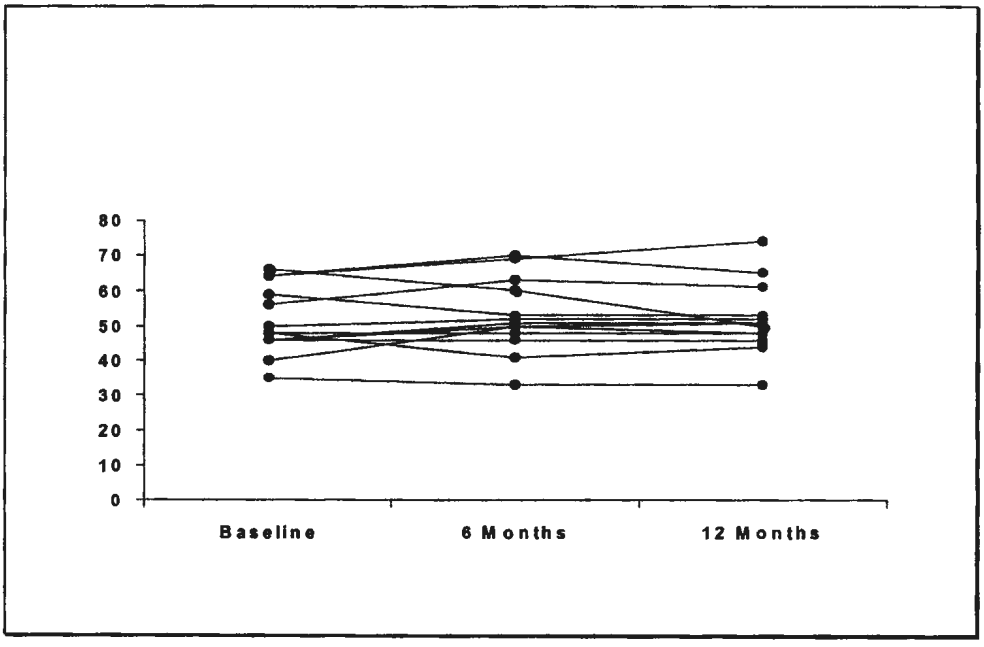

Figure 4.24: LVCF CISS Task Scores in Control Group

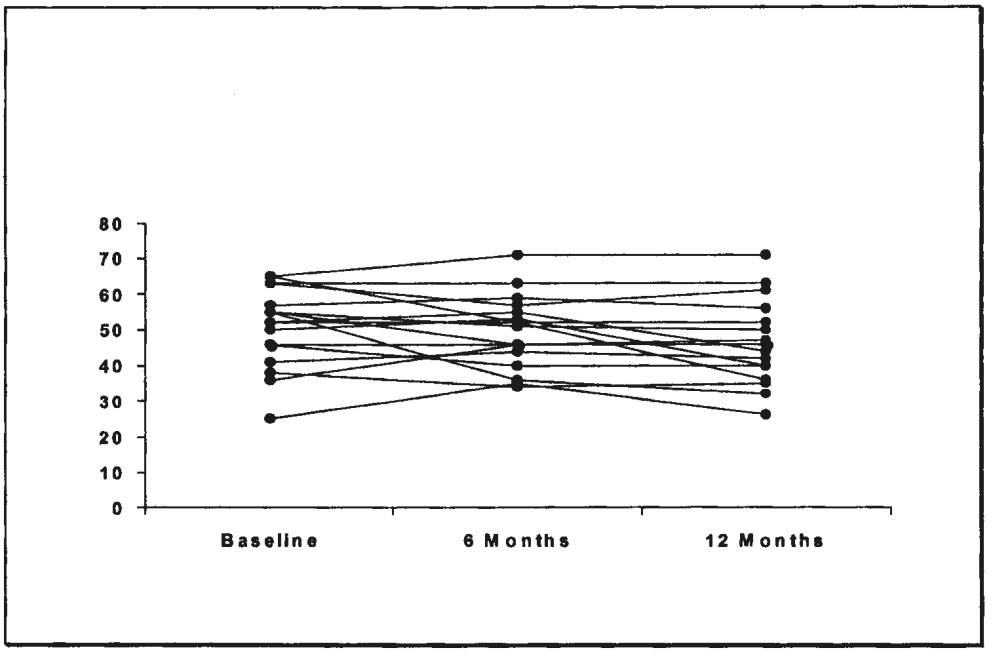

Figure 4.25: LVCF CISS Emotion Scores in Treatment Group

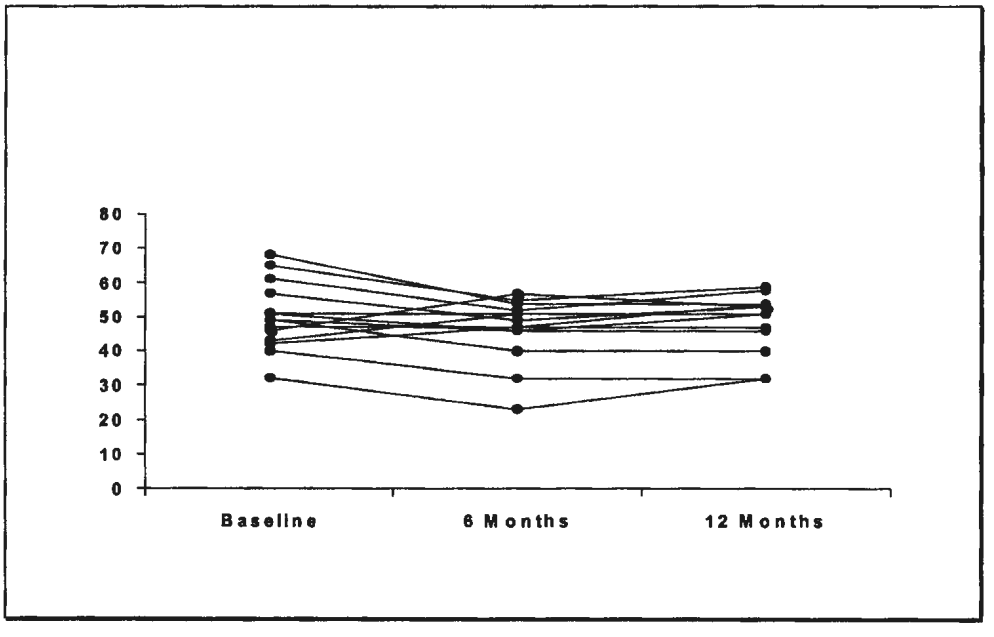

Figure 4.26: LVCF CISS Emotion Scores in Control Group

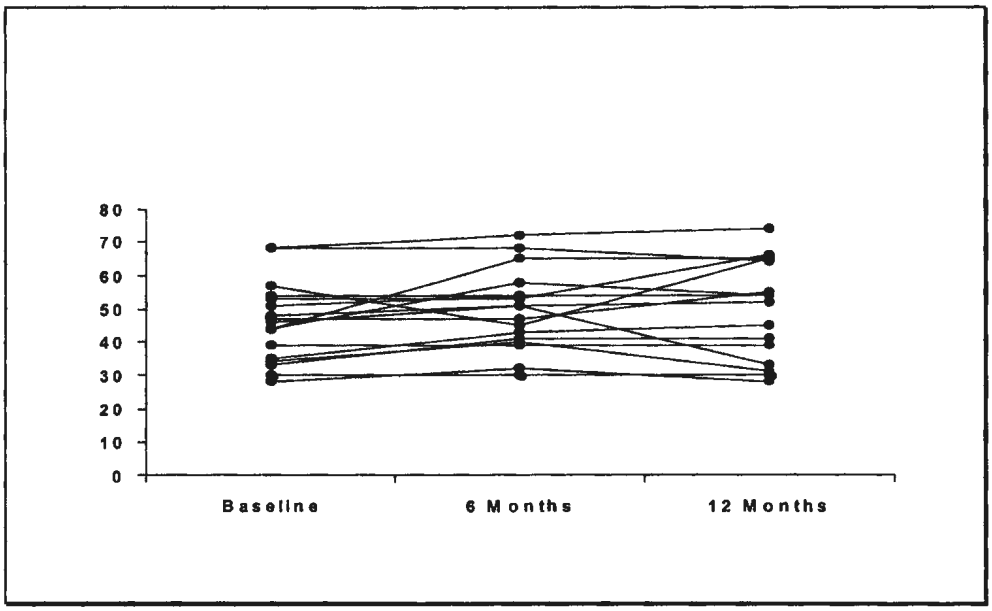

Figure 4.27: LVCF CISS Avoidance Scores in Treatment Group

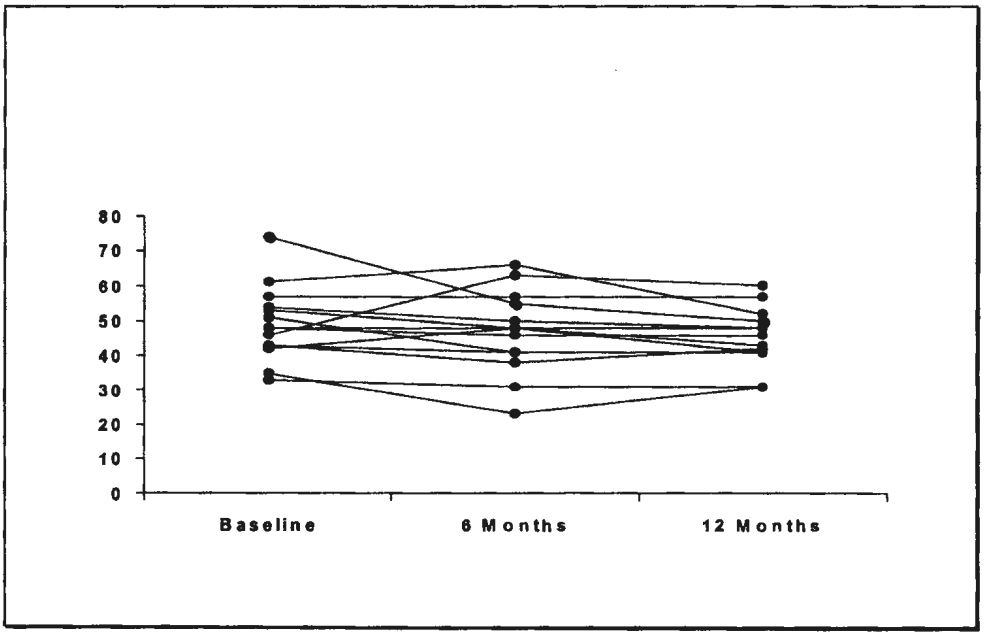

Figure 4.28: LVCF CISS Avoidance Scores in Control Group

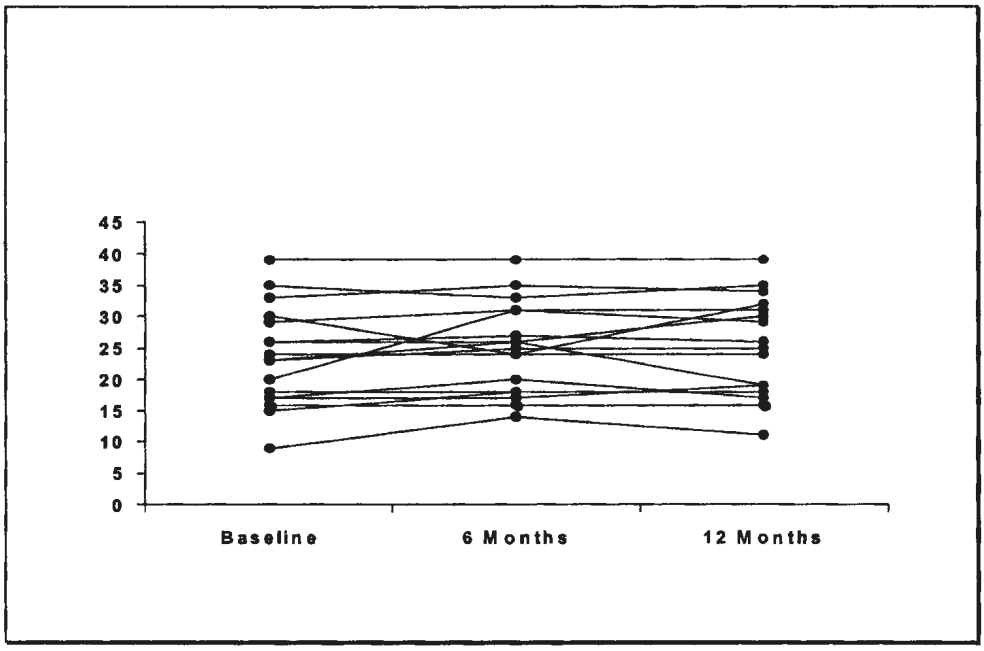

Figure 4.29: LVCF CISS Distraction Scores in Treatment Group

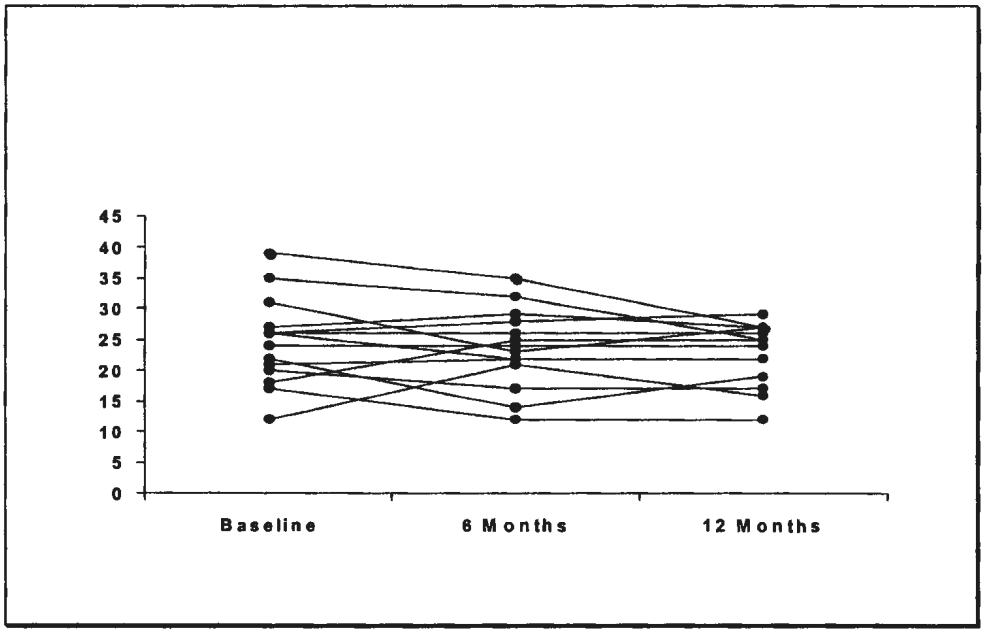

Figure 4.30: LVCF CISS Distraction Scores in Control Group

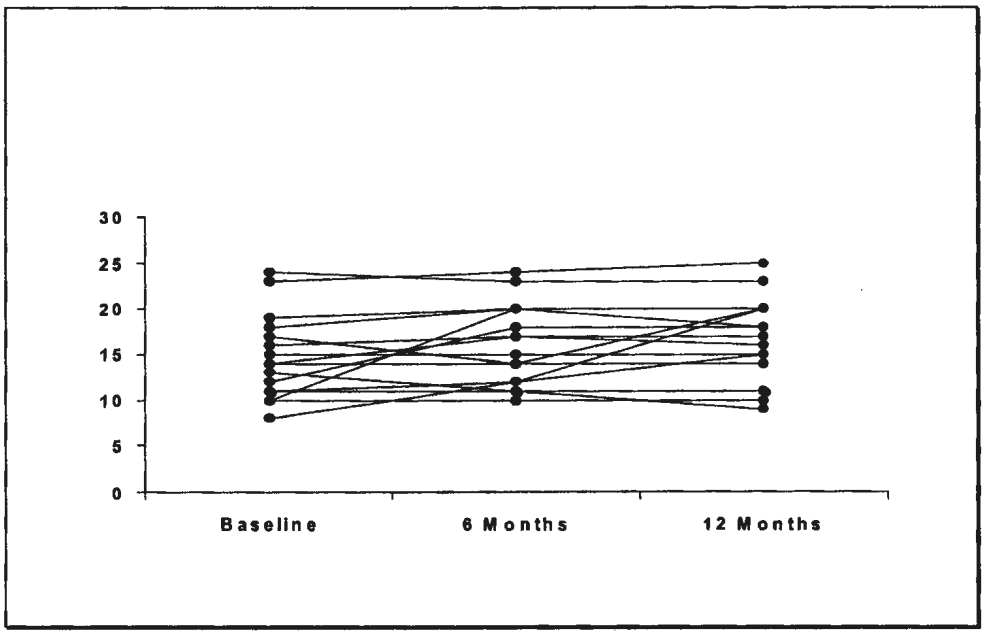

Figure 4.31: LVCF CISS Social Diversion Scores in Treatment Group

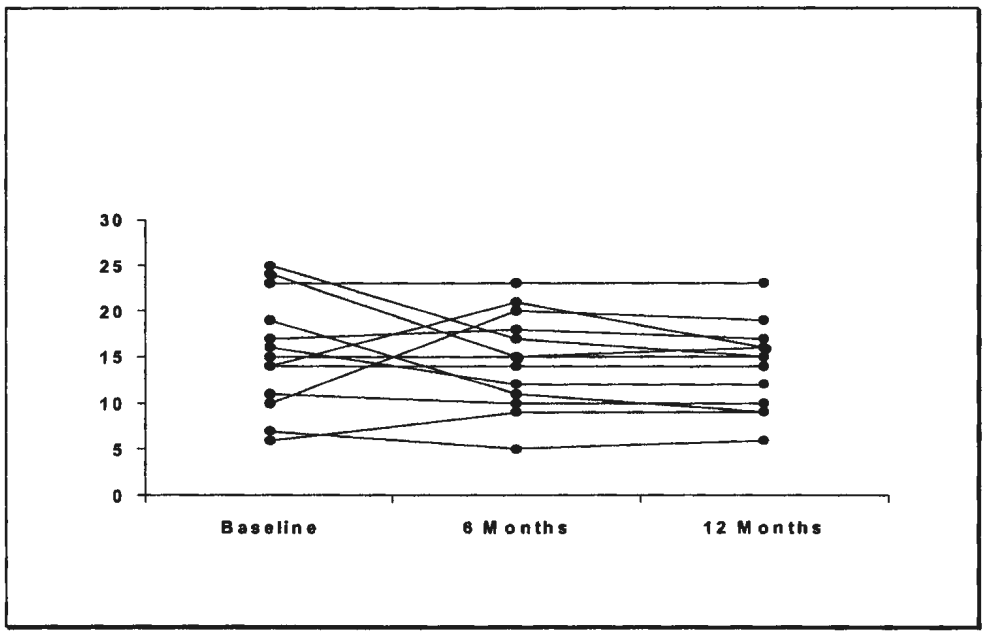

Figure 4.32: LVCF CISS Social Diversion Scores in Control Group

4.4 Adjusted Analysis of Baseline Differences

The linear regression analysis, adjusting for gender, age, marital status (described as living with partner in table 4.1), sexual orientation and route of transmission yielded similar findings to the primary analysis. None of the variables was significantly related to the 6-month change in depression. Only treatment and stratification were associated with change in BDI at six months.

An adjusted analysis of the secondary outcome measures yielded no meaningful differences between the results obtained from the primary analysis. The mean CISS Avoidance 12-month scores was significantly higher in the treatment group. Though statistically significant, this change was a clinically unimportant difference since values for both groups fell in the same diagnostic category.

4.5 ANCOVA Without Stratification As Covariate

The ANCOVA of the primary and secondary outcome measures, without stratification as a covariate, yielded results similar to the ANCOVA with stratification as a covariate.

CHAPTER 5

DISCUSSION

5.1 BDI Related Outcomes

The current study, unlike the majority of related studies, examined the impact of psychotherapy in a heterogeneous population of persons living with HIV/AIDS. Most studies enrolled patients who were male, gay or bisexual. This study enrolled males and females, heterosexuals and homosexuals. Generally, the trials investigating the efficacy of psychotherapy in HIV either included only subjects who had depression scores in the moderate/severe range, or had scores indicating mild depression. Subjects had BDI scores ranging from mild to severe (BDI scores 2-41). Numerous trials excluded HIV patients who were symptomatic and no RCTs investigating psychotherapy and HIV could be found which included patients with AIDS. In the trial reported in this thesis CD4 cell counts were used as a marker of disease severity and trial subjects ranged from asymptomatic to AIDS (CD4 cells/mm^3 879-0). Most of the RCTs in the literature excluded subjects with a history of a major psychiatric disorder. Patients with previous psychiatric disorders were included in this thesis trial. The majority of related trials investigated the provision of psychotherapy for periods of under 4 months duration. This thesis reports findings of the intervention group subjects who were provided psychotherapy for 12 months.

The primary goal of this trial, was to examine psychotherapy in the context of the management of persons living with HIV disease, not limit its investigation to selected subgroups of HIV positive patients. From the clinical team experience with HIV patients, many presented with histories of psychiatric disorders, dysfunctional personal relationships, physical abuse, drug and alcohol abuse, etc. It was the team belief that, for many of the patients, HIV was exacerbating previous or existing problems, not the sole cause of decreased psychological well-being. Team members also observed that patients reported feelings of depression and/or hopelessness independent of disease symptomology, indicating that improving physical outcomes alone may not ensure improved psychological well-being. In Newfoundland and Labrador the proportion of females and heterosexuals was higher than the proportions observed nationally, and it was felt that these groups should be represented in a clinical study, at least to the degree that subjects were available. The small population of Newfoundland and Labrador presented challenges for patients to keep their HIV immune status unknown and the clinical team felt that psychotherapy might be beneficial in addressing the psychological stress associated with forced or unplanned disclosure. It was felt that these outcomes might be associated with depression, and in conjunction with the psychological burden associated with living with HIV and AIDS, suggest a role for psychotherapy in the management of HIV disease

Measures of the severity of depression at six months showed that patients in the intervention group had scores that were indicative of mild depression, whereas patients in the control group had scores indicating moderate depression.

After 12 months of psychotherapy there was an even greater difference in mean scores between the treatment and control group. The treatment group had depression scores in the minimal range, whereas control group subjects had scores in the high end of the moderate range. There was a systematic decline in depression scores in the treatment group, whereas there was an increase in depression scores from baseline to 12 months in the control group.

Beck depression scores above 15 are thought to be indicative of depression that may require a clinical intervention. At both the six-month and 12-month intervals, the mean BDI scores did not indicate depression that may require clinical intervention in the treatment group, but suggest depression warranting clinical intervention in the control group.

5.1.1 Discussion of Studies Related to HIV and Depression after 1996

Chapter two presented a review of trials up to 1996, that were related to the thesis primary outcome measure of depression in HIV positive patients. At that time, there was a less clear role for psychotherapy in the management of HIV/AIDS. There was an absence of consistent and reliable information to identify if there was benefit to the provision of psychotherapy in managing depression in HIV positive patients, and which groups of patients, if any, might benefit from psychotherapeutic interventions. In this section I wish to evaluate some of the trials published after the commencement of RCT discussed in this thesis.

Table 5.1 provides a comparison of the trials discussed at length in this thesis, which were related to the primary outcome. Generally, the trials support a role for psychotherapy in the management of HIV. Group therapy orientations dominate the literature but improvements in depression have been observed from the provision of individual psychotherapy. In only one of the studies was there no benefit of psychotherapy in reducing psychological distress and the outcome was most probably related to a ceiling effect. Many of the studies were weakened by the absence of a control group, bringing into question the strength of the conclusion that psychotherapy ameliorates depression in persons living with HIV. The randomized controlled nature of the thesis RCT provides confidence in the conclusion of benefit of psychotherapy in the management of depression and hopelessness in persons living with HIVAIDS.

Antoni *et al.* (2000) investigated the effects of a cognitive-behavioral stress management (CBSM) intervention on anxiety, 24-hour Urinary Norepinephrine output and T-cytotoxic suppressor cells in symptomatic HIV- infected gay men. Participants were randomized to either a 10-week group based manualized CBSM treatment condition or wait-list control. Only 74 of the 96 men completed the study but were similar at baseline to those who did not, and equal proportions of subjects in both groups were noncompleters. There were no significant differences in baseline measures between groups.

Mood measures were assessed by the Profile of Mood States (POMS) and the Perceived Stress Scale (PSS). Compared to the control group, men assigned to CBSM showed significantly lower post treatment levels of self-reported anxiety, anger, total

mood disturbance, and perceived stress; and less norepinephrine (NE) output. The authors also state that at the individual level, anxiety decreases paralleled NE reductions. Additionally, significantly greater numbers of T-cytotoxic/suppressor (CD3+/CD8+) lymphocytes were found six to 12 months later in subjects assigned to CBSM. The authors also demonstrate that greater decreases in NE output and a greater frequency of relaxation home practice during the 10-week CBSM intervention period predicted higher CD3+/CD8+ cell counts at follow-up.

The authors were unable to demonstrate any significant differences in CD3+/CD4+ or CD3+/CD8+ cell counts immediately following the intervention. This is consistent with this researchers RCT finding of non-significant differences between groups on CD4 cell counts. Both this study and the thesis RCT may not have been sufficiently powered, due to small sample sizes, to detect immune marker differences.

Enrollment in this trial was very restrictive. Subjects were gay, had relatively asymptomatic HIV infection, had minimal psychological problems, including no major depressive disorder, and no drug or alcohol dependency. Subjects were all college educated and had full time employment. This clearly restricts generalizations from the study findings, particularly to HIV positive heterosexuals, HIV positive females, HIV positive patients with psychiatric problems, patients with AIDS, less educated HIV positive patients and unemployed HIV positive patients.

Less than 37 % (N=35) of the trial subjects had follow-up data. This brings into question the validity of the authors' conclusion of significantly higher CD3+/CD8+ cell counts favouring the CBSM group.

Depression was measured using the Hamilton Rating Scale for Depression (HRSD) but the authors state depression was not an outcome of interest but used to screen subjects. Subjects with corrected HRSD scores greater than 15 were excluded form the trial limiting specific comments regarding the effectiveness of CBSM on depression.

Depression score change was the primary outcome of the thesis RCT, and the lack of reporting of this outcome by Antoni *et al.* prevents this researcher from drawing parallels in relation to depression. Both this trial and that of the thesis author suggest improvements in psychological well-being through the provision of psychotherapy. However, Antoni *et al.* used a group model with a selected homogenous population whereas this researcher used an individual psychotherapy model with a heterogeneous population. These two differences limit comparisons of the two trials.

A RCT was conducted by Goodkin *et al.* (1999) to assess the effects on psychological distress and grief of a bereavement support group intervention in HIV seropositive and seronegative homosexual men. A total of 197 subjects were randomized to either a bereavement support group intervention or a community standard of care control condition. Thirty-one subjects did not complete the study follow-up, however all were accounted for.

The Texas Inventory of Grief (TIG) was used to measure grief level and the POMS was used to assess distress. A grief overall distress composite score was derived from the two tests producing a score representing the outcome variable, distress. The

Structured Interview Guide for the Hamilton Anxiety and Depression (SIGH-AD) rating scale was used as a secondary distress outcome measure to supplement the POMS.

After the intervention the bereavement experimental group had significantly lower distress scores than the control group. The authors conclude a brief group intervention can significantly reduce overall distress and accelerate grief reduction in a sample of bereaved subjects. However there was no significant difference post-intervention between groups on clinically rated depression and anxiety, assessed with the HRSD and Hamilton Anxiety Rating Scale (HARS). The authors conclude this may have been due to the relatively compressed range of variation observed on these measures in this sample, which was less depressed than a typical clinical population. This finding limits conclusions regarding the benefits of bereavement support groups with more severe distress and psychopathology. Both this study and the thesis RCT support a beneficial role for psychotherapy in the treatment of psychological issues confronting persons living with HIV.

The finding of no difference in depression scores post treatment is contrary to the findings in this thesis RCT. The short term nature of the Goodkin *et al.* trial and the fact that it is a group psychotherapy format, limits comparisons with the thesis RCT, which was long term individual psychotherapy.

All the subjects were homosexual males, generally healthy, and had no history of past or current psychiatric disorders. This limits generalizabilty of the study findings to HIV positive heterosexuals, HIV positive females, and severely ill HIV positive populations.

Weiss *et al.* (1999) investigated the effects of a 4-month supportive-expressive group (SEGT) intervention in 85 HIV positive gay men. Subjects were assessed using the BDI and the Hopkins Symptom Checklist (HSCL). The authors found no significant differences on distress, coping, or social support between the treatment group receiving supportive-expressive interventions and written material and the control group, which only received the written materials. The authors conclude that in the absence of clear indications for treatment, supportive-expressive group intervention may be no more effective at reducing distress than is provision of the written information.

All trial subjects were asymptomatic gay males making it difficult to determine the effects of supportive-expressive group therapy in HIV positive heterosexuals, HIV positive females and less healthy HIV positive populations.

The findings of no group differences in distress or social support are contrary to both the RCT findings of this researcher and other authors reported in this thesis. In discussion with the principal author he noted that the patients in this study had minimal distress scores at the start of the trial, therefore it may not have been possible to detect differences in distress due to a "ceiling" effect.

In an RCT to compare the effect of a CBSM on distress outcomes Lutgendorf *et al.* (1998) randomized 40 HIV+ gay men to either a 10-week CBSM intervention or 10-week wait-list control. Patients' mood was assessed using BDI and POMS; coping ability using COPE and perceptions of social support using the Social Provisions Scale (SPS). Patients were mildly symptomatic; free of AIDS symptomology, had no present or previous major psychiatric disorders, and were not clinically depressed. No significant

differences were observed between the groups at baseline. After completion of the 10-week CBSM intervention there were significant differences in the social supports and cognitive coping strategies favouring the treatment group. The authors conclude a CBSM group intervention can significantly attenuate dysphoria, anxiety and total mood disturbance in symptomatic HIV seropositive gay men.

The authors did not present data directly related to comparisons between intervention and control groups on measures of BDI or POMS. Instead authors were interested in correlations with BDI and POMS on subscales of COPE and SPS. The authors observed that increased acceptance and increased positive reframing was significantly associated with lower POMS depression, anxiety and total mood disturbance (TMD) and lower BDI depression at 10 weeks. They also observed that increased active coping was correlated with decreased distress but not correlated with changes in BDI scores. Denial coping was not significantly associated with distress. Increases in SPS scales of attachment, guidance, reliable alliance and social integration were significantly associated with lower POMS anxiety, depression, and TMD but not BDI.

In the absence of direct comparisons of mood measures between the treatment and control groups, only very limited comparisons can be made between the Lutgendorf trial and the thesis RCT. There does appear to be mood related improvements in both studies, which are related to the provision of psychotherapy.

Lutgendorf *et al.* acknowledged that small sample size might have limited their ability to detect differences and that some of the non-significant results are probably attributable to the small number of subjects.

Lutgendorf *et al.* utilized group psychotherapy whereas the RCT discussed in this thesis was individual psychotherapy, limiting comparisons between the two studies. Because the sample was restricted to men who were free of major mental health problems it is unclear what role this group intervention would have in treating patients with more severe mental problems.

With only HIV positive gay male subjects there are limitations to the generalizabilty of the findings to HIV positive females and HIV positive heterosexuals.

Most subjects were college educated and employed and it is uncertain how this intervention might impact less educated or unemployed subjects. In addition, using only mildly symptomatic subjects does not address the effectiveness of this intervention on moderately ill or severely ill patients.

Markowitz *et al.* (1998) randomized 101 HIV-positive subjects, with significant depressive symptoms, to 16-week interventions comparing interpersonal psychotherapy (IPT) (N=24), cognitive behavioural therapy (CBT) (N=27), supportive psychotherapy (SP) (N=24) and supportive psychotherapy with imipramine (SWI) (N=26). Depressive symptomology was assessed using the BDI and the Hamilton Depression Rating Scale (HAM-D). The authors observed that subjects randomized to interpersonal psychotherapy and supportive psychotherapy with imipramine had significantly greater improvement on depressive measures than those receiving supportive psychotherapy or cognitive behavioral therapy. The authors suggest that depressive symptoms appear treatable in HIV positive patients and that IPT may have particular advantages as psychotherapy for HIV patients with depressive symptoms.

The authors suggest their supportive psychotherapy group approximate a control group however, it clearly is not a control group, at least in an epidemiological sense. This trial is a comparison of psychotherapies more so than an investigation of the impact of psychotherapy on depression in persons living with HIV.

All subjects had to score 15 or higher on Hamilton Depression Rating Scale (Ham-D) and have a clinical judgment of significant depressive symptoms. Subjects were rated "relatively medically asymptomatic." Females accounted for 15 % of the trial sample and 80 % of the subjects were gay or bisexual. This limits generalizabilty of the finding to less severely depressed HIV positive patients, HIV positive women and HIV positive heterosexuals. In the RCT presented in this thesis, a heterogeneous patient sample was enrolled with no exclusion criteria related to scores on standardized depression scales.

Markowitz *et al.* demonstrated no significant difference on baseline measurements between groups. At midpoint and at termination, scores on the Ham-D decreased significantly for all treatment groups. BDI scores fell significantly by midpoint for IPT and SWI and for all groups by termination. A similar finding of decrease in BDI scores favouring psychotherapy was shown in this thesis RCT. There was no difference in CD4 cell counts amongst the groups at the conclusion of the trial. A similar finding was observed in this thesis RCT.

There was no follow-up reported in this study so little can be said about the longer-term effects of these interventions in controlling depression. The authors claim the relatively small sample size might have reduced statistical power to detect treatment

differences. The authors did not account for the absence of the 32 patients not included in their analysis of trial completers. Minimal information, only that 4 patients refused randomization and 15 completed < 4 sessions was provided. A thorough reporting of the trial subjects would have enabled a more critical appraisal of the authors' conclusions.

Zisook *et al.* (1998) conducted a randomized double-blind, placebo controlled trial to compare the efficacy and safety of fluoxetine plus group psychotherapy versus group psychotherapy alone. The 47 subjects enrolled were referred from either a cohort of 500 subjects being followed by the University of California, San Diego (UCSD) HIV Neurobehavioral Research Centre (HNRC) or the UCSD outpatient psychiatry services. Subjects were HIV-seropositive males and currently experiencing a major depressive episode of moderate to severe intensity.

Subjects were randomized to a fluoxetine group or placebo group. All subjects were exposed to a seven-week group supportive psychotherapy treatment phase following randomization.

By endpoint the intervention patients treated with fluoxetine experienced greater mean reductions from baseline compared to the placebo group on HAM-D and BDI-13 depression measures. Subjects who were treated with fluoxetine showed significantly more improvement on self and observer rated depression by the end of the first week of treatment. The authors conclude this study supports the efficacy and safety of fluoxetine over and above group psychotherapy alone for the treatment of HIV-associated major depression. It can not be concluded from this study that there would be advantages of fluoxetine over psychotherapy in patients with less severe depression. In addition it is

difficult to compare the Zisook *et al.* trial with the thesis RCT since the former is a group intervention and the latter is individual psychotherapy.

The authors acknowledge theirs was not a true placebo controlled trial in that all subjects received supportive psychotherapy and the trial was not designed to test the efficacy of group psychotherapy. The presence of a control group receiving no psychotherapy would have permitted an examination of the efficacy of group psychotherapy. In addition, the authors note that a more structured, systematized form of group therapy might have further improved the efficacy of the group therapy plus placebo cohort.

The authors compared a subgroup of patients with major depressive diagnosis of mild severity and found significant decrease in depression scores in both groups. The authors conclude that group psychotherapy may be sufficient for the treatment of major depressive episode of mild severity, but medications are an important component of treatment for more severe episodes. This finding supports a role for psychotherapy in the management of depression and is consistent with the findings of this thesis RCT.

In a randomized controlled trial comparing the influence of interpersonal psychotherapy (IPT) on psychosocial variables and immune function in depressed males, Gruettert *et al.*, (1998) found IPT to significantly reduce psychological distress. The authors found no significant psychoimmunological effect of psychotherapy. These findings related to the provision of psychotherapy are consistent with the finding in this thesis RCT.

The authors report IPT has advantages over supportive therapy, which is inconsistent with other reports, which clearly demonstrates a consistent failure to show one psychotherapy to offer any advantage over another (Brown, 1996). Despite efforts to locate a published article for this abstract, one could not be found.

Lutgendorf *et al.* (1997) investigated the effects of a 10-week group cognitive-behavioral stress management intervention on mood and immunologic function in 52 HIV-seropositive gay men. All patients were symptomatic but none had a diagnosis of AIDS. Only 40 subjects completed the trial but there was no difference in the proportions lost in each group. Subjects were randomized to the treatment group or wait-list control. All participants' psychological measures were assessed with the BDI and POMS. Blood samples were taken on all patients. There were no significant differences between subjects at baseline.

The treatment group subjects showed significant decreases in self reported dysphoria, anxiety, and total distress as well as significant decreases in herpes simplex virus - type 2 (HSV-2) antibody titers. The BDI scores were significantly lower at post intervention compared to the control group. This finding is consistent with the thesis RCT. A problem with the Lutgendorf et al. study is that subjects were involved in outside therapy and support groups and it is unclear what effects these interventions had on the CBSM group.

There were no significant differences between treatment and control groups on CD8+ and CD4+ cell counts. The finding regarding CD4+ cell counts is consistent with

the results reported in the thesis RCT. The small sample sizes of both these trials may have limited the ability to detect differences in CD4 cell counts.

The homogeneity of the trial subjects limits the generalizabilty of the findings to HIV positive heterosexuals, HIV positive females and people with AIDS.

The authors conclude that even in progressed symptomatic HIV disease, stress management interventions may enhance psychological adjustment and influence the immune system in a meaningful way. The authors' statement regarding immune function improvement is not strongly supported by their trial results.

The author of this thesis RCT concludes that provision of individual psychotherapy is effective in ameliorating depression in a heterogeneous population of persons living with HIV/AIDS. In addition, the author feels that routine psychotherapy, as a component of HIV disease management may have a preventive effect on depression.

Table 5.1: Comparison of Trials Related to Thesis RCT Primary Outcome

Reference	Subjects	Intervention	Measure	Effect
Antoni et al. 2000	Gay males N = 96 (74) [1]	CBSM group therapy vs. control 10 weeks	POMS PSS NE output CD3+CD8+	+ + + +
Goodkin et al.	Gay males N = 197 (166) [1]	Bereavement support group therapy vs. control 10 weeks	TIG/POMS SIGH-AD	+ NS
Weiss et al. 1999 Conference report	Gay males N = 85	SE group therapy vs. control 16 weeks	BDI HSCL	NS NS
Lutgendorf et al. 1998	Gay males N = 52 (40) [1]	CBSM group therapy vs. control 10 weeks	COPE SPS	+ +
Markowitz et al. 1998	Males N =85 Females N=15 80% gay/bi	IPT, CBT, SP, and SWI 16 weeks	BDI HAM-D CD4+	+[4] +[4] NS
Zisook et al. 1998	Males 47 (37) [1]	SP group therapy + Fluoxetine vs. SP 7 weeks	HAM-D BDI-13	+ +
Gruettert et al.[2] 1998 (Abstract)	Males [3]	IPT vs. SP	Psychosocial CD4+	+ NS
Lutgendorf et al. 1997	Gay males N = 52 (40) [1]	CBSM group therapy vs. control 10 weeks	BDI POMS HSV-2 HSV-1 CD4+ CD8+	+ + + NS NS NS
Markowitz et al. 1995	Gay/Bi males N = 32 (30) [1]	IPT vs. SP 16 weeks	BDI HRSD	+[4] +[4]
Targ et al. 1994	Gay males N = 20 (18) [1]	ST group therapy + Fluoxetine vs. ST for 12 weeks	HAM-D POMS CD4+ CD3+	+ + NS NS
Mulder et al. 1994	Gay males N = 39 (27) [1]	CBT group therapy, ET vs. Control 15 weeks	BDI GHQ POMS	+ + +

Table 5.1: Comparison of Trials Related to the Thesis RCT Primary Outcome (Continued)

Reference	Subjects	Intervention	Measure	Effect
Kelly et al. 1993	Males 94 % gay/bi N = 115 (68)[1]	CBT group therapy, SST vs. control 8 weeks	CES-D SPS SCL-90-R MHLCS	+ + + +
Markowitz et al. 1992	N = 23	IPT 16 weeks	HRSD	+[4]
Mugford thesis RCT	N = 31 (26)[1]	Psychotherapy vs. control 26 weeks	BDI BHS CISS CD4+	+ + NS[5] NS

[1] Number of subjects included in analysis of primary outcome.
[2] No article could be found.
[3] Number of subjects not reported in abstract.
[4] There was significant difference between baseline scores and endpoint scores.
[5] Some subscales were statistically significant but no scales were clinically significant.

5.2 BHS Related Outcomes

This thesis study also examined the efficacy of long-term psychotherapy on hopelessness. At six months the treatment group had scores that indicated mild hopelessness whereas the control group had scores in the moderate range.

This finding of improvement in hopelessness scores favouring the treatment group at the six-month interval is again observed at the 12-month period. Over the 12-month period scores in the treatment group continue to decline whereas scores in the control group are not only higher than the treatment group but continue to increase from baseline levels.

Hopelessness scores of nine or more are reported to be a predictor of eventual suicide in depressed people with suicide ideation. Therefore the decrease in hopelessness scores resulting from the psychotherapy intervention is an even stronger recommendation for its use in HIV management.

5.2.1 Discussion of Studies Related to HIV and Hopelessness

A search of the literature for RCTs investigating the efficacy of psychotherapy on hopelessness in persons living with HIV/AIDS revealed no trials where hopelessness is measured independently. Hopelessness is discussed in some trials, but only as component of depression, and was generally measured on a subscale of distress and mood state measures. This thesis RCT is the only known RCT to measure hopelessness directly as an outcome variable distinct from depression or distress in examining the efficacy of psychotherapy.

Despite the lack of RCTs investigating hopelessness, terms such as hope, despair or hopelessness were detected in several reports, as important elements in the lives of persons with HIV or AIDS (Kylma *et al.*, 2001). Feelings of hopelessness may be present at varying times throughout the course of HIV disease. Kylma *et al.* (2001) indicated the need for further research on the dynamics of hopelessness in persons living with HIV/AIDS. The author of this thesis trial observed measurable increases in hopelessness over time in the HIV positive control subjects.

Rabkin *et al.* (2000) investigated the psychological effects of highly active antiretroviral therapy (HAART) on 173 HIV+ gay or bisexual men with symptomatic HIV illness. The subjects had mild to moderate distress assessed using the Structured Clinical Interview for DSM-IV, BDI, Endicott Quality of Life Enjoyment and Satisfaction Questionnaire, and BHS. Generalized mental health improvement was not related to individual medical improvement of markers of HIV illness progression. Patients classified as medically improved were no more likely than those who remain unimproved to report greater decline in measures of distress and hopelessness. The authors concluded that patients whose CD4 cell count and HIV RNA viral load reflected successful treatment were no more likely than others to be relieved of the psychological burden of illness. The finding by Rabkin *et al.* of a weak association between medical improvement markers and decline in hopelessness and distress is consistent with the findings of the thesis RCT, of no difference in CD4 cell counts despite significant reductions in depression and hopelessness scores.

This trial was not an investigation of the efficacy of psychotherapy but an investigation of the impact of antiretroviral therapy on measurements of psychological distress. Only very limited comparisons between this trial and the thesis RCT are possible. This trial was included, however, because it provides relevant information which suggests that the improved physical health related to the provision of antiretroviral therapy may not be sufficient to improve psychological distress associated with living with HIV and AIDS.

Swindells *et al.* (1999) in an observational study followed 138 HIV positive patients and compared measures of hopelessness, coping and quality of life (QOL) with perceived satisfaction with social support. The authors concluded hopelessness, emotion-focused coping, avoidant coping and AIDS were predictors of poor QOL. They also found that employment, higher income, satisfaction with social support, and problem-focused coping were associated with significantly better QOL. They suggested that interventions to alleviate hopelessness, maladaptive coping and enhancement of satisfaction with social support may improve overall QOL in HIV-infected patients. Psychotherapy may be conceptualized as containing aspects of social support and the provision of psychotherapy significantly reduced hopelessness in the treatment group of the thesis RCT, supporting the conclusions of Swindells *et al.*.

In a study to assess the effects of 12 weeks of fluoxetine on mood and immune status in depressed patients with HIV, Rabkin *et al.* (1994) treated 23 patients with either fluoxetine alone or fluoxetine plus dextroamphetamine. Patients were assessed using the HRSD, Brief Symptom Inventory, Clinical Global Impressions Scale and BHS. All patients experienced decreases in psychological distress. There was no effect of fluoxetine on CD4 cell counts. The authors conclude fluoxetine alone and fluoxetine plus dextroamphetamine were an effective treatment for patients with HIV illness and Axis I depression. This thesis authors observed a similar finding of minimal impact on CD4 cell counts with successful management of depression and hopelessness. A similar problem in both the thesis RCT and the study by Rabkin *et al.* is insufficient power to detect significant changes in immune markers.

Van-Servellen *et al.* (1993) presented a paradigm for viewing mental health states of depression and hopelessness as outcomes that are dependent on stressors, physical health states, and stress-resistance resources. From psychological assessments and interviews of 30 males with AIDS, the authors report satisfaction with social support, intrapersonal hope and global hope were all significantly negatively associated with hopelessness. The authors also reported a significant positive relationship between negative life events and the measure of depression and number of complications. The authors concluded, depression and hopelessness are major problems in persons with AIDS and stress-resistance resources are important in promoting mental health. Developing stress resistance skills may be viewed as an aspect of psychotherapy and with this conceptualization in mind, the thesis RCT finding of decreased hopelessness in response to psychotherapy is consistent with the paradigm presented by Van-Servellen *et al.*

Catalan *et al.* (1992) compared the prevalence of psychosocial problems in a cross-sectional study of 24 HIV positive and 25 HIV negative gay men. The authors concluded that psychological morbidity was associated with hopelessness, previous psychiatric illness, symptomatic HIV disease and low self-esteem. Comparisons of findings of this study to that of the thesis RCT are limited by the nonexperimental nature of Catalan *et al.* trial and the differences in intent of both groups of authors. However the author of this thesis RCT observed decreases in depression and hopelessness as a result of the provision of psychotherapy and decreases in depression paralleled decreases in hopelessness.

Using CD4 cell counts as a measure of disease severity, the author of this thesis RCT did not observe a strong relationship between hopelessness and symptomatic HIV disease. Patients who demonstrated significant decrease in both measures of psychological morbidity, depression and hopelessness, did not differ on disease severity measures compared to the control group who were observed to have significantly higher levels of depression and hopelessness.

In conclusion, the provision of psychotherapy was effective in ameliorating hopelessness in a heterogeneous population of persons living with HIV/AIDS. In addition the availability of routine psychotherapy throughout the disease course may have had a preventive effect in relation to feelings of hopelessness. A decrease in feeling of hopelessness can motivate patients to take control of their lives and pursue a course which will enhance their quality of life. It is conceivable that believing there is no hope for the future and nothing good can ever happen, both aspects of hopelessness, will inhibit processes which promote quality of life. Significantly decreasing hopelessness is likely to motivate patients to make choices that will enhance their lives.

5.3 Coping Related Outcomes

In the specific application of coping to depression, the results of a number of studies have shown that depressed individuals use more emotion related coping behaviors than nondepressed individuals (Billings and Moos, 1984; Endler and Parker 1990b). In

addition there is empirical evidence for a negative relationship between depression and task-oriented coping behaviors (Mitchell and Hodgson, 1983).

An examination of the subscales of the Coping Inventory for Stressful Situations (CISS) using the interpretative guidelines established by Endler and Parker (1990a) provided an overview of the coping skills of patients in this thesis clinical trial. At baseline, both treatment and control group scores are in the average range for task and social diversion. The psychotherapy group was in the average range for avoidance whereas the control group was in the slightly above average range. Both groups are in the slightly above average range for emotion and distraction.

At the 6-month interval subjects in both groups scores were in the average range for task, emotion and social diversion. Scores were in the slightly above average category for avoidance and distraction subscales. Despite the finding of a statistically significant difference on raw scores for avoidance coping at the 6-month interval, both the intervention group score and control group score fall into the category "slightly above average".

By 12 months, both groups were in the average range for task, emotion and social diversion, and both groups were in the slightly above average on avoidance and distraction.

The avoidance scale and the two Avoidance subscales, distraction and social diversion, are not correlated with depression (Endler and Parker, 1990a), thus little information is gained from the differences between treatment and control scores on avoidance coping at the 6-month interval.

5.3.1 Discussion of Studies Related to HIV and Coping

A literature search for RCTs, coping, HIV/AIDS, and CISS yielded very limited information. A review of these articles suggests a relationship between coping and psychological well-being. Uehara *et al*, 1999 looked at the relationship between stress coping, as measured by CISS, and personality in 60 outpatients who were in remission from major depressive disorder. Their findings supported current opinions that coping is related to the pathology and course of mental disorders. They found task-oriented coping to be related to extraversion and frustration tolerance, whereas emotion-oriented coping was closely associated with neuroticism, esoteric tendencies, and isolation tendencies.

In a study using a pretest-posttest design Heckman *et al.* looked at providing a coping improvement intervention to 16 older adults living with HIV/AIDS. Though this trial is weakened by the absence of a control group, the authors concluded that the provision of the coping skills training intervention increased participants' perceptions of social support, produced higher perceptions of social well-being, and enabled more planful problem solving, confrontive coping and future optimism.

In an effort to determine whether quality of life (QOL) in patients with HIV is influenced by satisfaction with social support, coping style and hopelessness Swindells *et al.* (1999) studied 138 HIV positive patients. Amongst their findings were that problem focused coping was associated with significantly better QOL, whereas emotion focused coping, avoidant coping, and hopelessness were predictors of poorer QOL.

In a trial investigating the effects of coping skills training on 40 symptomatic HIV gay males Lutgendorf *et al.* (1998) found that cognitive coping training was strongly related to lower dysphoria, anxiety and total mood disturbance in the intervention group compared to the controls. In this thesis RCT no significant relationship was observed between coping scores and significant decreases in depression and hopelessness.

Significant correlations between ineffective coping and low quality of life have also been demonstrated by Leiberich *et al.* (1997). From their study of 61 HIV positive persons in all stages of infection, they conclude that after an initial phase of sorrow and lack of orientation regarding their future life, most HIV positive persons deal effectively with the demands of HIV infection but HIV positive patients with a high degree of distress and evasive regressive coping patterns need professional support such as psychotherapy.

Normative data have not yet been established for the CISS scores in HIV populations. It is therefore impossible to compare the results of this thesis RCT with a normative sample. The thesis author feels the CISS scale would be more appropriately used to examine how individual patients are doing compared to a normative sample. In addition, it is likely that there were insufficient numbers of patients to test some of the subgroup comparisons.

5.4 CD4 T-lymphocytes Related Outcomes

The finding of no significant difference between the treatment and control groups at six and 12 months was expected since the author was aware that the study would not have the power to detect significant changes in CD4 cell counts. The majority of the trials reporting the impact of psychotherapy on immune markers appear to be insufficiently powered to detect significant change.

5.4.1 Discussion of Studies Related to HIV T-lymphocytes

It has often been surmised that improved psychological well-being in the medically ill would lead to improvement in immune function. A review of the literature reveals conflicting opinions regarding the effects of psychotherapy on immune responses. Though some studies have not shown improved immune function directly related to the provision of psychotherapy there is evidence demonstrating psychotherapy leads to improved immune function (Cruess, *et al.*, 2001). Much of the early literature utilizes weaker research designs and small sample sizes. There is a need for randomized clinical trials which are sufficiently powered to examine the efficacy of psychotherapy in improving CD4 T cell production

Antoni *et al.* (2002) examined the effect of a stress management model of psychotherapy on immune system reconstruction in 25 HIV-infected males. The authors found that the group receiving stress management had higher CD4+/CD45RA+/CD29+

cell counts at follow-up compared to the control group. This was independent of initial number of T cells and the HIV virus load. In this thesis RCT no differences were observed on CD4 cell counts between treatment and control subjects.

Mohr *et al.* (2001) examined the relationship between the alleviation of depression and interferon gamma (IFN-gamma) production by peripheral blood mononuclear cells in patients diagnosed with relapsing-remitting multiple sclerosis (MS) and major depressive disorder. They concluded the production of the proinflamatory cytokine IFN-gamma in relapsing-remitting MS is related to depression and treating the depression resulted in decreased IFN –gamma production.

Antoni *et al.* (2000) found that HIV positive gay men assigned to a group based cognitive behavioral stress management (CBSM) intervention had significantly lower 24-hour urinary norepinephrine levels and decreased anxiety compared to the control group. In addition they found that the men with the greatest reductions in distress and norepinephrine level at 10 week follow-up had greater numbers of T-cytotoxic/suppressor (CD3+/CD8+) cells at 1-year follow-up.

In a two group comparison of 35 asthmatic children, the group receiving a 6-month psychosocial intervention in addition to conventional antiasthmatic therapy showed significant reduction in the specific Immunoglobulin E (IgE) responses against Ascaris lumbricoides (intestinal parasite), a significant increase in natural killer (NK) cells, an augmented expression of the T-cell receptor for Interlukin 2, and a significant decrease of leukocytes with low affinity receptors for IgE (Castes *et al.*, 1999).

In a study of 26 asymptomatic HIV positive homosexual men Mulder *et al.* (1995) found no differences in rate of decline of CD4 cells or T cell responses from pre to post psychosocial group intervention. However, they report those subjects who showed larger decreases in distress showed a smaller decline in CD4 cell counts.

In a comparison of the long term and immediate effects on immune function in patients with malignant melanoma, Fawzy *et al.* (1990) observed that patients receiving a 6 week structured psychiatric group intervention showed improvement in affective state, coping, and the NK lymphoid cell response system. Intervention group patients had significant increases in the percent of large granular lymphocytes and natural killer cells along with indications of increase in NK cytotoxic activity; and a small decrease in percentage of CD4+ T cells. Additionally they state affective rather than coping measures showed some significant correlations with immune cell changes.

The reduction of mitogen-induced Ca2+ signals in T cells is felt to be a reliable state marker in depressive illness. Successful treatment with interpersonal psychotherapy has been shown to reverse this reduction (Aldenhoff *et al.*, 1997).

Udelman, (1983), in an overview of psychoimmunology, reports studies which have demonstrated suppression of T and B lymphocytes for 6 months to a year in response to bereavement, correlation between degree of depression and suppressed chemiluminescence, as well as correlations between hope and T and B cell counts. The authors conclude adequate psychological defenses would be of aid in reducing vulnerability to illness and that the psychotherapist is confronted by a newly measurable challenge to aid in control of not only emotional, but also physical illness.

In conclusion there is conflicting evidence of a relationship between improved immune function and the provision of psychotherapy. In this clinical trial, an investigation of the effects of psychotherapy on immune function, particularly CD4+ T cells, was included only to observe trends. Before the start of the project, the researchers determined there would be insufficient sample size to adecquately study the relationship between psychotherapy and CD4 T cells.

5.5 Strengths and Limitations

The thesis study was designed, and powered, to examine the impact of psychotherapy on psychological parameters. It does not have adequate statistical power to detect an impact on markers of HIV progression, such as CD4 cell counts. It would have been of interest to restudy the psychological parameters at a moderately long interval after the conclusion of the trial. The anticipated attrition of sample size and the resultant dilution of statistical power made this impractical. Similarly, the relatively high dropout rate seen in other studies like this presents analytical challenges. The author chose, in the first instance, to bolster the sample size in proportion to the anticipated attrition rate. In retrospect, the observed and expected attrition rates were similar. In the second instance, the author made the *a priori* decision to do supplementary analyses in which previous values were brought forward to replace missing values. The major conclusions were similar using both strategies.

There is limited evidence regarding the long-term effects of psychotherapeutic interventions to ameliorate depression in persons living with HIV and AIDS. This is partially due to insufficient sample size at the post intervention trial period. Where sample size may have been adequate at the start of the trial, losses by the end of the trial have presented analytical problems. In earlier trials, efficacious antiretroviral therapy was not readily available and many patients died or were too medically ill to permit follow-up assessments. Improvements in antiretroviral treatments have helped delay deaths and poor health and should help maintain sample sizes for long-term follow-up.

A second problem in terms of patient follow-up, was that sufficiently large numbers of patients moved away from the study area, to larger centers, for reasons which included fear of ostracism by the community and a belief that more effective treatments were available outside the province. Increased acceptance has encouraged people to continue to live in their communities. Greater access and knowledge regarding drug management of HIV has also encouraged HIV positive patients to remain in their communities. Changes such as these may help investigators maintain the power to investigate long-term effects of psychotherapy in the future. There is a need for RCTs with sufficient power to investigate the long-term effects of psychotherapeutic interventions on both psychological outcome measures and immune variables. A result of widely accepted HIV/AIDS management guidelines ensures reasonably similar comparison groups, making it more feasible to conduct multi-centered trials that can bolster sample size.

Many studies utilize group psychotherapy in order to achieve a balance between the numbers of people requiring the service and the increased time and monetary costs of delivering individual psychotherapy. There is evidence that psychological distress is reduced with the provision of group psychotherapy, at least for less psychologically ill populations. An important issue in the provision of psychotherapy is that many patients are uncomfortable, unwilling or unable to participate in group psychotherapy, and efforts to employ this model have led to increased psychological distress as well as direct refusal.

In retrospect this study relied on the therapist being willing to be available to patients on 24-hour call for the duration of the trial. It would have been desirable to have at least two therapists providing the intervention. Funding was not available to employ two therapists.

The introduction to this thesis highlighted the prevalence of HIV infection globally, nationally, and locally. It would be difficult to implement the psychotherapeutic model of this RCT on a global scale, or perhaps even a national scale. Most therapists would be unable or unwilling to provide weekly or biweekly therapy to more than 20 or 30 patients. There would be insufficient therapists to treat the millions of people living with HIV/AIDS. In addition, the cost would be exorbitant, especially in the third world were money for food is often unavailable, and money for the provision of psychotherapy is unlikely to become available. Countries, such as Canada, with a national health plan could more easily provide similar interventions. For patients with private health insurance, or financial stability, it may be feasible to avail of routine psychotherapy.

However, it is possible to implement psychotherapeutic interventions as part of HIV disease management in areas such as Newfoundland and Labrador and Labrador where the number of patients is relatively small. The cost to deliver the services available in this trial could be provided for $50,000.00 per year per therapist.

Substantial costs have been associated with the treatment of psychological distress, not only in terms of medical management, but also in terms of lost productivity. Improved psychological function would likely lead to increased productivity for patients, thus reducing the financial burden.

Further studies are needed to investigate the impact on immune function associated with the provision of psychotherapy. If conclusive evidence can be obtained demonstrating improved immune function there may be cost savings related to treating less medically ill patients. From patient self-reports and clinical team observations, patients in the psychotherapy group were more adherent to drug therapy than control patients, and appeared to be healthier and to require less clinic visits. It would not be difficult to study the impact of psychotherapy on utilization of hospital and physician services, nor to investigate cost effectiveness of the provision of psychotherapy to persons with HIV infection. The possibility exists that interventions such as those discussed in this trial might lead to improved health of patients thus decreasing cost of care. Putting aside the issues of financial cost, one can argue that we are just as entitled to good psychological health as we are to good physical heath, and treatment of patients should focus on all aspects of care that contribute to the highest possible quality of life.

One explanation often put forward to explain the improvement on measures of depression and hopelessness is the increase in effectiveness and availability of antiretroviral medications. There are clear benefits of these medications in treating persons living with HIV and AIDS. However, if these medications were responsible for the improvement of psychological measures of distress then control subjects treated with similar medications, should improve along these measures also. In fact, by the 6-month point is this trial, control patients have higher measurable psychological distress than treatment subjects. This observation is seen again at the 12-month period. There is evidence from this trial, which is supported by other investigators, that the psychotherapy contributes to improvement in psychological well-being.

A visual examination of the baseline characteristics of the study subjects revealed some differences which the author felt might be associated with the primary outcome. These differences, which included marital status, age, sexual orientation, gender, and route of transmission, were examined in order to assess their impact on the primary and secondary outcomes measures. None of these characteristics were found to be significantly associated with depression, hopelessness or CD 4 T cell counts. A statistically significant association was found with the 12- month CISS subscale avoidance, however this was clinically nonsignificant, as avoidance scale values for both treatment and control were in the same diagnostic category "average". Analyses that adjusted for the above baseline factors failed to change the study conclusions. These findings provide support for the conclusions that the improvements seen in depression and hopelessness were due to the psychotherapy.

5.6 Implications for Clinical Practice and Health Provider Education

The findings related to depression and hopelessness reported in this thesis provides support for the provision of psychotherapy as part of the routine management of persons living with HIV and AIDS. It appears there is benefit to providing psychotherapy service to all HIV positive patients, not just when they are in crisis but as an ongoing intervention. The goal is to explore psychological deficits and promote skills training that empowers the patients to resolve issues before they reach crisis levels. There appears to be benefit to more formal screening to assess psychological dysfunction, which will permit earlier interventions. Additionally, a therapist as part of the clinical team, can provide information regarding the psychological well being of patients, training in early recognition by team members of symptoms of psychological dysfunction, skills building of team members which will enhance their ability to treat psychological deficits, as well as provide emotional support for other team members who are confronted with the psychological problems which often accompany HIV disease.

Following this clinical trial, and in part, as a response to the outcomes observed, a psychiatrist who provides psychotherapy when required has now become a member of the HIV team meetings. In addition, the team, under the guidance of the psychiatrist, has implemented routine screening using the SCL-90-R (Derogatis, 1994).

The results of this trial also suggest that there is a role for more in-depth training for all health care professionals concerning the psychological well-being of patients living with chronic illness such as HIV. This increased focus on the patients'

psychological well-being needs greater emphasis in the undergraduate curriculum of health professional schools and faculties within universities. Interdisciplinary education, which promotes the understanding of each discipline's role and the advantages of an interdisciplinary care approach while emphasizing mutual respect for all members of the team, should be provided at the earliest levels of each discipline's educational program.

This therapist has become involved in health professional undergraduate education and has been assisting in the implementation of an interdisciplinary educational module involving nursing, social work, pharmacy and medical students. In postgraduate resident education, this psychotherapist has presented during academic half day for psychiatry residents and has consulted with psychiatrists and psychiatry residents on HIV patients. As a member of the HIV team the therapist has assisted in the development of province-wide interdisciplinary HIV clinics, which emphasize both the physical and the psychological management of the disease. This investigator has developed and participated in interdisciplinary CME events, which encourage the need for ensuring the psychological well-being of HIV positive persons. In collaboration with the HIV care team this investigator has applied for, and received, industry funding to run interdisciplinary education sessions across the Province of Newfoundland and Labrador.

This investigator, in collaboration with faculty from pharmacy, nursing and social work, developed a health care provider needs assessment. This work was an extension of the ideas developed during the RCT and was funded by the Health Canada/Association of Canadian Medical Colleges HIV Scholar in Residence program. In addition, this work

has led to presentations to Health Canada on interdisciplinary approaches to health care delivery.

Interdisciplinary professional development remains a key issue. While new curricula are being developed to introduce interdisciplinary learning and care, traditional practices are being maintained in the community. In order for the new generation health care professionals to incorporate these patterns of practice in their future careers, clear functional models within current practice have to be established and maintained. Research is also needed to evaluate the impact of the changing practice patterns on patient care.

5.7 Conclusions

An attractive feature of this trial was the heterogeneity of the subject sample. A wide range of depression and hopelessness scores was observed, and the subjects differed in terms of sexual orientation, gender, age, stage of illness and mode of disease transmission. The study sample represented a large proportion of the HIV positive population in Newfoundland and Labrador. These characteristics suggest the findings are generalizable. The study is, however, limited to a single centre, and a single therapist. It would be desirable to have a larger study, in multiple centres. The logistics of completing such a trial are challenging. Despite its limitations, however, this study suggests that

regular psychotherapy has a place in the day-to-day care of patients living with HIV infection.

Traditionally, psychotherapeutic interventions are offered to patients when they show clear signs of depression or when they are in crisis. Study patients who continued to receive routine psychotherapy maintained depression scores which were not indicative of clinically significant depression. Patients receiving a crisis intervention model of delivery maintained significantly higher scores on measures of depression and hopelessness. A model of psychotherapy which provided for routine psychotherapy sessions appears more effective at reducing depression and hopelessness than a model of psychotherapy delivery only when the patient was thought to be in crisis. This conclusion is supported by the significantly lower depression and hopelessness scores observed in the intervention group subjects. The results of the RCT reported in this thesis suggests that crisis intervention, which focuses on immediate needs, does not empower the patient to develop strategies for dealing with episodes of depression and hopelessness that can follow a diagnosis of HIV infection.

The real success of this clinical trial is not measured in changes in scores on psychological questionnaires or changes in lab values obtained from blood samples, but is the individual patients who were able to regain their autonomy and experience happiness, hope for their future, and relief from feelings of worthlessness.

Brief statements regarding a few of the patients who were enrolled in this clinical trial helps demonstrate the efficacy of psychotherapy. One of the patients not only completed high school equivalency but also obtained a nursing degree. Another patient,

whose greatest regret was her inability to have children, was able, through therapy, to come to realize she has not only value as a person but also the skills to fulfill her dreams, and is deserving of them. She now has two healthy children and is a role model for successful autonomy. Another patient came to see that her beliefs that she was worthless and only deserved abuse, has left her abusive situation and has found successful employment and a new stable supportive relationship. A patient, for one of the very first times in his life, felt he could trust another person and asked for the therapist's support to end his life. He brought his child to therapy so that she could learn more about the finer qualities of her father and the implications of his death. One of the patients was able to work through so much repressed anger that he was able to reestablish a loving marriage that had been battered by the loss of his infant son to HIV. One of the patients, who experienced bi-weekly confrontations with the police, now has intervals of many months between police interventions and suicide attempts. A patient with a history of frequent IV drug use and prostitution was almost a year without IV drug use and participation in the sex trade. Currently, there is a substantive decrease in his IV drug use and prostitution. Another patient was able to find the self-respect to accept the truth that someone could love her. One patient learned to both talk to and trust his adoptive parents. This patient acquired self-respect and came to believe he had entitlement to more than just abusive relationships.

These are only a very few of the many stories of patients achieving autonomy and happiness through psychotherapeutic support, and reinforces the evidence that

psychotherapy helps improve the lives of those people confronted with the challenges of living with HIV and AIDS.

From a personal perspective, this researcher has no regrets related to the demands of this research project. Working with HIV patients has been, and continues to be, an extremely humbling experience. I have witnessed incredible triumphs in the quest to find happiness in a world that was oftentimes cruel, frightening and bleak. I have witnessed laughter from patients, whose physical pain is beyond the scope of most peoples' experiences. I have watched people recapture their autonomy after periods of total hopelessness and desires to be dead. I can only hope that my experience with people living with HIV/AIDS has made me a more understanding, gentler and giving person.

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Appendix A

Patient Consent Form

FACULTY OF MEDICINE
MEMORIAL UNIVERSITY OF NEWFOUNDLAND
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CONSENT TO PARTICIPATE IN BIO-MEDICAL RESEARCH

TITLE: **The Effect of Psychological Counselling in Patients with HIV/AIDS**

OFFICIAL TITLE: EFFICACY OF PSYCHOTHERAPY IN HIV/AIDS

INVESTIGATOR(S): **M. Ian Bowmer, J.E.G. Mugford, Constance Campbell**

Your doctor will already have asked you if you would be willing to take part in this study. The purpose of this form is to explain the study and then record your consent if you decide to take part.

Purpose of study:

Previous research in chronic illness shows that providing psychological counselling support may reduce hospital admissions and patient visits. This study is designed to examine the effectiveness of providing psychological counselling support to people with HIV/AIDS.

Description of procedures and tests:

You understand that if you agree to enter the study, you will have a 50:50 chance of receiving counselling. If you are assigned to the counselling group then the frequency of counselling will be determined by you and your counsellor. You understand that the counselling sessions will be a time commitment above and beyond your routine clinical visits. Each meeting with the counsellor will be scheduled for one (1) hour. You understand that counselling is not normally ended abruptly and that a schedule of reduced frequency of visits will be developed with the counsellor as the end of the study is approached.

Your participation in the study means you will complete three standard psychological tests which will help measure your level of depression, self esteem and ability to cope. **(THESE TESTS ARE NOT USED TO MEASURE INTELLIGENCE)**. These tests will occur at the beginning of the study and at approximately three month intervals until the end of the study. Testing time is approximately one hour and your counsellor will try to schedule these tests during your regular clinic visits.

Patient's Initials: _____

Date: _____

Foreseeable risks, discomforts, or inconveniences:

You understand that stopping counselling abruptly may cause anxiety. Inconveniences will include the time spent completing the psychological questionnaires and the time required to attend the counsellimg sessions.

Benefits which the subject may receive:

You understand that while it is possible that there may be no benefit to you, your participation in this study may help others with HIV/AIDS.

Alternative treatment for those not entering the study:

All routine care and support will be available to you if you choose not to enter the study.

Confidentiality:

Documentation of your participation in this study will be permanently included in your health record at the General Hospital and your hospital chart will be viewed by the study investigators.

Unless required by law or hospital policy, only your doctor, the counsellor, and the HIV Co-ordinator may have access to your General Hospital health record or any confidential documents pertaining to your participation in this study that may identify you by name. This access will only be permitted in the presence of the researcher or one of his representatives. Furthermore your name will not appear in any report published as a result of this study.

Voluntary participation in the study:

Your participation in this study is voluntary. You may refuse to participate or may withdraw at any time during the study, without any penalty or prejudice to the quality of the medical care you may require in the future. Furthermore, your physician may require you to be withdrawn without your consent if you do not respect the study protocol.

Liability statement:

Your signature on this form indicates that you have understood to your satisfaction the information regarding your participation in the research project and agree to participate as a subject. In no way does this waive your legal rights nor release the investigators, sponsors, or involved institutions from their legal and professional responsibilities. Funding for this project comes from the General Hospital and Health Canada.

Patient's Initials: _____

Date: _____

I,_____, the undersigned, agree to my participation or to the participation of _____ (my child, ward, relative) in the research study described.

Any questions have been answered and I understand what is involved in the study. I realize that participation is voluntary and that there is no guarantee that I will benefit from my involvement. I acknowledge that a copy of this form has been given to me.

_____ _____
(Signature of Participant) (Date)

_____ _____
(Witness Signature) (Date)

To be signed by investigator:

To the best of my ability I have fully explained to the subject the nature of this research study. I have invited questions and provided answers. I believe that the subject fully understands the implications and voluntary nature of the study.

_____ _____
(Signature of Investigator) (Date)

Phone Number: _____

If Appropriate:

_____
(Signature of Minor Participant)

(Age _)

Relationship to Participant Named Above _____

NOTE TO USERS

apx B-D